

Ethical and legal challenges in enrolling adolescents in medical research in South Africa: implications for HIV vaccine trials[‡]

A. Strode^{a*}, C. Slack^b, C. Grant^c and M. Mushariwa^a

IN THIS PAPER WE REVIEW LEGAL AND ETHICAL challenges to the enrolment of children in HIV vaccine trials, and discuss two main questions: 'When can children participate in research, such as HIV vaccine trials?' and 'Who can consent to child participation in such trials?' In examining the first question, we discuss the constitutional framework for research with children, and in particular the meaning of section 12(2)(c) of the South African Constitution. We submit that while there are no laws specifically prohibiting the enrolment of adolescents (provided that the research protects a child's constitutional rights and 'best interests', and is not against

'public policy'), there are challenges related to the absence of an objective standard in law for acceptable research-related risk for adolescents. We outline some ethical challenges to enrolment; namely, that ethical guidelines regarding what parents may consent to their children participating in are inconsistent, and that some guidelines take a restrictive stance, effectively precluding HIV vaccine trials with children. With regard to who can consent to child participation in such trials, we discuss current law, as well the new National Health Act. We explore possible inconsistencies between the Act and principles found in other children's law, as well as inconsistencies in current ethical guidelines, and the implications this may have for HIV vaccine research. Finally, we make recommendations for future work.

Introduction

South African children are at high risk of HIV infection. One study has found that

6.2% of 2–9-year-olds and 4.7% of 10–18-year-olds are HIV-infected.¹ Another study has also found that more than 4% of 10–18-year-olds were infected with HIV and that 31% of persons under 17 had experienced sexual intercourse.² Of this group, 31% had been sexually active before the age of 14. In this context, it is uncontroversial that children are in need of preventative interventions. Safe and successful HIV vaccines could form a critical component of a comprehensive HIV prevention package to reduce HIV infection and disease in this group.

In order to develop safe and effective vaccines for adolescents, they themselves will have to take part in clinical trials designed to assess vaccine safety, immune responses and efficacy. The South African AIDS Vaccine Initiative (SAAVI), in collaboration with the HIV Vaccine Trials Network, is currently planning an adolescent vaccine trial protocol for South Africa which is scheduled to begin around 2006 (H. Jaspen, pers. comm.). This provides an opportunity to debate in advance the range of ethical-legal complexities that relate to adolescent participation in HIV vaccine trials.

This article focuses on the ethical-legal complexities related to the *enrolment* of adolescents in HIV vaccine research,

[‡]This article is based on a paper presented by Ann Strode and Catherine Slack at the Fifteenth International AIDS Conference, Bangkok, Thailand.

^aSchool of Law, University of KwaZulu-Natal, Private Bag X01, Scottsville, Pietermaritzburg 3209, South Africa.

^bHIV/AIDS Vaccines Ethics Group, School of Psychology, University of KwaZulu-Natal, Pietermaritzburg.

^c9 Second Street, Parkhurst 2193, South Africa.

*Author for correspondence. E-mail: strodea@ukzn.ac.za

namely legal challenges relating to when adolescents may participate in vaccine trials, and who may consent to adolescent participation. Post-enrolment challenges, such as the management of disclosed high-risk or unlawful activities by adolescents, are discussed elsewhere.³

In this article, adolescents are viewed as persons between 13 and 18 years of age. It should be noted that we use the term 'child/children' interchangeably with 'adolescent', and submit that a child is a person below the age of 18 years, in keeping with section 28(3) of the Constitution⁴ and section 1 of the Child Care Act;⁵ a minor is a person under the age of 21.⁶ Some confusion arises, however, with the undefined and apparently interchangeable use of the terms 'child' and 'minor' in the National Health Act.⁷ The proposed Children's Bill⁸ should clear up this inconsistency in our law, by setting the age of majority at 18.

Background

Investigators seeking to enrol adolescents in HIV vaccine trials will have to recruit teenagers who are healthy, not infected with HIV and prepared to undergo regular high-risk behaviour assessments and HIV testing. Early trials may not confer many direct health-related benefits and a number of risks are possible, including discomfort from vaccine administration; unknown risks related to the vaccine product itself, the potential for testing false-positive on standard HIV tests; anxiety and discomfort from intrusive questions relating to risk behaviour; stress from repeated HIV testing; discomfort from blood draws for a range of tests; and potential for stigma or discrimination should participation be disclosed.

Section 12(2)(c) of the Constitution of the Republic of South Africa⁴ (hereafter referred to as the Constitution) states that everyone has 'the right to bodily and psychological integrity, which includes the right not to be subjected to medical or scientific experiments without *their* informed consent'. This constitutional principle forms the over-arching framework for South African laws and guidelines on research with human volunteers. All laws, policies and ethical guidelines must be consistent with this provision. Within this framework, we consider two key ethical-legal challenges in enrolling adolescents in HIV vaccine research:

- When, if at all, can adolescents participate in research, such as HIV vaccine trials?
- Who can consent to adolescent participation in such trials?

When can adolescents be enrolled in research such as HIV vaccine trials?

Legal framework

There has been academic debate on the nature of the constitutional framework for research with children. Van Oosten⁹ argues that the use of the word 'their' in the constitutional prohibition on experimentation without informed consent means that consent to research will be valid only if it is given by a person who is competent to consent him or herself. As a result, Van Oosten submits that, generally, a parent or guardian may not give proxy consent for a child to participate in research, where the child him or herself is not legally competent to provide this consent.

Others, such as Van Wyk,¹⁰ argue that a literal interpretation of the words used in section 12(2)(c) of the Constitution⁴ is inappropriate, and that a value-based or purposive interpretation is required. Accordingly, Van Wyk argues for an interpretation that promotes the constitutional values of human dignity, equality and human rights and recognizes that the purpose of the right is to protect individuals from being research subjects without informed consent. This interpretation allows for a parent or guardian to provide informed consent, where a child is not capable of doing so.

We submit that the approach adopted by Van Wyk is the correct one, for a number of reasons. Firstly, the Constitutional Court has favoured a value-based interpretation of the Constitution over a literal approach, particularly as section 39 of the Constitution itself requires this approach.¹¹ This section¹² states that '[w]hen interpreting the Bill of Rights a court, tribunal or forum ... must promote the values that underlie an open and democratic society based on human dignity, equality and freedom'. Furthermore, section 39 of the Constitution requires courts to consider international and public international law, and allows for consideration of foreign law in the interpretation process. Research on children, with proxy consent, is considered acceptable in many countries such as Australia,¹³ the United States¹⁴ and Scotland,¹⁵ provided various requirements are met, such as that the research includes acceptable levels of risk.¹⁶

We submit that the framework created by the Constitution for research on children is that research may only take place provided informed consent is obtained, (whether by the individual or another legally authorized person) and

other constitutional rights and obligations are respected.

While there is currently no law prohibiting adolescent participation in research, current legislation does not deal specifically with consent for adolescent participation, nor how to determine acceptable levels of research-related risk to which lawful consent for adolescent participation may be given. In the absence of specific legal provisions, therefore, we submit that currently a court would consider a child's participation in research such as HIV vaccine trials to be lawful if:

- the research protected and promoted the constitutional rights of the adolescent;
- consent to participate in the research was not 'against public policy'; and
- the research was 'in the best interests of the child'.

These are discussed in more detail below.

Protecting and promoting the constitutional rights of adolescents in research

Section 7(2) of the Constitution provides that 'The state must respect, protect, promote and fulfil the rights in the Bill of Rights'. This is a positive obligation to ensure that rights are fulfilled. In this context, 'the state' would include organs of state such as the Medical Research Council (MRC). For research to protect the constitutional rights of adolescents, the research should not infringe any of the adolescent's rights (such as the rights to equality or dignity). This means that a negative duty is placed on researchers to prevent adolescent participants from harm that infringes their rights. There is also a corresponding obligation to promote the constitutional rights of trial participants; that is, a positive duty is placed on researchers to take active steps to ensure the constitutional rights of adolescent research participants are realized.

Ensuring research is not against public policy

In terms of South African common law, no person may consent to something that is contrary to 'public policy'.¹⁷ Recently, the courts have held that constitutional values, including human dignity, equality and non-sexism, should be used to determine 'public policy'. 'Public policy' should also reflect the 'interests of the community'¹⁸ and therefore the consent would have to be in line with the concept that parents have responsibilities towards, rather than rights over, their children.¹⁹ In this context, consent to research would be lawful where it protected and promoted

an adolescent's rights to equality and dignity, did not expose them to undue harm, and recognised a parent's or guardian's responsibility to protect adolescents when enrolling them in research.

Ensuring the best interests of the child

Section 28(2) of the Constitution states that 'a child's best interests are of paramount importance in every matter concerning the child', and research involving adolescents would need to take due consideration of this principle.

The 'best interests' principle requires that a range of factors be considered during decision-making in order to promote a child's physical, moral, emotional and spiritual welfare.²⁰ The best interests principle is useful, as it requires consideration of what may harm or benefit the child. Although South African courts have not applied this principle to research, they may well follow the approach of English law, which recognizes that it would be contrary to a child's 'best interests' to submit a child to an unacceptable level of research-related risk.²¹ This argument is supported by the fact that section 71(2)(a) of the National Health Act⁷ specifically states that 'therapeutic research' may only be undertaken if it is in the child's 'best interests'. It is more complex to determine the application of this principle to so-called 'non-therapeutic' research. It is argued by some that while such research may not be in an individual child's best interests, it may be in the best interests of children as a class.²²

The new National Health Act

The National Health Act⁷ was brought into operation on 2 May 2005, by a presidential order in the *Government Gazette* (No. 27503, 19 April 2005). However, section 71 of the Act, which deals with research on or experimentation with human subjects, has not been put into operation. The reason for its delayed implementation is not known.

Nevertheless, in line with international trends, section 71 of the Act provides specifically for research with children. Importantly, it establishes that consent by parents and legal guardians to medical research is lawful in certain defined circumstances.²³ In establishing the conditions under which such consent would be valid, the Act deals separately with so-called 'therapeutic' and 'non-therapeutic' research, although the Act fails to define these terms.

With regard to therapeutic research, section 71(2)(a) of the National Health Act⁷ requires such research to be in a

child's best interests. This demands an assessment of whether submitting an adolescent a particular intervention is in their best interests by weighing up various factors, such as the probability and magnitude of risks, and benefits. It requires risk to be determined on an individual basis rather than setting an objective standard independent of the particular adolescent. This individual application has been held to be both the strength and the weakness of the best interests principle. The Constitutional Court has averred that the principle's lack of content allows an investigation into the needs of specific children in specific circumstances,²⁴ while some academic writers argue that its lack of content has meant that it has failed to provide a reliable and determinate standard.²⁵

With regard to non-therapeutic research on children, the National Health Act⁷ replaces the best interests principle with a risk standard. Section 71(3)(b)(iv) of the Act states that the research must be approved by the minister of health, and she may not authorize such research if it poses a 'significant risk' to the health of a child, or 'some' risk that is not outweighed by benefit. If early HIV vaccine trials are classified as non-therapeutic, as is possible (see below), the minister must determine whether the magnitude and probability of the risks in HIV vaccine trial interventions pose a significant risk to adolescents. Difficulties may arise as the Act does not define 'significant risk', nor is it a term used in South African ethical guidelines.

To sum up, in terms of current law, a parent, guardian or child could not consent to participation in unacceptable research. The types of research that would be considered unacceptable include studies that infringe the constitutional rights of participants, trials that expose adolescents to unacceptable risks, since this would be contrary to 'public policy', and trials that are not in the 'best interests of the child'. Although the new National Health Act attempts to create legal certainty regarding child participation in research, it fails to provide objective, clearly defined risk standards for determining when it is lawful for a parent or guardian to consent to research with an adolescent.

Ethical framework

In the absence of a clear legislative framework on the participation of adolescents in research, we argue that the courts would also seek guidance from national ethical guidelines, to establish the norms

and standards of ethical research. Current ethical guidelines do establish the conditions under which adolescents or their parents/guardians may consent to participate in research, including the level of research-related risk to which adolescents may be exposed. However, these ethical guidelines pose challenges to those planning and reviewing trials as there is currently no one set of national guidelines, there is some inconsistency among guidelines, and one set of influential guidelines appears to preclude HIV vaccine research with adolescents.

Existing ethical guidelines

The current MRC guidelines on medical ethics, *General Principles*,²⁶ are very restrictive and limit parental consent to research classified as 'non-therapeutic' to 'observation' research with risk levels that are 'negligible' (that is, the risks of daily life in a stable society, and routine physical or psychological tests). Importantly, no increase over this 'everyday risk' (referred to as 'minimal' in some guidelines) is allowed. HIV vaccine trials do not fit easily into either one of the classifications of 'therapeutic' or 'non-therapeutic' research; however, in terms of these guidelines they are likely to be classified as non-therapeutic, as the guidelines provide that, *by definition*, healthy volunteers will participate in non-therapeutic research. HIV vaccine trials are more accurately intervention research and not observation, and are likely to involve interventions with risks exceeding 'negligible' or 'everyday risk'.

The other set of widely used guidelines for clinical trials are the Department of Health's *Good Clinical Practice Guidelines* (GCP).²⁷ They would not preclude adolescent participation in HIV vaccine trials, as these guidelines do not restrict parental consent to certain kinds of study designs. They also allow a more flexible risk level. Specifically, they assert that generally (there are exceptions) adolescents should be exposed to research risk commensurate with daily life or routine tests. However, research involving a greater than 'everyday risk' is allowed. If the research does not hold out direct benefit, a minor increase in risk is justified by the development of 'generalizable knowledge'. If the research holds the prospect of direct benefit, the increased risk is justified by this direct benefit.

Future ethical guidelines

The MRC recently released guidelines specifically on research ethics for HIV preventative vaccine trials.²⁸ These guide-

lines state that adolescents are eligible for enrolment provided the risks of interventions that will not confer direct benefit (for instance, additional blood draws for lab tests) approximate 'everyday life' risk, or a slight increase over this risk is justified by a risk-knowledge ratio; and interventions that will confer direct benefit are justified by the benefits (for example, providing counselling on ways to reduce HIV infection).

Now that the National Health Act⁷ is operational, the National Health Research Ethics Committee established in terms of section 78(1) will be empowered to issue national ethical guidelines. This may provide the best opportunity for harmonizing certain contradictions in existing ethical guidelines.

To sum up, while current ethical guidelines provide detailed guidance on the kinds of studies parents may consent to adolescent participation in, and the acceptable levels of research-related risk, the guidelines are inconsistent. Furthermore the MRC's *General Principles*,²⁶ which apply to all MRC-related research, are highly restrictive and would in all likelihood prohibit adolescent participation in MRC-related HIV vaccine research. Currently, the MRC — through its lead research programme, SAAVI — coordinates all HIV vaccine trials in South Africa. However, the MRC guidelines on HIV vaccine trials will supersede the MRC's *General Principles* because of their recent publication and their endorsement by the Interim National Health Research Ethics Committee.

In summary

The key challenges regarding when adolescents can be enrolled in research relate to the failure of our existing common law and the National Health Act to set a clear, objective risk standard for research on children or adolescents. This is compounded by a lack of uniformity in the ethical guidelines. These challenges make it difficult to determine what sort of research is acceptable, and courts would have to consider a range of constitutional and common law principles, as well as ethical guidelines, in each instance.

When section 71 the National Health Act is implemented, the acceptability of adolescent participation in HIV vaccine trials will depend on how the research is classified; if vaccine trials are classified as 'therapeutic', it will have to be shown to be in the best interests of adolescents to participate. If vaccine trials are classified as 'non-therapeutic', the minister of health may approve trials only if they pose less than 'significant risk', or if the risk is outweighed by the potential benefits of the research.

Who consents for adolescent participation in research, such as HIV vaccine trials?

Legal framework

Until they reach adulthood, children have limited legal capacity to make decisions without assistance. Accordingly, our common law provides that children are generally unable to consent to medical treatment unless their parents or guardians provide proxy consent on their behalf.¹⁷ A number of statutes have altered the common law by providing children with the capacity to make independent choices in certain defined circumstances. Thus, children are able to consent to the use of contraceptives and HIV testing at 14, to sex at 16, or to a termination of pregnancy at any age.²⁹⁻³¹

Independent consent by the child to research

Currently, there is no law setting out the age at which children may consent independently to medical research, as alluded to above. However, section 39 of the Child Care Act⁵ allows a child of 14 years or older to consent independently to medical treatment. Some legal scholars have argued that therapeutic research can be likened to medical treatment in terms of the Child Care Act, implying that a child of 14 years or older can also consent independently to therapeutic research, and a parent or other legally authorized person may provide proxy consent to therapeutic research on a child below 14 years.³²

The National Health Act⁷ changes this assumption. Section 71(2)(a) provides that therapeutic research must be carried out with the consent of the parent or guardian of the child and, if the minor is capable of understanding, with the consent of the minor. Therefore, once section 71 is implemented, even therapeutic research will require the consent of a parent/guardian, and children will be unable to consent independently to any form of medical research until they reach adulthood.

Persons authorised to provide proxy consent for the child

Which persons are authorised by law to consent on a child's behalf? The common law provides that parents, guardians or, failing either, the High Court as the upper guardian of all minors, would have authority to provide consent for actions which the child is unable to consent to. Section 39 of the Child Care Act⁵ deals specifically with consent to medical treatment, and provides that a parent or guardian must consent to 'medical treatment' on behalf of a child who is under 14.

Section 53(1) further provides a person who is given custody of a child under the Act or the Criminal Procedure Act³³ the authority to consent to the provision of medical treatment for a child, provided such treatment is not 'attended with serious danger to life'. So, those who equate therapeutic research with medical treatment may (until the implementation of section 71 of the National Health Act) argue that parents, guardians and persons who are the custodians of the child can consent to therapeutic research on children under 14.

The draft Children's Bill³⁴ also recognizes the parental rights and responsibilities of other caregivers, with respect to consent for medical treatment. However, as discussed above, the National Health Act⁷ provides only parents or guardians with authority to consent to child participation in research. Other caregivers will *not* have the authority to provide consent, even though they may be the *de facto* parents of the child.

The participation of the child in decisions affecting the child

Our law shows an increasing focus on child participation. For example, even if children do not have the capacity to consent or act on their own, section 31 of the Children's Bill³⁴ provides that in any major decisions which are likely to change significantly, or have an adverse effect on a child's health, due consideration must be given to any views and wishes expressed by the child, bearing in mind the child's age, maturity and stage of development. By contrast, the National Health Act⁷ provides for additional consent of the child only where he or she 'is capable of understanding'.

To sum up, while the National Health Act provides much-needed direction on who may consent to adolescent participation in research, the provisions appear to be inconsistent with broader principles contained in other children's legislation, such as the move towards allowing children to act independently at certain ages, promoting child participation in decisions that affect them, and recognizing the parental rights and responsibilities of persons other than parents and guardians.

Ethical framework

Ethical guidelines adopt differing views regarding the persons with authority to consent for incompetent children. The GCP²⁷ guidelines provide for consent from a child's 'parents or legal guardians' for clinical trials. If HIV vaccine trials are classified as more than minimal risk ('everyday risk') with no direct benefit,

permission from *both* parents is required. Trials classified as more than minimal risk, but of likely direct benefit (which may be so with Phase III HIV vaccine trials) require the permission of *one* parent.

The MRC's *General Principles*²⁶ take an apparently restrictive approach by precluding parental consent to adolescent participation in non-therapeutic intervention research; however, they take an apparently permissive approach by bypassing parental consent for children over 14 to research classified as therapeutic. The MRC's recently released guidelines on research ethics for HIV preventative vaccine trials²⁸ allows that 'a parent' or guardian must give consent, and a child must give assent to preventative HIV vaccine trials.

To sum up, currently, major ethical guidelines are not well harmonized on the point of who consents for adolescent participation in research.

In summary

The key challenge regarding the question of 'who consents for adolescent participation in research?' is that the law does not provide adolescents with the independent capacity to consent to medical research. This position in the current law is not alleviated by the National Health Act, which requires parents or legal guardians (not other caregivers) to provide proxy consent to all forms of medical research on children and minors. This is compounded by the inconsistency in the approach of ethical guidelines regarding who may consent for adolescent participation in medical research and trials.

This has several implications for HIV vaccine research, including that it may be difficult to recruit adolescents who may be reluctant to involve their parents or guardians in trials that monitor sexual behaviour. Additionally, an adolescent with a caregiver who is not a parent or legal guardian would lack the required authority to provide consent and so be unable to participate.

Conclusions and recommendations

There are many challenges to enrolling adolescents in medical research, including HIV vaccine trials in South Africa. Currently, there is no legally defined risk standard, and we argue that the new National Health Act⁷ still fails to provide an objective, clear risk standard for 'therapeutic' and 'non-therapeutic' research. Now and in the future, research ethics committees (RECs) and our courts will need to rely on the principles emerging from the Constitution,⁴ 'public policy', the 'best interests of the child' and ethical guidelines to guide decision-making

around when lawful consent to adolescent participation in research may be given.

This means that different conclusions may be made regarding the lawfulness of adolescent participation in HIV vaccine trials, on a case-by-case basis. However, we submit that where due consideration is given to the principles underlying public policy and the best interests of the child, as well as the view of more recent ethical guidelines, adolescent participation in HIV vaccine trials will be considered lawful.

As a result, key areas for future work include:

- Advocating for the development of a clear risk standard in law for beneficial and non-beneficial research interventions with children
- Establishing the meaning of the term 'significant risk'
- Obtaining clarity on how HIV vaccine trials enrolling adolescents will be classified in terms of the provisions in section 71 of the National Health Act⁷
- Establishing the criteria that can be used to apply the 'best interests of the child' principle in a non-individualistic way, so that it is useful in the context of research
- Harmonizing key ethical guidelines on child participation in research in the development of new national ethical guidelines
- Developing the capacity of key stakeholders, such as RECs, to understand, apply and implement the new criteria for establishing the lawfulness and ethical nature of research with adolescent participants in medical trials.
- Building consensus amongst key gatekeepers such as RECs on the kinds of protocols that could be considered ethically and legally sound.

The authors are members of the HIV/AIDS Vaccines Ethics Group, University of KwaZulu-Natal (Pietermaritzburg) (www.saavi.org.za/haveg). We thank R. von Maltzhan for assistance.

1. Human Sciences Research Council, South African Medical Research Council, Cadre, and ANRS (2002). *Nelson Mandela/Human Sciences Research Council Study of HIV/AIDS: South African National HIV Prevalence, Behavioural Risks and Mass Media: Household Survey 2002*. Human Sciences Research Council, Cape Town.
2. Pettifor A.E., Rees H., Steffenson A., Hlongwa-Madikizela L., McPhail C., Vermaak K. and Kleinschmidt I. (2003). *HIV and Sexual Behaviour Among Young South Africans: A National Survey of 15-24 Year Olds*. Lovelife, Johannesburg.
3. Strode A. and Slack C. (2004). Ethical-legal complexities in adolescent participation in HIV vaccine trials: a South African case study. In *Proc. Fifteenth International AIDS Conference, Bangkok*.
4. Constitution of the Republic of South Africa 1996, No. 108.
5. Child Care Act 1983, No. 74.
6. Age of Majority Act 1972, No. 57, s1.
7. National Health Act 2003, No. 61.
8. South African Children's Bill, s17. (<http://www.uct.ac.za/depts/ci/plr/cbill.htm>).

9. Van Oosten F. (2000). The law and ethics of information and consent in medical research. *Tydskrif vir Hedendaagse Romeins-Hollandse Reg* 63, 5-31.
10. Van Wyk C. (2001). Guidelines on medical research ethics, medical experimentation and the Constitution. *Tydskrif vir Hedendaagse Romeins-Hollandse Reg* 64, 3-22.
11. Devenish G.E. (1998). The Bill of Rights. In *A Commentary on the South African Constitution*, pp. 43-102. Butterworths, Durban.
12. Constitution of the Republic of South Africa 1996, No.108, s1(a), Footnote 4.
13. National Statement on Research Involving Children, s4.1. (<http://www.nhmrc.gov.au/publications/pdf/e35.pdf>).
14. Code of Federal Regulations, s46, 406. (<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>).
15. Statutory Instrument No. 1031. The Medicines for Human Use (Clinical Trials) Regulations 2004. (<http://www.legislation.hmso.gov.uk/si/si200410.htm>)
16. Council for International Organizations of Medical Sciences (2002). *International Ethical Guidelines for Biomedical Research Involving Human Subjects*. CIOMS, Geneva. (http://www.cioms.ch/frame_guidelines_nov_2002.htm).
17. McQuoid-Mason D.J. (2001). Legal aspects of medical practice. In *Introduction to Medico-Legal Practice*, eds M.A. Dada and D.J. McQuoid-Mason, pp. 5-32. Butterworths, Durban.
18. Harms L.T.C. and Rabie P.J. (1994). *Contract Law of South Africa*, para. 165-167. Butterworths, Durban.
19. Bosman F.J. and Van Zyl G.J. (1997). Children, young persons and their parents. In *The Law of Children and Young Persons in South Africa*, ed. J.A. Robinson, pp. 49-94. Butterworths, Durban.
20. McCall v McCall. (1994). 3 SA 201 (C), para. 204-205.
21. Kennedy I. and Grubb A. (2000). Research. In *Medical Law*, 3rd edn, pp. 1665-1749. Butterworths, Oxford.
22. Stobie M., Strode A. and Slack C. (in press). The dilemma of enrolling children in HIV vaccine research in South Africa: What is in the child's 'best interests'? In *AIDS and Ethics in Africa*, eds A. Van Niekerk and L. Kopelman. David Philips, Cape Town.
23. National Health Act 2003, No. 61, s71 (Footnote 11).
24. Minister for Welfare and Population Development v Fitzpatrick and Others (2000). 7 *Butterworths Constitutional Law Reports*, 713 (CC), para. 18.
25. De Waal C. and Erasmus G. (2001). Children. In *The Bill of Rights Handbook*, 4th edn, pp. 455-468. Juta, Lansdowne.
26. Medical Research Council (2001). *Guidelines on Ethics of Medical Research: General Principles*. Cape Town. (<http://www.sahealthinfo.org/ethics/ethicsbook1.pdf>).
27. Department of Health. (2000). Guidelines for Good Conduct of Clinical Trials in Human Participants in South Africa. Pretoria. (http://www.d1.oh.gov.za/docs/policy/trials/trials_contents.html).
28. Medical Research Council (2003). Guidelines on Ethics of Medical Research: HIV Preventative Vaccine Trials. Cape Town. (<http://www.sahealthinfo.org/ethics/ethicsbook5.pdf>).
29. Child Care Act 1983, No. 74 (currently footnote 17).
30. Sexual Offences Act 1957, No. 23, s14.
31. Choice of Termination of Pregnancy Act 1996, No. 92, s5.
32. Van Wyk C. (2003). The participation of minors in preventative HIV research trials in South Africa: Legal and human rights considerations. *Medicine and Law* 22, 589-598.
33. Criminal Procedure Act 1977, No. 51.
34. South African Children's Bill. (<http://www.uct.ac.za/depts/ci/plr/cbill.htm>).