Following the adoption of the Nuremberg Code in 1947, health research with children was subjected to severe limitations in the western world. Children were effectively excluded from participating in research if the research was not intended to be of direct benefit to the child participants and carried some risk of harm. However, by protecting children in this way, they were also excluded from the benefits of research. It is now widely accepted that if children's health and well being is to be promoted they should be involved in research, subject to special safeguards to protect their rights and interests.

New Zealand's principal guideline for ethical review of health research is the National Standard for Ethics Committees 1996, currently under review. Section 5.1.4 deals with vulnerable participants, which includes children. This section is unsatisfactory in several respects, which are detailed below. We have therefore developed a set of guidelines which we believe will ensure that worthwhile health research with children can be carried out, whilst at the same time providing appropriate safeguards to protect the needs and interests of child participants and their families. The Guidelines are based on the leading international and foreign guidelines and have been endorsed by the Paediatric Society of New Zealand.

Criticisms of the National Standard
Our first criticism of the National Standard is that children are grouped with other vulnerable participants, including people with a physical or mental disability and unconscious patients. We believe that the issues relating to children are sufficiently different from those of other vulnerable people to warrant a separate section. Children are vulnerable not only because they lack capacity to give legally effective consent, but also because they are physically, psychologically, mentally and emotionally different from adults. They have unique characteristics which distinguish them from the other groups mentioned in section 5.1.4.

Second, the risk formulation is ambiguous and thus unhelpful as a guide to ethics committees. It provides:

Proxy consent cannot authorise research which carries significantly greater risk to the research participant than normal clinical treatment would pose.

What is a significantly greater risk? What is normal clinical treatment? How does one assess risk if there is no normal clinical treatment, as in non-therapeutic research?

Third, unlike all other international and foreign guidelines, the National Standard does not distinguish between therapeutic and non-therapeutic interventions in health research with children. Overseas guidelines make this distinction both in formulating the degree of permissible risk to which a child participant may be exposed and in relation to the child's consent. Stricter conditions are imposed on non-therapeutic interventions than on therapeutic interventions.

Fourth, the National Standard ignores the child's capacity in its consent requirements. It insists on valid proxy consent irrespective of the child's age or capacity. This is in breach of New Zealand law and the United Nations Convention on the Rights of the Child. On the other hand, a child's refusal is always deemed to be effective, according to the National Standard, again irrespective of the child's age or capacity to understand the consequences thereof. There may be circumstances where participation in research is of clear benefit to the child and where a child's refusal may be overridden by proxy consent.

Fifth, the Standard fails to address inducements to consent, both for parents and children.
Other New Zealand instruments provide even less guidance than the National Standard. The HRC Guidelines on Ethics in Health Research and the Interim New Zealand Guideline for Good Clinical Research Practice, for example, barely mention children as research participants. Ethics Committees are thus forced to look to foreign or international instruments for guidance. Though some of these guidelines are more detailed and focussed, they differ from each other on important points.

**Issues in Health Research With Children: Risk and Consent**

The two crucial issues in health research with children are the degree of permissible risk and the child's consent. While many of the international instruments have a broadly similar approach to these issues, there are significant differences. For instance, some guidelines define risk from the viewpoint of the children, taking into consideration the fear that some interventions generate in children, rather than the risk of actual physical harm. Most adopt a more objective stance looking at risk in terms of the probability and severity of physical harm.

The British Paediatric Association (BPA) listed the types of interventions that could be conducted on children in different forms of research. In the context of non-therapeutic research the list excluded all forms of invasive interventions and procedures, such as blood sampling by venepuncture, because of children's fear of needles. Criticisms that this very restrictive approach prevented valuable research prompted the BPA's successor, the Royal College of Paediatrics and Child Health (RCPCH), to adopt a slightly more lenient stance in the 1999 revision of the Guidelines. If there is no benefit to the child participant, or only a slight or uncertain one, interventions such as venepunctures ‘deserve serious ethical consideration’. They are permissible if the parents fully understand the reasons for the interventions and have balanced the risk to their child. The reasons for the interventions should be carefully explained to the children and their consent obtained if at all possible:

It is completely inappropriate to insist on the taking of blood for non-therapeutic reasons if a child indicates either significant unwillingness before the start or significant stress during the procedure.

Other guidelines tend to provide greater flexibility as regards risk by defining the various grades of risk in broad terms. For non-therapeutic interventions the risk is usually defined in relation to daily experiences or routine medical examinations which would probably not exclude venepunctures. Some guidelines, such as the National Standard, are too vague to be useful.

The second issue relates to consent. Section 10 of the New Zealand Bill of Rights Act 1990 provides:

> Every person has the right not to be subjected to medical and scientific experimentation without that person's consent.

This section appears to apply to persons of any age and could be read to preclude research with children who are not competent to consent. It does not appear to leave any room for proxy consent. We have argued elsewhere that such a narrow construction is neither necessary nor intended. However, the section does clearly reflect the importance of obtaining consent from research participants and this principle ought to apply to children as well to the greatest extent possible.

None of the guidelines deal with the consent issues very well. There are important differences in regard to the effectiveness of the child’s consent or refusal and the need for parental consent. None of the guidelines incorporate the UN Convention on the Rights of the Child, even though most countries in the world, including New Zealand, have agreed to be bound by it. Articles 5 and 12 of this Convention require children's views to be given due weight and to recognise the child's evolving capacities. Yet several guidelines state, or at least imply, that parental consent is necessary until the age of majority, which in New Zealand is attained at the age of 20. None differentiates between the various types of research or the risks associated with the research in relation to the consent requirements. Ten year olds may well have the necessary competence to consent to a non-invasive health survey, but will probably lack the competence to consent to a drug trial.

In each case the critical question should be: does this child have the necessary competence to make an informed decision about participation in this research project? If the
child has that competence, the child’s consent should be sufficient and his or her refusal should be binding. Proxy consent should only be sought where the child lacks the necessary competence to make an informed decision.\textsuperscript{17}

A fixed age below which proxy consent is always required would be easier to administer, but that is not the law.\textsuperscript{18} Nor is it in our view ethical to deny the child’s right to self-determination in such an arbitrary manner. The focus should be on the child’s rights, not the parents’ rights. If there is uncertainty about the child’s competence the child’s consent should be sought to involve the parent in the consent process. The child’s refusal to this request may justify excluding the child from participating in the research.

Even if the child obviously lacks the necessary competence to make an informed decision and parental consent is required, the child’s assent or willing co-operation should be obtained. This requirement is included in all the guidelines and is integral to the Code of Rights.\textsuperscript{19} The child’s refusal should be respected unless the child is to receive treatment for a condition for which no other medically acceptable therapy is available.\textsuperscript{20}

\textit{The Guidelines}

The Guidelines below should be read in conjunction with the ethical guidelines applicable to health research in general and the Guidelines for Researchers on Health Research Involving Maori. The following Guidelines set out the special conditions that we believe should apply to health research with children.

\textbf{Ethical Guidelines For Health Research With Children}

These Guidelines are based on six principles, which are mostly taken from the RCPCH Guidelines (1999) and the European Convention 1996.\textsuperscript{21}

\textbf{Principles:}

1. Research involving children is important for the benefit of all children and should be supported, encouraged and conducted in an ethical manner.\textsuperscript{22}

2. Children are not small adults; they have their own unique set of interests.

3. Research should only be done with children if comparable research with adults could not answer the same question and the purpose of the research is to obtain knowledge relevant to the health needs of children.

4. A research procedure which is not intended directly to benefit the child participant is not necessarily unethical.

5. All proposals involving health research with children should be submitted to an accredited ethics committee.

6. Legally valid consent should be obtained from the child, parent or guardian as appropriate. When parental consent is obtained, the assent or consent of the children should wherever possible also be obtained by the researcher.

\textbf{Guidelines:}

\textit{Nature and design of research}

1. Before undertaking research with children the investigator must ensure that:
   \begin{itemize}
   \item[(i)] children will not be involved in research that might equally well be carried out with adults;\textsuperscript{23}
   \item[(ii)] the purpose of the research is to obtain knowledge relevant to the health needs of children;\textsuperscript{24}
   \item[(iii)] if a choice of age groups is possible, older children should be involved in preference to younger ones;\textsuperscript{25}
   \item[(iv)] the research is designed or supervised and carried out by people experienced in working with children;\textsuperscript{26}
   \item[(v)] the number of children involved is limited to the number which is scientifically and clinically essential.\textsuperscript{27}
   \end{itemize}
Risk

2. Research procedures or interventions which are intended to provide direct therapeutic benefit to the child participants may be undertaken if
   (i) the risk is justified by the anticipated benefit to the child participants; and
   (ii) any relation of the anticipated benefit to the risk is likely to be at least as favourable to the child participant as any available alternative.

3. Research procedures or interventions which are not intended to be of direct benefit to the child participants, but which are likely to yield generalizable knowledge about the child's disorder or condition which is of vital importance for the understanding or amelioration of the child's disorder or condition, may be undertaken if
   (i) any risk represents a minor increase over minimal risk; and
   (ii) the interventions or procedures present experiences to the child participants which are reasonably commensurate with those inherent in their actual or expected medical, psychological, social or educational situations.

4. Research procedures which are not intended to be of direct benefit to the child participants, and do not come within the scope of 2 or 3 above, may be undertaken only if the risk presented by the interventions to the child participant is
   (i) minimal; and
   (ii) commensurate with the importance of the knowledge to be gained.

Informed consent

5. Information:
   When inviting children to participate in any research the investigator must ensure that the children, and where appropriate the children's parents, guardians or caregivers, have been fully informed about the research in a manner best suited to their needs.
   (i) Each child must be given full information about the research in a form that he or she can readily understand.
   (ii) Children must be advised of their right to decline participation and their right to withdraw from the research at any time without giving a reason.
   (iii) Investigators must give the children an opportunity to ask questions and to have those questions answered to the children's satisfaction.
   (iv) If proxy consent is required, the proxy must also be given full information about the research and be advised of the child's right to decline participation or withdraw from the research at any time.
   (v) The proxy must be given an opportunity to ask questions and have them answered to the proxy's satisfaction.

6. Consent:
   Before undertaking research with children the investigator must ensure that appropriate consent is sought on the basis of the information provided:
   (i) the consent of a child of or over the age of 16 must be obtained and has the same effect as if the child were of full age.
   (ii) If the child is below the age of 16, but has the competence to understand the nature, risks and consequences of the research:
       (a) the consent of the child must be obtained and
       (b) that consent will have the same effect as if the child were of full age.
   (iii) If the child is below the age of 16, and lacks the necessary competence to give legally effective consent:
       (a) the child's parent or legal guardian must give permission for the child's participation.
       (b) the child's assent must be obtained unless the child is unable to communicate.
       (c) the refusal of a child to participate in research must be respected unless
according to the research protocol the child would receive therapy for which there is no medically acceptable alternative; or
the research comes within the scope of category 3. above.

(iv) Care must be taken to ensure that no pressure is placed upon a child to consent to participate in research, especially if the procedures are not intended to be of direct benefit to the child participants (as in categories 3 and 4 above).

(v) The requirement for written consent should take into consideration the age and competence of the child.

Inducements
7. Families and children shall not receive any financial payments or other reward for participating in the research. Only expenses resulting from participation may be reimbursed.

Health research data
8. Retention and use of personally identifiable health research data:
   (i) Research data pertaining to the child participants should be retained by the researcher for ten years after the child has attained the age of 16.
   (ii) Children have the right to withdraw consent to the continued use or retention of personally identifiable health research data once they attain the age of 16.

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Notes

2. The following instruments were consulted:

International:
Nuremberg Code (1947);

World Medical Association (1964 as amended). Declaration of Helsinki;
United Nations (1966). International Covenant on Civil and Political Rights, GA Res. 2200 (XXI);
Committee for Proprietary medicinal Products (1997), Note for Guidance on Clinical Investigation of medicinal Products in Children, CPMP/EWP/462/95 [CPMP Guidelines];

United Kingdom:

British Paediatric Association (1992). *Guidelines for the Ethical Conduct of Medical Research Involving Children*, [BPA Guidelines];

Royal College of Paediatrics and Child Health (1999). *Guidelines for the Ethical Conduct of Medical Research Involving Children*, [RCPCH Guidelines, see also note 4 below].

**United States of America:**


**South Africa:**

**Australia:**

National Health and Medical Research Council (1999). *National Statement on Ethical Conduct in Research Involving Humans*, [NHMRC Statement].

3. A child is a person under the age of 20: s2(1) Guardianship Act 1968.

4. CIOMS Guidelines, Guideline 5 and US Code, [see note 2].

5. For example, s25 Guardianship Act 1968 and the New Zealand Court of Appeal’s approval in re J [1996] 2 NZLR 134 of the House of Lords’ decision in *Gillick v West Norfolk and Wisbech Area Health Authority* [1986] AC 112. See also Right 7 Code of Health and Disability Consumers’ Rights 1996.


7. CIOMS Guidelines, Guideline 5 and South African Guidelines: 6.2.2.2, [see note 2].

8. Definition of ‘minimal risk’ and the Introduction to the BPA Guidelines, [see note 2].


10. Note 9, p.179.

11. Idem.

12. Peart (2000) [see note 1], pp.428-31. The Australasian College Statement is similarly defective [see note 2].


15. England’s Department of Health requires parental consent for 16 and 17 year olds unless it would be against the child’s interests to comply with this requirement. Peart (2000) [see note 1], p.436.


17. Paterson (1998) [see note 16], pp.49-50. The Institute of Medical Ethics is of the view that parental consent should be sought for all children below the age of 16, even though children over the age of 14 have been found to be as competent as adults: Nicholson R.H. (ed.) (1986). *Medical Research with Children: Ethics, Law and Practice*, Oxford: Oxford University Press, p.151.

18. As Fraser points out: “there is no one particular age at which all children can consent to all health and disability services. Indeed, the development of the law in this area demonstrates a trend away from age-related thresholds, and instead focuses on the competence of the individual child” (Fraser A. (1998). The Informed Consent Process and the Application of the Code to Children. *Consent in Child and Youth Health*. Wellington: Ministry of Health, p.51.

19. Fraser (1998) [see note 18], p.53.

20. CIOMS Guidelines, Guideline 5 [see note 2].


22. This principle is now universally accepted: Peart (2000) [see note 1], pp.424-7. Concern about the lack of information on treatments in regular use with children prompted the US House of Representatives to urge the National Institute of Health to establish priorities for paediatric research. The NIH
issued a Policy and Guidelines on 6 March 1998 to increase the participation of children in research.

23. CIOMS Guidelines, Guideline 5; European Convention, Art 17; NHMRC Statement 4.1. [see note 2].


25. RCPCH Guidelines [see note 9], p.178; CIOMS Guideline 5 [see note 2], p.20.

26. CPMP Guidelines, Guideline 5.2.

27. Idem.

28. Reference is made to procedures and interventions as being therapeutic or non-therapeutic, rather than the research as a whole being therapeutic or non-therapeutic. Therapeutic research commonly includes non-therapeutic interventions and it is these interventions which should be carefully considered by researchers and ethics committees.

29. CIOMS Guidelines, Guideline 5 and US Code [see note 2], 46.405.

30. This provision is taken from the US Code of Federal Regulations [see note 2], 46.406. None of the other Guidelines have included this additional class of research.

31. ‘Minimal risk’: the probability and magnitude of harm or discomfort anticipated in the research are no more likely and not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. (US Code 46.102 (h)). While ‘a minor increase over minimal risk’ is vague, there may be instances where valuable research would not be possible without some greater leniency in the degree of permissible risk.

32. US Code [see note 2], 46.406.

33. See note 31. A broad definition of risk has been chosen, rather than the narrow list of permissible interventions in the RCPCH Guidelines to ensure greater flexibility. The RCPCH Guidelines define minimal risk as: “procedures such as questioning, observing and measuring children. Procedures with minimal risk include collecting a single urine sample (but not by aspiration), or using blood from a sample that has been taken as part of treatment”: RCPCH Guidelines [see note 9], p.179. Procedures which cause brief pain or tenderness, and small bruises or scars are described as low risk. Injections and venepunctures are included in this risk group, rather than the minimal risk group because many children fear needles. The BPA was of the view that “it would be unethical to submit child subjects to more than minimal risk when the procedure offers no benefit to them, or only a slight or very uncertain one”: BPA Guidelines, p.9. The RCPCH Ethics Advisory Committee has ameliorated this stance slightly. See above.

34. US Code [see note 2], 46.407.

35. Right 5 Code of Health and Disability Consumers’ Rights. See also RCPCH [see note 9], p.180. If the children are young it may be more appropriate to provide a verbal explanation rather than a written information sheet.

36. A written information sheet and a verbal explanation would normally be required.

37. Section 10 New Zealand Bill of Rights Act 1990. See page 4 above.

38. This accords with s25(1) Guardianship Act. Though this provision applies to medical treatment primarily, it has been argued that it should also apply to health research: Peart (2000) [see note 1] pp.436-7.

39. See Gillick v West Norfolk and Wisbech Area Health Authority [1986] AC 112; re J [1996] 2 NZLR 134; Right 7 Code of Health and Disability Consumers’ Rights. This does not preclude the involvement of parents in the consent process, if the child consents thereto. If the child refuses to agree to the parents’ involvement, and the researchers would prefer their involvement, it may be better not to include the child in the research.

40. Permission: parents of children give permission, rather than consent.

41 Assent: the acquiescence of younger children who lack the necessary understanding to give informed consent is required in addition to parental consent. See also Right 7(3) Code of Health and Disability Consumers’ Rights.

42. Communication should be interpreted broadly to include verbal as well as non-verbal communication.

43. A child’s refusal may be expressed verbally or non-verbally, eg by screaming, resisting or withdrawing.

44. CIOMS Guidelines, Guideline 5 [see note 2]. This principle recognises the distinction between medical treatment and health research.

45. RCPCH Guidelines [see note 9], p.180.

46. Ethics committees are advised to require investigators to inform parents and their children of appropriate lines of communication to enable child participants to exercise this right.