

# Standard 1: Consent and Recruitment

## DILEMMA

A 4-year-old boy with a serious metabolic disorder is eligible for a trial of a new enzyme replacement, the first potential option to treat this disease. His parents have little understanding of the disease or trial, even with careful explanation, but eventually they consent to entry in the trial. The treating clinician doubts whether their consent is valid.

This and similar dilemmas face pediatricians in research every day. Many of the therapeutic options for children have not been tested with the rigor applied to similar treatments in adults. This highlights the need for research to improve the evidence base of children's medicine, for more pediatricians to undertake research, and for more children and families to participate.<sup>1</sup> Each of these components is more challenging when research is proposed in vulnerable participants, such as children. Well-designed consent procedures are vital for ethically sound recruitment.<sup>2</sup>

This article highlights some of the many ethical problems encountered when considering clinical trials in children, provides recommendations for practice (Table 1), and suggests directions for future research on recruitment. We discuss (1) who should give consent to enrollment of children, (2) information requirements, (3) recruiting in vulnerable populations, (4) payment for participation, (5) the roles of clinicians versus investigators, and (6) why eligible patients are sometimes not approached.

## GUIDANCE

### 1. Who Should Give Consent for Children in Research?

An 8-year-old child is diagnosed with pneumonia and asked to participate in a trial of oral versus intravenous antibiotic treatment. The parents consent, but the child says he does not want to take part because he does not like taking oral medicines. Should his view be considered?

Consent to research involving children is complex, providing a challenge for researchers and for ethics review bodies,<sup>3</sup> and guidance or legal requirements on this topic vary between countries.<sup>4</sup> Although adults provide their own consent to participate in research, children depend on others, usually parents or carers. Therefore, the person consenting is not the one exposed to the risks, burdens, or potential benefits of the research. Further, even when the parent's or legal carer's permission is obtained for research, this process may be compromised by their level of understanding, caregiver neglect, and in special settings of research such as emergency care.<sup>5</sup>

Investigators also have an ethical and legal obligation to obtain the child's permission (assent) for participation in research.<sup>6,7</sup> Assent is defined as a child's "affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent."<sup>8</sup> Although the process of seeking assent is not globally

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This is the first in a series of standard articles resulting from an ongoing process in which a group of invited experts called a standard development group from StaR Child Health assembles and exchanges information about methods for pediatric trial design, conduct, and reporting. More detailed information about this topic can be found in the introductory article of this supplement or at the StaR Child Health Web site ([www.starchildhealth.org](http://www.starchildhealth.org)).

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**TABLE 1** Recommendations for Practice

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Investigators always have ethical and legal obligations to obtain consent and assent (when age-appropriate) to undertake research. However, when a child objects to research participation, his or her dissent should be recognized and taken in the context in which it presents (such as the clinical procedure).
Investigators should minimize decisions not to approach every eligible patient for trial participation and when patients are not approached should justify their actions. The information provided for parents and children should always be age-appropriate, clear, concise, and on-going.
Researchers should always ensure that the presentation of payments does not influence parents and children to look upon payments or incentives as a benefit of the research. However, when payment is made to vulnerable populations, ethics committees need to ensure that research payment will not lead families to take unnecessary risks. In this situation, ethics committees and supporting communities need further development and empowerment.
Clinicians acting as investigators should always clearly differentiate the roles and aspects of care that are standard or part of research when approaching their own patients for research participation. In this situation, the best option is for another researcher not involved in the care of the patient to obtain the informed consent, although it may be the child's clinician who explained the trial to the family.

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recognized, nor sufficient to authorize participation in research,<sup>6</sup> the act of obtaining assent demonstrates respect for children and reinforces their importance in the process even when they do not have decisional authority.<sup>9,10</sup> When assent is given, it is important to consider the voluntariness of a child's decision in the context of research. Is a child really able to disagree when his or her parents and doctors are enthusiastic about a study?

A child's dissent or objection should clearly be respected,<sup>11</sup> although it may be difficult in practice to define what constitutes true objection, and in some countries, a child's objection is not considered binding.<sup>12</sup> How can we determine whether a child's objection to procedure within a trial represents true and meaningful dissent to trial participation or is the sort of response a child would normally have to the same procedure outside a trial? As a general rule, it is reasonable to suggest that a child may be deemed to object if his/her behavior clearly differs in nature or degree from that normally displayed by the child when confronted with diagnostic or therapeutic procedures. Therefore, if the child would normally object to taking oral medication, it would be reasonable to assume that his or her objection does not represent true dissent.

## 2. What Information Is Necessary to Obtain Consent?

The parents and their 13-year-old daughter, who has cystic fibrosis, agree to her participation in a commercial, placebo-controlled trial of a new antibiotic. They have had several days to read information on the trial, which spans 16 pages for the adult version and an additional 10 pages for the child version. After the consent form is signed, the parents state that they wanted to participate to get the "new and better" antibiotic. The parents have been informed about the trial but do they understand?

There is a tension between providing "enough" information about a trial in adherence to local regulatory requirements and giving so much information that a child and family are left confused and overwhelmed. Information should be provided not only to parents but also in an age-appropriate manner to children to demonstrate respect, preserve trust, and facilitate cooperation. However, developing age-appropriate information further complicates the extent, content, and format of the material provided.

Comprehensive information describes the protocol design and duration, what it involves for the child including potential benefits, discomfort, risks, payments, plans for treatment or compensation if

harmed, the right to refuse or withdraw, alternative treatments, sources of funding, conflicts of interest and the researcher's contact details. Guidance on this content is provided within the Declaration of Helsinki<sup>2</sup> and national regulatory and ethics bodies.

Despite compliance with these existing standards, parents and children may still be left with a poor comprehension of the research and its implication.<sup>13,14</sup> This suggests the need to continue to inform children and families about the research process even after formal consent has been given. This must be balanced with the knowledge that excessive information undermines understanding and is negatively perceived by families.<sup>15</sup> Research on children's and families' information preferences highlights the need for brevity, age-appropriate material (fifth- or sixth-grade reading level) in friendly plain language, and preferably consultation with parents and families on the design of this information.<sup>16–18</sup> Parents' comments in 1 study assessing perception of the consent process included terms such as "a lot to read," "wordy," "intense," and "overwhelming."<sup>19</sup> Whether adapting to these preferences affect recruitment to studies remains uncertain.

## 3. Research in Extra Vulnerable Children: Equitable Opportunity or Exploitation?

A placebo-controlled trial of a new vaccine was conducted in a developing country in Asia. Children in the trial had easy access to the health center and free medications; check-ups and laboratory examinations were performed as part of the protocol. Is this an equitable opportunity for the children to access health care or exploitation in a low-resource setting?

Two special circumstances make children particularly vulnerable to exploitation in research: (1) children in institutions, such

as medical or correctional facilities<sup>20,21</sup> and (2) children in low-resource settings, such as those in minority ethnic groups, developing countries, and disadvantaged groups within developed countries. Within medical institutions, children in emergency or intensive care settings are especially vulnerable due to the urgency of their health care needs.<sup>22</sup>

<sup>23</sup> Similarly, in low-resource settings, the perception of risk and benefit is complicated by multiple compounding factors. The 2002 World Health Organization Ethics Committee Report<sup>24</sup> identified the following as rendering children from developing countries vulnerable to exploitation: (1) socioeconomic inequalities, (2) limited access to health care, (3) high burden of illness, (4) lower educational attainment of caregivers, (5) limited understanding of scientific research, including language barriers, and (6) cultural and gender norms. A further disadvantage is the underdevelopment of local ethics committees in developing countries. Recruitment of children from these settings may be considered resource-effective but raises ethical dilemmas. Is consent given independently and voluntarily? Are the benefits and risks of joining the study appropriately presented and properly weighted?

In low-resource settings, there should be clear justification of the scientific need to involve that population and an equitable sharing of benefits and risks among possible involved groups and communities. Community consultation can be helpful in appraising the potential benefits, harm, and the appropriateness of the study methodology but does not replace the need for individual consent. Local ethics committees are critical in protecting the rights of vulnerable children<sup>25</sup>; their composition and expertise should be strengthened. Existing international guidelines to safeguard

vulnerable children in research must be implemented and properly monitored.

To protect these vulnerable populations, ethics committees must take extra measures to minimize the risk of exploitation. Most national legislation<sup>26</sup> and international guidelines have prohibited conducting trials involving institutionalized children, except when trials are of direct potential benefit to the subjects or when the trials could not be conducted without the participation of persons of the same category as the subject. In these situations, extra attention should be given to informing parents or guardians to obtain true consent. This could be realized by separating the roles of investigator and clinician in institutions when recruiting (standard 5 below).

#### **4. Payment for Research: Justified or Unethical?**

In a trial in a developing country, parents of children eligible to be recruited were told that they would receive a transportation and meal allowance for each visit that was 3 times the minimum daily wage. Is this fair reimbursement or an unfair incentive to recruitment?

Payment in research is common but controversial.<sup>27</sup> Financial and non-financial payment can enhance recruitment; however, it may also lead participants to undervalue risks, thereby compromising voluntariness. In research involving children, the offer of payment is doubly problematic because often the person receiving payment is the parent or guardian when it is the child who is being exposed to the risk and burden of the study.<sup>28</sup>

Some have argued that parents should not receive monetary payments for their child's research participation,<sup>29</sup> whereas others believe that payment can reimburse research-related expenses and failure to compensate for these expenses may lead to the exclusion of poorer families. Payment can also compensate

for time and inconvenience, act as a token of appreciation after children have participated, or act as an incentive to encourage participation.<sup>30</sup> Wendler et al<sup>30</sup> write that reimbursement and compensation are ethically acceptable, whereas appreciation payments are unnecessary and incentive payments generally indefensible. Such distinctions may help ethics committees assess the appropriateness of payments; however, this sentiment is not embraced by all.<sup>31</sup> Although payment of competent adult research participants to compensate them for engaging in higher-risk research that does not directly benefit them is sometimes permissible, payment for children's participation in research to compensate them for the risk associated with research is not acceptable.<sup>29</sup> Excessive payment to parents may unwittingly or intentionally distort their decision-making, and payment to children may also be problematic because they have limited experience with money.<sup>30</sup> Payment is particularly controversial when offered to vulnerable children and families (section 3 above). Researchers offering payment or incentives in these situations need to ensure, in the context of their research, payment will not lead to families taking unnecessary risks.

Some studies provide payment, eg, movie tickets, after a child's participation is complete, but this may still distort decision-making about participation. Families may learn of this and assume they will receive something for participating.<sup>32</sup> In the school setting, incentives for return of a parental notification form (rather than for consent for trial participation) can help ensure that parents are informed about the study without distorting decision-making.<sup>33</sup> The current consensus is that incentives or payments are acceptable except when they lead participants or those deciding for them to ignore, misunderstand, or significantly undervalue serious risks.

## 5. Can a Child's Clinician Also Be the Investigator?

A chief investigator is told that his or her research funding will end unless the recruitment for his or her trial improves within 2 months. The next day, the chief investigator sees a child in his or her clinic who is eligible; can the investigator be objective?

A child's clinician is usually a trusted health professional to both the child and the family. Can the roles of clinician and researcher exist concurrently? This depends in part on whether the ethical issues in research are considered to be encompassed by those governing clinical care or distinct.<sup>34</sup> A key perspective is whether research is regarded as an integral part of good care (ie, as in oncology) or an "extra" activity. These views have to be considered in the context where many therapeutic options for children have little evidence base.

Studies reveal that families trust their doctors to explain research,<sup>35,36</sup> and engagement in research may suffer when others are substituted to this role. However, for the clinician to discuss a research study, there should be "clinical equipoise" (genuine uncertainty within the expert medical community) over the research question.<sup>37</sup> For the clinician, his or her personal equipoise may also be influenced by his or her culture, beliefs, experience, and standard practice and the potential for harm from participation as well as the setting for research (ie, community, ambulatory or emergency department).<sup>38-40</sup> An oft-quoted conflict relates to the potential rewards available to the investigator. These may be direct (financial or promotion) or indirect (status), but the perception of reward rather than their true value is most relevant. Guidance on the role of clinicians as investigators is provided in the Declaration of Helsinki,<sup>2</sup> in Good Clinical Practice, and in national bioethics guidelines (eg, United States).

These generally indicate the need for a clear differentiation of roles and aspects of care that are "standard" or part of research. Although this is not always easy when research is entwined in care, clinicians should be open about their dual clinician-investigator role when discussing trials with children and parents.<sup>41</sup>

## 6. They Were Eligible for the Trial so Why Were They Not Invited?

An investigator screens her clinic lists for a study of the impact of an educational and behavioral intervention for chronic pain. In addition to the eligibility criteria set in the study protocol, she decides to exclude children with a single parent because the study imposes a significant burden on the carer. Is she sensitive to the needs of her patients or prejudicial to the success of the study?

Children may be eligible to participate in a trial yet not be invited for many reasons. Clinicians may think it inappropriate to ask particular families because they are too distressed or unlikely to be compliant with the research protocol. There may be procedural complexities, for example, in school-based recruitment an invitation letter may not even reach families. Clinicians report the need to exercise discretion in deciding who to approach, for instance to avoid straining their relationship with a family who could be upset by being asked to consider a trial.<sup>42</sup> However, using criteria over and above those listed in the trial's eligibility criteria compromises the applicability of the study to all relevant patients. In some situations, preselection may also lead to poor accrual and delays, particularly in trials of treatments for rare diseases.<sup>43</sup> Ethically, informal preselection potentially leads to unfairness in sharing of the risks and benefits of research within society. Families consistently say that they want to be told when a trial is available for their child, they do not want

clinicians to decide on their behalf.<sup>44,45</sup> Existing guidelines reinforce this view by advising clinicians to ensure recruitment is "free from discrimination" and that all reasonable steps are taken to ensure that people eligible to participate are given equal access.<sup>46</sup> Nevertheless, families recognize the dilemmas faced by clinicians in recruiting to trials, reporting that in the case of "other" more vulnerable families, they want clinicians to exercise judgment and discretion in deciding which eligible families to approach.<sup>44</sup> Investigators have to find a proper balance in recruitment; achieving this takes time and requires adequate resources.

## RESEARCH AGENDA

This standard development group has identified a number of areas for future research. The highest priorities are as follows:

- To identify and develop an assessment tool of the criteria needed to assess children's decision-making capacity.
- To identify and develop an assessment tool to assess children's dissent or objection to research participation.
- To identify and evaluate different formats of presenting information on research to parents and children.
- To explore in vulnerable populations, parents' and children's perspectives on being approached for research.
- To determine how payments or incentives influence decisions about children's participation in trials.
- To evaluate whether the training, specialty, and beliefs of clinicians affect professional and patient participation in research.
- To identify the evidence supporting or refuting that preselection is damaging to research.
- To explore what influences clinicians to avoid approaching eligible patients.



## CONCLUSIONS

Few child health professionals would argue against the need for more research in pediatrics; the question is how to do it better? Improving the quality of research in children relates to the entire research path: from study question, through design, recruitment, and conduct to reporting and implementation of research findings.

Developing appropriate and ethical strategies for recruitment, information, and consent are key elements of any research study but more challenging

for those involving children. Responding to this challenge is fundamental to the success of a study. This means going beyond the minimum standard practice of obtaining consent and listening to the child's decision on participation. Recruitment information must be tailored from the regulatory requirements to a format that is accessible to the child and family. Investigators and ethics committees must be aware of these requirements and be vigilant to potential conflicts of interest, particularly in vulnerable groups or settings.

Research in children is challenging and requires that special time and attention be devoted to appropriately educating all eligible children and families. Pediatricians are highly skilled in achieving these standards in their clinical care, taking the time to explain, ensuring the environment is right for a child's care, and adapting treatments to their special needs. We accept this as routine clinical care, and we need to achieve similarly high standards in research involving children.

## REFERENCES

1. Klassen TP, Hartling L, Craig JC, Offringa M. Children are not just small adults: the urgent need for high-quality trial evidence in children. *PLoS Med*. 2008;5(8):e172
2. World Medical Association. Declaration of Helsinki, Ethical Principles for Medical Research Involving Human Subjects. 59th World Medical Association General Assembly; October 2008; Seoul, South Korea
3. Spriggs M. Ethical difficulties with consent in research involving children: Findings from key informant interviews. *AJOB Primary Research*. 2010;1(1):34–43
4. European Commission. Recommendations of the ad hoc group for the development of implementing guidelines for directive 2001/20/EC. 2008 Ethical considerations for clinical trials on medicinal products conducted with the paediatric population (annex 1: questionnaire). European Commission, Brussels, Belgium. Available at: [ftp://ftp.cordis.europa.eu/pub/fp7/docs/ethical-considerations-paediatrics\\_en.pdf](ftp://ftp.cordis.europa.eu/pub/fp7/docs/ethical-considerations-paediatrics_en.pdf). Accessed April 16, 2012
5. Chamberlain JM, Lillis K, Vance C, Brown KM, Fawumi O, Nichols S, et al. Perceived challenges to obtaining informed consent for a time-sensitive emergency department study of pediatric status epilepticus: results of two focus groups. *Acad Emerg Med*. 2009;16(8):765–770
6. Miller VA, Nelson RM. A developmental approach to child assent for nontherapeutic research. *J Pediatr*. 2006;149(suppl 1):S25–S30
7. Informed consent, parental permission, and assent in pediatric practice. Committee on Bioethics, American Academy of Pediatrics. *Pediatrics*. 1995;95(2):314–317
8. United States. Code of Federal Regulations. Title 45 Public Welfare, Department of Health and Human Services Part 46. Protection of Human Subjects, Revised January 15, 2009. [February 23, 2011]; Available at: [www.hhs.gov/ohrp/policy/ohrpregsulations.pdf](http://www.hhs.gov/ohrp/policy/ohrpregsulations.pdf). Accessed April 10, 2012
9. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont report: ethical principles and guidelines for the protection of human subjects of research. Available at: [www.ohsr.od.nih.gov/guidelines/belmont.html](http://www.ohsr.od.nih.gov/guidelines/belmont.html). Accessed February 27, 2011
10. Spriggs MP, Gillam LH. Consent in paediatric research: an evaluation of the guidance provided in the 2007 NHMRC national statement on ethical conduct in human research. *Med J Aust*. 2008;188(6):360–362
11. Leikin S. Minor's assent, consent or dissent to medical research. *IRB*. 1995;15:1–7
12. National Health and Medical Research Council (NHMRC) ARCAV-CC. *National Statement on Ethical Conduct in Human Research*. Canberra, Australia: Australian Government; 2007
13. Featherstone K, Donovan JL. Random allocation or allocation at random? Patients' perspectives of participation in a randomised controlled trial. *BMJ*. 1998;317(7167):1177–1180
14. Bergenmar M, Molin C, Wilking N, Brandberg Y. Knowledge and understanding among cancer patients consenting to participate in clinical trials. *Eur J Cancer*. 2008;44(17):2627–2633
15. Shilling V, Young B. How do parents experience being asked to enter a child in a randomised controlled trial? *BMC Med Ethics*. 2009;10(1):1
16. Tarnowski KJ, Allen DM, Mayhall C, Kelly PA. Readability of pediatric biomedical research informed consent forms. *Pediatrics*. 1990;85(1):58–62
17. Ogloff JR, Otto RK. Are research participants truly informed? Readability of informed consent forms used in research. *Ethics Behav*. 1991;1(4):239–252
18. Eder ML, Yamokoski AD, Wittmann PW, Kodish ED. Improving informed consent: suggestions from parents of children with leukemia. *Pediatrics*. 2007;119(4). Available at: [www.pediatrics.org/cgi/content/full/119/4/e849](http://www.pediatrics.org/cgi/content/full/119/4/e849)
19. Harth SC, Thong YH. Parental perceptions and attitudes about informed consent in clinical research involving children. *Soc Sci Med*. 1995;41(12):1647–1651
20. Advisory Committee on Human Radiation Experiments. *The Human Radiation Experiments*. New York, New York: Oxford University Press; 1996
21. Diekema DS. Conducting ethical research in pediatrics: a brief historical overview and review of pediatric regulations. *J Pediatr*. 2006;149(suppl 1):S3–S11
22. Day Watts D. Informed consent in emergency research: what every emergency nurse should know. *J Emerg Nurs*. 1997;23(1):70–74
23. Cook DJ, Blythe D, Rischbieth A, Hebert PC, Zytaruk N, Menon K, et al. Enrollment of intensive care unit patients into clinical studies: a trinational survey of researchers'

- experiences, beliefs, and practices. *Crit Care Med*. 2008;36(7):2100–2105
24. Initiative for Vaccine Research of the Department of Vaccines and Biologicals, World Health Organization. Ethical considerations arising from vaccine trials conducted in pediatric populations with high disease burden in developing countries. WHO/IVR ethics meeting. November 26–28, 2002. Accra, Ghana. Available at: [http://whqlibdoc.who.int/hq/2004/WHO\\_V&B\\_04.04.PDF](http://whqlibdoc.who.int/hq/2004/WHO_V&B_04.04.PDF). Accessed April 10, 2012
  25. Lemaire F, Brun-Buisson C. Are institutional review boards effective in safeguarding patients in intensive care units? *Curr Opin Anaesthesiol*. 2000;13(2):195–201
  26. Ministry of Health, Welfare and Sports. Dutch regulations on medical research involving human subjects (WMO). Stb.1998,161. Den Haag, The Netherlands: Sdu Uitgevers; 1998.
  27. Grady C. Payment of clinical research subjects. *J Clin Invest*. 2005;115(7):1681–1687
  28. Weise KL, Smith ML, Maschke KJ, Copeland HL. National practices regarding payment to research subjects for participating in pediatric research. *Pediatrics*. 2002;110(3):577–582
  29. Institute of Medicine. 2004. Payments related to children's participation in clinical research. In: Field M, Berman R, eds. *Ethical Conduct of Clinical Research Involving Children*. Washington, DC: The National Academies Press; 211–228
  30. Wendler D, Rackoff JE, Emanuel EJ, Grady C. The ethics of paying for children's participation in research. *J Pediatr*. 2002;141(2):166–171
  31. Friedman RL. *Children in Medical Research*. Oxford, United Kingdom: Clarendon Press; 2006
  32. Spriggs M. Understanding consent in research involving children: the ethical issues. 2010. Available at: [www.mcrci.edu.au/projects/ConsentInResearch/media/handbook.pdf](http://www.mcrci.edu.au/projects/ConsentInResearch/media/handbook.pdf). Accessed November 2010
  33. Esbensen FA, Melde C, Taylor TJ, Peterson D. Active parental consent in school-based research: how much is enough and how do we get it? *Eval Rev*. 2008;32(4):335–362
  34. Brody H, Miller FG. The clinician-investigator: unavoidable but manageable tension. *Kennedy Inst Ethics J*. 2003;13(4):329–346
  35. Chappuy H, Doz F, Blanche S, Gentet JC, Pons G, Treluyer JM. Parental consent in paediatric clinical research. *Arch Dis Child*. 2006;91(2):112–116
  36. Caldwell PH, Hamilton S, Tan A, Craig JC. Strategies for increasing recruitment to randomised controlled trials: systematic review. *PLoS Med*. 2010;7(11):e1000368
  37. Freedman B. Equipoise and the ethics of clinical research. *N Engl J Med*. 1987;317(3):141–145
  38. Zeibland S, Featherstone K, Snowdon C, Barker K, Frost H, Fairbank J. Does it matter if clinicians recruiting for a trial don't understand what the trial is really about? Qualitative study of surgeons' experiences of participation in a pragmatic multi-centre RCT. *Trials*. 2007;8:4
  39. Miller FG, Joffe S. Equipoise and the dilemma of randomized clinical trials. *N Engl J Med*. 2011;364(5):476–480
  40. London AJ. Clinical equipoise: foundational requirement or fundamental error? 2007. Available at: <http://repository.cmu.edu/cgi/viewcontent.cgi?article=1394&context=philosophy>. Accessed April 4, 2012
  41. Byrne-Davis LM, Salmon P, Gravenhorst K, Eden TO, Young B. Balancing high accrual and ethical recruitment in paediatric oncology: a qualitative study of the "look and feel" of clinical trial discussions. *BMC Med Res Methodol*. 2010;10:101
  42. Caldwell PH, Butow PN, Craig JC. Pediatricians' attitudes toward randomized controlled trials involving children. *J Pediatr*. 2002;141(6):798–803
  43. Weijer C. Selecting subjects for participation in clinical research: one sphere of justice. *J Med Ethics*. 1999;25(1):31–36
  44. Caldwell PH, Butow PN, Craig JC. Parents' attitudes to children's participation in randomized controlled trials. *J Pediatr*. 2003;142(5):554–559
  45. Shilling V, Williamson PR, Hickey H, Sowden E, Smyth RL, Young B. Processes in recruitment to randomised controlled trials of medicines for children (RECRUIT): a qualitative study. *Health Technol Assess*. 2011;15(15):1–116
  46. General Medicine Council. *Good Practice in Research and Consent to Research*. London, United Kingdom: GMC; 2010

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## **Standard 1: Consent and Recruitment**

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