

## CHAPTER 19

# **BIOMEDICAL EXPERIMENTATION WITH CHILDREN: BALANCING THE NEED FOR PROTECTIVE MEASURES WITH THE NEED TO RESPECT CHILDREN'S DEVELOPING ABILITY TO MAKE SIGNIFICANT LIFE DECISIONS FOR THEMSELVES**

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### **INTRODUCTION**

The use of children as research subjects can be traced back to various experiments conducted with smallpox vaccines in the 1700s among children in England and in the North American colonies.<sup>1</sup> While children were used, sporadically, as test subjects to develop vaccines, their infrequent selection hindered the development of specific regulations for the protection of their welfare as participants in research. In 1772, for example, Queen Caroline of England had ten orphans vaccinated against smallpox as a precautionary test before consenting to the vaccination of her own children.<sup>2</sup> Edward Jenner and Benjamine Waterhouse vaccinated their own children prior to vaccinating the children of others. Thomas James vaccinated 48 institutionalized children under his care and then inoculated the children with

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<sup>1</sup> S. Lederer & M.A. Grodin, "Historical Overview: Pediatric Experimentation" in M.A. Grodin & L. Glantz, eds., *Children as Research Subjects: Science, Ethics, and Law* (New York: Oxford University Press, 1994) 3 at 4.

<sup>2</sup> R.G. Mitchell "The Child and Experimental Medicine" (1964) 1 *British Medical Journal* 721 at 722; A. Holder, "Constraints on Experimentation: Protecting Children to Death" (1988) 6 *Yale Law & Policy Review* 137 at 155.

smallpox to test the effectiveness of his vaccine.<sup>3</sup> Similar trials were conducted with measles vaccines. During the latter half of the Nineteenth Century and the first half of the Twentieth Century, the common practice of institutionalizing members of special populations rendered children (and other institutionalized populations) attractive subjects for research. The apathy of investigators in safeguarding their subjects' well-being reflects the low esteem in which these populations were held. For example, at the turn of the century, Alfred Hess, Medical Director of the Hebrew Infant Asylum in New York, conducted research on the children in his institution because the conditions there were similar to the "conditions which are insisted on in considering the course of experimental infection among laboratory animals, but which can rarely be controlled in the study of infection in man".<sup>4</sup> Unfortunately, there are many such examples of abuse, with extreme examples occurring as recently as a few decades ago in New York at the Willowbrook State School.<sup>5</sup>

Poor sanitation and acute overcrowding at the Willowbrook facility created a breeding ground for hepatitis. Researchers proposed to test a vaccine by inoculating children upon admission and then infecting them with the disease. Parents wishing to place their children in the school were informed that participation was a condition of admission and that, as research subjects, their children would be isolated from the general population and so would receive superior care. It was pointed out that children who were placed among the general population would be expected to contract hepatitis and/or measles, shigellosis, and other parasitic or respiratory infections that were beyond the supervision and control of the investigators.<sup>6</sup> Research ethicists of the day looked beyond the deplorable conditions at the Institution to raise questions about whether the study should have been conducted in the way that it was and whether the consent so obtained was valid; the questions raised at that time have figured prominently in the subsequent debate on the participation of children in research.

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<sup>3</sup> See Lederer & Grodin, *supra* note 1 at 5.

<sup>4</sup> *Ibid.* at 1.

<sup>5</sup> D.J. Rothman & S.M. Rothman, *The Willowbrook Wars* (New York: Harper & Row, 1984); S. Krugman, "Experiments at The Willowbrook State School (letter)" (1971) 1 *Lancet* 966. Another example worth noting is the case of the Fernald School in Massachusetts where experiments were conducted on mentally retarded children in the late 1940s. These studies were reviewed in detail by the Massachusetts Task Force on Human Subject Research and the Presidential Advisory Committee on Human Radiation Experiments. Although the Fernald School radiation studies were not as dangerous as those conducted at Willowbrook, the Fernald researchers were criticized on the basis that they took advantage of a vulnerable pool of subjects (institutionalized children), concealed certain key details from their parents (such as the use of radioisotopes in the studies), and solicited participation unfairly (by offering inducements that were coercive in the circumstances, such as extra milk and special outings for the children). See Task Force on Human Subject Research, *A Report on the Use of Radioactive Materials in Human Subject Research that Involved Residents of State-Operated Facilities within the Commonwealth of Massachusetts from 1943 to 1973* (Submitted to Philip Campbell, Commissioner, Commonwealth of Massachusetts Executive Office of Health and Human Services, Department of Mental Retardation, April 1994); Advisory Committee on Human Radiation Experiments, *Final Report* (Washington, D.C.: U.S. Government Printing Office, 1995).

<sup>6</sup> See Krugman, *ibid.*

## DEFINING "CHILDREN"

Simply stated, children are persons between birth and the age of majority, the latter often being established by statute.<sup>7</sup> Many jurisdictions have also enacted legislation that sets a specific age as the point at which a child may consent to treatment without parental authorization.<sup>8</sup> Under that age, parental permission is required, although there are significant exceptions to this requirement. In those Canadian jurisdictions that have not established a specific age at which a child may consent to treatment without parental authorization, the so-called "mature minor" rule applies.<sup>9</sup> Provincial legislation also provides that the parents' right to refuse treatment for their children may be overridden where a court believes the treatment necessary to preserve life or health.<sup>10</sup>

It follows from the above definition of "children" that their rights and obligations are not comparable to those of adults. Their dependency and statutory incompetence necessitate that parents or guardians act as their representatives. Children therefore have a special, and perhaps even a privileged, place within the legal framework of society. They have been accorded a distinctive status in relation to their health care, entitling them both to receive adequate health care and to rely on others, generally their parents, not only to be vigilant concerning the need for medical intervention

<sup>7</sup> In half of Canada's twelve jurisdictions, for example, the age of majority is eighteen years; otherwise it is nineteen.

<sup>8</sup> In New Brunswick, for example, treatment may be administered to a child under the age of 16 where the health care practitioner is of the opinion that the procedure is in the best interests of the child, the child is capable of making a decision, and/or this opinion is supported in writing by another practitioner. See *Medical Consent of Minors Act*, R.S.N.B. 1976, c. M-6.1, ss. 1-3.

<sup>9</sup> The essential elements of this common-law rule were summarized in *Ney v. Canada (Attorney General)* (1993), 79 B.C.L.R. 47 (S.C.) at 58-59:

[A]t common law a child is capable of consenting to medical treatment if he or she has sufficient intelligence and maturity to fully appreciate the nature and consequences of a medical procedure to be performed for his or her benefit. It appears that the medical practitioner is to make this determination. If the child is incapable of meeting this test then the parents' consent will be required for treatment. It is not clear whether parental control yields to the child's independence or whether there are concurrent powers of consent. But it is clear that the parents may not veto treatment to which a capable child consents, and that neither child nor parents can require a medical practitioner to treat.

The "mature minor" rule is upheld by the *Health Care and Consent Act, 1996*, S.O. 1996, c. 2, which presumes that any person can make a treatment decision unless there is a finding of incapacity. See generally B.F. Hoffman, *The Law of Consent to Treatment in Ontario*, 2nd ed. (Toronto: Butterworths, 1997).

<sup>10</sup> See *Re McTavish et al. and Director, Child Welfare Act et al.* (1986), 32 D.L.R. (4th) 394 (Alta.Q.B.); *Re E and Minister of Social Services et al.* (1987), 36 D.L.R. (4th) 683 (N.S.C.A.); *Re K. (R.)* (1987), 79 A.R. 140 (Prov. Ct. Fam. Div.). In the case of *B. (R.) v. Children's Aid Society of Metropolitan Toronto*, [1995] 1 S.C.R. 315, the Supreme Court of Canada ruled that the Ontario legislation that permitted the overriding of a parental refusal to permit treatment (*Child Welfare Act*, R.S.O. 1980, c. 66) did not violate the *Canadian Charter of Rights and Freedoms*.

but also to be diligent in making sure that it is actually provided.<sup>11</sup> To the extent that they are not capable of meaningful involvement in decisions regarding their health care, children are also entitled to rely on the fact that the medical treatment to which they are subjected does not pose a risk of serious harm. Yet, to the extent that children are capable of meaningful involvement, they are equally entitled to participate in any decision-making process affecting the nature and quality of the medical treatment that they receive.

### *Children as a Vulnerable Population*

To say that children enjoy a special status is perhaps not entirely accurate, in that their entitlement to these assurances is no different from that of other vulnerable populations incapable of making independent health-care decisions.<sup>12</sup> Yet, children differ substantially from other vulnerable populations.<sup>13</sup> Four of these differences are worth mentioning.

The first of these differences is the universality of childhood dependency. It is the only inevitable dependence during the course of our lives, and so the need to establish and maintain mechanisms for others to make health care decisions on behalf of children is universally accepted. The operation of these decision-making mechanisms has a direct impact on the lives of all children as well as on those who have the obligation to care for them. Arguably, childhood is the relationship of dependence with the greatest repercussions for the general population.

The second consideration pertains to the mechanisms that permit others to make decisions on behalf of children. As a vulnerable population, children are the only

<sup>11</sup> The provision of adequate health care for children is assured through the various duties imposed on their caregivers and through the encouragement and resources provided to their caregivers by their communities. The effectiveness of this care is ensured by the criminal law and by a number of legislative measures that become operative should those who are responsible for a child's care fail in that responsibility. See e.g. *Public Hospitals Act*, R.S.O. 1990, c. P-40; *Family and Child Services Act*, R.S.O. 1990, c. C-11. Under s. 215 of the *Criminal Code*, R.S.C. 1985, c. C-46, parents and guardians are obligated to provide their children, who are younger than 16 years of age, with the "necessaries of life" and they will be found to have committed an offence if, without lawful excuse, they do not secure adequate medical treatment when a child is in danger of dying or suffering permanent injury. In *R. v. Naglik* (1993), 83 C.C.C. (3d) 526, the Supreme Court of Canada ruled that liability under s. 215 is imposed on an *objective* basis and that the relevant standard is that of the reasonably prudent parent or guardian.

<sup>12</sup> Seiber states that children are a vulnerable population because:

- (1) they have a limited psychological, as well as legal, capacity to give informed consent;
- (2) they may be cognitively, socially, and emotionally immature;
- (3) there are external constraints on their self-determination and independent decision-making;
- (4) they have unequal power in relation to authorities, such as parents, teachers, and researchers;
- (5) parents and institutions, as well as the youngsters themselves, have an interest in their research participation; and
- (6) national priorities for research on children and adolescents include research on drug users, runaways, pregnant teenagers; and other sensitive topics, compounding the ethical and legal problems surrounding research on minors.

See J. Seiber, *Planning Ethically Responsible Research: A Guide for Students and Internal Review Boards* (Newbury Park, N.J.: Sage, 1992) at 111.

<sup>13</sup> For a discussion of the notion of "vulnerability" in the context of non-therapeutic experimentation, see Chapter 18.

group for whom there is another clearly defined class of persons obligated to shoulder this responsibility. Furthermore, as discussed above, the situation of children is unique insofar as the adults who are legally accountable for providing them with health care are presumed to have the necessary authority to give a valid consent to the administration of treatment.<sup>14</sup>

Thirdly, there are the age-specific limits of the dependency. Most children are engaged in developing their own ability to provide or withhold consent.<sup>15</sup> Concern for their welfare must include balancing the need to obtain substitute consent on their behalf and the need children have to develop their own capacity to give consent.

The fourth concern relates to the fact that children have not yet developed values to which a substitute decision-maker can look in order to assess what the child would do if competent.

### ***Statutory Incompetence and Consent to Research***

The competence of children to consent to *treatment* sheds light upon the question of their capacity to consent to *research*, because competence to consent relies in part on the ability to understand the nature and consequences of the procedure to be performed. However, although a lack of capacity to consent to treatment might suggest an inability to consent properly to participation in research, the converse is not automatically true. For example, the *Civil Code of Quebec* permits children aged fourteen or more to make their own, independent decisions concerning therapeutic interventions and minimal-risk medical care not required by the state of their health; however, only persons of "full age" are entitled to give their consent to participate in an "experiment".<sup>16</sup> Perhaps the most important aspect of the Quebec legislation with respect to non-therapeutic experimentation is the explicit recognition that parents (or tutors) may give substitute consent to the participation of children provided that certain safeguards are respected. The *Civil Code* does not, however, recognize that older children themselves might be competent to consent to participate in an experimental protocol, and that the approval of the parent or tutor would not be required.

In common law jurisdictions, the question remains: Should children be statutorily restricted from consenting to participate in non-therapeutic experimentation before reaching a certain age? As will be discussed below, the answer must take into consideration the modern evolution of mental competency law and general principles which support the empowerment of children to make autonomous decisions concerning their personal welfare whenever they are able.

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<sup>14</sup> Of course, this presumption may be rebutted where the parent or guardian is unavailable, incapable, or irresponsible.

<sup>15</sup> This situation may be contrasted with that facing the mentally disordered, whose capacity to give consent is *fluctuating*; the developmentally disabled, whose capacity to give consent is *static*; and the elderly whose capacity to give consent is potentially *diminishing*.

<sup>16</sup> For a discussion of the law governing non-therapeutic experimentation in Quebec, see Chapter 10.

## AN INTERNATIONAL SURVEY OF ETHICAL AND LEGAL PRINCIPLES

*Canada*

With the exception of Quebec, there is a notable absence of legislation in relation to biomedical experimentation with children in Canada. Furthermore, it is uncertain whether such experimentation is permissible under the common law.<sup>17</sup> The principal consequence of this gap is that guidelines internal to the medical and research professions themselves define the ethical permissibility of research with children.

Until recently, the *Guidelines on Research Involving Human Subjects* of the Medical Research Council of Canada in conjunction with publications by the National Council on Bioethics and Human Research were the most influential directives "regulating" experimentation with children. The *MRC Guidelines*, however, have been criticized for not providing sufficient guidance in areas in which the law is unclear.<sup>18</sup> The MRC has consistently opposed the enactment of legislation regulating research involving children, preferring instead to rely on the continued application of the *Guidelines*. The Law Reform Commission of Canada took an opposing view and recommended that Parliament enact legislation restricting the use of children in experimental protocols. The proposed legislation would have permitted non-therapeutic experimentation involving children provided that:

- (1) the research was of major scientific importance and not possible to conduct using adult subjects;
- (2) it was directly related to infantile diseases or pathologies;
- (3) did not involve serious risks for the child;
- (4) consent of the parent or independent third party (a judge, ombudsman, or the child's lawyer) was obtained; and
- (5) wherever possible, the consent of the child was obtained, with refusals being honoured whatever the child's age.<sup>19</sup>

Against this backdrop, the Consent Panel Task Force of the NCBHR revised its *Report on Research Involving Children* in 1993. The NCBHR recognized the need for research involving children and offered numerous examples of the benefits such research provided and of the deleterious consequences resulting from its absence. The *Report* was premised on the assumption that "research involving children [is] an activity of valued collaboration between investigators and children (and their parents or guardians), [and] such activity in Canada [should be] encouraged, subject to [certain] limitations".<sup>20</sup> The Consent Panel Task Force established a tripartite

<sup>17</sup> See Chapter 8.

<sup>18</sup> See F. Baylis & J. Downie, "An Ethical and Criminal Law Framework for Research Involving Children in Canada" (1993) 1 *Health Law Journal* 39 at 53.

<sup>19</sup> See Law Reform Commission of Canada. *Working Paper No. 61: Biomedical Experimentation Involving Human Subjects* (Ottawa: Law Reform Commission, 1989) at 61.

<sup>20</sup> See National Council on Bioethics in Human Research, Consent Panel Task Force, *Reflections on Research Involving Children* (Ottawa: NCBHR, 1993).

categorization of authorization required for research involving children. For a very young child (under seven years), the “informed and voluntary authorization” of the parents or guardians would be required. For children between seven and fourteen, the assent of the child would be required in addition to parental consent. Finally, for children over fourteen, only the consent of the child would be required. Furthermore, it was recommended that the dissent of children unable to give consent should be given serious consideration and the refusal of a child capable of consent must be respected.

The *MRC Guidelines* have since been superceded by the *Code of Ethical Conduct for Research Involving Humans*, adopted by the three principal federal funding agencies.<sup>21</sup> The *Code* continues to endorse the conduct of experimentation with children, but only in specific circumstances where: authorization is first obtained from a parent or guardian, risk is within normally acceptable limits, and where research is likely to be of sufficient social benefit. Lastly, the assent (or dissent) of the child must be confirmed wherever appropriate. Of course, consent should be sought directly from the child whenever it is possible to do so.<sup>22</sup>

### ***International Declarations, Codes, and Guidelines***

International covenants that protect children from undue risk of harm as participants in research can best be understood if examined within the context of those covenants that entitle children to receive the benefits of medical advances made possible through research with child participants. These rights are contained in both the *Universal Declaration of Human Rights*<sup>23</sup> and the *International Covenant on Economic, Social and Cultural Rights*.<sup>24</sup> The recent statement that children are entitled to the “highest attainable standard of health” contained in the *Convention on the Rights of the Child*,<sup>25</sup> which Canada has signed, arguably strengthens the obligation to fashion its laws to permit research involving child subjects, particularly when such research would directly benefit the health of children.

The early international documents, by requiring free and informed consent *by the subject*, effectively circumscribed research involving children.<sup>26</sup> This position was

<sup>21</sup> See Tri-Council Working Group, *Code of Ethical Conduct for Research Involving Humans* (July, 1997). The three funding agencies consist of the Medical Research Council of Canada, the Natural Sciences and Engineering Research Council of Canada, and the Social Sciences and Humanities Research Council of Canada.

<sup>22</sup> *Ibid.* at Part 2, pp. 3–4; Part 3, pp. 35–36.

<sup>23</sup> *Universal Declaration of Human Rights*, G.A. Res. 217A, UN Doc A/810 (1948), art. 27.

<sup>24</sup> *International Covenant on Economic, Social and Cultural Rights*, 993 U.N.T.S. 3 (1966), art. 15(b).

<sup>25</sup> *Convention on the Rights of the Child*, G.A. Res. 44/25, UN Doc. A/RES/44/25 (1989), art. 24.

<sup>26</sup> See the *Nuremberg Code*, s.10 (2). The *Nuremberg Code* is part of the judgment articulated in the case of *U.S. v. Karl Brandt et al.*, *Trials of War Criminals Before the Nuremberg Military Tribunals Under Control Council Law No. 10* (October 1946-April 1949); *International Covenant on Civil and Political Rights*, 19 December 1966, Can T.S. 1976 No. 47, 999 U.N.T.S. 171, 6 I.L.M. 368, s. 7.

relaxed subsequently.<sup>27</sup> The latest restatement of the international consensus on the permissibility of research involving children was enunciated in the guidelines of the Council for International Organizations of Medical Sciences, prepared in collaboration with the World Health Organization, and promulgated in 1993. This document placed significant restrictions on the research that could be conducted with children by identifying a number of conditions that must be met before children may be involved:

- children will not be involved in research that might equally well be carried out with adults;
- the purpose of the research is to obtain knowledge relevant to the health needs of children;
- a parent or legal guardian of each child has given proxy consent;
- the consent of each child has been obtained to the extent of the child's capabilities;
- the child's refusal to participate in research must always be respected unless according to the research protocol the child would receive therapy for which there is no medically-acceptable alternative;
- the risk presented by interventions not intended to benefit the individual child-subject is low and commensurate with the importance of the knowledge to be gained;
- interventions that are intended to provide therapeutic benefit are likely to be at least as advantageous to the individual child-subject as any available alternative.<sup>28</sup>

### *The United States*

Department of Health and Human Services (DHHS) Regulations contain specific provisions protecting children involved in research. The Regulations divide research with children into four categories: (1) "research not involving greater than minimal risk"; (2) "research involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects"; (3) "research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition"; and (4) "research not otherwise approvable, but that presents an opportunity to understand,

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<sup>27</sup> In 1975, the *Declaration* was amended explicitly to permit research involving children, if the informed consent of the child's legal guardian was obtained in accordance with national legislation. In 1983, the *Declaration* was further amended to require the child's consent to participate in research if the child was able to provide it. See the World Medical Association, *Declaration of Helsinki*. Adopted at the 18th World Medical Assembly in Helsinki in June 1964. Amended at the 29th World Medical Assembly in Tokyo in October 1975; the 35th World Medical Assembly in Venice in October 1983; and the 41st World Medical Assembly in Hong Kong in September 1989. [Reprinted in (1991) 19 Law, Medicine & Health Care 264.]

<sup>28</sup> See Council for International Organizations of Medical Sciences, in collaboration with the World Health Organization, *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (Geneva: CIOMS, 1993) at 20.

prevent, or alleviate a serious problem affecting the health or welfare of children".<sup>29</sup>

The Regulations require that the investigator obtain the assent of the child subject, when, in the judgment of the Institutional Review Board, the child is capable of providing an assent.<sup>30</sup> Assent is defined in the Regulations as "a child's affirmative agreement to participate in research".<sup>31</sup> The IRB should take into account the age and psychological state of the child in determining whether or not the child is mature enough to provide a meaningful assent. The assent of the child is not required if it is determined that the child is not capable of providing a meaningful assent or if the well-being of the child requires participation in the research project.<sup>32</sup>

For research that involves more than minimal risk but offers the potential of direct benefit for the child subject, the risk must be justified with respect to the potential benefit, and the relation between the risk and benefit must be as favourable as it is for the best alternative treatment.<sup>33</sup> The IRB will also approve research that involves more than a minimal risk to the child but that does not offer the potential of direct benefit for the child. The risk, however, must be a minor increase over minimal risk, the intervention must be consistent with the life experience of the child, and there must be a likelihood that the procedure will generate generalizable knowledge about the subject's disorder that is of vital importance.<sup>34</sup> For research that would not be allowed under the mechanisms just described, the Secretary of Health and Human Services, after consultation with a panel of experts, must determine whether the research presents a "reasonable chance of furthering the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children".<sup>35</sup>

### *The United Kingdom*

The United Kingdom has not legislated with respect to medical research involving human subjects; however, in 1990, the Royal College of Physicians published guidelines developed from the legislation and jurisprudence in related areas of

<sup>29</sup> 45 C.F.R. 46 (1991) § 46. 404–46.407.

<sup>30</sup> *Ibid.* § 46. 408 (a). Grisso notes that the requirement of obtaining the permission of the parent *and* the assent of the child seeks a balance in providing adequate protection in two respects. Firstly, were the decision solely that of the minor, often we would be concerned about whether the minor understood the research procedures to which he or she was making a commitment. Secondly, a parent-only decision places the minor — whose participation is being requested — in the role of one who is "lent out" to the researcher, so to speak, ignoring the fact that the minor is a person who may have his or her own reasons for not wishing to undergo the procedure. See T. Grisso, "Minor's Assent to Behavioural Research Without Parental Consent" in B. Stanley & J. Seiber, eds., *Social Research on Children and Adolescents: Ethical Issues* (Newbury Park, N.J.: Sage, 1992) 109 at 111.

<sup>31</sup> 45 C.F.R. 46 (1991) § 46. 402 (b).

<sup>32</sup> *Ibid.* § 46. 408 (a).

<sup>33</sup> *Ibid.* § 46. 406 (a)(b).

<sup>34</sup> *Ibid.* § 46. 406 (a)–(c).

<sup>35</sup> *Ibid.* § 46. 407 (a)(b).

health law.<sup>36</sup> The Royal College's *Research Involving Patients* and the *Guidelines on the Practice of Ethics Committees in Medical Research* recommend that research with children be limited to that involving minimal risk, an example of a minimal risk procedure being venepuncture.<sup>37</sup> Both reports conceive that research involving higher degrees of risk might be permissible in exceptional circumstances that promise great benefit.<sup>38</sup> On the question of consent, the College recommended that parental consent be required for all children under the age of 18,<sup>39</sup> and indicated that the consent cannot be given if it is against the child's interests.<sup>40</sup> The consent of a child capable of understanding is also required.<sup>41</sup> According to the report, *Research Involving Patients*, the objection of the child who is incapable of understanding must be considered, while the *Guidelines* recommend that such refusal be treated as binding.<sup>42</sup>

The Medical Research Council of the United Kingdom published "The Ethical Conduct of Research on Children" in 1991.<sup>43</sup> The MRC recommended that children be included in research only if the following three conditions are met: (1) the relevant knowledge could not be gained through research with adults, (2) the appropriate Local Research Ethics Committee approves the protocol, and (3) either the subjects have given consent, or a parent or guardian has given consent on their behalf, and those included do not object or appear to object in either words or action.<sup>44</sup> With therapeutic research, the benefits to the child participant must outweigh the possible risk of harm; with non-therapeutic research, participation cannot place a child in more than at a negligible risk of harm.<sup>45</sup>

The British Paediatric Association published guidelines in 1978 which provided:

- that research involving children is important for the benefit of all children and should be supported and encouraged and conducted in an ethical manner.
- that research should never be done on children if the same investigation could be done on adults.

<sup>36</sup> Royal College of Physicians of London. *Guidelines on the Practice of Ethics Committees in Medical Research Involving Human Subjects*, 2d. ed. (London: RCP, 1990); Royal College of Physicians of London, *Research Involving Patients* (London: RCP, 1990) [hereinafter *RCP Research Involving Patients*].

<sup>37</sup> See Royal College of Physicians of London (1990), *ibid.* at 27; *RCP Research Involving Patients*, *ibid.* at 19–20.

<sup>38</sup> See *RCP Research Involving Patients*, *ibid.* at 19; Royal College of Physicians of London (1990), *ibid.*

<sup>39</sup> See Royal College of Physicians of London (1990), *ibid.*

<sup>40</sup> See *RCP Research Involving Patients*, *supra* note 42 at 20.

<sup>41</sup> *Ibid.*

<sup>42</sup> *Ibid.*; Royal College of Physicians of London (1990), *supra* note 42 at 27.

<sup>43</sup> See Working Party on Research on Children. *The Ethics of Research on Children* (London: MRC, 1991).

<sup>44</sup> *Ibid.* at para. 6.1.2.

<sup>45</sup> *Ibid.* at paras. 6.2.2 and 6.3.4. The MRC defines "negligible risk" as risks of harm no "greater, considering the probability and magnitude of physiological or psychological harm or discomfort, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests". *Ibid.* at para. 6.3.3.

- that research which involves a child and is of no benefit to that child (non-therapeutic research), is not necessarily either unethical or illegal.
- that the degree of benefit resulting from a research should be assessed in relation to the risk of disturbance, discomfort, or pain, (the “risk/benefit ratio”).<sup>46</sup>

The British Paediatric Association did not establish a threshold of risk that child subjects could be exposed to in non-therapeutic research other than that the risk must be proportionate to the benefit that is expected to result from the research.

### *Australia*

The National Health and Medical Research Council issued a revised version of its *Statement on Human Experimentation* in 1992.<sup>47</sup> The NHMRC will not fund research involving children that exposes the subject to more than minimal risk unless the research has the potential of benefiting the subject himself.<sup>48</sup> The NHMRC therefore establishes minimal risk as the threshold for non-therapeutic research. The consent of the child’s parents or guardians must be obtained, as well as the consent of the child where appropriate.<sup>49</sup>

In 1981, the Australian College of Paediatrics issued a report supporting research with children. Acknowledging that research on children is essential to advance knowledge on childhood disease, it recommended that the research be based on sound scientific concepts; that it be performed only when information could not be sought in practice with other groups; and that it be planned and conducted in such a fashion as to ensure that definite conclusions can be obtained. Informed consent is to be obtained from parents or guardians in all but the most exceptional circumstances, and from the children themselves when they possess sufficient maturity and intelligence. The Australian College of Paediatrics suggested that a risk/benefit ratio be used to determine whether therapeutic research be undertaken. For non-therapeutic research, the College suggested that the risks be “so minimal as to be little more than the risks run in every day life”. It also recommended that an ethics committee be established in all centres responsible for research in children. This committee is responsible for: protecting the rights and welfare of children involved in research; determining the acceptable level of risk as weighed against the potential benefit; obtaining informed consent; encouraging the performance of necessary and appropriate research in children; and preventing unscientific research.<sup>50</sup>

<sup>46</sup> British Paediatric Association, “Guidelines to Aid Ethical Committees Considering Research Involving Children” in F. Cockburn *et al.*, “Research Ethics” (1980) 55 *Archives of Disease in Childhood* 75.

<sup>47</sup> See National Health and Medical Research Council, *Statement on Human Experimentation and Supplementary Notes* (Canberra: NHMRC, 1992).

<sup>48</sup> *Ibid.* at 9.

<sup>49</sup> *Ibid.* at 8.

<sup>50</sup> Australian College of Paediatrics, “Report on the Ethics of Research in Children” (1981) 17 *Australian Paediatrics Journal* 162. See principles 1–5. For a further discussion of research involving children in Australia, see C.A. Berglund, “Children in Medical Research: Australian Ethical Standards” (1995) 21 *Child: Care, Health and Development* 149.

### France

France enacted legislation regarding human experimentation in 1988<sup>51</sup> under the title, *Loi relative à la protection des personnes qui se prêtent à des recherches biomédicales*.<sup>52</sup> This new law amended *La code de la santé publique*. Article L. 209-6 of the new Code now stipulates three basic requirements for non-therapeutic research involving children: (1) the absence of serious risk, (2) the prospect of a benefit to those of similar age as the subjects, and (3) the impossibility of conducting the research on competent adults.<sup>53</sup> Article L. 209-10 provides that the consent of the parent(s) is required for therapeutic or non-therapeutic research, or, in the case of a child under curatorship, the consent of the tutor is required for therapeutic research that does not pose a serious risk. For all other research, the authorization of the Family Council or a Tutorship Judge is required. This article also requires that assent be obtained from children able to express their will and that their withdrawal of consent, or their refusal to participate, be respected.

### Summary

A review of the scientific literature reveals a well-established consensus regarding the importance and necessity of conducting research with children.<sup>54</sup> The fact that drug safety and efficacy in adults can rarely be extrapolated to children is well-recognized; moreover, developmental influences on psychopathologic features and pharmacological effects necessitate the use of children as subjects in clinical research.<sup>55</sup> It is not surprising, therefore, that national and international documents consistently endorse non-therapeutic research involving children so long as their participation is subject to strict safeguards. These restrictions can be summarized as follows:

- children should not be exposed to more than “minimal risk”;
- children should not participate in non-therapeutic research if the research could be carried out with competent adults;
- the research should be concerned with the health needs of children;
- the consent of the child’s parent or guardian should be obtained;

<sup>51</sup> See *Loi relative à la protection des personnes qui se prêtent à des recherches biomédicales*, *Loi No. 88-1138 du 20 décembre 1988*, J.O., 22 December 1988.

<sup>52</sup> For a detailed discussion of the French law on experimentation, see Chapter 9.

<sup>53</sup> Article L. 209.6 Code de la santé publique.

<sup>54</sup> In fact, it has been suggested that children have been *over-protected* in the research context, resulting in the creation of a new class of “therapeutic orphans”. See L.E. Arnold *et al.*, “Ethical Issues in Biological Psychiatric Research with Children and Adolescents” (1995) 34 *Journal of the American Academy of Child and Adolescent Psychiatry* 929 at 931; and C. Levine, “Children in HIV/AIDS Clinical Trials: Still Vulnerable After All These Years” (1991) 19 *Law, Medicine and Health Care* 231 at 235.

<sup>55</sup> B. Vitiello & S. Jensen, “Medication Development and Testing in Children and Adolescents: Current Problems, Future Directions” (1997) 54 *Archives of General Psychiatry* 871 at 872. See also J.G. Simeon & D.M. Wiggins, “The Placebo Problem in Child and Adolescent Psychiatry” (1993) 56 *Acta Paedopsychiatrica* 119.

- the assent of the child should be obtained to the extent that it is possible to do so; and
- the refusal of the child to participate should be respected.

### **GENERAL SAFEGUARDS FOR EXPERIMENTATION WITH CHILDREN**

It is important to bear in mind that children may belong to one or more of the other vulnerable populations which require the protection of special safeguards in the context of non-therapeutic experimentation. For example, a child may be developmentally disabled and may also be institutionalized. Therefore, it is necessary to underscore the principle that such children should be given the benefit of all the protective measures that apply to the members of the other vulnerable populations concerned.<sup>56</sup> For example, this would require that a potential subject receive the benefit of the safeguards that apply not only to children in general but also to the developmentally disabled and/or those individuals who are institutionalized.

Child subjects are particularly vulnerable to trauma that may be caused by the invasiveness of the procedure itself. They may be profoundly affected by the immediate discomfort or pain of some procedures even though such procedures may be associated with only a low degree of risk. A child may be mature enough to anticipate the unpleasantness of a procedure and may object to it. Accordingly, it is our view that this refusal should be sufficient to halt the procedure and the child should be immediately withdrawn from the study. However, there are many other cases in which the child subject does not have the experience or understanding to object in advance to a particular procedure and, therefore, it is not possible to anticipate their reaction to it. For example, in the case of immunization, a variety of factors may affect the likelihood that a child will object to the procedure, including: the specific character of the child, the reassurance of the parent, and the skill of the medical personnel in administering the injection. It is, therefore, not easy to anticipate whether a child is likely, for example, to develop a strong aversion to injections in general as a result of their experience with routine immunizations. Accordingly, it is necessary for researchers to assess the risks of psychological harm posed by the discomfort or the invasiveness of the procedure, quite separately from the risks of physical injury that may, in fact, be considerably less likely to occur.<sup>57</sup>

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<sup>56</sup> Kaufmann has noted that "institutionalized children, both handicapped and non-handicapped, are at increased risk for exploitation". Furthermore, he argues that "surrogate consent presents special problems in this population. Therefore, these children should not be included in clinical trials unless they directly benefit from participation and/or the subject of the trial pertains to their special circumstance of being institutionalized". See R. Kaufmann, "Drug Trials in Children: Ethical, Legal, and Practical Issues" (1994) 34 *Journal of Clinical Pharmacology* 296.

<sup>57</sup> As Grodin and Alpert note, "(t)here are very few empirical data on children about the assessment of risk. While it is clear that different scales or standards might exist for infants as opposed to young children or adolescents, how to assess discomfort, pain, or inconvenience in these 'incompetent' vulnerable populations is problematic". See M.A. Grodin & J.J. Alpert, "Children as Participants in Medical Research" (1988) 35 *Pediatric Clinics of North America* 1389.

Furthermore, the significance or meaningfulness of an adverse reaction by the child subject to a particular procedure, whether this reaction is anticipated or not, may best be gauged by members of the family; they are particularly well-placed to interpret such a reaction and to take the necessary countermeasures on behalf of the child.

Therefore, it is our view that children should not be exposed to a more than a minimal level of risk in the course of biomedical experimentation. This limitation should only be exceeded in exceptional cases, and should require specific authorization by a research ethics review board especially established for this purpose. Furthermore, in all those cases where it is possible to do so, the assent of a child must be obtained before enrolling him or her as a subject in a biomedical experiment.

### **THE ROLE OF SOCIETY AND THE FAMILY IN THE CONSENT PROCESS**

As discussed above, children form the only vulnerable group which readily lends itself to a presumption of incompetence.<sup>58</sup> As children grow towards adulthood, they develop decision-making capacity, with a correspondingly decreasing reliance on their parents or guardians. The most important consideration when discussing bases for providing consent on behalf of children is the fact that, unlike adults, the former have not led mature lives, and have therefore never expressed wishes or values which could be applied towards the substitute decision-making process. It is only possible to anticipate the future values and/or wishes of a child. As such, it becomes important to examine the role of both society and the family in the consent process.

Society's agents in the research enterprise are the institutional research ethics committees, which are generally comprised of interdisciplinary teams of individuals whose expertise and/or experience enables them to make the complex assessments necessary to determine whether a protocol is scientifically and ethically meritorious and, therefore, whether it is appropriate to ask parents to enroll their children.<sup>59</sup> Although the review process certainly functions as an important "line of first defence" insofar as it prevents parents from being asked to enroll their children in ethically unacceptable research, the final decision to allow a specific procedure whose primary purpose is research should not be made by the researcher, the research ethics committee, or by any other representative of society at large; it must

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<sup>58</sup> See generally D.N. Weisstub (Chair), *Final Report: Enquiry on Mental Competency* (Toronto: Queen's Printer, 1990) at 122–152. [hereinafter *Enquiry on Mental Competency*]

<sup>59</sup> The correct identification of the potential benefits to the health of children that are made possible by research and the accurate assessment of the risk of harm to child participants posed by such research are both essential elements in the review of protocols by research ethics committees. This harm/benefit ratio, along with other ethical requirements such as scientific validity, scientific merit, and confidentiality, serve as the basis upon which a decision may be made as to whether a research protocol should be implemented. For a review of general ethical principles that should guide research involving vulnerable populations, see Chapter 18. For a discussion of research ethics committees generally, see Chapter 17.

be made by the parents or guardians, or by the child on whom the procedure is to be performed.

### *The Family and the Child's Developing Ability to Consent*

One problem associated with attempting to establish a climate within which children may be considered free to give or withhold their consent to participate in research is the likely reliance of children on their parents' guidance in making this decision. This guidance may be explicit; it may also be implicit and, as is frequently the case, considerably more subtle in its influence. However, regardless of the impact of parental guidance, considerable benefits may be derived from the dynamic involvement of children in the consent process. Foremost among these benefits is the development of a sense of responsibility in the child and the inculcation of an understanding of what issues are important in the context of making such a critical decision. These benefits may well be of much greater importance to the child's development than the actual final decision to participate in research.

Gaylin has examined the converse situation exemplified by a parent who, hoping to foster a sense of social responsibility in his child by encouraging him to participate in an experiment, was frustrated by the insistence that he respect his child's resistance to participation.<sup>60</sup> Although the situations are very different, in each case the central concerns of those involved are not focused on the ultimate inclusion of the child in the protocol, but rather on the effect on a child's personal development of being asked to volunteer, and on the appropriate degree of parental influence on the decision.

These two situations underscore the sense in which a child's developing ability to give or withhold consent may amount to considerably more than a major stumbling block to be resolved to the satisfaction of ethicists and lawyers. To the child, rather than serving as an obstacle to participation in research, the process of consent may instead present an opportunity to develop the ability to evaluate the potential benefits to others and to medical science against the potential harm to herself, and to place this evaluation in the context of her own personal priorities. Clearly, fostering the ability to respond effectively to this challenge has considerable social merit. For example, in examining the development of this ability as a critical step in the achievement of responsible adulthood, Weithorn has argued that positive psychological functioning and well-being in children is promoted by involving them in decision-making from an early age.<sup>61</sup>

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<sup>60</sup> W. Gaylin, "Competence No Longer All or None" in W. Gaylin & R. Macklin, eds., *Who Speaks for the Child* (New York: Plenum Press, 1982) 27.

<sup>61</sup> L. Weithorn "Children's Capacities for Participation in Treatment Decision-Making" in D.H. Schetky & E.P. Benedek, eds., *Emerging Issues in Child Psychiatry and Law* (New York: Brunner/Mazel, 1985) 22 at 27. Weithorn contemplates a range of involvement possibilities for children, including autonomous decision-making in the event that the child is capable, consultation with the child about the treatment option with the child's preferences taken into account, and lesser decisions within the framework of the regimen selected by the parent, such as deciding the balance between increased medication and increased adverse effects of the medication.

### ***Family Consensus and the Voluntary Activities of Childhood***

Children participate in a broad range of activities and pursue a variety of endeavours unhampered by their legal incapacity. Decisions about their participation in sport-related,<sup>62</sup> cultural, community, and religious activities are all made through some form of familial consensus. While all of these activities have earned the approval of society as being beneficial to the development of the children who participate in them, they are nevertheless recognized as being optional; indeed, any one of them might be regarded as unacceptable by some individuals or groups. Families, for example, may well differ on the importance of competitive sports.<sup>63</sup>

Experience demonstrates that the process of giving consent to the participation of children in optional or voluntary activities evinces a broad range of decision-making patterns. Sometimes parents, after signing children up for an after-school activity, discover that their children are not enjoying it, and elect to withdraw them. At other times, parents agree to enroll children in activities with great reluctance and only after extensive entreaties by them. There will always be dutiful children who persevere with extracurricular activities, in spite of difficulty or boredom, in order to please their parents; similarly, there will always be families who feel so strongly about religious or cultural education that they are unwilling to defer to their children's preference for other activities. In other words, the differing desires and responsibilities of family members and the ways in which conflicts between them are resolved are observed in a variety of circumstances, and are not limited uniquely to the conduct of research with children. To construct a model of decision-making that is indifferent to the importance, and the influence, of this age-old process is, at best, artificial and, at worst, injurious.

The notion that the family should play a significant role in the consent process is not a novel one. Hauerwas, writing for the National Commission on the Protection of Human Subjects of Biomedical and Behavioral Research, contended that "the child ought to be conceptualized as a family member, and because of this vulnerable position the consent and guidance of parents is relevant to the participation of children".<sup>64</sup> These arguments were reviewed but not incorporated into the National Commission's final recommendations, perhaps because they could not be adapted to fit a decision-making model that revolved around the relationship between the autonomous individual, on the one hand, and society, on the other.

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<sup>62</sup> Because a principal concern related to the decision to participate in research is the assumption of risk of physical harm, Baylis & Downie focused extensively on the freedom of parents to enroll their children in minor league hockey. See F. Baylis, & J. Downie, "An Ethical and Criminal Law Framework for Research Involving Children in Canada" (1993) 1 *Health Law Journal* 39 at 62.

<sup>63</sup> A. Holder, "Disclosure and Consent Problems in Pediatrics" (1988) 16 *Law, Medicine & Health Care* 219 at 225. Holder cites R.G. Mitchell, *supra* note 2; A. Holder, "Mental Illness and Parental Rights" (1971) 216 *Journal of the American Medical Association* 575. See also P. Keith-Spiegel, "Children and Consent to Participate in Research" in G.B. Melton, G.P. Koocher & M.J. Saks, eds., *Children's Competence to Consent* (New York: Plenum Press, 1983) 179 at 187.

<sup>64</sup> See National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, *Research Involving Children: Report and Recommendations* (Washington, D.C.: U.S. Government Printing Office, 1977) at 107.

Evidently, much has changed in the intervening decades with respect to the understanding of childhood and the role of the family. As two Canadian authors recently observed, "the courts and the legislature have increasingly turned back towards respecting the subjective actual familial, social unit of the child and have spurned the more objective social models of the 1970s".<sup>65</sup> A striking illustration of the change can be found in the statement contained in the opening paragraphs of the report in which the NCBHR Task Force said:

The natural advocates for the children in all such development and in the matter of their "concerns" and "interests" are the child's parents or guardians; they are to act as protectors and nurturers, seeking to protect and enhance the child's growth to adulthood. This familiar relationship between the child and the child's parents or guardians, between the child, siblings and parents, is of serious importance in any therapy or research context - not only insofar as there is parental responsibility to minimize harm and promote benefit to the child, but also in terms of the child's evolving independence of the family.<sup>66</sup>

It is important to note in this passage that parents are identified as the natural "advocates", or spokespersons, for the interests of their children and, in many cases, it will be they who express the familial consensus regarding participation.<sup>67</sup> However, it is implied that this advocacy will only benefit the development of the child's sense of independence if it is the articulation of a consensus that is influenced by the child's wishes (at least, to the extent that the child is capable of forming a judgment on the matter).

In formulating their proposals for an ethical model suited to the needs of children, the NCBHR Consent Panel Task Force struggled to defer to the principles of the *Belmont Report*,<sup>68</sup> notably the first principle of "respect for persons".<sup>69</sup> In so doing, it was observed that this principle advocated not only treating persons as autonomous agents but also protecting those who experience any form of diminished autonomy. After careful reflection, the Task Force recommended replacing the principle of "respect for persons" with "respect for the child", arguing that it is "more applicable and relevant in discussing research involving this group".<sup>70</sup> As a consensus has emerged that it is no longer as imperative to fit every decision-making situation affecting personal rights into the model of contractual autonomy, the opportunity emerges to adjust the model to suit the very particular needs of the child as a child.

<sup>65</sup> See C. Bernard & B.M. Knoppers, "Legal Aspects of Research Involving Children" in B.M. Knoppers, ed., *Canadian Child Health Law: Health Rights and Risks of Children* (Toronto: Thompson Educational Publishers, 1992) 259 at 318.

<sup>66</sup> See NCBHR (1993), *supra* note 27 at 10.

<sup>67</sup> See Levine, *supra* note 54 at 233.

<sup>68</sup> See National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *The Belmont Report: Ethical Principles for the Protection of Human Subjects of Research* (Washington D.C.: U.S. Government Printing Office, 1978).

<sup>69</sup> *Ibid.* at 4-9.

<sup>70</sup> See NCBHR (1993), *supra* note 27 at 18.

### ***Societal Assistance to the Family in Decision-Making***

To say that the child's interests are often best represented through family consensus is not to say that the most vocal family member should be presumed to represent the family as a whole nor that society has no interest in ensuring that the child is content with the final resolution. Indeed, as research is not a requirement for the child's physical health, residual disagreement should generally be identified and respected, by withdrawing the child from the protocol.

Moreover, the one overwhelming reality of medical research with children is that a large part of it must be conducted with children who are seriously ill. Apprehension associated with the illness of a child is liable to affect the judgment of parents and to distort the consent process in a variety of ways. Parents who are confused and concerned about the diagnosis or prognosis of their child's condition may find it very difficult to grasp the fact that they have been asked to authorize a procedure for the purposes of research. In addition, their ability to comprehend the nature and probability of the risks involved may be seriously impaired. Overwhelmed by their own helplessness, and by their gratitude for the efforts of health-care providers, they may be eager to do anything they can to assist.<sup>71</sup> Indeed, in this respect, the sick child is placed in a very difficult position with regard to decision-making — a task that is perhaps rendered virtually impossible by young age or the debilitating effects of illness.

It is unfortunate that a considerable amount of medical research is conducted under circumstances that render the process of obtaining consent difficult and potentially unreliable. Yet the prospect of a family's being placed at risk of making a poor decision with lasting negative consequences for a child was not created by the possibility of conducting medical research with children. Indeed, there is a veritable panoply of rules and regulations establishing minimum ages for everything from the consumption of alcohol and the minimum age to drive a vehicle to the freedom to withdraw from formal education. These age limits have been a staple of legislation in many countries. In addition to ensuring that each child reaches a certain age free from the risks or unfortunate consequences associated with engaging in various dangerous activities, these laws protect families from pressures, both from within and without, that may tend to compromise their judgment in a way that could result in harm to the child.

### **THE GROWING INDEPENDENCE OF THE CHILD**

In growing up, a child undergoes many radical transformations. It would be fictitious to treat childhood as a unitary state. Accordingly, any formulation of a model for

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<sup>71</sup> Outwater examined the special ethical problems arising in the context of pediatric care, noting that "although the process of obtaining informed consent from distraught parents may be difficult, the family may benefit from having someone explain their child's disease, the therapy being used, and potential outcomes and problems one more time". However, in view of the limited discretion appropriate to decisions in this context, and the often uncertain efficacy of informed consent under such circumstances, the possibility of designing protocols "to render the process of informed consent unnecessary or inappropriate" was considered. K.M. Outwater, "Ethics of Research in Pediatric Critical Care" in G.D. Koren, ed., *Textbook of Ethics in Pediatric Research* (Malabar, Fla.: Krieger, 1993) 107.

obtaining consent that may be considered appropriate to childhood must inevitably take into account the growing autonomy of the child.

### ***Capacity and Disagreement among Family Members***<sup>72</sup>

Differences of opinion between family members in the administration of therapeutic treatment, on the one hand, are likely to have significant consequences because treatment decisions are intended to produce effects on the recipient; on the other hand, procedures performed primarily for research are not intended to have any significant ramifications for the participant. Consequently, it is arguable that differences of opinion in the context of research should simply result in the withdrawal of the child from the protocol. If this is the case, then those responsible for obtaining consent should closely examine any meaningful expression of reticence from the child, however subtle.<sup>73</sup> Furthermore, if there is any indication that the child's willingness to participate appears to be the result of parental pressure, this inquiry should be conducted in the absence of the parent.

The interest of society in protecting the welfare of the child militates against exposing them to unnecessary risk in the research process. Therefore, when there is disagreement between members of the family the question should be whether there are circumstances in which a child's desire to participate should prevail over parental opposition.

Since the family also risks suffering harm through the responsibility of caring for any injury that may be incurred or risks the potential disharmony resulting from the child's defiant participation, the factors in favour of permitting participation in these circumstances would have to be very weighty indeed.<sup>74</sup> In view of the serious implications of dispensing with parental authorization, we believe that the threshold requirements for permitting the child's participation should include: (1) the capacity to make the decision independently, (2) research ethics committee approval of the protocol as a valuable study that could not otherwise be conducted if parental authority were required, and (3) the provision of independent advice for the child.

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<sup>72</sup> Although this discussion considers disagreement between parents and child subjects, it is acknowledged that disagreement could also arise between parents. It is our view that the permission of one parent should be considered sufficient, provided that this parent attests to the absence of disagreement on the part of any other person legally responsible for the child's welfare and that the researcher has no basis for believing that disagreement exists. This recommendation would, of course, only apply to those research protocols that involve nothing more than a purely minimal risk of harm.

<sup>73</sup> Not only should signs of reticence or objection be actively sought but, if they exist, they should be treated as an indication of a lack of the child's assent, which must be pursued whenever possible.

<sup>74</sup> According to Lynch, the distinction between an emancipated minor and one who is "socially immature" (e.g. living at home) is valid in determining the necessity of parental authorization for research participation. She argued that "social maturity", i.e. living independently from one's parents, is a good indicator of competence to consent to research. See A. Lynch, "Research Involving Adolescents: Are They Ethically Competent to Consent/Refuse on Their Own?" in G.D. Koren, ed., *Textbook of Ethics in Pediatric Research* (Malabar, Fla.: Krieger, 1993) 125. However, so-called "emancipation" may also be a signal for caution in the process of obtaining consent. For example, emancipated children may, for various reasons (including familial abuse), find themselves totally outside the family support system and may be particularly susceptible to peer pressure.

There are, of course, limitations that are currently placed upon the treatment of children without parental knowledge, particularly where it is administered in relation to distinctive conditions such as those related to adolescent sexual activity.<sup>75</sup> It is, therefore, anticipated that approval for research without parental approval would be restricted to those protocols that are designed to bring about an improvement in the treatments that are currently permissible without such approval. In any event, it is necessary for all those involved in the research enterprise to be particularly mindful of the social and practical consequences that may flow from the application of those standards that are ultimately developed as a means of determining the capacity of children to make decisions concerning their own participation.

### *The Nature of the Decision to Participate*

Capacity should be determined with reference to the specific decision in question rather than on a global basis.<sup>76</sup> Moreover, varying outcomes in the application of procedures designed to determine capacity may well reflect differences in the nature or significance of a proposed treatment. We must be acutely aware of the essential differences between research and therapy when considering the developing capacity of children and the nature of the actual decision-making process that is involved in the process of obtaining consent.<sup>77</sup>

Simply stated, as society has sought to minimize the possibility of negative consequences flowing from biomedical research, the decision to participate in research is both more complex and less consequential than a decision to accept treatment. Given these divergences from other forms of medical decision-making which focus on different requirements and results, it is not surprising that the appropriate standard for determining whether there is capacity to consent to research has not yet been considered in depth. It is also not surprising that, given the very complexity of the question of capacity to consent to research, confused results were obtained by a Consent Survey that asked a range of leading American authorities in

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<sup>75</sup> For a discussion of the legal and ethical issues surrounding research conducted on adolescents without parental knowledge, see G. Melton, "Ethical and Legal Issues in Research and Intervention" (1989) 10 *Journal of Adolescent Health Care* 36S.

<sup>76</sup> This is referred to as the "functional" model of capacity assessment. See generally *Enquiry on Mental Competency*, *supra* note 58 at 67.

<sup>77</sup> The capacity to consent to participation in research differs from the capacity to consent to the administration of treatment in at least two important ways. The first difference is that, when performed for purely research purposes, a biomedical procedure is intended to have little if any practical effect (either beneficial or harmful) on the subject. From the subject's point of view, evaluating the desirability of undergoing the procedure does not involve assessing its potential efficacy in attaining a treatment goal but rather an assessment as to the likelihood that it will cause no significant deleterious effects. Secondly, since the benefits of research are intended to accrue to society as a whole through improvements in medical knowledge, the value of that benefit must be weighed by child participants against the cost to them of the effort or discomfort involved. These two calculations, clearly, are a great deal more complex than those made for the purposes of consenting to treatment and, when considered from the standpoint of child participants, they are significantly more challenging. For a detailed discussion of the distinction between "therapy" and "non-therapy" in the research context, see Chapter 6.

the field of child development to specify the age at which children may be considered as capable as adults to consent to a study that was relatively easy to describe. In fact, the responses ranged from age 2 to age 17 with "no 'modal age agreement' emerging".<sup>78</sup>

Despite the confusion and uncertainty about the capacity of children to make the decision to participate in research,<sup>79</sup> there is notable agreement on two issues. Firstly, there are two points in child development that are particularly significant to the child's involvement in the decision whether or not to participate in research. Secondly, it is possible to identify the chronological ages at which these points of development are usually reached.

A variety of studies have considered these aspects of the issue of children's capacity to give consent, including the work of:

- *Janofsky and Starfield*, on the assessment of risk in research with children, in which three-quarters of the researchers studied made the determination of capacity on the basis of clinical judgment rather than chronological age;<sup>80</sup>
- *Piaget and Kohlberg*, on cognitive development in which children were found to develop the ability to engage in rule-governed behaviour by the age of seven, that the understanding of consensual behaviour began to develop at approximately ten years of age, and that an appreciation of society's perspective concerning one's behaviour began to emerge at age fourteen;<sup>81</sup>
- *Lewis, Lewis and Ifekwunigwe*, on consent to participation in the swine flu

<sup>78</sup> See Keith-Spiegel, *supra* note 66 at 193. See also G. Koren "Informed Consent in Pediatric Research" in G. Koren, ed., *Textbook of Ethics in Pediatric Research* (Malabar, Fla.: Krieger, 1993) 3, for a discussion of the ages that have been set in other countries for independent consent. See also G. Koren *et al.*, "Maturity of Children to Consent to Medical Research: The Babysitter Test" (1993) 19 *Journal of Medical Ethics* 142 at 147, for their argument that there are "deep inconsistencies in society's perception of a child's perception of a child's maturity with respect to participation in research, as compared to assuming the role of a babysitter". See also L. Lee, "Ethical Issues Related to Research Involving Children" (1991) 8 *Journal of Pediatric Oncology Nursing* 24; M.E. Broome & K.A. Stieglitz, "The Consent Process and Children" (1992) 15 *Research in Nursing and Health* 147.

<sup>79</sup> Keith-Spiegel recommends the articulation, for the purposes of research, of a range of questions concerning the capacity of children and ways in which they might be assisted to make decisions concerning their participation responsibly and independently. See Keith-Spiegel, *ibid.* at 204–207. See also R. Abramovitch *et al.*, "Children's Capacity to Consent to Participation in Psychological Research: Empirical Findings" in G. Koren, ed., *Textbook of Ethics in Pediatric Research* (Malabar, Fla.: Krieger, 1993) 11, for an examination of an interesting series of studies designed to determine the independence of judgment exercised by children of various ages.

<sup>80</sup> See J. Janofsky & B. Starfield, "Assessment of Risk in Research on Children" (1981) 98 *Journal of Pediatrics* 842.

<sup>81</sup> J. Piaget, *The Moral Judgement of the Child*, trans. M. Gabain (London: Routledge & Kegan Paul, 1932); L. Kohlberg, "Moral Stages and Moralization: The Cognitive-Developmental Approach" in T. Lickona, ed., *Moral Development and Behaviour: Theory, Research and Social Issues* (New York: Holt, Rinehart & Winston, 1976) 31.

vaccine trial in which it was determined that all but the six-year-olds were able to elicit the information necessary to make an informed decision;<sup>82</sup>

- Perrin and Gerrity,<sup>83</sup> Millstein, Adler and Irwin,<sup>84</sup> Kister and Patterson,<sup>85</sup> and Eiser *et al.*,<sup>86</sup> on the knowledge children have of their bodies and of health and illness, which showed that children generally have considerably less basic understanding than we tend to realize, and so may be less equipped to make rational decisions than we might otherwise believe; and
- Susman, Dorn and Fletcher,<sup>87</sup> on the capacity of children, young adults, and adolescents to assent and consent to research, which demonstrated that the elements of the research protocol relating to concrete experiences in the lives of the subjects were most often understood.

These studies provide a sampling of the mixed research findings concerning those factors relevant to determining a child's capacity to make decisions on participation in research. It is certainly true that researchers currently favour a *functional*, rather than a *chronological*, determination of capacity; however, this surely begs the question as to the criteria that should anchor their assessment of capacity. Although an appreciation of rule-governed conduct would seem critical for participation in the process of consent, we have seen that the substance of the decision to participate in research is far more complex with respect to its costs and consequences than even "ordinary" health-care decisions. In this vein, although Lewis *et al.* determined that children aged seven and above were able, as part of a group, to ask the questions necessary for them to make an informed decision regarding the administration of a vaccine, it should be remembered that a vaccine is a medically advisable and routine procedure; therefore, this finding would not necessarily reflect the ability of the children concerned to make a decision regarding a non-therapeutic procedure. Furthermore, it seems essential to the task of gaining an appreciation of the risks posed by any particular procedure that a potential participant have a clear

<sup>82</sup> C.E. Lewis, M.A. Lewis & M. Ifekwunigwe, "Informed Consent by Children and Participation in an Influenza Vaccine Trial" (1978) 68 *American Journal of Public Health* 1079. It should be noted that "(t)he children involved were already involved in a program whereby they were given increased decision making power regarding the school health care system, and were thus more accustomed than average children to making their own health care decisions". It may be the case that children in this sample would be more likely than average to make the decision to participate in the study themselves, without parental involvement. If this assumption is correct, then the number of children wishing for parental involvement would be higher in the general population than the study would indicate.

<sup>83</sup> E.C. Perrin & P.S. Gerrity, "There's a Demon in Your Belly: Children's Understanding of Illness" (1981) 67 *Pediatrics* 841.

<sup>84</sup> S.G. Millstein, N.E. Adler & C.E. Irwin, "Conceptions of Illness in Young Adolescents" (1981) 68 *Pediatrics* 834.

<sup>85</sup> M.C. Kister & C.J. Patterson, "Children's Conceptions of the Cause of Illness: Understanding of Contagion and Use of Immanent Justice" (1980) 51 *Child Development* 839.

<sup>86</sup> C. Eiser & D. Patterson, "'Slugs and Snails and Puppy-Dog Tails': Children's Ideas about the Inside of their Bodies" (1983) 9 *Child: Care, Health and Development* 233; C. Eiser, D. Patterson & J.R. Eiser, "Children's Knowledge of Health and Illness: Implications for Health Education" (1983) 9 *Child: Care, Health and Development* 285.

<sup>87</sup> E. Susman, L. Dorn & J. Fletcher, "Participation in Biomedical Research: The Consent Process as Viewed by Children, Adolescents, Young Adults and Physicians" (1992) 121 *Journal of Pediatrics* 547.

comprehension of the basic functioning, and significance, of the various body parts that might be affected by the procedure in question; without such a basic comprehension, the informational basis for making the decision, whether or not to participate, would be seriously deficient.

Weithorn, and Grisso and Vierling, have found that on “a scale of capacity ranging from the mere ability to manifest a choice to the ability to appreciate the nature of treatment, fourteen-year-olds were capable of the highest standard of mental reasoning”.<sup>88</sup> Grodin and Alpert determined that,

[c]hildren less than seven years of age employ reasoning structures which may not be entirely rational . . . [while] children from age seven to thirteen years . . . will see the world in concrete terms and not employ the magical thinking of the younger child. They suggest that the child of this age will have difficulty anticipating the future, however, thus limiting the ability to provide informed consent.<sup>89</sup>

### ***Two Developmental Milestones: Ages Seven and Fourteen***

It is manifestly clear that the whole question of the capacity of children to make decisions about participation in research is an extraordinarily challenging one and that a multitude of cognitive, social and consequential factors are involved. Nevertheless, there is a compelling level of agreement among researchers concerning the existence of two critical points of development and the age at which these points are generally reached. In the view of Nicholson, the following conclusions may be drawn from the research literature concerning the significance of these two developmental milestones:

Before the [developmental] age of 7 years . . . attempts to obtain a child's assent . . . are likely to be meaningless, and it is more important simply to tell the child, as much as possible using his level of language, what is going to be done . . . . The nearer the child is to 14 years old, the more important does his assent to a research procedure become . . . . (I)f the research procedure is . . . non-therapeutic, it should not in general be carried out if the child refuses assent. From the age of 14 years upwards, the adolescent subject's refusal . . . should be binding . . . . (T)he parents' or guardian's refusal of consent should probably only be binding in the case of non-therapeutic research.<sup>90</sup>

The consistency with which these ages are recognized as being significant in developmental terms extends to the recent NCBHR Report on the subject. In this Report, the Task Force responds to the question “Who are the children to be involved in this research?” by stating that it “agreed . . . to focus its attention on three age groups within the ‘child’ population”: those from birth to seven years of age, those from seven to fourteen years of age and those from fourteen years to the

<sup>88</sup> *Ibid.* at 144–45. T. Grisso and L. Vierling, “Minors' Consent to Treatment” (1978) 9 *Professional Psychology* 412; L. Weithorn, “Developmental Factors and Competence to Make Informed Treatment Decisions” (1982) 5 *Child and Youth Services* 85; L. Weithorn and S. Campbell, “The Competency of Children and Adolescents to Make Informed Treatment Decisions” (1982) 53 *Child Development* 1589.

<sup>89</sup> *Ibid.* at 145. *The Enquiry on Mental Competency* cites M.A. Grodin & J.J. Alpert, “Informed Consent and Pediatric Care” in G.B. Melton, G.P. Koocher & M.J. Saks, eds., *Children's Competence to Consent* (New York: Plenum Press, 1983) 93 at 96.

<sup>90</sup> See R.H. Nicholson, ed., *Medical Research with Children: Ethics, Law, and Practice* (Oxford: Oxford University Press, 1986) at 150–51.

age of majority.<sup>91</sup> While there is widespread support for recognizing these developmental milestones,<sup>92</sup> the question remains as to how best to harmonize this approach with the mutual interests of society and the family, not only safeguarding the welfare of children but also nurturing their growing independence in relation to their participation in research.

## CONCLUSION

In exploring the type of decision-making structure most appropriate to facilitate the participation of children in research, it was recognized that there is a growing need to cultivate their decision-making capacity in collaboration with their families. There is an increasing degree of respect for the capacity of children to participate initially as partners in the decision-making process and, ultimately, to make such decisions for themselves. Moreover, the family as a whole and the potential research subject in particular should be given effective assistance in this by establishing a system of ethics review to protect children against undue risk and by introducing a regulatory régime to provide concrete support to children who are developing an independent ability to give informed consent to participation in research.

In light of our review of existing practice that has emerged on the issue of children's participation in non-therapeutic research, it is possible to articulate some major goals that should be aimed at by any attempt to establish a statutory framework to regulate such research activity. These goals include: (1) the facilitation of much-needed medical research, (2) the protection of the welfare of child subjects, (3) the promotion of the integrity of the family, and (4) the supportive development of decision-making abilities in children.

## SUMMARY

It is our position that research involving children is necessary for the continued advancement of children's health and welfare. However, non-therapeutic experimentation with children necessitates a compromise between advances in medical knowledge and the exposure of children to risk.<sup>93</sup> Owing to the legal uncertainty surrounding substitute consent for children in procedures that may not be in their best interest, including non-therapeutic experimentation, we further believe that the law with respect to biomedical experimentation involving children requires clarification.

With respect to the participation of children in biomedical experimentation, we make the following recommendations:

<sup>91</sup> See NCBHR (1993), *supra* note 27.

<sup>92</sup> See also Group for the Advancement of Psychiatry, Committee on Child Psychiatry, *How Old is Enough? The Ages of Rights and Responsibilities: Report 126* (New York: Brunner/Mazel, 1989), who acknowledge the significance of the ages of seven (as generally coinciding with the development of social cognition) and fourteen (as generally coinciding with the growing adeptness with abstract principles) in the development of decisional capacity.

<sup>93</sup> J. Pearn, "A Classification of Clinical Paediatric Research with Analysis of Related Ethical Themes" (1987) 13 *Journal of Medical Ethics* 26 at 26.

- (1) Non-therapeutic research should never be conducted on children who are not capable of making their own decision to participate, if it is possible to conduct the same research with *adults* or with *competent children*.
- (2) Non-therapeutic research should not be conducted with children if the risk is *greater than "minimal"* unless *exceptional* approval is obtained from a research ethics review board especially established for the purpose of reviewing protocols involving biomedical experimentation with members of vulnerable populations. Such approval may be given only after the child, if capable, has given consent, or, where the child is not capable of making an independent decision, then only after a parent has consented.
- (3) Protocols should encourage children and their parents to make *joint decisions* concerning the participation of the former in biomedical research. However, children who are capable of making an independent decision should be permitted to give their consent to participation without parental approval.
- (4) Children who have reached 14 years should be *presumed* to be capable of making an independent decision to participate in biomedical research. If there are any doubts as to the capacity of a child of 14 or more to make such a decision, an assessment should be conducted to determine whether this capacity exists. In accordance with modern trends, there should be a *functional* determination of capacity.
- (5) Children under the age of 14 may be capable of making independent decisions concerning participation in biomedical research. However, the existence of this capacity should be established by an appropriate assessment. Furthermore, before a child under the age of 14 may make an independent decision to participate in research, the child should be given *independent advice* by an individual with special expertise in communicating with children.
- (6) Where a child is found to be incapable of making the decision to participate in research, consent may be given by a parent, *provided there is no objection on the part of the child*. Every effort should be made to provide the child with as much information as is possible in the circumstances and the child must be informed of the absolute right to refuse to participate in or to withdraw from the research project in question.
- (7) An objection by a child may be overridden where an innovative therapy, as part of a research protocol, is employed as a life-saving device or for the purpose of significantly improving the long-term quality of life of the subject. In such cases, the consent of the legal guardian should be reviewed by a research ethics review board.
- (8) In no circumstances may non-therapeutic research be either commenced or continued where there is a clear objection on the part of a child. Current objections must override any previous consent that may have been given to participation in such research.