

# Article 5: The Role of Parents in the Proxy Informed Consent Process in Medical Research involving Children

*Sheila Varadan*

PhD Candidate, Leiden University, the Netherlands

*s.r.varadan.2@gmail.leidenuniv.nl*

## Abstract

Medical research involving child subjects has led to advances in medicine that have dramatically improved the lives, health and well-being of children. Yet, determining when and under what conditions a child should be enrolled in medical research remains an ethically vexing question in research ethics. At the crux of the issue is the free and informed consent of the child participant. A child, who is presumed legally incompetent, or lacks sufficient understanding to exercise autonomous decision-making, will not be able to express free and informed consent in the research setting. Rather than exclude all such children from medical research, a parent (or legal guardian) is designated as a proxy to consent on the child's behalf. However, the concept of proxy informed consent and the framework for its implementation present practical and ethical challenges for researchers, particularly in navigating the relationship between proxy decision-makers and child subjects in the medical research setting. Article 5 of the UNCRC may offer guidance on this point: (1) it places boundaries around how parental authority should be exercised; (2) it offers a model for parent-child decision-making that is participatory, collaborative and linked to the child's enjoyment of rights under the UNCRC; (3) it respects and supports the autonomy of child participants by recognising their evolving capacities to give informed consent. This paper concludes that greater consideration should be given to Article 5 as a complementary framework for researchers engaged in medical research involving children.

## Keywords

Article 5 – parental responsibility – informed consent – medical ethics – autonomy – evolving capacities – children's rights

## 1 Introduction

Children have been described as the ‘little medical heroes’ of science (Lenz, 1940; Lederer, 2003; Lederer and Grodin, 1994). James Phipps, an eight-year old boy, was among the first human subjects to test the smallpox vaccine (Lenz, 1940; Lederer, 2003: 2–4). James Greenlees, an 11-year old boy, was the first human subject to undergo a carbolic acid treatment to prevent wound infection, after he suffered a compound leg fracture (Lenz, 1940; Lederer, 2003: 2–4). Joseph Meister, a ten-year old boy, was the first human subject to receive a rabies vaccination, after he had been bitten 14 times by a rabid dog (Lenz, 1940; Lederer, 2003: 2–4). But, for each of these scientific breakthroughs, there have been countless other instances in which a child was subjected to undignified treatment and unnecessary suffering for the purposes of advancing scientific or medical knowledge for the benefit of others (Lederer and Grodin, 1994; Jonsen, 1999; Wiendling, 2016).

At the crux of human subject research is the tension it poses between the pursuit of knowledge for the benefit of human progress, and the need to preserve the inviolability, and dignity of all persons. Informed consent represents an attempt to negotiate that tension through a process that seeks to respect, as widely as possible, the autonomy of persons, expressed in the voluntary, uncoerced and fully informed consent of the human subject in research. It is likely for this reason that informed consent remains among the most important ethical requirements in medical research and the *sine qua non* of all research involving human subjects (Perley *et al.*, 1992; Emanuel *et al.*, 2000; Emanuel *et al.*, 2004). However, it is also for this reason that medical research involving a child, who may be unable to give informed consent, presents an ethical dilemma for researchers seeking to further knowledge of child-related illness and disease (Beecher, 1959; McCormick, 1974; Perley *et al.*, 1992; Katz, 1992).

Children stand to benefit significantly from advances made through medical research and experimentation. The exclusion of children from medical research has been said to render child-related illnesses the ‘therapeutic orphans’ of medicine, and deny children as a class of persons, access to the collective benefits of medical progress (Nuffield Council, 2015: xvi). Moreover, relying on adult data to inform the clinical care of children, even on everyday matters such as drug-dosing, places the individual child at risk, given the differences in children’s pharmacokinetic and pharmacodynamic profiles from adults (Spriggs and Caldwell, 2011: 664; Nuffield Council, 2015: xvi).

To resolve the ethical impasse, children have been categorised as ‘vulnerable’ subjects in research with additional ethical protections imposed on research involving them (Belmont Report, 1979; Declaration of Helsinki 2000, 2004, 2008, 2013). Amongst these protections, consent by proxy provides the

basis to obtain informed consent on behalf of the child in medical research (Draft Code of Ethics on Human Experimentation, 1962; Declaration of Helsinki, 1964, 1975, 1983, 1989, 1996, 2000, 2004, 2008, 2013). Because children below 18 years of age are generally presumed incompetent under the law, and a young child may lack sufficient understanding and independence to say “no” to adult researchers, consent by a parent or legal guardian (“proxy”) provides an added layer of protection for the vulnerable child participant, while also serving as the legal basis to authorise the child’s enrolment in the study (Belmont Report, 1979; Spriggs and Caldwell, 2011: 665).

However, the concept of proxy consent and the framework for its implementation present significant practical and ethical challenges for researchers. What are the parameters of proxy decision-making authority? What is the role of the child in the informed consent process? To what extent should a child’s autonomy be recognised and enabled in the proxy informed consent process? The absence of any standardised regulatory framework for proxy informed consent and the resultant variations that have emerged in ethical guidelines have led to uneven approaches in how children are recognised, supported and enabled in the proxy informed consent process.

There are no straightforward answers to these questions, and this paper does not seek to resolve them. However, what is considered is the extent to which the framework of the United Nations Convention on the Rights of the Child (UNCRC), and more specifically Article 5, may offer a different vantage point for researchers contemplating these issues in the research setting.

For clarity, and to avoid the use of contested terms such as “therapeutic” and “non-therapeutic” research, this paper defines medical research as follows: a subset of health research that deals specifically with human subject experimentation, undertaken for the primary purpose of acquiring generalisable scientific or medical knowledge to further understanding of the causes, development and effects of human disease and improve preventive, diagnostic and therapeutic interventions (Declaration of Helsinki, 2013, principle 6; CIOMS 2016, Preamble).

This paper does not directly focus on parental consent in medical treatment or experimental treatment in the clinical care of a child. Its aim is to consider the complexities surrounding proxy informed consent, where a parent (or legal guardian) is designated to authorise a child’s enrolment in research that does not envisage a direct medical benefit to the child. It contemplates the relevance of the UNCRC, and Article 5, as a complementary framework for researchers, navigating the relationship between parents and children in the informed consent process.

What follows is a three-part analysis which expounds upon Article 5 and its potential relevance in the proxy informed consent process in medical research

involving children. Part I provides a brief history of informed consent and an overview of proxy informed consent provisions in existing international ethical guidelines and instruments. Part II considers the relevance of the UNCRC in medical research and the unique vantage point that Article 5 may provide in respect of the parent-child relationship in proxy informed consent. Part III examines how Article 5 could be used to guide researchers navigating the proxy informed consent process. This paper posits that Article 5 and the UNCRC framework may be useful in three respects. First, it introduces boundaries around how proxy authority should be exercised in the informed consent process. Second, it promotes a model for parent-child decision-making that is participatory, collaborative and linked with the child's enjoyment of rights under the UNCRC. Third, it fosters respect for and support of children's autonomy by recognising the child's evolving capacities to provide informed consent in medical research. The paper concludes that greater consideration should be given to Article 5 as a complementary framework in medical research involving children.

## 2 Part I – Overview of Informed Consent in Medical Research Ethics

### 2.1 *History of Informed Consent in Human Subject Medical Research*

That human subjects should voluntarily consent to medical research was not widely accepted when it was codified under Principle One of the Nuremberg Code (Katz, 1992: 229; Jonsen, 1999; Lederer, 2003; Faden and Beauchamp, 1986: 152). Because medical experimentation tended to take place within the context of medical treatment, the rights and protection of human subjects were viewed through the prism of the physician-patient relationship, as part of the physician's duty to act in the patient's best interest (Faden and Beauchamp, 1986: 152). A participant's consent was seen as more of a practical consideration, to facilitate cooperation, rather than an ethical duty to respect the autonomy of the participant (Katz, 1992; Beecher, 1966; Lederer, 2009).

The gravity and magnitude of atrocities committed during the Nazi era under the guise of medical experimentation (Wiendling, 2016) was a reckoning for the medical profession (Perley *et al.*, 1992; Faden and Beauchamp, 1986; Lederer, 2009). As the Nazi Doctors' Trial (*United States v. Karl Brandt*) unfolded, the ethical practices of the international medical community came under scrutiny: the accused defendants drew attention to the use of prisoners, institutionalised children and the mentally-ill in human experimentation, and challenged the assertion that voluntary participation was a common practice that 'generally occurred' in human subject research (Faden and Beauchamp, 1986: 155; Katz, 1992). In rejecting these claims, the Tribunal pronounced a set of ten 'basic

principles' to 'satisfy moral, ethical and legal aspects' of research, which placed central importance on the voluntary participation of the human subject in research (Lederer, 2009; Faden and Beauchamp, 1986: 155). That the Nuremberg Code focused on experimentation with prisoners (unrelated to medical treatment) did not diminish the universality of its principles or the stature of the Code (Faden and Beauchamp, 1986: 156; Annas and Grodin, 1992). The Nuremberg Code was a watershed moment for the autonomy and dignity of human participants in scientific and medical experimentation, and to this day, remains the most influential statement on the rights of human subjects in research (Katz, 1992).

By the late 1950s, however, concerns began to emerge over the practicability and enforceability of the Code, particularly in a rapidly expanding field of drug development and clinical research (Beecher, 1959; Perley *et al.*, 1992: 157; Faden and Beauchamp, 1986: 156; Lederer, 2003). There were fears that strict adherence to the informed consent requirements under the Nuremberg Code would 'effectively cripple' research in mental illness and 'render experimentation on children impossible' (Beecher, 1959; Lederer, 2003: 10). There were also doubts over practicability and enforceability of an absolute requirement of informed consent, after it was revealed that physician-researchers were not consistently implementing the Code's informed consent requirements in clinical research settings (Beecher, 1966).

In the early 1960s, the World Medical Association (WMA) began a process to develop a code of professional ethics (drafted by physicians for physicians) to provide guidance to physician-researchers across a wider range of clinical research settings (Lederer, 2003: 10). Led by the British Medical Research Council, Harvard Medical School, and the British Medical Association, a draft code was drawn up in 1961. It replicated the structure and aims of the Nuremberg Code (Katz, 1992: 233; Perley *et al.*, 1992). However, the WMA delegates could not agree on the draft and a protracted period of revisions ensued between 1962 and 1964 (Beauchamp and Faden, 1986; Lederer, 2003). When the draft code was finally adopted at the 18<sup>th</sup> WMA Assembly in Helsinki, Finland in 1964, its provisions on informed consent were significantly changed (Katz, 1992: 232; *Ethics of Human Experimentation*, 1964).

The Declaration of Helsinki departed from the Nuremberg Code in a number of important respects. It introduced the possibility of conducting research on persons incapable of providing voluntary, free and informed consent, breaking from the absolute requirement under Principle One of the Nuremberg Code (Declaration of Helsinki, 1964, part II, principle 1, part III, principle 3a). It proposed a concept of "consent by proxy" for persons incapable of providing informed consent to enable their participation in research (Declaration of Helsinki, 1964, part II, principle 1, part III, principle 3a). It introduced a distinction

between medical research combined with clinical care (therapeutic research), for which informed consent was not strictly required (Declaration of Helsinki, 1964, part II, principle 1), and medical research undertaken for the purpose of accruing scientific knowledge for the benefit of others (non-therapeutic research) for which free and fully informed consent was required (Declaration of Helsinki, 1964, part III, principle 3a) (Katz, 1992). The upshot of these changes was to introduce a concept of informed consent (by proxy) that departed from the autonomy-based model of consent envisaged under Principle One of the Nuremberg Code.

The Declaration of Helsinki has since been revised eight times – 1975, 1983, 1989, 1996, 2000, 2004, 2008, 2013 – and continues to be recognised as the foundational instrument in medical research ethics, from which all other international guidelines and national regulatory frameworks are based.

## 2.2 *International Ethical Guidelines on Informed Consent in Medical Research*

2.2.1 The Ethical Dilemma of Involving Children in Medical Research  
When the Declaration of Helsinki introduced the notion of proxy consent into medical research, it did so without explicating how such an informed consent process should be understood or implemented in the research setting. Who had the moral legitimacy to act as the proxy? On what basis did a proxy have moral authority to volunteer a child in research? What were the parameters of proxy decision-making authority? What was the child's role in the proxy informed consent process? To what extent should a child's preferences and views be elicited and prioritised in the proxy decision-making process? The uncertainty surrounding these questions led ethicists to debate the morality of involving children in medical research, particularly where the research did not overlap with the clinical care of the child (Jonsen, 2006; McCormick, 1974; Ramsey, 1976). Many of these questions remain unanswered, and the concept of proxy informed consent continues to stir unease among ethicists, characterised as an “insoluble dilemma” in human subject research (Moser, 1974: 433; McCormick, 1974: 19; McLean, 1992; Spriggs and Caldwell, 2011).

### 2.2.2 International Ethical Guidelines on Proxy informed Consent in Medical Research

In the meantime, international ethical guidelines and instruments have evolved myriad frameworks for proxy informed consent which confer wide authority to parents (or legal guardians) to act as decision-makers on behalf of their children in medical research. A brief survey of international research ethical guidelines and instruments (Table 1), reveals some notable differences in how

TABLE 1 Informed Consent under International Medical Research Ethical Codes and Guidelines

Instrument	Recognition of the child	Disclosure and participation in decision-making	Respect for child's agreement ('assent')	Respect for child's refusal ('dissent')	Weight given to child's preferences / authority of proxy
<i>Declaration of Helsinki (2013)</i> World Medical Association <b>Principle 28, 29</b>	Children identified as persons 'incapable of giving informed consent'	<b>No.</b> There is no explicit requirement for engaging or involving children in decision-making	<b>Yes.</b> If a child is able to agree to participate, physicians must obtain assent alongside consent	<b>Yes.</b> A child's dissent or refusal must be respected	<b>The child's refusal is <u>determinative</u></b> <b>Assent is required alongside informed consent from a parent or legal guardian</b>
<i>CIOMS Guidelines (2016)</i> Council of Medical of International Organizations of Medical Sciences <b>Guidelines 9, 15 and 17</b>	Children and adolescents recognised as having 'evolving capacities to give informed consent'	<b>Yes.</b> Age-appropriate information must be provided to children, and they must be involved in discussions in accordance with their evolving capacities	<b>Yes.</b> Agreement must be obtained in keeping with the child's evolving capacities	<b>Yes.</b> Refusal must be respected over parents/guardian permission, unless participation in research is the best medical option for the child	<b>The child's refusal is <u>determinative</u> if it does not interfere with his or her best interests in clinical care</b> <b>Assent is required alongside permission from a parent or legal guardian</b>
<i>Good Clinical Practice: Consolidated Guidance (1995, 2006, 2016) ICH Para 4.8.12</i>	Children identified as 'vulnerable subjects'	<b>Yes.</b> Children should be informed about the nature of the research to the extent of their understanding	<b>Yes.</b> If the child is deemed capable of assenting, he or she may sign the informed consent form	<b>No.</b> Only parent or guardian may withdraw a child, and only if she or he appears unduly distressed.	<b>The child's refusal is <u>not</u> recognised and <u>not</u> determinative</b> <b>Informed consent is required from a parent or legal guardian</b> <b>Assent may be obtained if the child is capable.</b>

TABLE 1 Informed Consent under International Medical Research Ethical Codes and Guidelines (*cont.*)

Instrument	Recognition of the child	Disclosure and participation in decision-making	Respect for child's agreement ('assent')	Respect for child's refusal ('dissent')	Weight given to child's preferences / authority of proxy
<i>UNESCO Declaration on Bioethics and Human Rights (2005)</i> UNESCO Article 7	Children identified as 'persons without capacity to consent'	Yes. The child should be involved to the greatest extent possible in decision-making	Not required	Yes. If research does not envisage a direct benefit, a child's refusal must be respected	The child's refusal is <u>determinative</u> . Authorisation is required from a parent or legal guardian
<i>Regulation (EU) No 536/2014 on clinical trials on medicinal products (2014)</i> European Parliament Article 32	Children identified as 'minors' incapable of providing informed consent	Yes. The child must be engaged in a way adapted to their age and mental maturity	Not explicit. However, deference is given to national laws to determine where and when a child may give 'assent'	Yes. If a child refuses to participate or wishes to withdraw, his or her views must be respected	The child's refusal is <u>determinative</u> . Informed consent is required from a parent or legal guardian
<i>Oviedo Convention, (1997)</i> Council of Europe Arts 5, 6, 17	Children identified as 'minors'	Yes. The child must be engaged in discussions and informed of his or her rights as prescribed by law	Not explicit. However, the child's views will be afforded increasing weight subject to age and maturity	Yes. If the child refuses, her or his wishes must be respected	The child's refusal is <u>determinative</u> . Informed consent is required from a parent or legal guardian
<i>Add'l Protocol on Biomedical Research (2005)</i> Council of Europe Article 14, 15	Children identified as 'minors'	Yes. The child must be engaged in discussions and informed of his or her rights as prescribed by law	Not explicit. However, the child's views will be afforded increasing weight subject to age and maturity	Yes. If the child refuses, her or his wishes must be respected	The child's refusal is <u>determinative</u> . Informed consent is required from a parent or legal guardian



children are recognised, supported and enabled in the proxy informed consent process.

These differences are further magnified at the national level where an estimated 1,100 laws and regulations inform human subject research across 131 countries (OHRP, 2019). A recent survey of informed consent provisions in 27 European countries revealed significant differences in age requirements, legal definitions for consent and assent, and proxy requirements (Lepola *et al.*, 2015). What we are left with, then, is an uneven ethical and regulatory framework for proxy informed consent that provides little assurance to the child that her rights and autonomy will be respected and supported in the informed consent process in medical research.

### 3 Part II – The UNCRC and Informed Consent in Medical Research

#### 3.1 *The Role of the UNCRC in Medical Research with Children*

Despite its adoption over 30 years ago, the UNCRC seldom appears in international ethical guidelines and instruments. The Declaration of Helsinki – revised five times since 1989 – makes no reference to the UNCRC or the rights of children in its preamble or principles (Declaration of Helsinki, 1996, 2000, 2004, 2008, 2013). The technical guidelines for clinical practice issued during the International Conference on Harmonisation (ICH-GCP) also make no reference to the UNCRC (ICH-GCP, 1995, 2016). The Guidelines of the Council of International Organizations of Medical Sciences (CIOMS), developed in collaboration with the WHO in 1982 and subsequently revised in 1993, 2002 and 2016, also make no reference to the UNCRC, despite mentioning the ‘evolving capacities of the child’ in its provisions on informed consent (CIOMS 2016, Guideline 17).

The Convention on Human Rights and Biomedicine (Oviedo, 1997) mentions the UNCRC in the preamble, but the rights of the child are not explicitly referenced in its provisions. The Convention has been criticised for failing to recognise ‘children’s evolving capacities’ and ‘right to be heard and participate in decision-making’ in the informed consent process (Liefwaard, Hendriks and Zlotnik, 2017: 4, 5, 27, 28).

For its part, the Committee on the Rights of the Child has stated that the UN Convention applies in the medical research setting, and ‘...academics, private companies and others, undertaking research involving children [must] *respect the principles and provisions of the Convention*’ alongside research ethical guidelines and codes (emphasis added) (CRC General Comment No. 15: para 85).

The CRC Committee has further emphasised the importance of respecting children's rights in the research setting:

Children have been subjected to unnecessary or inappropriately designed research with little or no voice to either refuse or consent to participation. In line with the child's evolving capacities, consent of the child should be sought and consent may be sought from parents or guardians if necessary, but in all cases consent must be based on full disclosure of the risks and benefits of research to the child (General Comment No. 3, para. 29).

Yet, the UNCRC does not explicitly address consent in medical research or treatment within its provisions. The UNCRC Working Group considered the issue late in the drafting process during its 1989 Working Group Session (Legislative History, Vol. 2, 2007: 601). A draft paragraph was tabled during the discussions on right to health (Article 24), which stated, 'that a child shall not be subject to any medical or scientific experimentation or treatment unless it is with the free and informed consent of the child or where appropriate that of the child's parents' (Legislative History Vol. 2, 2007: 601). A number of delegates strongly supported the inclusion of the paragraph. However, as discussions ensued, complex issues emerged, raising concerns about adopting such a provision without further consultation with experts (Van Bueren, 1995: 310–311). Given the late stage in the drafting process, it was decided that the proposed paragraph should be rejected (Legislative History Vol. 2, 2007: 601).

That the UNCRC did not address children's consent in medical research has been lamented as a missed opportunity to re-evaluate the issue of proxy informed consent: 'This Convention might have strengthened procedures, reassessed the whole issue of proxy consent and encapsulated tests to which all jurisdictions would be expected to subject proxy decisions were they authorised' (McLean, 1992: 189). Whether the proposed paragraph would have fulfilled these expectations will never be known. In the absence of any such a provision, this paper considers the extent to which Article 5 may offer guidance to researchers navigating these questions in the proxy informed consent process.

### 3.2 *Article 5 – A Unique and Necessary Provision of the UNCRC*

Article 5 is unique to the UNCRC, having no antecedent and no subsequent equivalent in any other international and regional instrument on the rights of the child (Tobin and Varadan, 2019: 159; Kamchedzera, 2012). When the Working Group began discussing Article 5, they were motivated by two equally

important concepts: the child as a rights holder with evolving capacities, and the duties, responsibilities and rights of parents, and legal guardians (Working Group Report, 1987). The ambition of Article 5 was to bring together these two important general concepts under one provision, striking a delicate balance between empowering the child in the exercise of her rights, while also respecting the role of parents and guardians in the upbringing of their children (Working Report, 1988: para. 28; Tobin and Varadan, 2019: 160).

An important aspect of Article 5 was its recognition of autonomy and rights as relational concepts under the UNCRC. As Tobin writes:

Rights for children under the CRC are not to be enjoyed in isolation from their parents and family ... the realization of children's rights will be deeply connected to, and interdependent with, the exercise of parental rights and responsibilities (Tobin, 2017: 21).

Because children are born in a state of dependency, there will be a period in a child's life, in which she will need to rely on parents and others to provide direction and guidance to enable her realisation and enjoyment of rights under the Convention (Eekelaar, 1994; Tobin and Varadan, 2019: 619). Respecting a child's autonomy as a rights-holder will thus require giving consideration to the involvement of parents in the child's life, not only to ensure the child's protection, but also to support and enable her exercise of rights under the Convention. Viewed in this way, the UNCRC introduces a conception of rights that does not abandon children to their autonomy but rather recognises the important role that relationships will play in supporting and enabling children's autonomy as rights-holders (Daly, 2017: 190). That said, Article 5 does not envisage a role for parents and family that is indeterminate or indefinite. The reference to the 'evolving capacities of the child' recognises that as a child grows, respect for her autonomy should concurrently increase, and a time will come when parental guidance and direction will no longer be needed (Tobin, 2013; Peleg, 2018: 16). In this respect, Article 5 should be understood as 'an enabling or scaffolding provision that is designed to protect the rights of the child, *not parents*, by demanding that parents and carers provide the direction and guidance necessary for children to enjoy their rights' (Tobin and Varadan, 2019: 177).

For this reason, Article 5 is also somewhat radical. It promotes a model of the parent-child relationship that departs from historical conceptions of the parent-child relationship, which were framed in terms of ownership over the child (Lansdown, 2005; Tobin, 2017). It introduces a conception of parenthood which should be understood as 'a form of stewardship ... or trusteeship' that

'perceives [the] child not as an object subject to the control and subjugation of an adult but rather an independent subject with discreet entitlements, the realisation of which is dependent on the assistance of adults' (Tobin, 2005). It promotes a parent-child decision-making relationship that is 'co-operative and interdependent', with emphasis on 'a dialogue of participation and mutual respect' (Tobin, 2005: 41). From the child's perspective, it reframes the role of parents as 'first and foremost duty-bearers expected to fulfil their obligation in the upbringing of the child', rather than 'rights-holders vis-à-vis the child' (Peleg, 2018:18). Article 5 thus introduces a model for parent-child decision-making that places the child at the centre of the process, with a right to receive appropriate guidance and direction from his or her parents, rather than a right of parents to have their authority respected by the State (Tobin and Varadan, 2019: 161; Peleg, 2018).

This paper suggests that Article 5 could offer guidance to researchers, where ethical guidelines and instruments have been unable.

#### 4 Part III – Article 5 and Proxy Informed Consent in Medical Research

This section examines how Article 5 could be applied in the research setting to support researchers navigating the relationship between parents (or legal guardians) and child subjects in the proxy informed consent process. It suggests that Article 5 may be useful in three respects: (1) it introduces boundaries around how proxy decision-making authority is exercised; (2) it promotes a model for parent-child decision-making that fosters participation, dialogue and collaborative decision-making in the proxy informed consent process; (3) it places an obligation on parents and legal guardians to support and enable a child's autonomy by recognising her evolving capacities for decision-making in the research setting. Each of these aspects of Article 5 is considered below.

##### 4.1 *Boundaries around Proxy Decision-making Authority*

For the most part, research ethical guidelines and instruments do not explicate the boundaries of proxy decision-making authority in informed consent. This was likely a deliberate decision to ensure respect for the authority of parents (or legal guardians) acting on behalf of their child in the research setting. However, situations can arise where a proxy's exercise of authority will not be consistent with the child's enjoyment of rights in the research setting. For example, Spriggs and others (2015) observed a practice in which parents

withheld information from their children in the informed consent process. In some cases, parents misrepresented the purpose of the research to the child. Spriggs and others (2015) found that while, '[t]hese kinds of situations were ... troubling for researchers', '[r]esearch ethics guidelines and regulations in the UK, Australia and the USA [had] nothing specific to say about the deception of children' by their parents (Spriggs *et al.*, 2015: 179, 180).

Article 5 may offer guidance to researchers on this point. While it respects the role of parents and adult carers to provide guidance and direction to their children, this authority is not unbounded. The nature of the 'responsibilities, rights and duties of parents' is informed by the other provisions of the UNCRC, specifically those relating to the responsibilities of parents (Articles 18, 27, 14 and 5). Any direction and guidance provided to children must also be "appropriate", which in the context of the UNCRC framework, is understood as consistent with the child's enjoyment of other rights under the Convention (Tobin and Varadan, 2019: 171, 172). Finally, guidance and direction provided by parents must take into account, 'the evolving capacities of the child', recognising that as children grow, the role of a proxy will need to be adjusted to enable more respect for the autonomy and agency of the child subject in the research setting.

#### 4.2 *The Parent-child Relationship in Proxy informed Consent*

Remarkably, research ethical guidelines and instruments have struggled to find an ethical basis to justify children's participation in the proxy informed consent process that is not linked with the determinative outcome of informed consent. This is due, in part, to individualistic conceptions of autonomy that have dominated the discourse on informed consent (Ramsey, 1974; McCormick, 1976; Faden and Beauchamp, 1986; Emanuel *et al.*, 2000). However, it is also due to traditional understandings of parent-child relationships, in which parents have been historically conferred with wide and unfettered authority to determine how and to what extent their child should be involved in decision-making in informed consent (Sibley *et al.*, 2016; Gaylin and Macklin, 1982).

The advent of concepts such as "assent", which appear in some ethical guidelines and instruments (Declaration of Helsinki, 2000, 2004, 2008, 2013; CIOMS 2016; ICH-GCP 2016) and not others (UNESCO 2005; EU Regulation 2014; Oviedo 1997; Additional Protocol 2005) has been widely criticised for introducing more confusion rather than clarity over children's participation in the proxy informed consent process.

The concept of "assent" and its use in the research setting are problematic for a number of reasons. First, there is no agreed definition for "assent" in medical research ethics (Nuffield Council, 2015: 60). This has led to uneven

understandings of what assent means, and how it should be obtained, which in some cases has resulted in age restrictions or other barriers being placed on children's participation (Wendler and Shah, 2003; Shah, 2004; Ungar, Joffe and Kodish, 2006). Second, variations in the assent process have resulted in disagreements over its role and function, prompting some to question the value of children's participation in the informed consent process (Baines, 2011). Third, the binary framework of "assent" and "dissent" has reduced children's participation to either "agreement" or "refusal", overlooking the wide range of perspectives in between, and undermining the value of children's expression in the proxy decision-making process.

These practical challenges have fed broader debates around the value and weight that should be given to children's participation in the proxy informed consent process. These perspectives have yielded a number of ethical approaches, which may be summarised as follows: (1) attributing value to a child's views to support and foster her developing autonomy in decision-making in informed consent (Bartholome, 1976; Nelson and Miller, 2006, 27; Navin and Wasserman, 2019; Nuffield Council, 2015; Joffe, 2003; Nelson, 2003; Diekema, 2003; Miller and Nelson, 2006; Sibley *et al.*, 2012); (2) attributing value to a child's views as a pedagogical exercise to nurture moral growth and development (Sibley *et al.*, 2016; Nelson and Miller, 2006; Joffe, 2003); (3) attributing value to a child's views as a show of respect for the individual child and her moral worth in the research setting (Sibley *et al.*, 2016: 6; Nuffield Council, 2015; Navin and Wasserman, 2019); (4) attributing value to a child's views as a reflection of the fluidity in the parent-child decision-making process, and the gradual devolvement of decision-making authority from the proxy to the child (Joffe, 2003; Diekema, 2003; Fisher, 2003; Rossi *et al.*, 2003).

The Nuffield Council on Bioethics, in its 2015 report on *Clinical Research with Children*, recognised the importance of involving children in the informed consent process, as a show of respect for the individual child 'regardless of their age or capacity' (Nuffield Council, 2015: 102). Navin and Wasserman (2019) agree with this approach, recognising that there is 'moral value' in involving a child that is 'not reducible to considerations of either autonomy or best interests' (Navin and Wasserman, 2019: 44). Sibley *et al.* (2016) have put forward an ethical justification for children's participation that is based on the 'moral worth' of the child, recognising the inherent value of involving a child even if she is 'not considered to have the necessary and cognitive capacities to give fully informed consent' (Sibley *et al.*, 2012; Sibley *et al.*, 2016; Navin and Wasserman, 2019).

Article 5 and the UNCRC framework could offer additional guidance to researchers on these issues. First, the UNCRC reinforces the notion that the child has moral worth and her participation has inherent value, through its

rights-based framework. Articles 5 and 12 together affirm that all children are holders of rights, with voice and agency, which, even if not determinative, must be listened to and respected by those adults, exercising influence over the child (Tobin, 2013: 407; Archard, 2004: 58; Tobin and Varadan, 2019: 173).

Second, Article 5 introduces a model for parent-child decision-making, which demands that, 'parents concede that they are not always the sole arbiters of a child's best interests' (Tobin, 2017: 24). It requires that parents work with their children to create decision-making systems that allow the child's views to be heard, taken into account and treated seriously in decision-making processes (Tobin, 2017: 24). This collaborative decision-making model promotes a relationship that is based on dialogue and participation, in which parents must not only involve the child in decision-making, but also explain to her why certain decisions are made (Tobin, 2017: 24). The Article 5 framework thus challenges the traditional proxy-child relationship in research ethics, in which the child is designated as "vulnerable" and the proxy (parent or guardian) empowered as "protector". It replaces it with a framework that recognises the evolving capacities of the child and, importantly, 'demands that parents (or guardians) support the child to develop her decision-making capacities' (Tobin, 2015: 177).

Third, Article 5, Article 12 and Article 18 provide a framework to guide researchers in how they attribute weight to the child's views in the proxy informed consent process. Article 18 requires that parents make the child's best interests their basic concern, while Article 5 requires parents to provide guidance and direction that is appropriate and in a manner consistent with the child's evolving capacities. However, Articles 5 and 18 together recognise the importance of respect for the views and preferences of the child in the assessment of her best interests. As the CRC Committee explains:

Assessment of a child's best interests must include respect for the child's right to express his or her views freely and due weight given to said views in all matters affecting the child. The two articles ... have complementary roles: the first aims to realize the child's best interests, and the second provides the methodology for hearing the views of the child ... in all matters affecting the child, including the assessment of his or her best interests (CRC General Comment No. 14: para. 43).

The CRC Committee further adds:

The evolving capacities of the child (art. 5) must be taken into consideration when the child's best interests and right to be heard are at stake ... as the child matures, his or her views shall have increasing weight in the

assessment of his or her best interests (CRC General Comment No. 14: para. 44).

Thus, as a child grows and her capacities evolve, greater weight must be attributed to her views and preferences in proxy decision-making setting. In this respect, Articles 5, 12 and 18 offer guidance to researchers faced with situations where a parent's use of proxy authority does not respect the views and preferences of the child subject in the research setting. Applying Articles 5, 12 and 18, if a child has sufficient understanding, capacity and maturity to express free and voluntary consent to participate in medical research, her views should be determinative in an assessment of her best interests (Tobin, 2019: 1417). This position aligns with the recommendations of the Nuffield Council which state, that 'where [children] are capable of understanding what is involved in taking part in a particular piece of research ... professionals have an ethical obligation to actively seek their consent ... regardless of any additional requirements of national legislation' (Nuffield Council, 2015: 151). Thus, while the UNCRC does not directly resolve the issue of children's right to consent in medical research, Articles 5, 12 and 18 at the very least, provide a framework that assures the views and preferences of the child will not be overlooked or disregarded in the informed consent process.

#### 4.3 *The Evolving Capacities Principle and the Autonomy of the Child*

For the most part, research ethical guidelines and instruments have generally presumed that all children under 18 years of age are incapable of informed consent, deferring to national laws and regulations to determine when and under what conditions a child may provide informed consent in medical research (Declaration of Helsinki, 2013: Principles 28, 29; CIOMS, 2016: Guideline 15, 17; ICH-GCP, para 4.8; UNESCO, 2005: Article 7; EU Regulations 2014: Article 32; Oviedo Convention, Article 5; Additional Protocol (2005), Article 14). However, because a young child may also lack sufficient understanding, and independence to engage in autonomous decision-making, children, as a group, have been designated as 'vulnerable subjects' in medical research (Belmont Report, 1979; Declaration of Helsinki, 2000, 2004, 2008, 2013; CIOMS 2016, Guideline 15). This combination of presumed incompetence and vulnerability has essentialised children as 'non-autonomous' beings, in need of protection rather than empowerment in the informed consent process (Emanuel *et al.*, 2000; Ramsey, 1974; McCormick, 1976).

Yet, there is an emerging body of empirical data that challenges the notion of children as non-autonomous, incapable and vulnerable in the research setting. Hein and others (2015) suggest that a child may be capable of autonomous



decision-making through 'shared' or 'co-consent' as early as 12 years of age (Hein *et al.*, 2015). Alderson and others have shown that children are able to engage in various levels of decision making at all ages (Alderson *et al.*, 2006; Alderson *et al.*, 2005; Alderson, 1990; Alderson, 1993) and are often able to express free and informed consent well before the age of legal competency (Alderson, 1993; Alderson and Montgomery, 1996). Although these perspectives are finding more support in the discourse on research ethics (Nuffield Council, 2015; Navin and Wasserman, 2019; Miller and Nelson, 2006), researchers continue to grapple with how to balance respect for parental authority with recognition of children's autonomy in the informed consent process.

Article 5 may provide guidance on this point. As Peleg observes, '[A]rticle 5 and the evolving-capacities principle is, essentially, a mechanism to achieve balance between autonomy and protection' (Peleg, 2019: 207). As the CRC Committee further elaborates, 'parents (and others) have a responsibility to continually adjust the levels of support and guidance they offer to a child' to 'take account of a child's interests and wishes as well as the child's capacities for autonomous decision-making and comprehension of his or her best interests' (CRC Committee, General Comment No. 7, para. 17). In other words, as a 'child grows and develops, respect for her autonomy should concurrently increase' and a time will come when the child has sufficient capacity that she will no longer need to rely on her right to parental guidance and direction to secure the enjoyment of her rights under the Convention (Tobin, 2013; Peleg, 2018: 16; Tobin and Varadan, 2019: 177).

In this respect, Article 5 and the evolving-capacities principle are not dissimilar to the often cited judgment of the House of Lords in *Gillick v. West Norfolk and Wisbech Area Health Authority* ([1986] 1 AC 112) (*Gillick*), in which reference was made to parental rights as a 'dwindling right' which terminates once a child has achieved sufficient understanding, intelligence and discretion to enable her to make a wise choice in her own interests (*Gillick*). Though *Gillick* predated the UNCRC, it embodied a vision of children's rights that aligns with the UNCRC, and Article 5 (Tobin, 2009: 600). It is likely for this reason that it has been often cited as a basis to recognise children's right to consent in medical research (Alderson, 2007; Alderson, 2012; Alderson, 2018; Nuffield Council, 2015). That said, the decision in *Gillick* focuses on children's consent in medical treatment, and its authority is confined to common law jurisdictions, whereas Article 5 provides a framework that is accessible to any researcher working in medical research across all of the 196 State Parties of the UNCRC.

It is important to emphasise that Article 5 does not 'render the involvement of ... parents mute or displace their authority' (Tobin, 2005: 32). It requires, and indeed expects, parents to provide, 'appropriate levels of protection' to prevent

the child from being forced to make decisions in circumstances when they themselves do not feel competent or comfortable doing so (Tobin and Varadan, 2019: 174). In this respect, Article 5 adopts a conception of autonomy that is relational and supported. It challenges individualistic notions of autonomy in the discourse on informed consent, which have historically characterised children as incompetent and 'non-autonomous'. Article 5 offers, in its place, a concept of 'supported autonomy' which Daly explains as, '[c]hildren [able] to have their autonomy respected without being given the same status as adults and without being abandoned to harmful fates unaided' (Daly, 2017: 132).

At the same time, the evolving capacities principle is not without concerns for the proxy informed consent process. The question of how a child's 'evolving capacities' will be assessed, and the process by which decision-making authority will devolve from the parent to the child are not addressed within Article 5 or practically considered by the CRC Committee. Making a child's exercise of autonomy conditional on her evolving capacities potentially 'opens up adults' discretion to decide who is capable' (Alderson, 2018), enabling paternalism through the rhetoric of rights (Tobin, 2009; Freeman, 2005). While there will be legitimate situations where a child's autonomy in decision-making will need to be constrained (Daly, 2017; Tobin, 2009; Gaylin, 1982), without further elaboration on how a child's "evolving" capacities will be recognised and practically enabled, there remains a risk that Article 5 could be used to undermine rather than support the autonomy of child subjects in the medical research setting.

Notwithstanding these concerns, Article 5 and the evolving-capacities principle may nonetheless offer guidance to researchers, providing a framework that fosters respect for a child's autonomy as she grows and develops (Peleg, 2018:18), and places responsibility on parents (or legal guardians) to exercise their authority in a manner that supports and enables the child's capacities to engage in autonomous decision-making in the informed consent process.

## 5 Conclusion

In the mid-1970s, two leading bioethicists – Paul Ramsey and Richard McCormick – were invited to discuss the morality of medical research involving children, in what would become a pivotal debate on the ethics and regulation of proxy informed consent in medical research. As McCormick and Ramsey laid out their arguments, a remarkably blunt conception of the child was revealed. For Ramsey, the child was not a moral agent (Ramsey, 1976: 25). For

McCormick, the child was neither legally competent nor factually capable of consent (McCormick, 1974: 2). In essentializing the child as 'vulnerable', 'non-autonomous' and 'incapable', Ramsey and McCormick effectively robbed children of voice and agency in the informed consent process, laying the foundation for a proxy consent process that prioritized protection over empowerment in the research setting.

In the 45 years since Ramsey and McCormick, research with children has challenged this narrow understanding of informed consent. Alderson and others offer evidence that children, from a very young age, are able to engage in various forms of decision-making at varying levels (Alderson, 1993; Alderson and Montgomery, 1996; Alderson, Sutcliffe and Curtis, 2006; Alderson, Hawthorne and Killen, 2005). Increasingly, it is recognised that child acquire capacities over a dynamic and evolving process that encompasses multiple dimensions – psychological, cognitive, emotional, social, cultural and spiritual.

Yet, the ethical framework for proxy informed consent in medical research remains unchanged, and the image of the child as vulnerable and non-autonomous continues to influence how children are viewed, recognised and supported in the proxy informed consent process in medical research.

This paper contemplated how Article 5 and the UNCRC framework could be applied to medical research to recognise, support and enable children's voice and agency in the proxy informed consent process. It is suggested that Article 5 may offer guidance to researchers in three broad respects. First, it introduces boundaries around how proxy authority is exercised, ensuring parental decision-making is undertaken in a manner that respects and supports the child's enjoyment of rights in the research setting. More practically, it provides a set of guiding principles to researchers to evaluate when and under what circumstances the exercise of parental authority will be inappropriate in the proxy informed consent setting. Second, it promotes a model for parent-child decision-making that values participation, dialogue and collaborative decision-making in the proxy informed consent process, ensuring that a child's views and preferences are respected and taken seriously at each stage of the decision-making process. Third, it places an obligation on parents to respect and support children's autonomy by recognising the evolving capacities of the child to engage in decision-making in the medical research setting.

It is undeniable that medical research has yielded advances in medicine that have dramatically improved the health, well-being and life expectancy of all human beings. This is particularly true for children, whose lives have been transformed over the past century as a result of medical progress in the

prevention, diagnosis and treatment of child-related illness and disease. Inclusion of children in research has been and will remain essential if further gains are to be made in children's health, and well-being. Yet, research ethical guidelines and instruments continue to grapple with how to involve children in research, in a manner that respects and supports the autonomy of the child participant. This paper did not set out to resolve the ethical dilemmas and legal uncertainties surrounding children's consent in medical research. What it sought to do is introduce a conception of the child as a rights holder in the medical research setting, whose voice and agency, even if not determinative of consent, must be listened to, respected and supported by parents and researchers in the proxy informed consent process.

### Acknowledgement

I would like to thank Elaine Sutherland, Claire Fenton-Glynn and Brian Sloan for the opportunity to attend the CRC-IP Colloquium on Article 5 (17–18 July 2019) in Cambridge. I would also like to thank Priscilla Alderson, Ton Liefwaard and Jaap Doek for their helpful comments and encouragement. All errors and omissions are my own.

### References

#### *International Research Ethical Codes and Guidelines*

- Nuremberg Code (1947), Judgement, *Trial of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10, Nuremberg Germany*, October 1946 – April 1949, available at: <https://history.nih.gov/research/downloads/nuremberg.pdf>.
- Draft Code of Ethics on Human Experimentation (1962), World Medical Association, reprinted in *British Medical Journal*, 2(5312), 1119.
- Declaration of Helsinki (1964), World Medical Association, adopted by the 18<sup>th</sup> World Medical Assembly, Helsinki, Finland, June 1964.
- Declaration of Helsinki (1975), World Medical Association, revised by the 29<sup>th</sup> World Medical Assembly, Tokyo, Japan, October 1975.
- Declaration of Helsinki (1983), World Medical Association, revised by the 35<sup>th</sup> World Medical Assembly, Venice, Italy, October 1983.
- Declaration of Helsinki (1989), World Medical Association, revised by the 41<sup>st</sup> World Medical Assembly, Hong Kong, September 1989.
- Declaration of Helsinki (1996), World Medical Association, revised by the 48<sup>th</sup> General Assembly, Somerset West, Republic of South Africa, October 1996.

- Declaration of Helsinki (2000), World Medical Association, revised by the 52<sup>nd</sup> WMA General Assembly, Edinburgh, Scotland, October 2000.
- Declaration of Helsinki (2004), World Medical Association, revised by the 55<sup>th</sup> WMA General Assembly, Tokyo, Japan, October 2004.
- Declaration of Helsinki (2008), World Medical Association, revised by the 59<sup>th</sup> WMA General Assembly, Seoul, Korea, October 2008.
- Declaration of Helsinki (2013), World Medical Association, revised by the 64<sup>th</sup> WMA General Assembly, Fortaleza, Brazil, October 2013.
- Belmont Report (1979), National Commission for the Protection of Human Subjects and Biomedical and Behavioural Research, Office of the Secretary, Department of Health, Education and Welfare, Baltimore: United States of America.
- International Ethical Guidelines for Health-related Research Involving Humans, CIOMS Guidelines (2016), Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO), Geneva: Switzerland.
- Handbook for Good Clinical Research Practice* (1995, 2005), World Health Organization, Geneva: Switzerland.
- Good Clinical Practice: Consolidated Guidance* (1995, 2016), International Conference on Harmonisation of technical requirement for registration of pharmaceuticals for human use, Geneva: Switzerland.
- Declaration on Bioethics and Human Rights (2005), UNESCO, adopted by acclamation at the 33<sup>rd</sup> session of the General Conference of UNESCO, 19 October 2005.
- Regulation (EU) No. 536/2014 on clinical trials on medicinal products for human use, European Parliament and of the Council, 16 April 2014.
- Convention on Human Rights and Biomedicine (Oviedo Convention), Council of Europe, entered into force on 1 December 2009.
- Additional Protocol to the Convention on Human Rights and Biomedicine, Concerning Biomedical Research, Council of Europe, entered into force on 1 September 2007.

### *UN Committee on the Rights of the Child*

- UN Committee on the Rights of the Child, General Comment No. 3 (2003), *HIV/AIDS and the rights of the child*, 17 March 2003, CRC/GC/2993/3, paras. 12, 20, 22, 23, 29, 40(f).
- UN Committee on the Rights of the Child, General Comment No. 7 (2005), *Implementing child rights in early childhood*, 20 September 2006, CRC/C/GC/7/Rev.1.
- UN Committee on the Rights of the Child, General Comment No. 12, *The right of the child to be heard* (2009), 20 July 2009, CRC/C/GC/12.
- UN Committee on the Rights of the Child, General Comment No. 14 (2013) on *The right of the child to have his or her best interests taken as a primary consideration* (Art. 3, para. 1), 29 May 2013, CRC/C/GC/14.

- UN Committee on the Rights of the Child, General Comment No. 15 (2013) on *The right of the child to the enjoyment of the highest attainable standard of health* (Art. 24), 17 April 2013, CRC/C/GC/15.
- UN Committee on the Rights of the Child, General Comment No. 20 (2016) on The implementation of the rights of the child during adolescence, 6 December 2016, CRC/C/GC/20.
- UN Working Group Session Reports on Drafting the UNCRC.
- United Nations Commission on Human Rights, "Report of the Working Group on a draft convention on the rights of the child" (1987), E/CN.4/1987/25.
- United Nations Commission on Human Rights, "Report of the Working Group on a draft convention on the rights of the child" (1988), E/CN.4/1988/28.

### *Secondary Sources*

#### Books

- Alderson, P., *Choosing for Children: Parents' Consent to Surgery* (Oxford: Oxford University Press, 1990).
- Alderson, P., *Children's Consent to Surgery* (Buckingham: Open University Press, 1993).
- Alderson, P. and Montgomery, J., *Health Care Choices: Making decisions with children*, (London: Institute for Public Policy Research, 1996).
- Archard, D., *Children, Rights and Childhood* (2<sup>nd</sup> edn., London: Routledge, 2004).
- Daly, A., *Autonomy and the Court: Beyond the Right to Be Heard* (Stockholm: Brill, 2017).
- Faden, R. and Beauchamp, T. with King, N., *A History and Theory of Informed Consent* (Oxford: Oxford University Press, 1986).
- Jonsen, A., *A Short History of Medical Ethics* (Oxford: Oxford University Press, 1999).
- Lansdown, G., *The Evolving Capacities of the Child* (Florence: UNICEF, 2005).
- Liefgaard, T., Hendriks, A. and Zlotnik, D., *From Law to Practice: Towards a Roadmap to Strengthen Children's Rights in the Era of Biomedicine* (Leiden: Leiden University/ The Committee on Bioethics of the Council of Europe, 2017).
- Nuffield Council of Bioethics, *Children and clinical research: ethical issues* (London: Nuffield Council, 2015).
- Office of the United Nations High Commissioner for Human Rights, *Legislative History of the Convention on the Rights of the Child*, Vols. 1 and 2, (New York/Geneva: United Nations, 2007).
- Office for Human Research Protections, U.S. Department of Health and Human Services, *International Compilation of Human Research Standards*, 2019 edn., accessed at: <https://www.hhs.gov/ohrp/sites/default/files/2019-International-Compilation-of-Human-Research-Standards.pdf> (15 October 2019).
- Peleg, N., *The Child's Right to Development* (Cambridge: Cambridge University Press, 2019).

Van Bueren, G., *The International Law on the Rights of the Child* (London: Martinus Nijhoff Publishers, 1995).

### Book Chapters

- Alderson, P., "Children's Consent and 'Assent' to Healthcare Research" in M. Freeman (ed.), *Law and Childhood Studies* (Oxford: Oxford University Press, 2012).
- Gaylin, W., "Competence: No Longer All or None" in W. Gaylin and R. Macklin (eds.), *Who Speaks for the Child: The Problems of Proxy Consent* (New York: Hastings Center).
- Kamchedzera, G., "Article 5 – The Child's Right to Appropriate Direction and Guidance" in A. Alen and others, *A Commentary on the United Nations Convention on the Rights of the Child* (The Netherlands: Martinus Nijhoff, 2012).
- Katz, J., "The Consent Principle of the Nuremberg Code: Its Significance Then and Now" in G. Annas and M. Grodin (eds.) *The Nazi Doctors and the Nuremberg Code* (New York: Oxford University Press, 1982).
- Lederer, S. and Grodin, A., "Historic Overview: Pediatric Experimentation" in M. Grodin and L. Glantz (eds.), *Children as Research Subjects: Science, Ethics & Law* (Oxford: Oxford University Press, 1994).
- Lederer, S., "Chapter 49: The Ethics of Experimenting on Human Subjects" in R. B. Baker and L. B. McCullough (eds.), *The Cambridge World History of Medical Ethics* (Cambridge: Cambridge University Press, 2008).
- McLean, S., "Medical Experimentation with Children" in P. Alston, S. Parker and J. Seymour (eds.), *Children, Rights and the Law* (Oxford: Clarendon Paperback, 1992).
- Peleg, N., "International Children's Rights Law: General Principles" in T. Liefwaard and U. Kilkelly (eds.), *International Human Rights of Children*, Singapore: Springer Nature Singapore, 2018).
- Perley, S., Fluss, S., Bankowski, Z. and Simon, F., "The Nuremberg Code: An International Overview" in G. Annas and M. Grodin (eds.), *The Nazi Doctors and the Nuremberg Code* (New York: Oxford University Press, 1992).
- Tobin, J., "Chapter 4: Fixed Concepts but Changing Conceptions: Understanding the Relationship Between Children and Parents under the CRC" in M. D. Ruck, M. Peterson-Badali, and M. Freeman (eds.), *Handbook of Children's Rights: Global and Multidisciplinary Perspectives* (London: Routledge Taylor & Francis Group, 2017).
- Tobin, J., "Article 36: Protection against All Other Forms of Exploitation" in J. Tobin and P. Alston (eds.), *The UN Convention on the Rights of the Child: A Commentary* (Oxford: Oxford University Press, 2019).
- Tobin, J. and Varadan, S., "Article 5: The Right to Parental Direction and Guidance Consistent with a Child's Evolving Capacities" in J. Tobin and P. Alston (eds.), *The UN*

*Convention on the Rights of the Child: A Commentary*, (Oxford: Oxford University Press, 2019).

### Peer-reviewed Journal Articles

- Unsigned, "Ethics of Human Experimentation", *British Medical Journal* 1964 (2(5402)) 135–136.
- Alderson, P., Hawthorne, J., Killen, M., "The Participation Rights of Premature Babies", *The International Journal of Children's Rights* 2005 (13) 31–50.
- Alderson, P., Sutcliffe, K. and Curtis, K., "Children's Competence to Consent to Medical Treatment", *Hastings Center Report* 2006(36(6)) 25–34.
- Alderson, P., "Giving Children's Views 'Due Weight' in Medical Law", *The International Journal of Children's Rights* 2018(26) 16–37. DOI:10.1163/15718182-02601001.
- Baines, P., "Assent for children's participation in research is incoherent and wrong", *Archives of Disease in Childhood* 2011(96) 960–962. DOI: 10.1136/adc.2011.211342.
- Bartholome, A., "Parents, Children, and the Moral Benefits of Research", *Hastings Center Report* 1976 44–45.
- Beecher, H., "Experimentation in Man", *Journal of the American Medical Association* 1959(169) 461–478.
- Beecher, H., "Ethics and Clinical Research", *The New England Journal of Medicine* 1966(274(24)) 1354–1360.
- Caplan, A., "Informed Consent: A History and Theory of Informed Consent" by Ruth R. Faden and Tom L. Beauchamp", *Journal of the American Medical Association* 1987 (257(3)) 386.
- Dorscheidt, J. H. H. M., "Medical Research Involving Children – Giving Weight to Children's Views", *The International Journal of Children's Rights* 2018(26) 93–116. DOI:10.1163/15718182-02601006.
- Diekema, D., "Taking Children Seriously: What's so Important about Assent?", *American Journal of Bioethics* 2003(3(4)), 25–26.
- Eekelaar, J., "The Interests of the Child and the Child's Wishes: The Role of Dynamic Self-Determinism", *International Journal of Law, Policy and the Family* 1994(8) 42–61.
- Emanuel, E., Wendler, D., and Grady, C., "What Makes Clinical Research Ethical?", *Journal of the American Medical Association* 2000 (283(20)) 2701–2711.
- Emanuel, E., Wendler, D., Killen, J. and Grady, C., "What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research", *Journal of Infectious Diseases* 2004(189) 930–7.
- Fisher, C., "A Goodness-of-Fit Ethic for Child Assent to Nonbeneficial Research", *American Journal of Bioethics* 2003 (3(4)) 27–28.
- Freeman, M. D., "Rethinking Gillick", *The International Journal of Children's Rights* 2005(13(1–2)) 201–218.



- Hanson, K. and Lundy, L., "Does Exactly What it Says on the Tin? A Critical Analysis and Alternative Conceptualisation of the So-called 'General Principles' of the Convention on the Rights of the Child", *The International Journal of Children's Rights* 2017(25(2)) 285–306. DOI:10.1163/15718182-02502011.
- Hein, I., De Vries, M., Troost, P., Meynen, G., Van Goudoever J. B. and Lindauer, R., "Informed consent instead of assent is appropriate in children from the age of twelve: Policy implications of new findings on children's competence to consent to clinical research", *BMC Medical Ethics* 2015(16(76)), 1–7. DOI: 10.1186/s12910-015-0067-z.
- Joffe, S., "Rethink 'Affirmative Agreement', but Abandon 'Assent'", *American Journal of Bioethics* (2003) (3(4)) 9–11.
- Jonsen, A., "Non-therapeutic research with children: the Ramsey versus McCormick Debate", *Journal of the American Medical Association* 2006 S12–S14.
- Lederer, S., "Children as Guinea Pigs: Historical Perspectives", *Accountability in Research* 2003(10) 1–16.
- Lentz, J., "Little Medical Heroes", *Hygeia* 1940 (18) 888.
- Lepola, P., Needham, A., Mendum, J., Sallabank, P., Neubauer, D. and de Wildt, S., "Informed consent for pediatric trials in Europe", *Archives of Disease in Childhood* 2016(101) 1017–1025.
- McCormick, R., "Proxy consent in the experimentation situation", *Perspectives in Biology and Medicine* 1974 (18(12)) 2–20.
- Miller, V. and Nelson, R., "A Developmental Approach to Child Assent for Nontherapeutic Research", *Journal of Pediatrics* 2006 S25–30. DOI:10.1016/j.peds.2006.04.047.
- Moser, R. H., "An Anti-Intellectual Movement in Medicine?", *Journal of the American Medical Association* (1974)(227(4)) 432–434.
- Navin, C. and Wasserman, J., "Capacity for Preferences and Pediatric Assent", *Hastings Center Report* (2019)(49(1)) 43–51. DOI: 10.1002/hast.980.
- Nelson, R., "We Should Reject Passive Resignation in Favor of Requiring the Assent of Younger Children for Participation in Nonbeneficial Research", *American Journal of Bioethics* 2003(3(4)), 11–13.
- Ramsey, P., "The enforcement of morals: non-therapeutic research on children", *Hastings Centre Report* 1976(6(4)) 21–30.
- Rossi, W., Reynolds, W. and Nelson, R., "Child Assent and Parental Permission in Pediatric Research", *Theoretical Medicine* 2003 (24) 131–148.
- Rothmire, J., Lasley, M. and Shapiro, G., "Factors Influencing Parental Consent in Pediatric Clinical Research", *Pediatrics* 2003 (111(5)) 1037–1041.
- Shepherd, L., Read, K. and Chen, D., "Children Enrolled in Parents' Research: A Uniquely Vulnerable Group in Need of Oversight and Protection", *IRB Ethics and Human Research* 2013(35(3)) 1–8.
- Sibley, A., Pollard, A., Fitzpatrick, R. and Sheehan, M., "Developing a new justification for assent", *BMC Medical Ethics* 2016(17(2)) 1–9. DOI: 10.1186/s12910-015-0085-x.

- Sibley, A., Sheehan, M. and Pollard, A., "Assent is not consent", *Journal of Medical Ethics* 2012 (38(1)) 3.
- Spriggs, M. and Caldwell, P., "The ethics of paediatric research", *Journal of Paediatrics and Child Health* 2011(47) 664–667.
- Spriggs, M. and Gillam, L., "Deception of children in research", *Journal of Medical Ethics* 2015(41) 179–182.
- Tobin, J., "Parents and Children's Rights under the Convention on the Rights of the Child: Finding Reconciliation in a Misunderstood Relationship", *Australian Journal of Professional and Applied Ethics* 2005 (7(2)) 31–46.
- Tobin, J., "Judging the Judges: Are They Adopting the Rights Approach in Matters Involving Children?", *Melbourne University Law Review* 2009 (33) 579–625.
- Tobin, J., "Justifying Children's Rights", *The International Journal of Children's Rights* 2013 (21(3)) 395–441. DOI: 10.1163/15718182-02013004.
- Tobin, J., "Understanding Children's Rights: A Vision Beyond Vulnerability", *Nordic Journal of International Law* (2015)(84) 155–182. DOI: 10.1163/15718107-08402002.
- Ungar, D., Joffe, S. and Kodish, E., "Children are not small adults: Documentation of assent for research involving children", *Journal of Pediatrics* 2006 S31–S33. DOI: 10.1016/j.peds.2006.04.048.
- Varadan, S., "The Principle of Evolving Capacities under the UN Convention on the Rights of the Child", *The International Journal of Children's Rights* 2019(27(2)) 306–338. DOI: 10.1163/15718182-02702006.
- Weindling, P., von Villiez, A., Loeweneau and Farron, N., "The victims of unethical human experiments and coerced research under National Socialism", *Endeavour* 2016(40(1)), 1–6.
- Wendler, D., "Assent in paediatric research: theoretical and practical consideration", *Journal of Medical Ethics* 2004(32) 229–234.
- Wendler, D. and Shah, S., "Should Children Decide Whether They are Enrolled in Non-beneficial Research?", *American Journal of Bioethics* 2003 (3(4)), 1–7.