MINORS AND BIOMEDICAL RESEARCH IN SINGAPORE

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This article examines the challenges of enrolling minors in biomedical research that does not offer participants any prospect of direct benefit. It does so in the context of the current Singapore regime for the protection of research subjects, and seeks to evaluate if this is adequate for the task. In the process, it reviews appropriate Commonwealth and U.S. precedents, regulatory instruments and guidelines that bear on three main issues raised by such research, and makes some recommendations on how they might be better addressed: first, the protective ceilings of risk prescribed beyond which minors may not be exposed to. Secondly, the allocation of decision-making authority and processes employed before a minor is permitted to enrol in such research. Finally, the particular regulatory oversight mechanisms that are needed to improve ethical and legal compliance.

I. INTRODUCTION

Human participation in research is generally thought of as a supererogatory obligation, particularly when the research does not otherwise offer any compensating therapeutic or medical benefit (‘non-beneficial research’).1 More specifically, research undertaken by a physician is motivated partly, if not exclusively, by the desire to increase generalisable medical knowledge, and not primarily the welfare interests of a patient participant. In order that such deviations from the Hippocratic paradigm are brought home to the participant in biomedical research, informed consent is the cornerstone of ethics and legal regulation in this area.2

This paradigm of voluntary, informed consent raises unique ethical and legal difficulties when the consent of participants is not possible because of their incapacity, whether transitory or permanent. These difficulties are heightened in non-beneficial research, when both informed consent and medical benefit are not forthcoming.

This article examines the current Singapore regime in place for the protection of minors in non-beneficial research. In doing so, comparisons will be drawn with equivalent U.K. regulatory provisions and professional guidelines to determine what approaches are adopted or common lessons can be learnt, in an attempt to evaluate if the former is adequate for the task. The next part briefly outlines the main regulatory challenges raised by the conduct of non-beneficial biomedical research involving minors and the ethical principles that bear on these issues. The article then evaluates three principal aspects of the current regulatory framework and makes some recommendations on how they might be improved, namely (a) the protective ceilings of risk or harm prescribed beyond which minors may not be exposed to, (b) the allocation of decision-making authority and processes employed before a minor is permitted to enrol in such research and (c) the particular regulatory oversight mechanisms that are needed to improve ethical and legal compliance.

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II. REGULATORY CHALLENGES

Minors, by legal definition, presumptively or conclusively lack the requisite competence to provide informed consent to a variety of activities. An important justification for exposing them to research-derived risks and inconvenience is therefore wanting. This ethical challenge cannot be side-stepped by relying on adult volunteers. Children have a different physiology and range of diseases that prevent the extrapolation of medical knowledge derived from research involving adults to the treatment of minors. In order to advance medical knowledge and the development of better therapies, the biomedical research effort must out of necessity recruit the very individuals it seeks to benefit as a group in the future, often without the assurance of demonstrable direct benefit for participants. An ethical and legal dilemma thus emerges. How do we balance the respect for a minor’s individual dignity and interests against their collective interest in the development of therapies appropriate for their unique physiology? To ignore the challenges posed by this dilemma is to condemn our children to continued medical ignorance about childhood illness, therapeutic orphanhood and to perpetuate the continuing risks associated with the ‘off-label’ use of pharmaceuticals in children. Historically, children were largely ignored in the development of pharmaceuticals. Significant gaps in knowledge concerning adolescent health and appropriate public health policy responses also exist.

As a matter of fiscal and health policy, the tide is shifting on the research front. Governments recognise the special needs of child and adolescent health and have in various ways sought to rectify, in particular, the therapeutic orphan status of minors in healthcare. The means have been both regulatory and fiscal, requiring the inclusion of children in biomedical research in general and clinical trials in particular. We can therefore expect that minors will be recruited in clinical trials and other research projects at an increasing rate. This phenomenon is also likely to spread internationally. With an eye on the substantial international paediatric drug market, pharmaceutical companies seeking to overcome limited paediatric patient populations and drug development resources are likely to look to other jurisdictions to support paediatric trials. This is facilitated by greater international harmonization of pharmaceutical registration data requirements in paediatric populations and increasing global advocacy for such research as

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6 Murphy & Goldkind, ibid.
9 R. Nelson, ‘Including Children in Research: Participation or Exploitation’ in Santoro & Gorrie, supra note 5, c. 4 at 69-70.
more countries seek to address paediatric health care issues. Singapore will eventually have to address these regulatory challenges. The biomedical sector has in recent times seen a significant increase in government and foreign research funding, and the republic is seen as a potential organisational hub for clinical trials in Asia. The Ministry of Health, through the National Medical Research Council, also strives to improve medical care and human health through medical research.

As a matter of research ethics, some international consensus has emerged on the basic ethical requirements for non-beneficial research involving minors. First and foremost, minors may only be enrolled in non-beneficial research that exposes them to “minimal” or “low” risk. The trouble of course is working out what we mean by these terms. Second, parental consent, or more accurately, ‘permission’ to enrol the minor is obviously necessary. This requirement respects parents’ prima facie authority and responsibility to protect their children from harm and determine the proper education and upbringing of the child, rather than their personal interests in the matter. In terms of risk analysis, parents are also generally better placed than investigators or institutional review boards (IRBs) to evaluate a research protocol’s subjective risks from the perspective of the particular minor’s unique vulnerabilities.

Third, the “assent” of the child is required as well. “Assent” roughly refers to the understanding and positive agreement of the child to participate in the trial, at least to the extent that he or she is capable of, and depends on the age, maturity and psychological development of the particular child. This requirement reflects the importance of respecting the developing capacity of the child to exercise autonomous choice. Furthermore, it is said that respecting the dissent of the child ensures that undue distress or harm are avoided, particularly when the research is non-beneficial in nature. Disagreement and uncertainty, however, exist over when assent should be required, and if the dissent of a non-competent child should be respected in every situation. On the other hand, should competent minors be allowed to independently consent to research participation before they attain majority status?

Finally, irrespective of the agreement of parents and assent of minors, all research protocols involving vulnerable populations such as minors should be independently evaluated by an IRB (or ethics committee) to ensure that their interests are protected. What is less certain is if and

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15 Chen Huifen, “Singapore well cut out to be clinical trial hub” The Business Times (5 April 2006).
17 CIOMS Guidelines, supra note 2, Guideline 9; UNESCO Declaration, supra note 2, Art. 7(b).
19 See CIOMS Guidelines, supra note 2, Guideline 14; cf. Helsinki Declaration, supra note 2, para. 24, which refers to the “informed consent” of a legally authorised representative of the incompetent subject.
22 CIOMS Guidelines, supra note 2, Guideline 14; Helsinki Declaration, supra note 2, para. 25.
23 CIOMS Guideline 14, ibid.
how such ethics review processes should be structured where research involving minors is concerned. These issues will be considered in turn.

III. RISK THRESHOLDS IN NON-BENEFICIAL RESEARCH

A. Regulations Governing Clinical Trials

Singapore currently lacks a comprehensive legislative framework regulating human biomedical research. Legal and ethical standards of conduct are derived from the patchwork of specific legislative regulations and ethical guidelines promulgated by professional and policy making bodies. First and foremost, clinical trials are subject to the provisions of the Medicines (Clinical Trials) Regulations\(^{26}\) and the Singapore Guideline for Good Clinical Practice.\(^{27}\) On the question of protective risk thresholds, the regulations provide that the surrogate or proxy granting ‘consent’ (whether independently or jointly with the consent of the minor of sufficient understanding\(^{28}\)) to participate must also “act in the best interests of person to be used as a subject in the clinical trial….”\(^{29}\) This is presumably a backdrop to the more specific requirement that parental or guardian consent alone is sufficient when the minor lacks “sufficient understanding” if there be “a prospect of direct benefit”.\(^{30}\) This prospect exists where:

(a) appropriate animal and other pre-clinical studies have been conducted which support the proposed use of the test material to provide direct benefit; and

(b) risks associated with the clinical trial are reasonable in relation to what is known about the medical condition of the subject, the risk/benefit profile of standard therapy, if any, and that of the proposed test material.\(^{31}\)

Several preliminary observations on permissible risk may be made here. The regulations unambiguously prescribe a ‘best interests’ standard for surrogate decision making in the context of clinical trial participation. In this respect, the minor’s recognisable interests appear to be strictly confined. From the definition quoted above, it seems reasonably clear that ‘benefit’ is narrowly defined to mean benefit derived from administration of the investigative drug alone, and not some indirect or ancillary benefit derived from the fact of participation, such as payments offered or enhanced medical care often associated with the conduct of a clinical trial.\(^{32}\) More significantly, by stipulating for direct benefit, the provisions structurally preclude any possibility that the best interests of a minor subject may encompass participation in a non-beneficial trial that falls outside the definition of direct benefit provided.

In contrast, the U.K.’s Medicines for Human Use (Clinical Trials) Regulations\(^{33}\) appear to be more permissive in its conditions for enrolling minors in clinical trials. The germane requirement here is that “[s]ome direct benefit for the group of [minor] patients involved in the clinical trial is to be obtained from that trial.”\(^{34}\) Furthermore, parental consent required for the enrolment of a minor

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\(^{26}\) 2000 Rev. Ed. Sing., Reg 3 [CTR].

\(^{27}\) Singapore: Ministry of Health, 1999 [SGGCP].

\(^{28}\) See supra note 26, Reg. 11(1) and (2).

\(^{29}\) Ibid., Reg. 11(6).

\(^{30}\) Ibid., Reg. 11(2).

\(^{31}\) Ibid., Reg. 11(9).


\(^{34}\) Ibid., Schedule 1, Part 4, para. 10.
in a clinical trial must represent the minor’s “presumed will”. Both these requirements have an immediate bearing on the permissible risk/benefit ratio of trial participation, but are somewhat unclear as to their interpretation and application.

For example, Welzing et al welcome the requirement of direct benefit for the group of patients as implying that it is not necessary for each individual child to directly benefit from participation. On the other hand, Hagger & Woods are concerned that the requirement of direct group benefit may be read too restrictively to continue to exclude non-therapeutic research, perhaps on the basis that group benefit for trial participants still requires that every minor participant must receive some direct tangible benefit. The recommendations of the European Commission Pharmaceuticals Unit’s ad hoc working group, in respect of the European Clinical Trials Directive on which the MHUCTR is based, take the former view. Group benefit “could be defined by increased knowledge of the condition and/or treatment, which would possibly result in better diagnosis, treatment or prevention.” In addition, the EC Guidelines also add that group, as opposed to individual, benefit can only be ethically balanced with either “minimal” or “minor increase over minimal risk”.

However, article 17(1) of the European Convention on Human Rights and Biomedicine requires as a general rule that the results of research must have “the potential to produce real and direct benefit to [the participant’s] health”. As an exception, article 17(2) allows research which has “the aim of contributing… to the ultimate attainment of results capable of conferring benefit to… other persons… afflicted with the same disease or disorder or having the same condition”, provided it entails only “minimal risk and minimal burden for the individual concerned; and any consideration of additional potential benefits of the research shall not be used to justify an increased level of risk or burden”. It would therefore seem that minor increase over minimal risk cannot be justified solely on the basis of group benefit, if the EC guidelines are to be faithful to the Biomedicine Convention (assuming ‘minimal risk’ bears the same meaning under both instruments). In this respect, the EC Guidelines have adopted the U.S. Federal Regulations definition of ‘minimal risk’ - the “probability of harm or discomfort not greater than that ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests,” but the concept is not defined in the Explanatory Report to the Biomedicine Convention apart from illustrations.

From the perspective of parental decision-making, the notion “presumed will” of the minor and its implications on permissible risk is likewise a source of conceptual uncertainty. If the basis of parental consent is what the minor would have wanted, one wonders why minors competent to make the participation decision could not simply be accorded respect by at least requiring

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38 Directive 2001/20/EC (4 April 2001), O.J. L121/34 1.5.2001 [ECTD]
40 Ibid. at 19, para. 12.
41 Ibid. at 20, para. 12.1
43 Supra note 39 at 17, para. 11.1.
44 Supra note 42 at paras. 111-114.
parents to involve them in the decision making, rather than presuming this. Instead, the MHUCTR only requires that the explicit wish of the minor to refuse or withdraw from the trial be “considered” by the trial investigator.\(^45\) Perhaps the assumption here is that all minors are insufficiently competent to decide whether the trial is of direct benefit to the group of participating patients. “Presumed will” then reflects a standard that asks what the minor would reasonably want in order to fulfill his interests and desires when offered trial enrolment. In implementation, this is unlikely to be very different from a best interests approach, broadly defined to encompass the individual’s values and preferences. Indeed, the draft guidance issued by the U.K. Department of Health adopts a best interests approach in interpreting “presumed will” under the MHUCTR.\(^46\) In comparison, the EC Guidelines appear to interpret this more broadly as representing the parents’ duty to protect the child and his interests based on their experience with the child up to that point in time.\(^47\) On the whole therefore, the MHUCTR appear to permit trials for the direct benefit of the group of patients provided only minimal risk is involved. It is much less clear if minor increases over minimal risk are also permitted, a traditional best interests test governs such risk/benefit assessments or if some less stringent albeit protective test applies.

B. Professional Ethical Guidelines

The recent third report of the Singapore Bioethics Advisory Committee (‘BAC’) on Research Involving Human Subjects: Guidelines for IRBs\(^48\) (‘Third Report’) took on regulatory force when the Director of Medical Services decreed that all health care professionals under the professional jurisdiction of the Singapore Medical Council must comply with the BAC’s recommendations in this area.\(^49\) The report provides recommendations for the ethical oversight of human subject research (‘HSR’) by institutional review boards (‘IRBs’). Of particular relevance to this discussion, the Third Report’s reaffirms the prior recommendations of the National Medical Ethics Committee (‘NMEC’) regarding the ethical principles on the protection of legally incompetent persons who are generally considered vulnerable in HSR.\(^50\)

First, on the question of acceptable risk thresholds, the NMEC’s recommendations in paragraph 2.5.5.1 relating to children recognise:

(a) that children should not be exposed to greater risks in biomedical research than those in their everyday lives.

(b) parents and legal guardians currently control this level of risk; and

(c) parents may therefore permit exposure to several instances of acceptable research risk, namely (i) the inspection of the child’s medical records, (ii) the collection and

\(^{45}\) Supra note 33 at para. 7.

\(^{46}\) U.K. Department of Health, Draft Guidance on Consent by a Legal Representative on Behalf of a Person Not Able to Consent under the Medicines for Human Use (Clinical Trials) Regulations 2003 (March 2003)

\(^{47}\) Supra note 39 at 18, para 11.1.

\(^{48}\) Singapore: BAC, 2004; online at <http://www.bioethics-singapore.org/resources/reports3.html> [BAC, Guidelines for IRBs].

\(^{49}\) Ministry of Health, Director of Medical Services Directive 1A/2006 (18 January 2006), para. 3, which states “The Singapore Medical Council would, in evaluating the appropriateness of a doctor's actions in research involving human subjects, rely on the BAC's recommendations as the standard for ethical conduct. Doctors are therefore expected to familiarize themselves with the BAC's recommendations and to comply with them”.

analysis of excreted materials and (iii) interventions that would otherwise involve minor legal assaults but do not involve pain or discomfort beyond “carefully defined limits”, such as a venepuncture.  

The NMEC’s recommendations are likely confined to “minimal risk” non-beneficial research pegged to the notion of risk in ‘everyday life’; otherwise, in the case of beneficial or therapeutic research, a reasonable analysis of the comparative risks and benefits in such situations would be unjustifiably restricted by a minimal risk requirement.

In contrast to an ‘everyday’ risks baseline, guidelines issued by the Royal College of Paediatrics and Child Health 52 (‘RCPCH’), Medical Research Council 53 (‘MRC’) and Royal College of Physicians 54 (‘RCP’) all acknowledge the permissibility of non-beneficial research on minors if the risks posed are “sufficiently small” that they can be said to be “not against the child’s interests” 55 and imposes “minimal burden”, thereby warranting parental consent. 56 A typology of risk is offered by reference to risks associated with common research procedures. According to the RCPCH Guidelines, such research is most clearly permissible where the research only imposes minimal risk, i.e. where procedures are non-interventional or do not impose any extra risk apart from procedures already administered on the minor for therapeutic purposes. 57 Alternatively, the MRC Guidelines would define minimal risk as “a very slight and temporary negative impact on the health of the person concerned”. 58

Non-beneficial research can also extend to “low risk” procedures that might cause “no more than brief pain or tenderness, small bruises or scars or very slight, temporary distress”, provided serious ethical consideration is given. 59 In this respect, the RCPCH Guidelines further specify that such low risk non-beneficial research should be permitted where the child understands the reasons for the procedure and agrees to participate for altruistic reasons. 60 “High risk” procedures, on the other hand, are impermissible unless accompanied by compensating direct benefit to the child. 61 In comparison, an earlier Institute of Medical Ethics report noted the inherent subjectivity of such perception-based categorisations and offered instead an arithmetical categorisation of risk correlated to existing categories in an attempt to improve the objectivity of risk assessment. 62

What is the legal status of such guidelines and the consequences of non-compliance by a researcher in Singapore? Their adoption as professional ethical standards 63 implies that any breach would render a researcher who is a registered medical practitioner subject to disciplinary proceedings before a disciplinary committee of the Singapore Medical Council. 64 However, not

51 Ibid.
52 RCPCH Ethics Committee, “Guidelines for the ethical conduct of medical research involving children” (2000) 82 Archives of Disease in Childhood 177 at 179 [RCPCH Guidelines].
54 RCP, Guidelines on the practice of ethics committees in medical research with human participants, 4th ed. (London: RCP, 2007) at paras. 5.11-5.14 [RCP Guidelines].
55 This test is taken from the House of Lords decision in S v. S, infra note 85.
56 Supra note Error! Bookmark not defined., at 180; note 53 at 5.1.4a. See also, Department of Health, Seeking Consent: working with children (November 2001) at 25-26.
57 Supra note 52.
58 Supra note 53 and RCP Guidelines, supra note 54 at para. 5.13.
59 RCPCH, supra note 52, MRC, supra note 53.
60 RCPCH, supra note 52. See also Part D.3 below.
61 Ibid. See also RCP Guidelines, supra note 54 at paras. 5.13-5.20.
63 See supra note 49.
64 Medical Registration Act (Cap 174, 2004 Rev. Ed. Sing.), Part VII.
all researchers are registered medical practitioners under the Medical Registration Act. Therefore, a regulatory gap exists in so far as non-registered professionals may also conduct HSR. Furthermore, as the BAC took pains to point out, their recommendations are not ipso facto pronouncements of legal principles or rules. Researchers, professionally affiliated or otherwise, must still ensure that their conduct in research complies with applicable legal standards governing the care and treatment of minors, which leaves open the possibility that such legal standards or rules may be stricter or more lenient. In the absence of a general legislative governance framework for biomedical research apart from clinical trials, recourse must therefore be had to the common law in search of answers (as the U.K. guidelines have also done).

C. Common Law

As a matter of general principle, decisions concerning the custody, care and upbringing of children are broadly subject to the ‘best interests’ standard, and implementation of this is subject to supervision and intervention by a court exercising the parens patriae jurisdiction. The ‘best interests’ approach reflects two broad principles in respect of decisions permitting bodily interventions involving children: first that the intervention must be consented to by the parent, and second, that this is consonant with the welfare of the child objectively assessed. The first describes the presumptive allocation of decision-making authority, based on the view that parents are generally the best placed to make decisions that promote the best interests of the minor, while the latter makes clear that parental discretion in these matters was nevertheless subject to legal scrutiny, especially where the vital interests of the minor are at stake. Courts however recognise that there are matters on which reasonable persons may disagree, such as religious and moral upbringing, and parental decisions will not be interfered with lightly.

In Marion’s case, the Australian High Court acknowledged that the ‘best interests’ standard is inherently imprecise and judges have to develop guidelines to give further content to the standard depending on the particular situations that call for judicial resolution. An important premise of the standard is that it generally requires the parent or a court to place first, paramount or overriding consideration for the interests of the child over third party and societal interests. Accordingly, there was an initial view that non-beneficial research offering no tangible medical or therapeutic benefits to a proposed minor participant was beyond the power of parental authority. This view was reinforced by the decision in Re Eve, where the Canadian Supreme Court drew a distinction between therapeutic and non-therapeutic medical interventions, and categorically rejected the latter as ever capable of advancing an incompetent person’s best interests. Transposed to the research context, it was suggested that non-beneficial research in minors might be outlawed on a similar basis.

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65 Ibid., s. 2; supra note 48 at paras. 2.30-2.35.
66 Supra note 48 at paras. 3.25-3.26.
67 See for e.g., Secretary, Department of Health and Community Services v. J.W.B. and S.M.B. (1992) 175 C.L.R. 218 at 269-272, 278-280, per Brennan J. [Marion’s Case]. In Singapore, the parens patriae jurisdiction in respect of minors is explicitly reserved for the High Court by s.17(d) of the Supreme Court of Judicature Act (Cap 322, 2007 Rev. Ed. Sing.). See also, G. Laurie, ‘Parens Patriae Jurisdiction in the Medico-Legal Context: The Vagaries of Judicial Activism’ (1999) 3 Edinburgh Law Review 95 at 98.
68 Marion’s Case, ibid. at 239-240, 258-259, per Mason C.J., Dawson, Toohey and Gaudron JJ.
69 Ibid. at 280-281, per Brennan J.
70 Ibid. at 259, per Mason C.J., Dawson, Toohey and Gaudron JJ. Cf. Brennan J. at 270-272.
71 Nicholson, supra note 62, c.6 at 134-135.
73 Ibid. at para. 86, per La Forest J.
74 See for e.g., R. Williams, “Pediatric Research and the Parens Patriae Jurisdiction in Canada and England”, (1999) 18 Medicine & Law 525 at 539, 545-546. These views raised concerns amongst many commentators uncomfortable with the implications for the advancement of knowledge and therapies for paediatric conditions and diseases: see
Nevertheless, there have been several instances where medical interventions in minors for the purpose of benefiting specified third parties have been authorised, and on which research participation might find analogous legitimacy. Kidney organ donation was permitted between identical minor twins in *Hart v. Brown*, on the grounds that the operation only presented negligible short-range risk in the form of anaesthesia and there was no demonstrable long-range risk to health and insurability. In *Curran v. Bosze*, the Illinois Supreme Court reviewed a line of American authorities and held that parents could only consent to the donation of bone marrow by their child (which involved a small but appreciable risk of death associated with the general anaesthesia administered in connection with the bone marrow harvesting procedure) where, *inter alia*, there was an existing, close relationship between the donor and recipient. In such circumstances, it was argued that there would be a recognisable psychological benefit in the very existence of a sibling relationship and its continuation, made more likely by the donation of bone marrow. This is not simply a ‘personal, individual altruistic’ benefit in an ‘abstract theoretical sense’, although this may be taken into consideration. However, in *In the Marriage of GWW and CMW*, bone marrow donation was permitted notwithstanding the absence of a close sibling relationship. The court seems to have placed equal emphasis on the understanding and desire of the minor donor to help his aunt and the relatively ‘minimal’ risk of the harvesting procedure when compared with major surgical risks associated with sterilisation in *Re Eve* and *Marion’s Case*. Thus, although these cases continue in the vein of *Re Eve* in emphasising the paramountcy of the welfare of the child, where risks are relatively low and the intervention conforms with the wishes of the minor, the court is more inclined to give weight to intangible ‘psychological’ benefits.

The closest decision in the U.K. to the pure research situation is that of *Simms v. Simms*, which involved the proposed administration of an experimental drug in an attempt to arrest the progress of variant Creutzfeldt Jakob Disease in two incompetent patients. In authorising the experimental therapy, the court similarly applied a broad best interests test that (apart from the possible medical benefit of the drug and associated risks) placed great weight on the views of family members and the effect of refusal of such an opportunity on their relationship with the patients. Although some commentators argue that there is a real distinction to be made between experimental treatment and pure research activity, and the relevant factors exceptional, the case does indicate that some form of the best interests standard will likely be applied in the latter context as well.


75 (1972) 289 A.2d 386 at 373-375 (Superior Court, Connecticut).
76 (1990) 566 N.E.2d 1319 (S.C. Illinois)
77 *Ibid.* at 1343-1344.
78 *Ibid.*. Apart from this psychological benefit, it was clear that the bone marrow donation was of no physical benefit to the child donor.
79 (1997) 21 Fam. L.R. 612 (Fam. Ct., Aus.)
80 See also *In re Y (adult patients)/bone marrow transplant* [1997] 2 W.L.R. 556, where the court was prepared to infer ‘benefit’ from the improvement of the incompetent’s relationship with her mother who very much desired the procedure and the eternal gratefulness of the donee sister.
81 [2003] Fam. 83.
However, the generally narrow approach of framing the ‘best interests’ by a minor’s individual self-interests is tempered by the decision of the House of Lords in *S v. S*,85 where the issue was whether a child should be subjected to a blood test for the determination of legitimacy. The court distinguished the ‘custody’ jurisdiction from the ‘protective’ jurisdiction vis-à-vis minors; whereas the overriding status of the welfare of the child prevails in the former, it does not in the latter:

The argument… is that a court can only order a blood test of a child in the exercise of the old Chancery jurisdiction acting on behalf of the Sovereign as *parents patriae*, and that when exercising that jurisdiction a court must act solely in the interests of the child disregarding all more general considerations. I greatly doubt that line of argument. … But even if one accepts the view that in ordering, directing or permitting a blood test the court should not go farther than a reasonable parent would go, surely a reasonable parent would have some regard to the general public interest and would not refuse a blood test unless he thought that would clearly be against the interests of the child.86

Thus, the paramount or overriding status of the welfare of the child is not the sole paradigm of decision-making.87 Where the intervention proposed is not clearly against the child’s interests, a reasonableness standard applies that endorses a parent’s choice for the minor even if it is not the ‘best’ alternative.88 The parent may also take into consideration other public interests apart from the minor’s individual interests. Second, the common law affords a parent a certain amount of discretion in the discipline and moral upbringing of a child, and will not interfere with parental decisions involving physical interference unless these are ‘cruel or excessive’.89

Some commentators refer to *S v. S* as recognising a ‘not against the best interests’ standard of decision making.90 Transposed to the context of non-beneficial research, this standard would warrant parental permission to participate where the risks are sufficiently low such that it could not be objectively shown that the child would clearly be harmed or made worse off. Yet, there is very little indication of how this risk threshold is to be determined. In *S v. S*, the blood test involved no appreciable harm save momentary discomfort,91 and there were considerations of the public interest in the administration of justice involved. Dickens argues that the inquiry should be based on what a reasonable parent would decide in discharge of his responsibility and discretion in regulating the conduct of his child in accordance with his own convictions, provided that this does not create a “real risk of harm” to the child.92

The best interests approach was only recently specifically applied in the context of non-beneficial research in *Grimes v. Kennedy Krieger Institute*,93 where children who were enrolled in a federally funded study on several lead paint abatement methods in their homes in Baltimore city sued the institute conducting the study for negligently permitting exposure to unreasonably high levels of

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86 Ibid. at 44, per Lord Reid [emphasis added].
87 Ibid. at 44, per Lord Reid; at 58, per Lord Hodson.
88 See the typology offered by L. Kopelman, “The Best Interests Standard as Threshold, Ideal, and Standard of Reasonableness” (1997) 22 Journal of Medicine and Philosophy 271 at 279-281. Kopelman articulates three senses of ‘best interests’: as a threshold for intervention in child abuse and neglect cases, an ideal to promote the good of children or establish prima facie duties, and as a standard of reasonableness based on what most informed rational people would do to maximise net benefits and minimise net harms.
89 Ibid. at 43.
91 Supra note 85 at 57, per Lord Hodson.
lead in their blood. The court took the opportunity in an interlocutory application to make very clear that:

We have long stressed that the “best interests of the child” is the overriding concern of this Court in matters relating to children. Whatever the interests of a parent, and whatever the interests of the general public in fostering research that might, according to a researcher’s hypothesis, be for the good of all children, this Court’s concern for the particular child and particular case, over-arches all other interests. It is, simply … not in the best interest of any healthy child to be intentionally put in a nontherapeutic situation where his or her health may be impaired, in order to test methods that may ultimately benefit all children.94

The rather absolute nature of this pronouncement prompted various interest groups to petition for reconsideration. The Grimes court then provided some qualification to its initial ruling by holding that the parental prohibition from exposing children to “any risk of injury or damage to the health of the [child] subject”95 referred to:

… any articulable risk beyond the minimal kind of risk that is inherent in any endeavor. The context of the statement was a non-therapeutic study that promises no medical benefit to the child whatever, so that any balance between risk and benefit is necessarily negative. As we indicated, the determination of whether the study in question offered some benefit, and therefore could be regarded as therapeutic in nature, or involved more than that minimal risk is open for further factual development on remand.96

Grimes represents a very restrictive view of parental authority to consent to research participation in that it places research participation within the overriding conception of the ‘best interest’ standard. ‘Minimal risk’ appears to be carved out as an exception to this framework of analysis on the basis that such research does not really pose any risk or harm to the minor at all, and would therefore offset the imbalance presented by the absence of medical benefit. This essentially reflects a non-consequentialist interpretation of ‘best interests’ that, by laying down a clear harm threshold, discourages a slippery slide in favour of the collective interest in the advancement of research at the expense of a minor’s interest in her health, bodily integrity and developing autonomy.97 Consequently, if any sacrifice on the part of children is sought for the sake of science, it is to be done when they “have reached the age of full and legal discretion when they can make that choice for themselves.” 98

How then does the concept of ‘minimal risk’ cohere with this best interests approach? A ‘minimal risk’ exception is perhaps allowed because such risks do not endanger (or render worse off) the minor’s health and well-being when compared to any other ‘endeavor’ he may be permitted to undertake. Being ‘inherent’, such risks are presumably unavoidable whatever the endeavour. This conception does not sit well with the court’s reference at another juncture99 to

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94 Ibid. at 852-853. In doing so, the court affirmed an earlier decision in T.D. et al v. New York State Office of Mental Health (1996) 228 A.D.2d 95 at 124 (S.C. App. Div., N.Y.), which held that “a parent or guardian… may not consent to have a child submit to painful and/or potentially life-threatening [greater than minimal risk] research procedures that hold no prospect of benefit for the child and that may have the same result as a denial of necessary medical treatment…”.

95 Ibid. at 858.

96 Ibid. at 862.

97 Grimes, supra note 93 at 853.


99 Grimes, supra note 93 at 856 fn 41.
the U.S. Federal Regulations’ definition of ‘minimal risk’. There are two components to this federal test: the risks of daily life standard or the routine examinations standard. Linkage to this conception of minimal risk is problematic in that it could possibly encompass significant risks that a child may experience in pursuit of activities that are otherwise for the child’s benefit (and therefore could have been foregone), or it could discriminate against children who by reason of their lower socio-economic status are exposed to greater environmental risks, such as the children in the Baltimore study that were likely to be exposed to unhealthy levels of lead in their normal daily environments. Even if this disadvantage be a social reality, it is not at all clear why it should be legal or ethical to intentionally expose children to these same risks for the sake of science. The law is asked to provide a normative justification, not a descriptive one. The alternative routine examinations standard is perhaps closer to the mark. Such examinations are unlikely to encompass anything more than commonly used physical and psychological assessments, including a single venepuncture, that pose negligible risk, and hence fit more closely with the notion of risk inherent in any endeavour.

Alternatively, the court may have merely sought to avoid placing an insurmountable negative burden of proof on researchers and parents. It would suffice to show, on the basis of the available evidence, the absence of any ‘articulable’ risk to the minor’s health and well-being, rather than to disprove the possibility of any risk associated with a proposed research protocol. However, even in this scenario, research participation often entails time away from the minor’s other educational and social activities, and possibly momentary discomfort or pain. On this ‘no articulable risk’ standard, must there still be some demonstrated collateral benefit to compensate for these drawbacks or the court implicitly stipulating a reasonableness standard as in S v. S., leaving discretion ultimately to the parent? The court leaves this open.

In summary, non-beneficial research participation will likely invoke the concerns of the ‘protective’ dimension of the parens patriae jurisdiction. The law is concerned to protect the minor from excessive and unreasonable exposures to harm, especially in situations where the activities do not purport to directly benefit the minor, but instead seek to advance the interests of third parties or society generally. From the foregoing review, at least two distinct approaches are discernable at common law in relation to decisions closely analogous to those that have to be made in non-beneficial research participation. The first confers overriding or paramount weight to the individual welfare interests of the minors, which therefore rules out any non-beneficial or self-interested activity. The second gives due consideration to the minor’s interests, but permits the decision maker to consider extraneous or public interests in coming to a reasonable decision, which need not represent the very best alternative for the minor.

It is submitted that these various approaches, regulatory, professional and common law, can be understood as a dynamic function balancing the level of risk or harm posed by the activity in question, the parents’ discretion concerning the nature of the minor’s upbringing and the minor’s capacity to understand and identify with the activity in question. First, the greater the risk, and in

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100 45 C.F.R. §46.102(i) (2006)
103 Wendler, supra note 101 at 38.
105 See Kopelman, supra note 88.
particular the potential harm to the minor’s primary interests in health and well-being, the greater the weight placed on the minor’s individual interests, to the exclusion of all other considerations. Where the risks are low and do not pose any discernable immediate or long term harm to the minor, parents may, in their discretion, allow participation in activities or procedures that serve primarily to benefit a third party or societal interest. This respects parental discretion in the social, educational and moral development of their children, whether because parents are best situated to do so, out of respect for family autonomy and privacy or simply a recognition that there are many areas in this socially important endeavour over which persons may reasonably disagree. The third dimension in this sliding scale of risk/benefit analysis is arguably the capacity of the minor to understand and identify with the activity or procedure in question. The greater this capacity and desire, the greater the leeway for risk exposure on the basis that this now also properly represents the individual minor’s developing autonomy interest. However, while it is clear that the courts and professional guidelines recognise this autonomy interest, it is less clear what risk ceiling beyond ‘minimal risk’ applies in this instance.

Within this more nuanced conception of the minor’s ‘best interests’, clinical trials in Singapore have been statutorily confined to direct benefit procedures apparently because a legislative judgment has been made at the outset that all other non-beneficial trials are likely to pose an unacceptably high level of risk to minors who do not have the condition or symptom under investigation. Phase 1 trials are considered to be beyond the level of acceptable minimal risk to expose a healthy child, and minor participation is usually justified on the basis that it offers the prospect of some direct medical benefit. Parents therefore have no discretion to enrol their healthy minors in such trials, or for that matter any other biomedical research that presents similar or greater levels of risk. However, this approach might rule out placebo-controlled trials where minors on the placebo-arm do not receive the investigative drug conferring the potential therapeutic benefit. Perhaps the ECTD and MHUCTR sought specifically to address this issue by stipulating instead for direct group benefit, but as discussed, this leaves open the question of what protective risk threshold applies to placebo-arm participants.

Extrapolating the CTR stance to all biomedical research involving minors regardless of risk level is likely to be unduly restrictive. Where the risks of harm presented are instead ‘minimal’ or ‘low’, the other considerations just outlined may properly come into play, and the various professional guidelines recognise that parents have discretion in respect of exposure to such risks. What is lacking is a principled way of determining just what is ‘minimal risk’ and how this can be more consistently interpreted by the relevant decision makers. Furthermore, Singapore law at present does not even make clear when, if at all, non-beneficial research in minors is permissible. The CTR applies an overriding “best interests” standard, and it is uncertain whether the alternative approaches adopted in the MHUCTR or foreign decisions will be applied here. The result is that important childhood and adolescent research may be impeded out of fear of litigation or unrealistic expectations in the ethical rigour of the decision-making process.

D. Clearer Legal Standards for Risk/Benefit Analysis

106 L. Glantz, ‘The Law of Experimentation with Children’ in Grodin & Glantz, supra note 136, c.4 at 104-111.
107 Ibid. at 105.
109 Marion’s Case, supra note 67 at 280, per Brennan J. Cf. Brock, ibid. at 197.
111 On the difficulties associated with judicial resolution or clarification, see Dickens, supra note 74 at 146-147.
How can risk-benefit analysis be improved to cohere with legal principle? ‘Minimal risk’ needs to be anchored in a specific decision-making context in order for it to have any normative value, otherwise it is merely a subjective concept dependent on the value system of the decision-maker. If we take our cue from the *Clinical Trials Regulations* and *Grimes* decision, minimal risk might reflect an idealised world where children may never be asked to sacrifice anything until their attainment of legal majority or functional competency, at which point the law then unceremoniously throws them in with the lot of adult martyrs, narcissists and the whole spectrum of life choices and ideologies in between. This all or nothing approach is quite unrealistic when compared to the actual choices society and the law allow parents to make in the daily upbringing of their children. As Ackerman rightly points out, parents are allowed to intervene in the life of their child not only for the purpose of enhancing their physical and psychological well-being, but also to inculcate character traits which allow them to develop into moral adults. Furthermore, parents may intervene to promote the interests of other persons, particularly family members and possibly even third persons in the context of inculcating moral development.

This indicates that the alternative ‘not against the best interests’ approach reflected in *S v. S* offers more nuanced starting point of legal analysis. Children are developing individuals, raised in a family context where intra-familial trade offs are often made to accommodate conflicting family interests and where the governing value system(s) are chosen and inculcated by parents. In this decisional context, ‘minimal risk’ should reflect the outer limit of parental discretion in respect of the legitimate goals of parenting and how they might reasonably be brought to bear on the question of research participation. When would or should responsible parents agree to allow their children to participate in non-beneficial research? Three approaches may be usefully adopted from the perspective of the discharge of parental duties.

1. **Risks of daily life, new experiences and charitable endeavours**

The NMEC guidelines articulate a “risks of everyday life” standard, observing that parents “currently control this level of risk”. This is a common standard adopted internationally in interpreting ‘minimal risk’. Freedman *et al* point out that the risks of everyday life is intended as qualitative or categorical standard, rather than a quantitative one. While it may be difficult to quantify such risks, they are well known to us all and if we are uncertain about the commonality of a risk of harm, it is necessarily excluded. Therefore, the risks of everyday life approximate a lowest common denominator of risk at which level most reasonable people feel is safe enough to ignore in making choices, and are therefore deemed socially acceptable. Freedman *et al* build on this foundational concept by arguing that parents are justified in further exposing their children to ‘minor’ increases over daily risks, on analogy to their decision concerning whether to allow their charge to participate in ‘new experiences’ that are sufficiently similar to their daily activities. This layered approach to risk analysis nicely mirrors the Federal Regulation’s categories of ‘minimal risk’ and ‘minor increase over minimal risk’, and might offer an explanatory account of the ‘minimal’ and ‘low’ categories in the U.K. guidelines.

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112 Ackerman, *supra* note 102 at 95-96. See also Dickens, *supra* note 92.
113 *S v. S*, *supra* note 85 at 45, per Lord Reid.
114 See Marion’s *Case*, *supra* note 67.
115 *Supra* note 50.
120 45 C.F.R §46.405 and §46.406 (2006) respectively.
There are several difficulties with this interpretation of minimal risk. Minors in an affluent society like Singapore have numerous social, educational and sporting opportunities in daily life. Short of a parent adopting a paranoid stance which precludes allowing a child to ever leave the home, the risk profile attached to the usual activities of a child vary widely depending on the activity, particularly where road travel, sport and play are involved. Many of these activities might not have been chosen after conscious consideration of all the attendant risks, so reference to common risk profiles would not be morally significant. Parents may desire the safest environments for their children, but the actual risks children are exposed to are a complex function of their psychological and economic ability to manage the risks. A nation-wide sample study of children under 15 in Singapore found a 19.5% prevalence rate of injury, many of which occurred in the home and were preventable. Childhood injuries, particularly in the home, are empirically significant and a common feature of daily life. Yet it seems clear that such a level of risk should not be used to justify deliberate exposures to risk in a research setting where risks are identified and disclosed at the outset before participation.

Secondly, when parents consciously deliberate over these activities, the acceptable risk level is not simply a function of what is inherently unavoidable or acceptable, but also of the potential benefit offered by the activity. Thus parents might reasonably permit young children to participate in a dangerous sport like wake-boarding, after considering not just the available reasonable precautions, but also the tangible psychological and physical benefits of the activity and also the interest of the child in the activity. It is therefore not particularly self evident what activities or subsets of daily life are within or without the underlying concept of ‘minimal risk’, nor whether these riskier but potentially beneficial activities like sport are properly taken into account. Freedman’s analogy with parental decisions concerning new experiences for the minor assumes that there is something beneficial about new experiences per se. It would be difficult to assume that all non-beneficial research, however exciting and important to the investigators, would necessarily possess this beneficial quality vis-à-vis the minor.

Thirdly, it is unclear whether benchmarking to daily risks is meant to be an objective or subjective exercise. The latter interpretation pegs minimal risk to the particular subjective experiences of minors likely to be recruited or targeted by the requirements of the research protocol, and has attracted much deserved criticism. Sick or disadvantaged children are more likely to satisfy the threshold simply by reason of the greater risks presented by their illness, treatment or socio-economic background. A rejection of the subjective ‘daily risks’ standard also reflects a concern of justice that seeks to treat all children fairly, and not disproportionately impose the burdens of paediatric research on those already less favourably treated by the lottery of life.

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121 A study by M.E.H. Ong et al., ‘A Review of 2,517 Childhood Injuries seen in a Singapore Emergency Department in 1999 – Mechanisms and Injury Prevention Suggestions’ (2003) 44(1) Singapore Medical Journal 12-19, found that a majority (56.4%) of observed injuries occurred in the home, while 14.4% were road, 8.2% sport and 7.4% playground related.
123 Freedman et al., supra note 117, adopt a subjective interpretation.
On the whole, the risks encountered in daily life reflect a broad range of intentional, inadvertent or negligent choices made in discharging parental duties which might be conceptually and ethically inappropriate to justify ‘minimal risk’ in a research setting. Ackerman proposes a more focussed test. Research procedures involving minimal risk are those “in which the probability and magnitude of physical and psychological harm is no more than that to which it is appropriate to intentionally expose a child for educational purposes in family life situations.” This test offers the immediate advantage of overcoming the shortfalls of an undifferentiated ‘daily risks’ test by zeroing on closely analogous activities as a guide to evaluating the acceptability of non-beneficial research related risk. Responsible parents are also concerned about the moral development of their children, and this can partly be achieved by exposing them to situations where they can be sensitive to the realities of acting beneficently to promote the interests of others instead of their own. This is rooted in the parental responsibility to inculcate values in their children, religious or otherwise. In order to achieve this, parents may have warrant to enrol their children in research even where there is no demonstrable medical benefit to them, if participation reasonably constitutes part of the range of charitable activities where children can learn altruism. This need not be restricted to activities that have some direct educational value of the virtues of charity. By “educational”, Ackerman also envisages more than research interventions that have the potential to offer scholastic benefits, to include research that has the potential to “enhance their development as moral persons”.

If a certain degree of risk or harm is acceptable in inculcating moral values, then non-beneficial research may be similarly justified within the same bounds. It is also important to take into account the age, emotional maturity and particular physical condition of the children in question when evaluating the commensurability of these risks. In the absence of empirical data, decision-makers may draw on their experience of socially accepted methods of disciplining children and charitable activities that parents often permit their children to evaluate research proposals, even if specific empirical data may be lacking on the risks associated with such activities. For example, charitable activities might include visits that schools in Singapore often organise to welfare homes or blood donation in the case of older minors.

2. Routine examinations and negligible risk

An important assumption underlying the charitable activities standard just discussed is that the minor must be capable of responding to the developmental objectives of non-beneficial research participation. This interpretation of ‘minimal risk’ would therefore not justify the enrolment of infants and very young children who are not yet capable of drawing basic moral lessons from participation or, at the very least, appreciating its purpose. Nevertheless, S’s S recognises that certain medical interventions such as a single venepuncture pose negligible risk and do not essentially harm the minor. Parents may then in their discretion consider third party or public interests in deciding whether to permit participation, even if there is no prospect of developmental benefit. It is suggested that such negligible risk interventions exist where accumulated evidence or experience demonstrates that the intervention in question poses

127 Ackerman, supra note 102 at 106-107 [emphasis added].
128 Ibid.
129 See F. Wender, “Assessment of Risk to Children” in Grodin & Glantz, supra note 4, c. 6.
130 Ackerman, supra note 102. See also Wendler, supra note 101 at 39-41.
131 For the Singapore Centre for Transfusion Medicine’s guidelines on blood donation by minors, see online: Health Sciences Authority <http://www.hsa.gov.sg/publish/hsaportal/en/health_services/blood_donation/can_i_donate/who_can_donate.html>.
essentially no risk and only minor, transient discomfort. International and domestic ethical guidelines often benchmark this notion of negligible risk to the risks associated with routine medical and psychological examinations for children.

Wendler criticises this interpretation of minimal risk on the ground that these routine examinations are in fact justified by the preventive care (and therefore benefit) of the child. The associated risks involved should not automatically justify similar risks in non-beneficial research without some prospect of direct benefit. This presupposes a ‘best interests’ paradigm which S v. S candidly acknowledges no longer controls where the risks are negligible. Instead, expressed positively, participation reflects the minor’s beneficent moral obligation. This moral duty to promote minors’ common interest in health care advancement has been framed variedly. Brock’s account argues that a duty to participate may rationally be constructed from the original position behind the Rawlsian veil of ignorance. This generates a reciprocal obligation to contribute to the advancement of research and health care of minors in general, from which ensuing social good the minor in question also benefits. Alternatively, the duty to contribute may be constructed in terms of the basic moral obligation to help others in need, which would extend to contributions by participation in such research that does not do them any appreciable harm. In permitting such research participation, parents in effect give appropriate recognition to this moral obligation on the part of the minor.

From this vantage, the negligible risk threshold reflects, albeit conservatively, the considered judgments of society’s appointed decision-makers on the most basic duties of all minors toward the promotion of their common interest in their health care. Criticism is rightly levelled that duty-based justifications for childhood participation in research offer no clear criterion for determining the acceptable level of risk. However, restricting parental recognition of a minor’s basic beneficent obligation to negligible risk interventions reflects a carefully controlled and restrictive authority. This prevents a free-fall into purely consequentialist justifications of any level of risk exposure if the research imperative is sufficiently weighty. After all, if adults are not generally subject to a duty except in limited instances to participate in or contribute to research, justice requires that minors should not be expected to do more. In this vein, greater specification is also given to the “not against the best interests” standard: parents may enrol their children in recognition of the child’s moral duty to participate in circumstances where the risks are demonstrably negligible.

3. Moral development and the child’s developing autonomy

133 See, for e.g., the assessment of the risks associated with blood sampling in Nicholson, supra note 71 at 90-92, 120; Wendler, supra note 101 at 38-39.
134 See, for e.g., CIOMS Guidelines, supra note 2, commentary on Guideline 9; D. Hull, ‘Guidelines for the ethical conduct of medical research involving children: Royal College of Paediatrics and Child Health’ (2000) 82 Arch. Dis. Child. 177 at 179.
135 Wendler, supra note 101 at 38-39.
136 Dan Brock, ‘Ethical Issues in Exposing Children to Risks in Research’, in Grodin & Glantz, supra note 4, c. 3 at 91-93.
139 Non-voluntary adult contribution to biomedical research is recommended in limited situations involving human tissue and personal information. See Bioethics Advisory Committee, Human Tissue Research (Singapore, BAC 2002), paras. 8.1-9.6; Personal Information in Biomedical Research (Singapore: BAC, 2007) at para. 5.16-5.33; online: BAC <http://www.bioethics-singapore.org/resources/reports.html>.
In the foregoing analysis, although the minor’s age and emotional maturity were relevant factors in assessing risk and benefit, ethically permissible research interventions were determined from the perspective of parental responsibility and discretion. Thus the minor’s cognitive capacities and emotional maturity were relevant in determining the likely subjective harm and the potential for moral development presented by research interventions. Another relevant consideration in determining acceptable risk is the minor’s developing capacity to understand and identify with the altruistic or charitable motivation in research participation. Children under 7 years generally lack such capacity, but those above that age have demonstrated the ability to understand abstract concepts, and the nature of charitable acts. If these capacities are in fact present, and the minor identifies with the purposes of the proposed research, then parents may be justified in allowing moderate increases over the charitable activities standard articulated above in recognition of the child’s developing autonomy. This also properly advances the moral development objective in a real sense beyond mere exhortations to do good and consider the interests of others. Inevitably, parents are also intimately involved in such choices. They assist the child in making reasonable choices consistent with his other social and educational activities and ensure that the risk is not disproportionate to the moral development potential of the research experience.

For children over 14 years with substantial decision-making capacity akin to adults, it might be argued that they should be allowed to take on more substantial risk provided they understand the nature and risks of the research participation, the lack of legal majority notwithstanding. Here, the question is whether the risk ceiling should be substantially relaxed since competence approaches that in adulthood and we should perhaps not be unduly restricted by notions of minimal risk. However, the complex realities of non-beneficial research participation should be borne in mind. They by definition do not offer any therapeutic benefit to the minor, and may impose substantial risks that minors may likely under assess by virtue of their lack of experience. Minors’ reasoning may also be distorted by the usual monetary or other incentives often offered by researchers to encourage participation. Furthermore, competence assessment is not an exact science. There is a lack of professional consensus on the interpretation of the concept, an absence of a gold standard in assessment tools, and frequent discordance of expert opinions on decisional capacity.

These factors suggest that generous dose of soft paternalism is in order. Minors who possess adequate functional decision making capacity including an understanding of altruistic endeavour.

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140 Weisstub et al., supra note 21 at 400-402 and Nicholson, supra note 71 at 150-151.
143 Weisstub et al., supra note 21; D. Wendler ‘Assent in paediatric research: theoretical and practical considerations’ (2000) 32 Journal of Medical Ethics 229 at 230-231.
should be allowed to enrol in greater than minimal risk research. This is provided that the research interventions do not expose them to a real or significant risk of harming their primary goods necessary for “successful participation in the central institutions of society that a minor can be reasonably expected to live as an adult” (for e.g. their education, health and emotional well-being) or, more generally, their developing capacity to mature into independent autonomous adults. This constitutes an outer limit of acceptable risk justified by both the minor’s capacity to identify with the research goals and the desire to encourage moral development and good citizenship.

It is acknowledged that these guidelines or standards require further interpretation, and therefore leave significant discretion or judgment to researchers, IRBs and proxy decision makers in determining if they will allow such non-beneficial research to proceed. Much will depend on the specifics of the research proposed, the context in which parents and their children are approached to participate and the specific minors in question. However, the more specific ‘responsible parent’ standard proposed is but one important pillar of minor protection, which also depends on appropriately designed review and approval processes to achieve the broad objective of protecting the welfare of minors.

IV. DECISION-MAKING PROCESSES: THE PARENT, MINOR AND THE STATE

A. Current Law and Practice

On the question of decision making authority, a clinical trial ‘subject’ who is below 21 years in age (and not married) may consent to participate in a trial provided the minor’s parent, guardian or other legal representative also consents. Unless a minor has been emancipated by marriage or lacks “sufficient understanding”, the default requirement is effectively that a joint decision to participate must be made where both the minor and her parent are persuaded of the benefits or merits of the trial. This is the case even though the minor may, under common law Gillick competency or the ‘mature minor’ doctrine in the U.S., possess adequate functional competence to understand the nature of the trial proposed, its implications, and be able to come to her own decision on the matter.

Dual consent may be dispensed with if the minor ‘subject’ of a clinical trial ‘lacks sufficient understanding to give such consent’, in which case a parent or legal representative may alone give consent to participate if the direct benefit requirement is satisfied. It is not clear what level of ‘understanding’ is required for a minor to give individual consent. This could be equated with common law Gillick competency or some lesser and subjective notion of ‘assent’ that involves eliciting willing cooperation to the extent permitted by the minor’s intelligence and maturity.

151 Supra note 28.
153 See Glantz, supra note 20 at 225-226.
154 Supra note 26, Reg. 11(2).
155 See, for e.g., CIOMS, supra note 2, Commentary to Guideline 14. The U.S. National Commission, supra note 138 at 16, distinguished ‘assent’ from a legally valid consent. The former represents a child’s ability to understand the purposes and procedures of research and indicate her wish regarding participation. The Federal Regulations define assent to mean a child’s “affirmative agreement to participate in research”: 45 C.F.R. §46.402 (2006).
By terminologically equating the minor’s ‘consent’ to that given by a parent or legal representative, the reference to ‘sufficient understanding’ arguably refers to the functional competence in *Gillick* needed to give legally valid consent. This goes further in objectively requiring the intelligence and maturity necessary to understand the risks and consequences involved in coming to a decision concerning trial participation. In contrast, the SGGCP draws a clearer distinction between ‘informed consent’ and affirmative agreement on the part of the minor based on his subjective understanding that falls short of informed consent.

In respect of biomedical research in general, the NMEC Guidelines explicitly recognise the concept of ‘assent’ which is contrasted to ‘legal consent’. A child “should have [the] power to decline invasive involvement with conclusive effect. Parental consent may be [a] necessary but not sufficient condition: the child’s negative preferences in such cases should be respected.” The emphasis here seems to be a negative one emphasising the dissent of the child, but it is unclear how, if at all, this differs from assent. Nevertheless, if child assent and parental consent are both necessary for enrolment in research, then the NMEC Guidelines make clear that even if the child is not legally competent, enrolment is unethical if child assent is not forthcoming.

In interesting contrast, the *MHUCTR* only requires individual informed consent from a person with parental responsibility in order to enrol a minor in a clinical trial. The minor must still receive information regarding the trial according to his capacity of understanding. However, his refusal to participate or to withdraw need only be ‘considered’ by the investigator and is therefore not binding. Secondly, the *MHUCTR* confers majority status on individuals who are 16 years or older, perhaps drawing a parallel with s.8 of the *Family Law Reform Act 1969* which provides for the equivalent right to consent to medical treatment. Based on the conditions applicable in respect of adults, such individuals may therefore consent to participate in a trial without the need to consult or inform their parents, nor are there any restrictions on financial inducements that may be offered.

In a similar vein, the U.K. professional guidelines generally adopt a broad individual model of consent. However, in contrast to the *MHUCTR*, they recommend that if a minor acquires *Gillick* competence, it is the minor’s consent alone that is required. The MRC also recommends that family be involved in the decision-making process unless the minor specifically requests otherwise. Where parental consent is necessary, the guidelines recommend that researchers should still obtain the ‘assent’ of minors so capable, and respect their refusal to participate notwithstanding legal incompetence. In notable contrast, the RCP considers it unwise to

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156 * supra* note 152 at 189, *per* Lord Scarman.
157 * supra* note Error! Bookmark not defined., para. 4.8.12 read with para. 4.8.5, which together provide that where a minor cannot give “informed consent”, “the subject should be informed about the trial to the extent compatible with the subject’s understanding and, if capable, the subject should sign and personally date the written informed consent”.
158 * supra* note 50.
159 * supra* note 33, Part 4, para 4. The MRC view this measure as additional protection device in that it disallows even competent minors (under 16 years of age) from consenting to participation in clinical trials: MRC Guidelines, * supra* note 53 at 25.
161 * supra* note 33, reg. 2.
163 See RCPCH Guidelines, * supra* note 52 at 180; MRC Guidelines, * supra* note 53 at paras. 5.1.3-5.1.3a, which also notes the different position in Scotland, where individuals aged 16 and above may give consent of legal effect in any transaction: *Age of Legal Capacity (Scotland) Act 1991*, c.50, s. 1.
164 MRC Guidelines, * supra* note 53 at para. 5.1.4.
include a Gillick competent child where the child agrees but the parents do not. On the whole, while there is consensus on the ability of a functionally competent minor to give informed consent, it is unclear whether proceeding without accompanying parental consent is ethical in all situations.

In the absence of general legislative specification, the common law prescribes the default rules concerning consent requirements outside clinical trials. The foregoing discussion makes clear that parents generally have the authority to give consent on behalf of minors to participate in therapeutic research and some instances of non-beneficial research. Valid parental consent operates as a defence to an action of battery. It is far less clear, however, what decision-making authority or input minors have in respect of non-beneficial research. Some decisions give implicit recognition to the developing autonomy of each minor. Lord Reid, for example, in S v. S suggests that where the child has understanding of the matter, then it would be unwise to override his wishes. In contrast, Gillick suggests that if the child attains sufficient functional competence, then he should have the authority to make decisions even in respect of research participation, to the exclusion of his parents since their authority has come to an end.

In the light of the subsequent decisions in Re R \(^{170}\) and Re W \(^{171}\) that allow parents to provide consent that furthers the child’s bests interests notwithstanding her refusal of medical treatment, it is unclear to what extent children have truly independent decision-making authority and if this extends to non-beneficial interventions. There is fortunately no necessity at common law that we be restricted to such binary outcomes. The U.S. decision in Bonner v. Moran offers a third option by requiring that both the consent of the competent minor and the parent are required to legitimate non-beneficial interventions, even ones that expose the minor to serious risk. None of these precedents however have been explicitly considered or applied in Singapore. These issues are not without practical significance since they are necessary determinations for researchers and research institutions as a matter of legal risk management, and may also have determinative influence where research cannot practically proceed if parental consent is always required.

B. Sorting out Consent, Assent and a Minor’s Legitimate Role

The first important question that needs to be resolved is whether a minor’s consent or agreement is necessary for non-beneficial research participation. Even if such authority is not warranted, should the law recognise or mandate some level of involvement by the minor in the decision-making process? First, the ethical principle of respect for persons urges that the minor’s developing autonomy should be recognised and respected. Children, with age and experience,

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166 The RCP Guidelines 2007, supra note 54 at para. 4.58, continues this advice, albeit in less absolute terms. In fact, the RCP’s earlier Guidelines on the Practice of Ethics Committees in Medical Research Involving Human Subjects (2nd ed., January 1990) advocated a dual consent approach for subjects below the age of 18 (at para. 13.1). A similar recommendation was made by the Institute of Medical Ethics working group in respect of non-beneficial research: Nicholson, supra note 62 at 151.

167 Marion’s Case, supra note 67 at 316, per McHugh J.

168 Supra note 85 at 45.

169 Supra note 156. See also Marion’s Case, supra note 67 at 316, per McHugh J; cf. Brennan J. at 280-281.


172 126 F.2d 121 (1941) (U.S.C.A., D.C.). See also, Glantz, supra note 20 at 227-229 and Re W, ibid. at 78-79, where Lord Donaldson observed obiter that it was inconceivable, in the context of organ donation, that doctors would proceed solely on the basis of the consent of a Gillick competent child without “supporting parental consent” or a court order.

often develop the cognitive capacities for understanding, reasoning and voluntary choice well before they acquire the age of majority.\textsuperscript{174} Second, to the extent that participation is ethically justified by the potential for the minor’s moral development, then it is imperative that the minor be involved in the decision-making in order that he can be exposed to the investigator’s and parents’ reasoning and their motivations for conducting the research or supporting it, in order to stimulate this development.\textsuperscript{175} Third, if as argued above, exposure to greater than minimal risks is justified in part on the minor’s ability to identify with and be motivated by altruistic actions that promote the interests of a third party or the common good, minors should be accorded a commensurate measure of decision-making authority once this level of competence exists.\textsuperscript{176} Finally, minors who are more involved in the process and agree to participate are more likely to be committed to complying with the research protocol requirements.\textsuperscript{177}

Consequently, it is submitted that a clear distinction should be drawn legally between the concept of consent\textsuperscript{178} and assent.\textsuperscript{179} Consent traditionally functions as a legal defence to what would otherwise be unlawful invasions or restraints of an individual’s bodily integrity and liberty respectively.\textsuperscript{180} This is closely tied to the law’s respect for the principle of autonomy and the presumed capacity of individuals to best assess and promote their personal interests. Thus the requirement of informed consent is a fundamental pillar that defines the legality of research interventions that otherwise impinge on the value that law places on an individual’s bodily integrity and liberty. Correspondingly, the competence of an individual should fulfil the basic hallmarks required by law to exercise autonomous choice – namely the capacity to understand, reason and evaluate research risks and benefits, and come to an independent voluntary choice.\textsuperscript{181} If minors come to possess this level of competence, they should have the authority to consent to or refuse non-beneficial research participation, and especially when it is this autonomous capacity that also mandates exposure to greater than minimal risk.

The concept of assent more appropriately relates to minors who fall short of this level of competence,\textsuperscript{182} but nonetheless possess some ability to understand the nature and purpose of the research, whether at a concrete or abstract level.\textsuperscript{183} At this level, explaining the nature of the research procedures, dealing with the minor’s concerns and pointing out the value of her involvement also serve both pedagogical and risk management functions. The potential for moral development is realised by engaging the minor to the extent possible, based on his cognitive and psychological development, on the purpose and motivations for participation.\textsuperscript{184} Any subjective fears or concerns are more likely to be revealed by such engagement and can be addressed in order to minimise the subjective risks associated with the proposed research participation.

\textsuperscript{174} Collogan & Fleischman, supra note 145 at 84-86.
\textsuperscript{175} Weisstub et al., supra note 21 at 394.
\textsuperscript{176} See Part III.D.3 above.
\textsuperscript{178} As recognised in the Clinical Trials Regulations, supra note 26, Reg. 14.
\textsuperscript{179} As recognised in the NMEC Ethical Guidelines, supra note 50, para. 2.5.5.1.
\textsuperscript{181} In re C (Adult: Refusal of Treatment) [1994] 1 W.L.R. 290 (Fam). This test was applied to a minor in Wolverhampton Metropolitan Borough Council v. DB [1997] 1 FLR 767 (Fam).
\textsuperscript{182} Cf. CIOMS Guidelines, supra note 155, which appears to conceive of assent as agreement to participate which falls short of legally valid consent solely on the score of the chronological age of majority.
\textsuperscript{183} See L. Weithorn, ‘Children’s Capacities to Decide about Participation in Research’ (1983) 5(2) Hastings Center Report 1 at 2.
\textsuperscript{184} S. Leikin, ‘An Ethical Issue in Biomedical Research: The Involvement of Minors in Informed and Third Party Consent’ (1983) Clinical Research 34 at 39.
The real test of assent is whether the minor’s dissent after such engagement must be binding. As the possible reasons for a minor’s dissent are varied, and parents have a broad discretion in how they should promote the minor’s moral development within acceptable risk thresholds, the latter should have the authority to override the child’s dissent.\(^\text{185}\) If, however, dissent is intractable and reveals anxieties or fears that cannot be allayed, then the risks presented are likely to exceed the minimal level articulated earlier and investigators and parents have a duty to not enrol him. In this instance, refusing participation is not based on the minor’s decision-making authority, but rather the parental duty to protect her from unjustified harms. Consequently, assent must be distinguished from traditional consent in that it does not principally serve a self-protective function or ensure respect for minor autonomy. In summary, assent is necessary in all situations where the minor has some rudimentary capacity to understand the basic features of research participation. When the competence of the minor reaches the level of adequate functional competency in the context of research participation, and especially where the risks are greater than minimal, the minor’s informed consent then becomes a necessary condition before research can proceed.

Two practical issues follow from this. Should the requirement of consent and assent rest on individualised assessments of the minor’s competency, or should the law provide age-based proxies of competence to facilitate minor recruitment in non-beneficial research? If the former, how should such assessments be conducted and in particular, by whom? There has been some study on the competence of minors to make research participation decisions using an informed consent paradigm. However, it appears that there is no one age at which all minors can uniformly be said to possess the requisite decisional capacity to consent to research participation.\(^\text{186}\) Nevertheless, there is some consensus amongst psychologists that age 14 years represents a significant milestone where a minor is likely to have progressed to the formal operations stage of development with the means to think abstractly and hypothetically,\(^\text{187}\) and generally possess the highest standard of mental reasoning in appreciating the nature of medical treatment.\(^\text{188}\)

Ideally, minors should be individually assessed to determine the appropriate nature of decision-making involvement, and whether they are capable of providing legally valid (though not necessarily sufficient) consent. This individualised approach has its clear costs of implementation, given the need for further research on the factors of development that bear upon a minor’s capacity to understand and make decisions,\(^\text{189}\) and the consequent lack of any standardised instruments of assessment.\(^\text{190}\) When the risks presented by non-beneficial research are minimal, it is argued that a presumptive rule based on chronological age may be usefully deployed to guide investigators and parents on appropriate assent or consent procedures without the necessity for an individualised competence assessment. This age threshold should ideally be determined by local empirical study on childhood competency in research contexts, where social and cultural factors may be properly accounted for.\(^\text{191}\) Where research entails greater than minimal risk and depends on the autonomous capacity of the minor for legitimacy, individualised assessments are warranted by the greater stakes involved. Finally, such assessments of competence should be made by a suitably trained professional who is independent of the

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\(^{185}\) Ackerman, \textit{supra note} 142. Cf. NMEC Guidelines, \textit{supra note} 50.

\(^{186}\) See generally, Collogan & Fleischmann, \textit{supra note} 145 at 83-85.

\(^{187}\) Ibid.

\(^{188}\) Weisstub \textit{et al.}, \textit{supra note} 21 at 399-403.


\(^{190}\) Wendler, \textit{supra note} 143.

\(^{191}\) See Nicholson, \textit{supra note} 71, c.7 at 148.
investigator or sponsor of the research in question, given the potential for conflict of interest on the part of the latter if they are allowed to render their own assessment before enrolling minors.192

C. The Sufficiency of Informed Minor Consent?

The second important question relates to the tension produced between a minor’s capacity to consent and the need for parental permission under a dual consent model. If a minor acquires functional competence to make a substantially autonomous choice, why should parental consent still be required? Thus far, functional competence was used specifically to justify the inclusion of minors in the decision-making process. Some commentators argue that the acquisition of functional competence should ipso facto entitle minors to make independent choices concerning research participation,193 and this approach is supported by various U.K. professional guidelines. However, as Scott et al point out, the functional competence test emphasises cognitive capabilities that adhere to an informed consent model developed in the context of respecting adult decisions in medical treatment and research.194 This model may not, as a matter of social and legal policy, be suitable for minors. Although Gillick heralded the rise of minor’s decision-making rights, the law has not whole-heartedly gone down this path. Subsequent cases such as Re R and Re W195 reveal paternalistic concerns in the continued overriding of minors’ decision-making rights. Furthermore, it is not uncommon for the legislature to draw a bright line in some instances by imposing age-based limits on independent choices by minors, regardless of their individual functional competence. The provisions of the Singapore Clinical Trials Regulations and Voluntary Sterilisation Act196 are instances where dual consent is required, while the prohibition on the sale of cigarettes to minors 18 years and below is an example of an absolute bright line prohibition.197

These restrictions on the freedom of functionally competent minors to make their own independent decisions reflect three broad policy concerns. The first appears to be based on the view that minors (or adolescents in particular) as a class have poorer judgment, and consistently choose different outcomes than adults which result in unacceptable social costs that fall primarily on minors themselves. If so, then there is a compelling public interest in preventing harm to this group.198 On a related note, the second major concern is that minors base these judgments on values and preferences that reflect common developmental characteristics that will predictably change with experience and maturity. If this is the case, then the respect for the autonomy of minors is less compelling as compared to adults, and the case for protecting the future adult from the cost of his immature youthful decisions more so.199 In view of this, some psychologists argue that decision-making capacity should be linked to both cognitive ability and previous life experiences.200 Others have advocated a richer “judgment” based framework for evaluating decision-making competence that better explains current approaches and restrictions to minor

193 Supra note 144.
195 Supra notes 170 and 171 respectively. In Ney v. Canada (Attorney General) (1993) 79 B.C.L.R. (2d) 47 (B.C.S.C.) the court noted that it was still uncertain at common law whether parental control yields to the child’s independence or whether there are concurrent powers of consent.
197 Infra note 219.
198 Scott et al, supra note 194 at 228.
199 Ibid.
competence and independence. This framework extends beyond value-neutral cognitive development factors to encompass dispositions such as responsibility, temperance and perspective, in the search for a fuller understanding of a concept of maturity in decision-making. This also suggests that the current *Gillick* test of competency based on understanding may not fully capture what is necessary for autonomous choice in view of what is at stake in research participation.

Although more research is needed to fill out our understanding of the development of these dispositions in minors, there is sufficient empirical evidence of adolescent development that would give weight to these concerns in the context of non-beneficial research participation. For example, research has indicated that adolescents are more likely than adults to act impulsively and be focussed on the current rather than their possible future situations. In general, they seem to discount the future more than adults, and to weigh more heavily the short term consequences of decisions, which often contribute to risky behaviour. Adolescents also seem to differ from adults in their perception of and attitude toward risk, and may sometimes be unaware of risks that adults perceive or calculate the probability or magnitude of a given risk. These researchers speculate that such differences may reflect the reality that adolescents have fewer life experiences and may possess greater uncertainty over their own futures, leading them to focus on short term consequences.

These specific findings and continuing need for more research on adolescent development raise a likelihood that minors in general do require greater protection than their independent informed consent alone can provide in non-beneficial research. Minors will be asked to weigh in the balance the physical and psychological risks that they may not be familiar with or appreciate, their personal values or value systems that are still developing and the monetary payments and other inducements that investigators frequently offer, whether as compensation or remuneration for time spent. These deliberations and trade-offs occur at a stage in life where minors are generally of limited independent financial means and the short term opportunities that these inducements afford are plentiful. Given these observed differences in perspective and disposition, and the lack of a clear picture of the systematic differences in decision-making processes between adults and minors, it does not make for sound policy to depend solely on the independent consent of minors to protect their own current and long term interests.

Thirdly, the continuing parental interest and responsibility in the social and moral development of their children should not be ignored. They have discretion in deciding how to go about this, subject of course to legally or ethically defined limits. Research may interfere with the daily routine parents plan for their children, and the consequences of any such risk that materialises...
are also generally borne indirectly by parents. Furthermore, by virtue of their knowledge and understanding of the minor’s individual needs and characteristics, parents are generally best placed to assist in the assessment of the risks and benefits of research participation.

Consequently, a dual consent model of decision-making provides an obvious remedy to safeguard against these concerns, and should be the preferred default requirement in non-beneficial research involving minors that involves significant risk. Dual consent formally recognises that both minor and parent have independent authority to withhold consent and therefore prevent research participation. Both are therefore entitled to the same consent procedures and statutorily mandated information disclosures and explanations. Investigators would be required to ensure in particular that the consent of the minor is voluntary, and this is probably best ensured if there is an independent third party who not only assesses the minor for adequate competence, but also engages the minor with explanations of and discussions about research participation to obtain the requisite consent. Finally, in order to facilitate the consent of both minor and parent, investigators or independent advocates would have an incentive to promote joint decision-making between parent(s) and the minor. One study has revealed that if parents were approached first, they were likely to decline. However, if minor adolescents were included in the decision making process, their different perspectives and greater willingness to participate could possibly influence a more favourable outcome. Although many decision-making styles have been observed within families in this context, joint decision-making is desirable as it appears to be typical of normal development and has the potential to encourage increased responsibility and maturity in minor decision-making while allowing for parental guidance and input on issues such as risk assessment. Much of the desired outcomes in decision-making of course depend on practical implementation, but just as with adult informed consent, this is question of responsible professional standards developed on the basis of experience and research on our understanding of adolescent-parent decision-making processes.

The law should also countenance several exceptions or modifications to this recommended baseline. First, where research presents no more than negligible risk or risk associated with charitable endeavours, additional protection for a functionally competent minor is unnecessary, given the carefully controlled levels of risk and assuming a reliable ethics review process. The minor’s individual consent would suffice. Parental permission would then be more of a practical issue if their cooperation is necessary for the minor to participate as required by the research protocol.

Secondly, it has been observed that the insistence on parental consent has inhibited research needed to improve health care for substance abuse, mental health, sexual activity and pregnancy concerning minors as they are reluctant to involve their parents. It is submitted that where the

208 In respect of clinical trial participation: Clinical Trials Regulations, supra note 26, Reg. 14.
209 See text accompanying note 192 above.
210 J. Brody et al., 'Comparisons of adolescent and parent willingness to participate in minimal and above-minimal risk pediatric asthma research protocols' (2005) 37 Journal of Adolescent Health 229 at 234.
214 As defined in Part D.2. above.
215 Collogan & Fleischman, supra note 145 at 91.
public health interest collides with parental prerogative, waivers of parental consent should be permitted where there is a pressing public health interest related to minors in the research and insistence on parental consent would make such research practically impossible. In either of these situations, a substitute process for protective review and advice by an independent minor advocate (especially where risk exceeds negligible levels) or consent by the competent minor alone would be sufficient assurance of protecting their welfare. Secondly, alternative decision-making authority should be recognised where parents are demonstrably abusive or neglectful and would not likely be able to discharge their responsibilities in this context.

Finally, compared to the age of majority prescribed in the U.K. regulations, the Singapore threshold of 21 years is rather high. It is submitted that a review of this chronological threshold is long overdue, at least in the context of medical treatment and research participation. Legislation in Singapore takes differing approaches to the presumptive age at which an individual acquires full legal competence to make decisions for herself. While the age of majority for contracting and marriage still remains at 21, 18 year olds are statutorily permitted to independently purchase tobacco products, make a gift of their body post mortem for research, educational or therapeutic purposes and, for male individuals, required to enlist for compulsory military service. As a matter of practice, 18 year olds are also allowed to make independent blood donations. While there is certainly a lack of coherency in the conferment of adult majority status, to the extent that some of these activities are found to pose commensurate minimal or greater than minimal risk, and/or involve similar or greater decision-making complexities, then existing or proposed research regulations should similarly be revised downwards in conferring independent decision making authority to participate in non-beneficial research posing minimal or even greater than minimal risk.

However, there is likely to be some hesitancy in setting this at 16 years, as has been done under the MHUCTR. If this corresponds to the universal age of transactional majority, then this arguably corresponds with a larger societal judgment about an appropriate point at which individuals are deemed to 'come of age'. Jurisdictions are likely to differ on this, perhaps reflecting different cultural attitudes towards adolescents and the usual course of adolescent development in a particular society. However, if the decision is based on an analogy drawn with consent to medical treatment, then there is cause for concern. Non-beneficial research participation offers no compensating direct benefit when compared to a therapeutic intervention. Participants may lack the protection of the advice of an attending physician professionally bound to act in their best interests. Even then, physician-investigators face an inherent conflict in serving the interests of their patients and their own interests in recruiting sufficient participants or their commitment to protocol observance. In short, it may not be prudent to assume that young people at 16 years of age are ready for the challenges posed by such research participation, especially when the risks are more than negligible and potentially grave.

D. The Role of Independent Research Oversight

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216 *Cf. Collogan & Fleischman, ibid. at 94.*
217 See, for e.g., the example given by 45 C.F.R. §46.408(c) (2006).
219 *Smoking (Control of Advertisements and Sale of Tobacco) Act (Cap. 309, 2003 Rev. Ed. Sing.), s.10.*
220 *Medical (Therapy, Research and Education) Act (Cap. 175, 1985 Rev. Ed. Sing.), s.3.*
221 *Enlistment Act (Cap. 93, 2001 Rev. Ed. Sing.), s.10.*
222 See *supra* note 131.
The third pillar of the decision-making process is the independent evaluation by a research ethics committee or IRB of the ethical soundness of a research protocol. The IRB evaluation serves a social oversight function, ensuring that the particular risk profiles and informed consent process cohere to the ethical principles governing HSR before parents and competent minors are recruited. Independent IRB review is a well-established legal requirement in Singapore for clinical trials and an emerging ethical requirement for all human subject research that involves direct intervention or interaction with the physical body of a research participant. In respect of clinical trials, this currently involves evaluation first by a hospital-based ethics committee, and subsequently by a national Medical Clinical Research Committee appointed by the Minister for Health.

In contrast, HSR apart from clinical trials currently lacks a statutory regime of governance. Indirect regulation via professional ethical guidelines however requires hospitals and healthcare professionals undertaking research to ensure ethical review by an institution-based ethics committee. The recent BAC guidelines for IRBs reemphasises this fundamental requirement and extends it to all investigators regardless of professional affiliation, but the report makes clear that it lacks legal force. Furthermore, while the BAC has expanded the recommendations governing the function, constitution and procedures of IRBs in Singapore, procedural guidelines on vulnerable populations have thus far not received any detailed attention beyond the general exhortation to pay particular attention to the protection of such persons. Quite apart from a more coherent articulation of substantive legal and ethical principles at play, it is argued that decision making procedures are equally important and also need revision in order to better achieve the welfare objectives in research involving minors.

An important first step in this direction would be the establishment of a national oversight committee focussed on the interests and needs of vulnerable persons, and minors in particular. Existing guidelines envisage research governance within a ‘flat’ structure of IRBs, without further extra-institutional ethical oversight or review. As evident from the foregoing discussion, standards on risk ceilings and childhood competency are still relatively general in nature. They require further specification in the light of experience derived from actual research protocol review, and further research into community standards on charitable activities and minor decision-making competency. Such specification needs to proceed in reflective equilibrium with the particular judgments of investigators and IRBs made on every new research project involving minors devised. As discussed, “minimal risk” is a broad concept that needs to be tested by community standards as to acceptable levels of risk associated with educational and altruistic endeavour on the part of minors. If so, IRB processes and evaluations cannot be isolated and opaque if our ethical and legal understanding of this area is to develop. IRBs should therefore be required to provide reasoned decisions for approving or disallowing research concerning minors, at least in respect of protocols that pose greater than negligible risk. This would

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224 Supra note 27.
226 SGGCP, supra note Error! Bookmark not defined. at 8, para 1.37.
227 BAC, Guidelines for IRBs, supra note 48 at para. 2.20.
229 Ibid. at para. 3.9 and 3.25 respectively.
230 Ibid. at para. 4.17(d).
231 Ibid at paras. 5.12-5.17: Although institutions may share IRBs or refer protocols to an IRB established by a parent organisation, these IRBs are still, by definition, principally institution based.
232 See Wendler, supra note 101 at 40-41.
233 See Scott et al, supra note 194; Steinberg & Cauffman, supra note 201.
exclude most run-of-the-mill observational studies and therefore keep IRB workloads manageable.

Such decisions could then be reviewed and disseminated by the national committee, in order to promote more consistent application by various IRBs and improve future assessments by gradually ‘filling’ out the broad standards articulated above based on the collective experiences and judgments of individual IRBs. Furthermore, in a small research jurisdiction like Singapore, individual institutions are unlikely to possess or have the resources to develop the necessary expertise to review specialist issues related to research involving minors. It would improve ethics review if IRBs in doubt could refer difficult issues to a national committee, which can better pool relevant expertise for cases deserving more careful scrutiny, whilst providing the initiative for ongoing review of applicable standards and guidelines. Finally, a national committee would have greater independence from institutional interests and agendas, and therefore promote better accountability in ethical evaluations of research projects that affect the welfare of minors.

V. CONCLUSION

In conclusion, it is ethical and should be lawful for parents and legal guardians to enrol minors in non-beneficial research, in exercise of their responsibility and discretion over the child’s development. The law should provide a clearer standard on the boundaries of this authority to guide these decision-makers, based on what a responsible parent should do in the circumstances. This standard more specifically reflects a multi-layered approach to risk ceilings in non-beneficial research, which permits minor participation where the risks:

(a) are negligible, acknowledging their reciprocal beneficent obligation to contribute to the furtherance of paediatric medical knowledge and therapy;

(b) are commonly associated with intentional parental interventions for the purpose of discipline or moral development; and

(c) exceed those in (b) but do not present a real risk to the primary goods or developing autonomy interests of the minor, which are justified in part by the minor’s capacity to understand and value the charitable or altruistic endeavour reflected in research participation.

In respect of decision making authority, a dual consent model is proposed in respect of non-beneficial research participation that involves risk exceeding those in senses (a) and (b) above. Where minors possess capacity to provide informed consent in accordance with current legal standards of competence, both parent and minor must consent to participation. Where this is not the case, or if insisting on parental consent would practically render the research impossible, then a functionally competent minor should be allowed to give independent consent to participate. The chronological age at which minors acquire independent decision making authority without the need for parental permission should be reviewed and perhaps revised downward to 18 years. Finally, their independent right to consent to or refuse research participation where risks are determined to be minimal in senses (a) and (b) above could also be tied to a chronological threshold in order to streamline recruitment procedures and reduce the need to assess minor competence individually. Ideally, this threshold should be based on empirical studies done locally.

235 Kopelman, supra note 126 at 757.
Even where minors do not possess sufficient functional decision making capacity, they should be involved in the process to the extent that their capacity permits by obtaining their assent. What procedures these entail are best left to IRBs and investigators to formulate based on professional best practices developed in the light of research on minors’ cognitive and independent decision making capacity development. Minor assent should not necessarily be binding, but the persistent dissent of a minor to participation affects risk assessment and should be a strong indication that enrolment is imprudent.

Finally, in order to enhance the application of these standards and processes, the structure of research oversight should be modified in respect of research involving minors. A national oversight committee with adequate resources and expertise should be established to review IRB decisions in respect of such research, with greater transparency and publicity of these decisions. This will hopefully facilitate a more reflective collective decision making process that enhances the overall welfare of minors in the conduct of research that is very much needed to promote their welfare.