Session 2: The Impact of Medical Research on Children

Does the Legal System Provide Adequate Protection for Children in Scientific Experiments? The Unanswered Question of Grimes v. Kennedy Krieger Institute

DR. WILLIAM J. WENNER

A child’s participation as a subject in a scientific experiment generates ambiguous feelings\(^1\) and conflicts of values.\(^2\) Experimentation on children has led to the discovery of overwhelming health benefits, including the obliteration or amelioration of threats of smallpox, measles, and other

---

\(^*\) Dr. William J. Wenner is a 2004 graduate of the University of California, Davis, School of Law, and is the former Director of Medical Quality for the Children’s Hospital of Philadelphia. He obtained a B.S. in biology at the University of Scranton, and a M.D. from Penn State University. He has been on the faculty at Penn State and the University of California, Davis, and has published over 30 articles and chapters in the fields of pediatrics and managed care, including THE PEDIATRICIANS MANAGED CARE MANUAL (Total Learning Concepts, Inc. 1999).


previously fatal childhood infectious diseases. 3 Yet history documents episode after episode of the appalling abuse of children in the name of the advancement of science. 4 A child can be remarkably vulnerable when participating as a subject in an experiment. 5 The child’s ability to speak and defend herself is by nature, and the law, severely limited. The parent, guardian, or the person conducting the experiment may be motivated by rewards rather than the child’s best interest. 6

The modern legal system has attempted to prevent such abuse and protect children through legislative action, regulatory structures, and the occasional judicial action. The legislative and regulatory approach has been one of pragmatism, reflecting a desire to provide some protection without unduly interfering with the advancement of knowledge. The judicial approach has been grounded in the common law’s respect for personal autonomy. 7 In 2001, the first judicial opinion to directly comment on the legality of experimentation on children was issued. 8 In Grimes v. Kennedy Krieger Institute, the tension between the pragmatic and the protective positions is evident. The Maryland Court of Appeals not only criticized the safeguards used by a noted academic institution when it placed children in a lead-contaminated environment for scientific purposes, but the

---

6 See Alexander M. Capron, Legal Considerations Affecting Clinical Pharmacological Studies in Children, 21 CLINICAL RES. 141, 146 (1972); Lederer & Grodin, supra note 4 at 11-18.
7 1 WILLIAM BLACKSTONE, COMMENTARIES 125. See also Kendall Ann Desaulniers, Legislation to Protect the Decisionally Incapacitated Individual’s Participation in Medical Research: Safety Net or Trap Door? 13 REGENT U. L. REV. 179, 215-221 (2000).
court also had significant concerns regarding the ethics of the research.  

The dearth of judicial opinions, the findings of the court in *Grimes*, the response of the research and regulatory community to *Grimes*, the ambiguities of current regulations, and the continuing evidence of adverse effects on children in scientific experiments all suggest a need to re-evaluate the legal protections offered to children involved in human experimentation.

*Grimes v. Kennedy Krieger Institute*

In *Grimes*, the plaintiffs of two separate actions had enrolled in a lead-paint abatement research program at Kennedy Krieger Institute, a prestigious research institute in Baltimore that is associated with Johns Hopkins University. Kennedy Krieger Institute is considered by the overall medical community to be the pioneer in lead poisoning treatment and prevention. The study was funded through sources such as the Environmental Protection Agency and the U.S. Department of Housing and Urban Development. The research study was designed to include five test groups, each consisting of 25 houses. Three groups consisted of houses with a considerable amount of lead dust in which different levels of abatement would be performed by the landlords and owners according to Kennedy Krieger Institute’s previously tested abatement methods, known as “alternative abatement methods” (alternatives to full abatement). The fourth group of houses had lead-based paint, but had the lead abated prior to enrollment and not as part of the study. The fifth group consisted of modern houses that never had lead dust.  

---

9 *Id.*

10 *Id.* at 811-12.


12 *Id.*

13 *Grimes*, 782 A.2d at 820.

14 *Id.* at 821; Pinder, *supra* note 11 at 477.

15 *Grimes*, 782 A.2d at 820.

16 *Id.*
The study was designed to do less-than-comprehensive lead paint cleanup in order to study the partial abatement’s potential effectiveness on preventing children’s exposure to lead. The study would, in theory, help determine if less expensive methods of making lead reduction in homes with children were equally effective as complete abatement.

The first plaintiff – Erika Grimes, a 10-month girl – was enrolled in the study by her mother after representatives of Kennedy Krieger Institute recruited her in March 1993. As part of the study she was to remain in her current home. She was considered to be one of the study’s “control groups” (Group 4, a residence where lead was abated prior to the study). Prior to the study, all lead dust had been previously removed from her house and no further repair or maintenance was done while the house was enrolled in the study. The first measurement during the study of lead in the house dust revealed levels higher than those of a completely abated house. The family was not told of these results until nine months after the sample was collected, and not until after the child’s blood was found to contain elevated levels of lead.

In her complaint filed in the Baltimore circuit court, Hughes sought to hold the Institute liable for negligence for failing to warn of, or abate, lead-paint hazards that the Institute allegedly discovered in the property during the study. The Institute then filed for summary judgment on the grounds the Institute did not owe a duty to the appellant. On July 26, 2000, the circuit court granted the Institute’s motion.

The second plaintiff – Myron Higgins, a four-year-old girl – was recruited into the study in May 1994. She lived in
a property that was not completely free of lead, one of the “study” groups. Dust samples collected immediately prior to enrollment revealed elevated lead levels. The plaintiff, however, contended they were not informed of the elevated levels until December 1994. A negligence suit was filed in the Baltimore circuit court on February 26, 1995. The Institute filed for summary judgment on the same grounds it did in the Grimes claims: The Institute did not owe any duty to Myron Higgins. On April 5, 2000, the circuit court granted the Institute’s summary judgment motion.

Both plaintiffs appealed the lower court’s decision to the Court of Appeals. The appeals court vacated the summary judgment and remanded for further proceedings. The Institute then filed for reconsideration, accompanied by amicus briefs from Johns Hopkins University, the University of Maryland Medical System, the Association of American Medical Colleges, and the Association of American Universities.

The court denied reconsideration.

In its opinion, the Maryland Court of Appeals noted that as far as it was aware, no federal or Maryland statutes mandate all research be subject to certain conditions. The judges, however, felt certain international codes, at least in theory, did establish standards. The court used, as they determined to be appropriate, those international codes; studies conducted by various government entities; treatises and other writings on the ethics of using children as research

---

26 Id. at 826.
27 Id. at 827.
28 Id. at 828.
29 Id. at 832.
32 Grimes, 782 A.2d at 815.
subjects; and the duties, if any, arising out of the use of children as subjects of research.  

The Maryland Court of Appeals highlighted the Nuremberg Code as being a source of ethics in research. This code of ethics for human research was prepared by the international tribunal that sat in judgment and convicted 23 Nazi doctors of murder, torture, and other atrocities committed in the name of medical science. While not precisely a U.S. court, it was established by the United States and its allies and four prominent American judges appointed by President Truman presided over the trial of the Nazi doctors. Some have argued the Code has the weight of a judicial decision in American courts, but no U.S. court has used it as precedent. Many of the atrocities committed by the Nazi doctors, especially those of the notorious Dr. Mengele, were experiments on children. Yet conspicuously absent from the opinion of the tribunal and its Code was any direct reference to children or pediatric research. Even absent direct reference to children, the Code might apply to children. It explicitly states as its opening clause: “The voluntary consent of the human subject is absolutely essential.”

33 Id.
34 Id. at 834-37 (providing a detailed discussion of history, legal status and application of Nuremberg Code).
37 Id.
interpreted literally, the Code would preclude research on children because children are unable to give consent.\textsuperscript{41}

Like the Nuremberg Tribunal, the Maryland Court of Appeals concluded consent was mandatory for participation in a human experiment.\textsuperscript{42} The Maryland court stated

\begin{quote}
[O]therwise healthy children should not be enticed into living in potentially lead tainted housing … [and] parents, whether improperly enticed by trinkets, food stamps, money or other items, have no more right to intentionally and unnecessarily place children in potentially hazardous non-therapeutic research surroundings, then do researchers. In such cases, parental consent, no matter how informed, is insufficient.\textsuperscript{43}
\end{quote}

In addition to concern about parents placing children at risk, the court addressed the oversight of the researchers. Commenting on current oversight methods used when children are the research subjects, the court felt the scientific and medical communities cannot be permitted to assume sole authority to determine what is right and appropriate in research projects involving young children.\textsuperscript{44}

In strong language, the court pointed out the experiments at issue presented similar problems\textsuperscript{45} as those in the Tuskegee Syphilis Study,\textsuperscript{46} the government’s intentional


\textsuperscript{43} Id.

\textsuperscript{44} Id. at 818.

\textsuperscript{45} Id. at 817.

\textsuperscript{46} \textit{The Tuskegee Syphilis Study}, 289 NEW ENG. J. MED. 730 (1973).
exposure of soldiers to radiation in the 1940s, \(^{47}\) the exposure of Navajo miners to radiation, \(^{48}\) and the government’s secret administration of LSD to soldiers by the Central Intelligence Agency. \(^{49}\)

The court also believed the current federal oversight system was flawed. Specifically, the court had concerns that the major instruments of federal oversight, the Institutional Review Boards (IRBs), are not designed to be sufficiently objective in the sense that “they are as sufficiently concerned with the ethicality of the experiments they review as they are with the success of the experiments.” \(^{50}\)

**Motion for Reconsideration**

When the Maryland Court of Appeals subsequently denied reconsideration, they noted as a matter of law that their only conclusion of summary judgment was improperly granted. \(^{51}\) But the court did take note that much of the arguments in support or against the motion for reconsideration centered on the question of what guidelines should govern the parents’ authority to provide informed consent for the participation of minor children in medical research. \(^{52}\) The court noted in the opinion that a parent, “cannot consent to the participation of a child ... in non-therapeutic research in which there is any risk of injury or damage to the health of the subject.” The court felt it was clear that by “any risk” they meant “any articulable risk beyond the minimum risk that is inherent in any endeavor.” \(^{53}\) This statement of court in its initial opinion was directed toward non-therapeutic studies that promised no medical benefit to the children whatsoever,


\(^{50}\) *Grimes*, 782 A.2d at 818.


\(^{52}\) *Id.*

\(^{53}\) *Id.*
so any balance between risk and benefit is unnecessarily negative.\textsuperscript{54} In the response to the motion for reconsideration, the court noted the determination of whether the study in question offered some benefit was open for further factual development on remand.\textsuperscript{55}

**Response of the Research Community**

During its arguments before the appellate court, the Krieger Institute asserted it did not have an obligation to warn participates about the study’s risks because neither the institution nor the researchers had a special relationship with the children in what was a potentially dangerous research study.\textsuperscript{56} The courts strongly rejected this argument. This argument was not part of any of the briefs for reconsideration.

The research and academic community responded in amici curiae to the motion for reconsideration and in academic publications regarding the Court of Appeals opinion, some in defense of the Krieger Institute and its research\textsuperscript{57} and some with guarded criticism.\textsuperscript{58} Most of the response to the opinion of the Court of Appeals, as evidenced by publications and amici curiae, focused on this issue of parental consent to non-therapeutic research.\textsuperscript{59} Some academic commentators believe that the Maryland Court of Appeals, in rejecting the petition for reconsideration, narrowed its interpretation of limits on pediatric research.\textsuperscript{60} In its original opinion, the court, by noting parents could not consent to non-therapeutic research

\textsuperscript{54} Id. at 2.
\textsuperscript{55} Id. at 1.
\textsuperscript{57} Lainie Friedman Ross, In defense of the Hopkins lead abatement studies, 30 J. L. MED. & ETHICS 50 (2002).
\textsuperscript{59} Lainie Friedman Ross, supra 57, at 50.
\textsuperscript{60} Loretta M. Kopelman, Pediatric Research Regulations Under Legal Scrutiny: Grimes Narrows Their Interpretation, 30 J. L. MED. & ETHICS 38, 41 (2002).
on their children, seemed to either be prohibiting such research or requiring another unstated mechanism of consent such as judicial approval of all such research. The wording used by the Court of Appeals in its rejection of reconsideration might imply they were retreating from this position as they chose to clarify “any risk.” However, it is just as likely the court, while acknowledging the conflict of progress versus protection, reaffirmed its commitment to the autonomy of the individual in a research study. The amici took strong issue with the language and scope of the court’s opinion with respect to the issue of parental consent, appealing that “the court should review, reconsider, and rescind that portion of the decision.”

Johns Hopkins University, the University of Maryland Medical School, the American Association of Medical Colleges, and the American Association of Universities filed amicus briefs in support of the Institute. Each took strong issue with the language and scope of the Court of Appeals’ opinion regarding the issue of parental consent for children participating in research. The University of Maryland argued:

[I]f the ruling stands, research in cases involving children and other and legally disabled individuals cannot take place in Maryland and the overall cost in terms of lost advances in medical and health knowledge and ultimately lost opportunities to cure diseases and prevent suffering and loss of life will far outweigh the asserted advantage of protecting individual rights.

But the court upheld its opinions regarding parental consent. It sent the case back to the lower court to determine

---

63 Id.
64 Id.
if the research was non-therapeutic and to balance the legal risk and benefits of the study.\textsuperscript{65}

As the original opinion of the Court of Appeal supports the primacy of the autonomy of the child, the ongoing conflict between the philosophies of the court and with the academic and research community indicates a need to re-appraise the compromises previously made on ethical issues in child experimentation. The methodology of regulation imposed on federally sponsored research was, and remains, a compromise. One of the key compromises was on the issue of who can consent to place a child at risk when there are minimal or no benefits to the child. Incidents continue to suggest the compromises of the federal regulations do not provide the needed protection for children from the risks of non-therapeutic research.

**Recent Events in Experiments on Children**

Current events may suggest flaws in the existing oversight framework for research conducted on children. Regulatory protection of children may not be meeting the needs of children and may require further judicial and legislative intervention.

Three months prior to the Maryland decision, a subject died while in an asthma study at Johns Hopkins University, the affiliate agency of Kennedy Krieger Institute. Subsequent increased scrutiny resulted in institutional improvements, but flawed studies continued to be approved.\textsuperscript{66} In a study on hormones in children, the Office of Human Research Protection of the Department of Health and Human Services, the federal agency responsible for research oversight, determined children in a Johns Hopkins study were subjected


\textsuperscript{66} Tom Pelton, Regulators encouraged by Hopkins; “Extraordinary effort” expended on reviews of medical studies; But concerns persist; 2 experiments draw agency’s criticism, 1 involving children. THE BALTIMORE SUN, Nov. 10, 2001, at B1.
to unacceptable risks. The consent forms provided to the parents failed to warn about potentially serious side effects. The study had received approval from the Johns Hopkins Institutional Review Board, and volunteers had already begun enrolling at the time of the agency’s findings suggesting the oversight provided by Johns Hopkins through its institutional review board was inadequate.

California’s attorney general investigated Stanford University’s conduct of research on 61 inmates with the California Youth Authority. When parents could not be found to provide permission, the CYA “consented” for the young men’s participation. Robert Presley – who as a California state senator had authored legislation on research in children and at the time of investigation was secretary of the Youth and Adult Correctional Agency – acknowledged: “In the legal sense, and maybe the moral sense, we missed the boat on this one.” The incident prompted a review of existing policies and the adoption of new ones, including the establishment of a Research Project Review Committee by the Youth Authority.

The University of Pennsylvania’s Institute of Human Gene Therapy was ordered to halt gene therapy experiments following the death of a young man participating in a study. The patient suffered a fatal immune-system reaction to the introduction of a modified common-cold virus after the Federal Drug Administration discovered “a number of serious problems in the Institute’s informed consent procedures and, more generally, a lapse in the researchers’ ethical

---

67 Id.
68 Id.
69 Id.
71 Id.
72 Id.
75 Id.
responsibilities to experimental subjects.” A study at the New
York State Psychiatric Institute and three other hospitals
recruited the brothers of adolescents who had been arrested for
various crimes.\textsuperscript{76} As part of the study, the children were given
a dose of the drug fenfluramine – later used for weight loss
and possibly associated with heart damage\textsuperscript{77} – to help
measure levels of a brain hormone related to antisocial
behavior.\textsuperscript{78} While the researchers and the institutional
oversight board concluded it was an appropriate study under
federal regulations, critics were concerned the children in the
study had no known illness.\textsuperscript{79} The researchers also offered a
$100 inducement to the child’s parents to encourage
participation. The researchers also approached children
directly, offering them $25 gift certificates for toys and telling
them by participating they would earn money for their
families.\textsuperscript{80}

In each of these examples, the internal oversight group,
the institutional review boards, had determined the research
was appropriate under current guidelines.

\textbf{Evidence of Systemic Problems with Pediatric Research}

The failure to protect children in research appears to
be more problematic than the few incidents reported in the
mainstream press. A study published in 2002 found 65
percent of published research on children did not comply with
federal requirements for consent or review.\textsuperscript{81} This lack of
compliance occurs despite the existence for more than 20
years of federal regulations and voluntary professional

\textsuperscript{76} Rick Weiss, \textit{Volunteers at Risk in Medical Studies; Complex Research
\textsuperscript{77} Id.
\textsuperscript{78} Id.
\textsuperscript{79} Id.
\textsuperscript{80} Id.
\textsuperscript{81} Eric Weil, Robert M. Nelson & Lainie Friedman Ross, \textit{Are Research
Ethics Standards Satisfied in Pediatric Journal Publications?} 110
PEDIATRICS 364 (2002).
guidelines stipulating compliance with the regulations as a requirement for publication.\textsuperscript{82}

A 2004 study found even when researchers follow the regulations protecting children, the application of the rules varies significantly.\textsuperscript{83} Often the institution’s interpretation is “contradicted by the available data on risks and the regulations themselves.”\textsuperscript{84} Dr. Robert Nelson, a national expert on pediatric research and bioethics, noted:

There exists an unacceptable variability in the interpretation and application [of Federal Research Regulations] indicating a failure to understand the moral underpinnings of the restrictions on the risk exposure for children involved in research.\textsuperscript{85}

Further evidence of ambiguity regarding the application of federal regulations – and possible risk to children – is suggested by the observation that while the federal regulations require institutions to request the approval of the secretary of the Department of Health and Human Services prior to certain high risk experiments, in the 20 years of existence, the institutional review boards had submitted requests fewer than 10 times.\textsuperscript{86}

\textbf{The Federal Regulations Regarding Experiments on Children}

Human subjects in experiments are generally protected by the so-called “Common Rule.”\textsuperscript{87} The Common Rule is

\textsuperscript{82} Id.
\textsuperscript{84} Id.
\textsuperscript{85} Nelson, \textit{supra} note 58, at 449 (2002).
\textsuperscript{86} Clifford C. Scharke, DHHS, letter to author, Apr. 9, 2002.
\textsuperscript{87} Subpart A of 45 CFR Part 46 is generally called the “Common Rule.” It has been adopted by many other Federal departments and agencies. 45 C.F.R. § 46.101 (2003).
composed of the set of regulations set forth in the Federal Regulations. These regulations apply to federal agencies and departments that fund or are otherwise involved in research involving human subjects. They also apply to entities that receive federal research funds or participate in federally funded research. Entities with federal funding document their adherence to the regulations by filing a required assurance of compliance with the Office of Human Research Protections (OHRP) of the Department of Health and Human Services.

The Common Rule, however, does not include the regulations that safeguard children in experiments. The regulations for children are contained in Subpart D, and were adopted by Health and Human Services on March 8, 1983, and subsequently amended on June 18, 1991. Because the regulations in Subpart D are not part of the Common Rule, the other signatory departments and agencies that have adopted the Common Rule have not universally shared them. The Children’s Health Act of 2000 corrected this incongruity when it required all research conducted, supported, or regulated by Health and Human Services to be in compliance with Subpart D.

Both the Common Rule and Subpart D regulations build their protection of research subjects upon two foundations: informed consent and oversight by an internal institutional review board (IRB). Since children are not legally competent to provide consent, the federal regulations require that, when the child is capable, assent must be solicited. In addition, the permission of each child subject’s

---

90 Id.
94 Id.
96 45 C.F.R. § 46.103(b) (2003).
97 45 C.F.R. § 46.408(a) (2003).
When research involves more than minimal risk to the child and there is no prospect of direct benefit to the child or research not otherwise approvable under the regulations, permission must be sought from both parents.

The institutional review board, usually part of the institution conducting the research, consists of a minimum of five members, with varying backgrounds that promote complete and adequate review of all research activities commonly conducted by the institution. The review board is required to pay special care to the needs of vulnerable populations (e.g., children, prisoners, disabled, pregnant women, economically disadvantaged). The foundation of the protections for children in research studies, found in the Federal Regulations is a complex interaction of factors: (1) risk to the child, (2) benefit to the child, (3) benefit to other children with similar conditions, and (4) the child’s ability to assent to the project.

These complex interactions allow the institutional review board to categorize research on children into one of four types: (1) research not involving greater than minimal risk, (2) research involving greater than minimal risk but presenting the possibility of direct benefit to the subject, (3) research involving greater than minimal risk and no prospect of direct benefit to individual subjects not likely to yield generalizable knowledge about the subject’s disorder or condition, and (4) research not otherwise approvable that

---

98 45 C.F.R. § 46.408(b) (2003).
100 45 C.F.R. § 46.408(b) (2003).
presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.\footnote{108}

\textit{Conflict from the Beginning: The Origin of the Federal Rules}

The Subpart D regulations are based on the recommendations developed by the National Commission for The Protection of Human Subjects of Biomedical and Behavioral Research.\footnote{109} Known as the National Commission and established in 1974,\footnote{110} research on children was one of several subjects to which the Commission paid particular attention.\footnote{111} The Commission's objective was to answer two questions: (1) under what conditions is the participation of children in research ethically acceptable, and (2) under what conditions may such participation be authorized by the subjects and their parents?\footnote{112}

The Commission was unanimous on most of its recommendations.\footnote{113} The final report, however, reflected a significant difference of opinion on the participation of children in research when the child receives no direct benefit, often called non-therapeutic research.\footnote{114} Two of the 11 commissioners wrote dissenting opinions on the issue of non-therapeutic research with children.\footnote{115} One of the two dissenters was the Commission’s sole attorney, Robert Turtle.\footnote{116}

\footnote{111} OHRP, supra note 109, at 3.
\footnote{112} Id.
\footnote{113} National Commission, supra note 110, at 123.
\footnote{114} Id. at 7, 123.
\footnote{115} Id. at 123.
\footnote{116} Id.
Commissioner Turtle felt the Commission’s approval of an oversight mechanism for research with no foreseeable benefit was a “clear error.” He wrote: “[The proposed regulations for allowing non-therapeutic research] were shams and there is no legal, ethical or social basis for subjecting sick children to more than minimal risks merely because a foreseeable benefit might accrue to an identifiable class of children in the future.” This is the precise issue in *Grimes* and while not cited by the Maryland Court of Appeals, the concerns of the commissioners are a reflected in the *Grimes* opinion. The recommendation to which some of the commissioners objected did serve as the basis of the relevant federal code: “Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition.”

**Ambiguity of Interpretation of Current Federal Regulations**

The regulations do not define terms critical to the protection of the children such as “minor increase over minimal risk,” “likely to yield,” or “reasonably commensurate with those inherent in their actual [life].” The lack of definitions has resulted in widespread differences in how and what research the institutional review boards approve. Chairpersons of the review boards are unable to agree on what is defined as risk, as illustrated in their classification of certain common research tests on children. When asked to classify allergy skin testing (which requires multiple small injections into the skin), 23 percent of review boards classified this test as minimal risk, 43 percent as a minor increase over minimal risk, and 27 percent as more than a minor increase over minimal risk. Another example of widespread differences involves a spinal tap (an insertion of a needle into the space surrounding the spinal cord to withdraw fluid) in an otherwise

---

117 Id. at 146.
118 Id. at 147.
120 See Shah et al., *supra* note 83; Weil et al., *supra* note 81.
121 Shah et al., *supra* note 83, at 479.
healthy child without sedation: two percent of the review boards considered it minimal risk, 16 percent a minor increase, and 78 percent more than a minor increase.\textsuperscript{122} There is similar confusion as to what is considered a benefit to the participant, as 10 percent of review boards felt payment was a direct benefit justifying research, 60 percent considered additional psychological counseling a direct benefit in justifying research,\textsuperscript{123} and added medical examinations were considered a benefit by 51 percent.\textsuperscript{124} The comments by the original commissioners do not suggest these factors are benefits.\textsuperscript{125} There seems to have been an expansion of acceptable elements and a lessening of the protection by those assigned the oversight, the review boards.

It is possible to conclude the lack of clear guidelines has allowed a gradual erosion of the protection intended by the regulations. It is difficult to imagine that over 20 years, only 10 proposed research projects met the criteria to require review and approval of the secretary of Health and Human Services.

\textit{Federal Recognition of the Regulatory Ambiguity}

The Children’s Health Act of 2000, which mandated the regulations that protect children apply to all federal agencies also directed the secretary of the Department of Health and Human Services to conduct a review of the regulations under 45 C.F.R. part 46 Subpart D.\textsuperscript{126} In accordance with this directive, the OHRP consulted experts in relevant fields and issued a report to Congress.\textsuperscript{127} The report concluded the current regulations are sound and effective, and well-crafted when institutional review boards properly implement them and investigators provide adequate and appropriate protections for children of all ages and maturity

\begin{itemize}
\item \textsuperscript{122} \textit{Id.}
\item \textsuperscript{123} \textit{Id.} at 478.
\item \textsuperscript{124} \textit{Id.}
\item \textsuperscript{125} See National Commission, \textit{supra} note 110, at 151-53.
\item \textsuperscript{126} 42 U.S.C. 42 U.S.C. § 289 (2003); OHRP, \textit{supra} note 109.
\item \textsuperscript{127} 42 U.S.C. § 289 (2003).
\end{itemize}
The report, however, suggested Health and Human Services provide additional guidance on certain terms and concepts, such as “the prospect of direct benefit for the individual subject,” “the parameters for defining a “minor increase over minimal risk,” and the proper procedures for recruiting children into research and providing them and their parents with some type of payment. The report to Congress clearly recognized the ambiguity at the heart of the regulatory protections of research on children. Unfortunately, this ambiguity has not been eliminated.

**Ambiguity over Parental Consent**

The federal regulations clearly state that except in rare circumstances, like research on child abuse, parental permission must be solicited prior to a child’s participation in research. The regulations do not use the word “consent,” neither do they specifically state parental permission fulfills the functions of legal informed consent nor do the regulations expressly override or invalidate state law on parental consent. Further, the regulations do not provide protection for when the parent’s interest is in conflict with the child’s best interest. This could occur when a parent’s consent is influenced by financial incentives.

There is little state or federal law, legislative or judicial, that applies to consent for non-therapeutic research in “decisionally-impaired” individuals. It is generally held children lack the legal ability to give proper informed

---

128 Id. at iii.
129 Id.
130 Id.
131 Id.
132 45 C.F.R. § 46.408(c) (2003).
133 45 C.F.R. § 46.408(b) (2003).
134 See Grimes, 782 A2d at 844.
consent.\textsuperscript{136} Some states have statutes requiring judicial approval or approval of a court appointed guardian for those who are decisionally-impaired.\textsuperscript{137} But these statutes do not explicitly address the issue of parental consent for children.\textsuperscript{138} In fact, most states have no statute that explicitly confers permission to the parents to consent to research for their child.\textsuperscript{139}

There is some indication of judicial precedent that non-therapeutic operations and procedures can be legally permitted on a minor as long as the parents or other guardians consent to the procedure. These cases were unique circumstances. In 1941, in \textit{Bonner v. Moran}, in an action for battery and assault, a District of Columbia court was asked if adequate consent was given for a 15-year-old child to undergo skin grafting for his cousin.\textsuperscript{140} The child had been “volunteered” as a skin donor by his aunt after his cousin who had been severely burned.\textsuperscript{141} The mother had not been informed and brought the action after she became aware that during the procedures, her child had suffered severe complications during his two-month hospitalization.\textsuperscript{142} The court held parental consent was necessary and the jury should have been so informed.\textsuperscript{143} It has been argued that in \textit{Bonner}, the court seemed to assume a de facto right of the parent to consent to procedures not for the benefit of the child.\textsuperscript{144} However, others have felt this is a “gross over-reading” of the holding and the court did not find an explicit authorization to

\textsuperscript{137} See \textit{Hoffman et al.}, \textit{ supra note 135}, at 126.
\textsuperscript{138} See \textit{CAL. HEALTH & SAFETY CODE} § 24175 (West 2003).
\textsuperscript{139} See \textit{Hoffman et al.}, \textit{ supra note 135}, at 126.
\textsuperscript{140} \textit{Bonner v. Moran}, 126 F.2d 121 (D.C Cir. 1941).
\textsuperscript{141} \textit{Id.} at 121-23.
\textsuperscript{142} \textit{Id.}
\textsuperscript{143} \textit{Id.}
parents to independently volunteer children for non-therapeutic procedures.\footnote{145}

In \textit{Hart v. Brown}, in 1972, after physicians refused to remove a kidney from a healthy twin for transplant into the twin with a malfunctioning kidney, a Connecticut court was asked for a declaratory judgment concerning the right of the parents of the twins to consent to this non-therapeutic operation and its inherent risks.\footnote{146} The court cited \textit{Bonner} and three unpublished Massachusetts cases in support of the principle that a parent could subject their child to non-therapeutic procedures.\footnote{147} In all the cited cases, a child was to undergo a risky procedure with no direct benefit to the child but a close relative would benefit. While the court considered the desires of the parents, they felt because the procedure was needed by the ill child, the parents’ consent was sufficient and a court order was not needed.\footnote{148} The court also discussed the extensive process that the parents and the court had undertaken.\footnote{149} They noted it appeared “the natural parents would be able to substitute their consent for that of the minor children after a close, independent and objective investigation of their motivation and reasoning.”\footnote{150}

These precedents do not involve research on children. Each procedure was for the benefit of a close relative that the child knew. In each, it was presumed there was a high probability of success for the recipient and low risk to the donor.\footnote{151} By definition, non-therapeutic research, in addition to offering no direct benefit, may only benefit unknown subjects and has an unknown probability of success.

When the New York Appellate Court in \textit{T.D. v. New York State Office of Mental Health}, held regulations affecting

\begin{footnotes}
\footnote{145}{See A. Capron, \textit{Legal Consideration Affecting Clinical Pharmacological Studies in Children}, 21 \textit{CLINICAL RES.} 141 (1973); Mitchell, supra note 3, at 919.}
\footnote{147}{Id.}
\footnote{148}{Id. at 387.}
\footnote{149}{Id. at 390.}
\footnote{150}{Id.}
\footnote{151}{Id.}
\end{footnotes}
mental health research in the state of New York were invalid, the court addressed the secondary issue of parental consent for minors to participate in nontherapeutic research that may be potentially harmful.\textsuperscript{152} It held: “a parent or guardian, let alone another adult who may be a member of the child's family, may not consent to have a child submit to painful and/or potentially life-threatening research procedures that hold no prospect of benefit for the child.”\textsuperscript{153}

The New York court noted their finding did not comport with the Federal Regulations regarding research supported by federal funds, and noted their holding only applied to research not funded with federal money.\textsuperscript{154}

Addressing the issue of child labor and religious freedom in \textit{Prince v. Massachusetts}, the U.S. Supreme Court held: “parents are free to become martyrs themselves. But it does not follow they are free...to make martyrs out of their children before they reach the age of full and legal discretion when they can make that choice for themselves.”\textsuperscript{155}

Extending this reasoning to scientific research, the court might conclude that even if motivated by a desire to help humanity through the advancement of medicine, parents might not have the right to determine their children should be the ones required to make the sacrifice.\textsuperscript{156}

\textbf{Conclusion}

The ambiguity of regulatory protections, the ambiguity in state and federal courts over the status of parental consent for non-therapeutic research on children, and recent events demonstrating that children have been placed in jeopardy through research have again focused attention on the

\textsuperscript{152} \textit{T. D. v. New York State Office of Mental Health}, 650 N.Y.S.2d 173, 173.
\textsuperscript{153} \textit{Id.} at 191-92.
\textsuperscript{154} \textit{Id.}
\textsuperscript{155} \textit{Prince v. Massachusetts.}, 321 U.S. 158, 170 (1944).
\textsuperscript{156} \textit{See} Mitchell, \textit{supra} note 3 (advocating application of Supreme Court standard of \textit{Prince v. Massachusetts} to research on children).
protection of children in research projects involving human experimentation.

Over 20 years has passed since the federal regulations regarding pediatric research were promulgated. While the current situation is nowhere near the environment that led to so many abusive events in the past, federal regulations still are not mandated for all research on children, are applied in situations closed to the public, are overseen by boards connected to the research institutions, and are not understood by the oversight boards who apply the regulations. These ambiguities may have contributed to the disturbing events in the news today.

When the current regulations were drafted, there was a significant difference over how to protect children in non-therapeutic research; that difference remains. Those involved in research and the oversight of research desire the advancement of knowledge and will often advocate for liberal protective mechanisms. Conservative perspectives on protection are more frequently reflected in the legal and judicial perspective of individual autonomy, as evidenced in the Maryland Court of Appeals decision in *Grimes v. Kennedy Krieger Institution*. Until the difference is resolved or at least the gap further narrowed, children in research and those who conduct it will continue in the no-man’s land of ambiguity. And the protection of those who can not speak for themselves, who are at greatest risk of abuse by research, will remain suboptimal.