
MEDICAL RESEARCH AND INTANGIBLE HARM

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ABSTRACT

Conventional wisdom assumes that human subjects participating in medical research face significant risk of pain, disability, and death. In fact, evidence suggests that, in the aggregate, research subjects fare as well therapeutically as patients with similar conditions not participating in clinical trials. Research subjects do, however, face unappreciated risk of intangible harm, even if not physically injured. Such intangible hazards include frustrated access to investigational technology, affront to dignitary interests, and participation in a study that fails to disseminate meaningful data in order to advance medical knowledge. This Article considers whether the intangible hazards faced by subjects should be cognizable to a greater degree. A more flexible approach has considerable advantages, including strengthening the needed respect for subjects as persons with individual dignity, remedying problematic informed consent, policing opportunistic conduct in the investigator-subject relationship, and promoting trust in research, an independent, socially important goal. At the same time, providing more robust remedies for a much wider range of intangible harm claims, while appealing for these reasons and for ethical considerations, remains difficult to reconcile with current case law doctrine and regulatory approaches, threatens to deter useful research activity, and poses numerous pragmatic problems as a legal matter, such as defining boundaries for such claims. This Article balances the competing considerations and concludes by arguing for a limited expansion in recognizing research subjects' intangible harm claims. One application is to address particularly problematic enrollment encounters where question exists whether a subject understood she participated in research at all. A second, related area would use broader intangible harm remedies to address abandonment hazards, such as when investigators and research sponsors readily frustrate and potentially

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exploit subjects' assumptions regarding study terminations and continued access to experimental technology. Similarly, subjects may be wrongfully abandoned, even if not physically injured, when the study fails to contribute to general medical knowledge through the public dissemination of research results. Such conduct forsakes and deserts subjects by disrupting their reasonable expectations and disregarding their considerable personal investments in clinical trials. Such conduct also raises serious concerns for the research enterprise generally, thus warranting greater recognition and sanction as legally cognizable harm.

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INTRODUCTION

Medical research with human subjects is booming. Private sector funding has more than tripled since the mid-1980s,¹ alongside generous

1. See Patricia C. Kuszler, *Curing Conflicts of Interest in Clinical Research: Impossible Dreams and Harsh Realities*, 8 WIDENER L. SYMP. J. 115, 118–19 (2001) (noting an increase in private sector funding from \$6 billion to \$19 billion).

federal support,² resulting in billions of dollars spent on clinical trials each year.³ The staggering number of investigations, approximately sixteen thousand to twenty thousand studies conducted annually, continues to grow in size and overall complexity.⁴ More than nineteen million individuals are estimated to have enrolled in medical experiments,⁵ with more than two million participating each year.⁶

By some accounts, this explosive increase in research activity should be cause for alarm. While clinical trials contribute to the improvement of therapeutic care, experimentation presents unknown hazards.⁷ Bioethics and health law emphasize research subject protection as essential to the appropriate conduct of medical experimentation.⁸ Yet, recent subject deaths at leading academic medical centers, such as the University of Pennsylvania⁹ and Johns Hopkins University,¹⁰ have

2. See NAT'L RESEARCH COUNCIL, TRENDS IN FEDERAL SUPPORT OF RESEARCH AND GRADUATE EDUCATION 4 (Stephen A. Merrill ed., 2001), available at <http://www.nap.edu/openbook/0309075890/htm/R1.html>.

3. See Wendy K. Mariner, *Human Subjects*, NAT'L L.J., May 13, 2002, at A25.

4. See Philip J. Hiltz, *In Tests on People, Who Watches the Watchers?*, N.Y. TIMES, May 25, 1999, at F1 (discussing General Accounting Office estimates). See also Lars Noah, *Informed Consent and the Elusive Dichotomy Between Standard and Experimental Therapy*, 28 AM. J.L. & MED. 361, 361-62 (2002).

5. Dan Vergano, *Drug Trial Deaths Go Unreported*, USA TODAY, Nov. 8, 2000, at 12D.

6. See Mariner, *supra* note 3, at A25 (referring to 2001 data). Some clinical trial activity estimates are even higher. CenterWatch, a patient advocacy group, reports that eighty thousand clinical trials have been conducted annually. See Michael D. Lemonick & Andrew Goldstein, *At Your Own Risk*, TIME, April 22, 2002, at 46. And Adil Shamoo, a University of Maryland bioethicist, suggests that approximately twenty million subjects were enrolled in clinical trials in 2001. See *id.*

7. See Frances H. Miller, *Trusting Doctors: Tricky Business When It Comes to Clinical Research*, 81 B.U. L. REV. 423, 437 (2001).

8. See, e.g., NAT'L COMM'N FOR THE PROT. OF HUMAN SUBJECTS OF BIOMEDICAL & BEHAVIORAL RESEARCH, THE BELMONT REPORT: ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH (1978) [hereinafter BELMONT REPORT], reprinted in INSTITUTIONAL REVIEW BOARD: MANAGEMENT AND FUNCTION 492, 494, 497 (Robert J. Amdur & Elizabeth A. Bankert eds., 2002). The influential Belmont Report emphasizes the principle of beneficence as one of the guiding ethical principles for medical research. The pursuit of beneficence requires maximization of benefits and minimization of harms to subjects and requires a commitment to protecting subjects. See *id.* See also 45 C.F.R. § 46.103(b)(1) (2005) (requiring institutions conducting research funded by the Department Health and Human Services to file assurances detailing the institution's commitment to "protecting the rights and welfare of human subjects").

9. In 1999, Jesse Gelsinger died after participating in a gene therapy study at the University of Pennsylvania. Numerous problems with oversight of the trial were later identified, including that investigators enrolled him in the study although he did not meet the criteria for eligibility, alleged failure to inform Gelsinger about previous subjects' deaths and the death of animal subjects that had received the technology, and alleged failure to tell him about the investigator's and University's financial interest in the experimental technology. See generally Jesse A. Goldner, *Dealing With Conflicts of Interest in Biomedical Research: IRB Oversight as the Next Best Solution to the Abolitionist Approach*, 28 J.L. MED. & ETHICS 379, 379 (2000); Sheryl Gay Stolberg, *The Biotech Death of Jesse Gelsinger*, N.Y. TIMES MAG., Nov. 28, 1999, at 136.

significantly shaken public confidence. Critical government reports have concluded that the current monitoring system suffers from patchwork coverage and lacks sufficient resources, leaving subjects exposed to danger.¹¹ Indeed, the research enterprise endures a painful crisis period.¹² At this critical juncture, a common refrain is that “all research subjects deserve better protection.”¹³

But protection from what exactly? Of the more than two million research subjects enrolled in clinical trials each year, how many really experience harm? And what kinds of harm? Lost in the general debates about “research subject protection,” an elusive and vague concept, has been a sufficiently serious consideration of the extent and different types of harms faced by research subjects. Current academic commentary features robust discussion of duties and rights arising in medical experiments.¹⁴ One must be careful not to skip over such necessary threshold questions. But it is also of paramount importance to focus more attention on pragmatic questions of injury and redress, evaluating the different hazards that research subjects actually face and what they realistically can do about them. Reversing the ordinary order of analysis helps to make overlooked subject harm more visible, forcing reconsideration of the appropriateness and practical availability of remedies for such risks.

Accordingly, this Article delves into the harm problem in detail. It explores the issue from the much misunderstood and increasingly controversial vantage point of intangible harm. A research subject faces a range of serious potential hazards that may materialize even if

10. In 2001, Ellen Roche, a healthy subject, died after participating in a Johns Hopkins University trial studying the effects of nebulized hexamethonium on the physiology of asthma. Numerous problems were identified with oversight of the trial, including the use of boilerplate consent forms that failed to mention that the Food and Drug Administration had not yet approved the drug and that failed to mention the drug's pulmonary toxicity. See generally Bette-Jane Crigger, *What Does It Mean to “Review” a Protocol?: Johns Hopkins & OHRP, IRB: ETHICS & HUM. RES.*, July-Aug. 2001, at 13, 13–15.

11. See, e.g., OFFICE OF INSPECTOR GEN., DEP'T OF HEALTH & HUMAN SERVS., INSTITUTIONAL REVIEW BOARDS: A TIME FOR REFORM (1998); OFFICE OF INSPECTOR GEN., DEP'T OF HEALTH & HUMAN SERVS., PROTECTING HUMAN RESEARCH SUBJECTS: STATUS OF RECOMMENDATIONS (2000); COMM. ON ASSESSING THE SYS. FOR PROTECTING HUMAN RESEARCH PARTICIPANTS, INST. OF MED., RESPONSIBLE RESEARCH: A SYSTEMS APPROACH TO PROTECTING RESEARCH PARTICIPANTS (Daniel D. Federman et al. eds., 2003).

12. See Robert J. Levine, *Institutional Review Boards: A Crisis in Confidence*, 134 ANNALS INTERNAL MED. 161, 161 (2001) (“There is a sense of crisis in the country about the effectiveness of the nationwide system that protects the rights and welfare of human research subjects.”).

13. Mariner, *supra* note 3, at A25.

14. See, e.g., Carl H. Coleman, *Duties to Subjects in Clinical Research*, 58 VAND. L. REV. 387 (2005); E. Haavi Morreim, *The Clinical Investigator as Fiduciary: Discarding a Misguided Idea*, 33 J.L. MED. & ETHICS 586 (2005).

participation in the experiment has not made the subject any therapeutically worse off than if she had not enrolled. Such hazards ordinarily do not generate economic loss directly traceable to physical injury caused by the experimentation. This harm includes not only emotional distress, but also lost opportunity costs, destruction of trust and confidence in the research process, clinical trial abandonment, affront to dignitary interests, breach of confidentiality, invasion of privacy, loss of meaningful choice about use of one's body as an experimental object, participation in a study that fails to disseminate trial data in order to advance medical knowledge, and frustrated access to perceived cutting-edge therapy. This Article refers to such risks collectively as "intangible hazards" or "intangible harm."¹⁵

Conventional wisdom, fueled by coverage of recent medical research scandals, assumes that experimental subjects confront significant risk of pain, disability, and death. Yet, the degree of physical harm experienced by research subjects is likely overstated. One recent estimate suggests that approximately five thousand subjects die each year in federally funded trials, with tens of thousands more suffering injuries.¹⁶ But such conclusions seem suspect and unreliable. First, many research subjects enroll in trials when already ill, making it difficult to distinguish between natural disease progression and research-related interventions as the cause of their later injuries. Second, no uniform reporting system exists for adverse events across federally and privately funded trials, making calculation of subject injury and death rates nearly impossible.¹⁷

Despite the problematic data, a likely conclusion is that a considerable number of research subjects fare as well or better therapeutically as patients with similar conditions receiving ordinary

15. Standard medical malpractice doctrine distinguishes between compensatory "economic" damages (lost wages, medical care costs, rehabilitation costs, and other directly related out-of-pocket expenses arising from the physical injury) and compensatory "noneconomic" damages (for subjective injuries such as pain and suffering, familial losses, and anguish). See Catherine M. Sharkey, *Unintended Consequences of Medical Malpractice Damages Caps*, 80 N.Y.U. L. REV. (forthcoming May 2005). In this Article the term "intangible harm" is used to describe primarily the noneconomic damage component, if viewed from the perspective of a medical malpractice claim. Of course, research subjects may assert non-tort claims as well. Hence, this Article uses the broader term "intangible harm." This term is intended to have a wider application than emotional distress alone. This definition covers harms that are hard to quantify or view tangibly through physical manifestation, as well as harms not readily traceable to direct economic loss or out-of-pocket remedial costs. This definition would, for example, include claims of injury arising from breach of trust and confidence that the subject places in the investigator and the research enterprise generally, even if the loss of trust or confidence does not result in emotional distress.

16. See Tom Pelton, *Medical Experiment Disclosure Hinges on a Flawed Honor System*, BALTIMORE SUN, Aug. 12, 2001, at A1 (discussing estimates of Adil Shamoo, a University of Maryland scientist).

17. See Lemonick & Goldstein, *supra* note 6, at 46; Barbara A. Noah, *Bioethical Malpractice: Risk and Responsibility in Human Research*, 7 J. HEALTH CARE L. & POLICY 175, 176 (2004).

medical care.¹⁸ For example, the Advisory Committee on Human Radiation Experiments's comprehensive review of federally funded research projects, from both radiation- and non-radiation-related disciplines, determined that most studies posed only minimal risks of harm.¹⁹ Others have speculated that the aggregate amount of injuries arising from medical research pales in comparison to total physical harms caused by more mundane activities such as walking.²⁰ Further, the emergence of improved technologies and techniques for managing experimental subjects suggests that whatever the physical risk from research participation, clinical trial safety is improving. A recent retrospective review of Phase 1 clinical trials²¹ of cancer drugs, considered the most dangerous phase of testing, concluded that, over a twelve year period, the odds of research subject death from an experimental intervention dropped to less than ten percent of the earlier likelihood.²² Moreover, some studies suggest the existence of a "trial effect," under which subjects in clinical trials fare better therapeutically than similarly situated patients not participating in research.²³

This evidence raises an interesting challenge for research subject

18. Part of the reason why research may not present significantly greater dangers than ordinary medical care is that the distinction between experimentation and standard therapeutic care has become increasingly blurred, as ordinary medical care includes a great deal of innovation and trial and error testing by individual physicians. See generally Noah, *supra* note 4.

19. See *Research Ethics and the Medical Profession: Report of the Advisory Committee on Human Radiation Experiments*, 276 JAMA 403, 408 (1996). See also ROBERT J. LEVINE, *ETHICS AND REGULATION OF CLINICAL RESEARCH* 39–40 (2d. ed. 1986) (summarizing data from several earlier studies regarding injuries to subjects and concluding that "the role of research subjects is not particularly hazardous").

20. See Philip Hamburger, *The New Censorship: Institutional Review Boards* (University of Chicago, Public Law Working Paper No. 95), available at <http://ssrn.com/abstract=721363>.

21. The Food and Drug Administration reviews drugs by stages of clinical testing. Phase 1 studies determine levels of tolerance to establish safe dosage levels. If deemed nontoxic, a drug passes into Phase 2, where it is tested to demonstrate efficacy and relative safety. Phase 3 studies involve expanded controlled and uncontrolled clinical trials. See 21 C.F.R. § 312.21 (2005).

22. See Thomas G. Roberts et al., *Trends in the Risks and Benefits to Patients With Cancer Participating in Phase 1 Clinical Trials*, 292 JAMA 2130 (2004).

23. See e.g., John D. Lantos, *The Inclusion Effect in Clinical Trials*, 134 J. PEDIATRICS 130 (1999). The trial effect applies to individuals receiving experimental treatment, as well individuals receiving standard therapy as "control" subjects on a protocol. Potential reasons for a trial effect include the more careful monitoring that research subjects receive, the fact that investigators follow well-defined protocols that have received the input of numerous experts, a placebo effect in which the subjects believe they are receiving cutting-edge and therefore better care, and a possible selection bias in which subjects more responsive to interventions are selected for inclusion in clinical trials. See *id.* Others state the "trial effect" may not be well supported as the data from many studies does not allow for a good comparison between research participants and nonparticipants. See, e.g., Jeffrey M. Peppercorn et al., *Comparison of Outcomes in Cancer Patients Treated Within and Outside Clinical Trials: Conceptual Framework and Structured Review*, 363 LANCET 263 (2004) (noting, however, that no studies show a "negative" trial effect in which research participants generally experience worse outcomes).

protection. If the current oversight system, however deficient, apparently works crudely but well enough to safeguard subjects' physical health at levels seemingly no worse than that enjoyed by patients outside of medical experiments, then the experience of research subjects needs to be contextualized further. A sincere commitment to research subject protection requires taking a harder look at the intangible harm side of the equation.

What should happen when research subjects may have been "wronged even if not injured?"²⁴ The issue is ripe for discussion. Thorny questions of how to account for intangible harm arising from research currently challenge the courts, regulatory agencies, and legislatures. In several recent lawsuits, subjects have raised relatively novel allegations about violation of "dignitary rights."²⁵ Other recent disputes have involved subjects' seemingly incongruous claims of harm arising from study terminations that denied them access to experimental technology apparently proven ineffective.²⁶ Meanwhile, concerns continue to be raised about the failure of research sponsors to disseminate clinical trial results,²⁷ conduct likely associated with intangible harm as it causes no physical injury but flagrantly breaches the implied covenant with subjects that their participation helps future patients by improving medical knowledge.

Currently, subjects principally concerned with such intangible harm face limited opportunity for relief. This Article explains how the legal and regulatory framework strains to adequately address intangible hazards experienced by research subjects. This Article further asks what, if anything, the law should do about it.

Some immediate qualifications are warranted. First, this Article does not rehash the long-standing debates in tort law about recovery for physical injury in contrast to the limited or no-duty rules applicable to claims for pure emotional and pure economic harm. Tort law's general conservative approach to emotional harm recovery explains, in part, the inability of research subjects to obtain relief for various hazards when not made physically worse off as a result of the research. But the harm considered in this Article is broader than simply emotional distress, as it includes intangible hazards that can develop even without serious mental anguish, such as affront to dignitary interests, loss of trust in the research process, or participation in research that does not yield publicly

24. E. Haavi Morreim, *Clinical Trials Litigation: Courts in Confusion*, 2 Med. Res. L. & Pol'y Rep. (BNA), No. 24, at 908-09 (Dec. 17, 2003).

25. *See infra* Part III.A.

26. *See infra* Part III.B.1.

27. *See infra* Part V.B.2.

available results. Second, the question of how to account for intangible hazards occurs in many areas and is hardly confined to medical research.²⁸ However, the unique context of medical experimentation presents special challenges, in light of the high priority of research subject protection as a matter of bioethics and health law, the social importance of medical innovation, and further demonstrated by recurring, problematic research controversies involving intangible harm. Third, this Article is intentionally limited to consideration of intangible hazards experienced by individual research subjects. Claims of group-based injuries, such as genetic research that may yield results damaging to the social reputation and economic standing of various ethnic or racial groups also raise interesting questions of intangible harm,²⁹ but these disputes involve distinct, complex issues of group identity and authority beyond this Article's intended scope.

Part I of this Article provides an overview of the medical research enterprise and the legal background, noting the law's ambiguous, vague record of demonstrated concern about intangible harm, and further explains how a changing research environment has created new apprehension about experimental subjects and intangible hazards. Part II discusses the traditional limited liability for research activities involving intangible harm. Part III examines a new wave of research-related litigation in which plaintiffs have attempted—with limited success—to overcome the traditional barriers to relief for intangible hazards. It also discusses other recent cases in which subjects with compelling cases of intangible harm have largely failed in recovering more conventional damages, suggesting the need for new approaches.

Part IV asks whether the intangible hazards faced by subjects should be cognizable to a greater degree. A more flexible approach has considerable advantages, including strengthening needed respect for subjects as persons with individual dignity, remedying problematic informed consent, policing opportunistic conduct in the investigator-

28. See e.g., Stanley Ingber, *Rethinking Intangible Injuries: A Focus on Remedy*, 73 CAL. L. REV. 772 (1985); Nancy Levit, *Ethereal Torts*, 61 GEO. WASH. L. REV. 136 (1992); Andrew J. McClurg, *Dead Sorrow: A Story About Loss and a New Theory of Wrongful Death Damages*, 85 B.U. L. REV. 1 (2005).

29. For example, members of the Havasupai Tribe recently sued Arizona State University researchers alleging that blood samples taken from them for a diabetes study were used for additional, unauthorized research regarding schizophrenia, inbreeding, and population migration. They asserted that the schizophrenia and inbreeding investigations stigmatized the tribe and that the migration research challenged their religious origin story. See Complaint, *Havasupai Tribe v. Arizona State Univ.*, No. 04-CV-1494 (D. Ariz. 2004). See also Charles Weijer, *Protecting Communities in Research: Philosophical and Pragmatic Challenges*, 8 CAMBRIDGE Q. HEALTHCARE ETHICS 501 (1999); Pilar Ossorio & Troy Duster, *Race and Genetics: Controversies in Biomedical, Behavioral, and Forensic Sciences*, 60 AM. PSYCHOLOGIST 115 (2005).

subject relationship, and promoting trust in research, an independent, socially important goal. At the same time, providing more robust remedies for a wider range of intangible harm claims, although appealing for these reasons and for ethical considerations, remains difficult to reconcile with current case law doctrine and regulatory approaches, threatens to deter useful research activity, and poses numerous pragmatic problems as a legal matter, such as defining boundaries for such claims.

Part V balances the competing considerations and concludes by arguing for a circumspect expansion in recognizing research subjects' intangible harm claims, either through common law actions or through regulatory mechanisms. It discusses representative scenarios, appropriately limited in scope. One application is to address particularly problematic enrollment encounters, regardless of whether physical harms materialize, where a question exists as to whether a subject understood that she participated in research at all or failed to understand, at the most basic level, how study protocols operate in conflict with desires for access to care and individually tailored treatment. A second, related area would use broader intangible harm remedies to address abandonment hazards. This contemplates situations where experimental goals of the study protocol, or pure business objectives of the trial sponsor, lead to egregious disregard of already enrolled subjects' legitimate interests in more than physical safety. For example, investigators and sponsors can readily frustrate and potentially exploit subjects' inaccurate assumptions regarding the duration of the experiment, proper reasons for terminating the study, and continued access to investigational technology. Similarly, subjects may be wrongfully abandoned, even if not physically injured, when the study fails to contribute to general medical knowledge through the public dissemination of research results. Such conduct forsakes and deserts subjects by disrupting their reasonable expectations and disregarding their considerable personal investments in clinical trials. Such conduct also raises serious concerns for the research enterprise generally, thus warranting greater recognition and sanction as legally cognizable harm.

I. OVERVIEW OF THE MEDICAL RESEARCH SYSTEM AND LEGAL BACKGROUND

Medical research with human subjects, a highly regulated endeavor, implicates various ethical standards, common law obligations, and numerous statutory and regulatory requirements. The ethical standards, rather broad and open-ended, provide some support for the need to

safeguard subjects from intangible hazards. However, this commitment is not mirrored in clear law or regulation, as a review of the major components of the current oversight system reveals an ambiguous, vague record regarding the law's concern with subjects' experience of intangible harm. At the same time, the changing research environment suggests new reasons for concern about intangible hazards in medical experiments.

*A. Commonly Recognized Ethical Standards:
Nuremberg Code and Declaration of Helsinki*

In the aftermath of World War II, the Nuremberg Military Tribunal drew public attention to atrocious actions by Nazi physicians performed under the guise of scientific research. In deciding charges against the Nazi investigators of war crimes and crimes against humanity, the judges identified ten basic principles, known as the influential "Nuremberg Code," to provide ethical guidance for medical research with human subjects. The Nuremberg Code (the Code) emphasized the need for voluntary consent and minimization of suffering and injury for the subjects involved.³⁰ While the Code urged researchers to design experiments "to avoid all unnecessary . . . mental suffering and injury,"³¹ it did not otherwise expressly discuss dignitary or other intangible harms to research subjects.

The Nuremberg Code responded to research with healthy subjects, as had been performed in many of the Nazi experiments. Many U.S. physicians perceived the Code as inapplicable to much of their research that involved ill subjects who might benefit from the experiment.³² As an alternative, and partially in response to reports of ongoing research abuses, the World Medical Association adopted the Declaration of Helsinki (the Declaration) in 1964.³³ The Declaration applied broadly to therapeutic and nontherapeutic research. It similarly emphasized the need for informed consent and harm minimization. However, the Declaration went further than the Nuremberg Code in expressly discussing the need to respect research subjects' intangible interests.

30. See Nuremberg Code, 2 Trials of War Criminals Before the Nuremberg Military Tribunals under Control Council Law No. 10 (1949) ¶ 1, 7, reprinted in INSTITUTIONAL REVIEW BOARD: MANAGEMENT AND FUNCTION, *supra* note 8, at 490–91.

31. *Id.* ¶ 3.

32. See Appendix C: *The Current Oversight System: History and Description*, in NAT'L BIOETHICS ADVISORY COMM'N, ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS 151 (2001).

33. See *World Medical Association Declaration of Helsinki*, reprinted in INSTITUTIONAL REVIEW BOARD: MANAGEMENT AND FUNCTION, *supra* note 8, at 499–500.

The Declaration states that researchers have a duty to protect the “life, health, privacy, and dignity of the human subject.”³⁴ In addition, the Declaration urges investigators to respect subjects’ right to “safeguard their integrity,”³⁵ and calls on investigators to minimize a study’s impact on each subject’s “physical and mental integrity and on the personality of the subject.”³⁶

B. Commonly Recognized Ethical Standards: The Belmont Report

The influential “Belmont Report, released in 1978 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, identifies commonly understood ethical guidelines for research with human subjects.”³⁷ The Belmont Report discusses three fundamental ethical principles: respect for persons, beneficence, and justice.³⁸ Of the three guiding principles, the respect-for-persons concept provides the strongest support for recognizing intangible harms because this principle incorporates aspects of personal autonomy, capacity for free will and choice, and an emphasis on “the basic human dignity in everyday life.”³⁹ Thus, research that debases subjects, overrides their free choice, or otherwise affronts their sense of individual personhood and dignity, even if physical injury is not caused, seemingly raises serious concerns under the Belmont Report guidelines.

Further, the Belmont Report states that all research with human subjects should have a favorable risk/benefit assessment.⁴⁰ In determining whether research presents acceptable risk/benefit tradeoffs, the Belmont Report expressly contemplates that subjects need protection from many types of harms, including intangible hazards:

Many kinds of possible harms and benefits need to be taken into account. There are, for example, risks of psychological harm, physical harm, legal harm, social harm, and economic harm, and the corresponding benefits. While the most likely types of harm to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked.⁴¹

34. *Id.* § B.10.

35. *Id.* § B.21

36. *Id.*

37. See BELMONT REPORT, *supra* note 8.

38. See *id.*

39. See Harold Y. Vanderpool, *An Ethics Primer for IRBs*, in INSTITUTIONAL REVIEW BOARD: MANAGEMENT AND FUNCTION, *supra* note 8, at 5.

40. See BELMONT REPORT, *supra* note 8, at 494–95.

41. *Id.* at 497.

Unfortunately, the Belmont Report is written at a considerable level of generality, as it tries to incorporate consensus views about commonly agreed upon principles from among many different philosophical traditions and ethical perspectives. As such, the Report does not develop many concepts to a great degree of specificity. For example, while the Report evidences concern about dignitary injuries to participants, it does not tackle harder practical questions such as the precise source of a research subject's dignitary interests, what types of injuries count as an affront to dignitary interests, and whether some dignitary harm can be tolerated to advance other interests.

*C. Current Federal Research Regulations, Agency Guidelines,
and the Oversight System*

Following the directive for additional regulations on medical experimentation in the National Research Act of 1974⁴² and the recommendations in the Belmont Report, the Department of Health and Human Services (HHS) and Food and Drug Administration (FDA) issued substantially revised research regulations in 1981.⁴³ The new rules more broadly reiterated previous agency guidelines that investigators obtain local institutional review board (IRB) approval for research protocols. IRBs are research review committees organized within academic institutions, comprised of scientists and layperson community members. The new regulations also renewed a requirement that investigators seek informed consent of research subjects.⁴⁴ These general provisions have continued, without significant change, to the present.

Clinical trials involving human subjects that are funded in whole or in part by HHS generally require IRB review. The IRB evaluates whether the research presents acceptable risks and whether informed consent procedures are followed.⁴⁵ Industry-funded clinical trials testing drugs and devices for FDA approval also generally require IRB review along the same lines.⁴⁶ For a small subset of studies, such as where physicians

42. Pub. L. No. 93-348, 88 Stat. 342 (1974) (codified as amended in scattered sections of 42 U.S.C.).

43. See Dep't of Health & Human Servs., Final Regulations Amending Basic HHS Policy for the Protection of Human Research Subjects, 46 Fed. Reg. 8366 (January 26, 1981); 46 Fed. Reg. 8942 (January 27, 1981) (FDA rules).

44. See generally Richard S. Saver, *Medical Research Oversight from the Corporate Governance Perspective: Comparing Institutional Review Boards and Corporate Boards*, 46 WM. & MARY L. REV. 619, 633-39 (2004).

45. See 45 C.F.R. §§ 46.101, 46.109 (2005).

46. See 21 C.F.R. §§ 50.1, 56.103.

conduct research in their private medical clinics and are not affiliated with a larger academic medical center, review is performed not by a local IRB but by a non-institutional review board, sometimes referred to as an "independent review board."⁴⁷ The monitoring system, largely dependent on the work of local IRBs, is ultimately overseen by the Office for Human Research Protections (OHRP) within HHS, as well as by the FDA, and each agency conducts a limited number of on-site audits.⁴⁸ However, some research remains completely unregulated under the federal rules. This includes nonfederally funded studies not seeking FDA approval for a drug or device, such as privately financed investigations into new surgical techniques.⁴⁹ Further, several states have enacted statutes regulating experimentation, but these laws are more limited in application and may be preempted in certain instances by the federal regulations.⁵⁰

1. Informed Consent Requirements

The federal regulations on research informed consent do not expressly mention the need to disclose to subjects that dignitary or other types of intangible harm may occur. Indeed, the regulatory requirements for risk disclosure are remarkably silent on what types of risk ultimately require discussion. The regulations simply state, in catch-all language, that informed consent means providing the subject with a description "of *any* reasonably foreseeable risks or discomforts"⁵¹ When serious, non-physical risks, such as mental distress or potential problems with insurability or loss of confidentiality, are likely to materialize, then arguably these hazards fall within the open-ended regulatory category of foreseeable harms. Accordingly, failure to apprise a subject of likely

47. Independent review boards operate outside of medical centers. They offer their review services to investigators who may not have a relationship with a local IRB or academic medical center, such as when the research is conducted in private physician offices. See OFFICE OF INSPECTOR GEN., DEP'T OF HEALTH & HUMAN SERVS., INSTITUTIONAL REVIEW BOARDS: THE EMERGENCE OF INDEPENDENT BOARDS i-ii (1998).

48. See Gary Chadwick, *Preparing for an FDA Audit*, in INSTITUTIONAL REVIEW BOARD: MANAGEMENT AND FUNCTION, *supra* note 8, at 359-64; Thomas Puglis & Michele Russell-Einhorn, *Preparing for an OHRP Site Visit*, in INSTITUTIONAL REVIEW BOARD: MANAGEMENT AND FUNCTION, *supra* note 8, 365-69.

49. See ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS, *supra* note 32, at 12.

50. See Richard S. Saver, *Critical Care Research and Informed Consent*, 75 N.C. L. REV. 205, 226-28 (1996).

51. 45 C.F.R. § 46.116(a)(2); 21 C.F.R. § 50.25(a)(2) (emphasis added). See also 45 C.F.R. § 46.116(b)(3); 21 C.F.R. § 50.25(b)(3) (requiring that, when appropriate, subjects be told about "[a]ny additional costs" that may result from research participation).

intangible harm technically violates the consent regulations. However, specific identification of such harm in advance becomes difficult for many intangible hazards precisely because of their intangible nature.⁵²

2. IRB Review

The regulations provide that an IRB may approve a protocol only if it determines, among other requirements, that risks are minimized through sound research design and risks are reasonable in light of the anticipated benefits.⁵³ Unfortunately, similar to the informed consent provisions, the IRB review regulations fail to provide clear guidance on the issue of intangible harm. The IRB rules do not further define the types of intangible risks that IRBs should focus on, if at all, other than mentioning the need to look for adequate privacy and confidentiality protections.⁵⁴ The regulatory provisions neither expressly mention nor preclude discussion of other intangible hazards.⁵⁵

Apart from the regulations, less formal guidance from OHRP contemplates a role for IRBs in evaluating certain non-physical risks, such as stress, feelings of guilt, and other psychological harm.⁵⁶ Similarly, the guidance encourages IRBs to remain sensitive to risks of breach of subject confidentiality, particularly with regard to sexual activity, drug use, or mental illness, as this can lead to stigma and embarrassment, and accompanying social or economic harm.⁵⁷

52. The regulations also provide a catch-all requirement for renewed disclosures to already participating subjects by requiring that subjects be told about "significant new findings developed during the course of the research which may relate to the subject's willingness to continue . . ." 45 C.F.R. § 46.116(b)(5); 21 C.F.R. § 50.25(b)(5). Thus, this regulatory provision provides an additional, albeit rather convoluted, hook on which to hang possible intangible harm claims when investigators fail to make new disclosures about continued participation and intangible hazards. *See also infra* notes 290–92 and accompanying text.

53. 45 C.F.R. § 46.111.

54. *See* 45 C.F.R. §§ 46.101(b)(2)(ii), 46.110, 46.111; Categories of Research that May Be Reviewed by the Institutional Review Board (IRB) Through an Expedited Review, 63 Fed. Reg. 60364 (Nov. 8, 1998), *available at* <http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm>. *See also* OFFICE FOR HUMAN RESEARCH PROTS., DEP'T OF HEALTH & HUMAN SERVS., GUIDANCE ON THE USE OF EXPEDITED REVIEW PROCEDURES (2003) (incorporating the previous guidance document by reference), <http://www.hhs.gov/ohrp/humansubjects/guidance/exprev.htm>.

55. The only limitation, in an attempt to restrain potentially open-ended IRB review of risks and benefits, is an instruction that IRBs should not consider "long-range effects of applying knowledge gained in the research . . ." 45 C.F.R. § 46.111(a)(2). This would involve, for example, IRB consideration of the public policy implications of applying the research results.

56. *See* OFFICE FOR HUMAN RESEARCH PROTS., DEP'T OF HEALTH & HUMAN SERVS., INSTITUTIONAL REVIEW BOARD GUIDEBOOK (1993), Chapter III(A), *available at* http://www.hhs.gov/ohrp/irb/irb_guidebook.htm.

57. *See id.*

IRB responsibilities do not end with initial review. They conduct continuing reviews of previously approved research projects at least once a year,⁵⁸ receive adverse event reports regarding unanticipated complications with research subjects,⁵⁹ and they have the authority to shut down studies that lead to unexpected serious harm.⁶⁰ These provisions certainly contemplate a vigilant role for IRBs in monitoring ongoing trials. They do not, however, provide more helpful guidance as to what intangible hazards, if any, should trigger IRB intervention.⁶¹

D. Uncertain Legal Claims to "Dignitary Rights"

Recognition of a dignitary right for research subjects could be a promising vehicle for bringing various claims for intangible harm relief, as dignitary concerns may arise independent of physical injury and even emotional distress. Whether research subjects have a viable, enforceable legal claim to be treated with dignity remains unclear. Several commentators assert that research subjects have such a right based on more general assertions of inalienable rights, without providing a concrete legal source for recognizing such claims.⁶²

A number of possible sources might, individually or in the aggregate, provide the foundation for a subject's legal right to dignity. As noted, medical ethics standards such as the Nuremberg Code and Helsinki Declaration provide support for safeguarding the intrinsic dignity of subjects, apart from issues of physical injury. However, ethics and law often diverge. It is debatable whether the Nuremberg and Helsinki provisions are anything more than aspirational ethical guidance. Several United States courts have been reluctant to find the international ethical guidelines legally binding in domestic private actions filed by aggrieved research subjects.⁶³

58. See 45 C.F.R. § 46.109(e).

59. See 45 C.F.R. § 46.103(b)(5); 21 C.F.R. § 56.108(b).

60. See 45 C.F.R. § 46.113.

61. See Sharona Hoffman, *Continued Concern: Human Subject Protection, the Institutional Review Board, and Continuing Review*, 68 TENN. L. REV. 725, 733 (2001) (noting the extremely limited overall guidance for IRBs performing continuing review).

62. See Samuel Hellman & Deborah S. Hellman, *Of Mice But Not Men: Problems of the Randomized Clinical Trial*, 324 NEW ENG. J. MED. 1585, 1587 (1991) ("The right to be treated as an individual deserving the physician's best judgment and care, rather than to be used as a means to determine the best treatment for others, is inherent in every person. This right, based on the concept of dignity, cannot be waived."); Richard W. Garnett, *Why Informed Consent? Human Experimentation and the Ethics of Autonomy*, 36 CATH. LAW. 455, 488 (1996).

63. See, e.g., *Robertson v. McGee*, No. 01-CV-60-C, 2002 U.S. Dist. LEXIS 4072, *9 (N.D. Okla. Jan. 28, 2002) ("This Court agrees with other jurisdictions which have found that there is no private right of action for an alleged violation of international law for the protection of human research

Domestic bioethical principles, reflected in the Belmont Report, regarding autonomy and respect for persons also support recognizing dignitary claims of subjects. These principles caution against merely using subjects as means to the end goals of the study.⁶⁴ Similar considerations would infer a research subject's right to dignity as arising from a patient's common law right of self-determination in medical decisionmaking. This common law right safeguards not only patients' physical health but also arguably advances their intrinsic worth as independent moral agents.⁶⁵ However, few courts so far have followed such reasoning to clearly recognize a research subject's right to remedy for affronts to dignity alone.

Claims of a research subject's right to dignity also potentially implicate constitutional rights, at least when the research involves state action through governmental actors. Courts have found that the Fourteenth Amendment's substantive due process guarantee protects a research subject's right to bodily integrity.⁶⁶ Constitutional protections for bodily integrity might similarly be found to more broadly encompass a right to be treated with dignity. Cases under the Fourteenth Amendment protecting personal decisions relating to marriage, procreation, contraception, family relationships, and education arguably protect choices implicating not only personal autonomy but also dignity.⁶⁷ Similarly, subjects have argued that the Fifth Amendment's

subjects under the Declaration of Helsinki and the Nuremberg Code."'). *But see In re Cincinnati Radiation Litig.*, 874 F. Supp. 796, 821–22 (S.D. Ohio 1995); *Grimes v. Kennedy Krieger Inst.*, 782 A.2d 807 (Md. 2001) (finding an investigator has a special duty to protect subjects and basing the duty on several different sources, potentially including the Helsinki Declaration and Nuremberg Code).

64. See generally TOM BEAUCHAMP & JAMES CHILDRESS, *PRINCIPLES OF BIOMEDICAL ETHICS* 181 (4th ed. 1994); Lawrence Gostin, *Ethical Principles for the Conduct of Human Subject Research: Population-Based Research and Ethics*, 19 L. MED. & HEALTH CARE 191, 192 (1991).

65. The seminal case articulating this concept is *Schloendorff v. Society of New York Hospital*, 105 N.E. 92 (N.Y. 1914). Judge Cardozo's opinion stated that "[e]very human being of adult years and sound mind has a right to determine what shall be done with his own body" *Id.* at 93.

66. See, e.g., *In re Cincinnati Radiation Litig.*, 874 F. Supp. at 810–11 (involving plaintiffs who were exposed to radiation by the Department of Defense and were not told that the exposure was part of a military experiment rather than treatment of their cancers).

67. See *Planned Parenthood of Se. Pa. v. Casey*, 505 U.S. 833, 851 (1992). For example, in *United States v. Stanley*, which involved a former soldier's suit against the Army for LSD exposure, Justice Brennan's dissent concluded that the military acted so egregiously in conducting unauthorized research on the plaintiff that it violated the basic tenets of the Nuremberg Code, failed to treat the subject with dignity, and could trigger constitutional violations. 483 U.S. 669, 708 (1987) (Brennan, J., dissenting) (lamenting that the soldier, treated as a mere experimental object, "will receive no compensation for this indignity" and further stating that "[s]oldiers ought not be asked to defend a Constitution indifferent to their essential human dignity"). See also *id.* at 708–09 (O'Connor, J., dissenting) (noting that the principles of the Nuremberg Code had been violated by unknowing and involuntary experimentation and commenting that the Constitution affords due process protections against such actions).

guarantee of liberty for all citizens creates an obligation, in research settings involving government actors, to treat subjects with a minimum level of dignity.⁶⁸

Despite these theoretical bases for constitutionalizing a dignity right for certain research subjects, the lower courts have thus far displayed reluctance to recognize such claims without clearer guidance from the United States Supreme Court. Plaintiffs asserting constitutional rights to dignity in recent research litigation, where the intangible harm claim was distinct from claims to bodily integrity, have generally not been successful.⁶⁹

E. A Changing Research Environment

A dramatically changing research environment has renewed concern about insufficient protection of research subjects. In this critical period, the research system faces new, significant challenges in not only safeguarding subjects from physical injury, but also addressing risk of serious intangible hazards.

1. Commercialization

The Bayh-Dole Act of 1980, which allows universities to retain title to intellectual property derived from research supported by the federal government, has spurred numerous, complex financial arrangements between academic medical centers, investigators, and industry for developing and commercializing new medical discoveries.⁷⁰ Additionally, private industry now sponsors a far greater number of clinical trials than in previous decades.⁷¹ As a result, today's research

68. See, e.g., Second Cause of Action, Complaint, *Steubing v. Kornak* (N.D.N.Y. March 18, 2003), available at <http://www.sskrplaw.com/gene/steubing/complaint.pdf>. That lawsuit arose from cancer drug trials conducted at Stratton Veteran Affairs Medical Center Hospital in which subjects alleged that defendants, among other actions, enrolled subjects who did not meet study protocol criteria and failed to follow study protocol procedures designed to monitor and safeguard the subjects.

69. See, e.g., *Ammend v. Bioport, Inc.*, 322 F. Supp. 2d 848, 872–73 (W.D. Mich. 2004) (“American constitutional jurisprudence has never recognized a right to human dignity.”) *Ammend* involved an action by current and former military members alleging various harms, including breach of the right to be treated with essential human dignity, after mandatory participation in an anthrax vaccination program administrated under the Department of Defense. *Id.* at 852. See also *Robertson v. McGee*, No. 01-CV-60-C, 2002 U.S. Dist LEXIS 4072 (N.D. Okla. Jan. 28, 2002) (discussed further at *infra* Part III.A.1).

70. See 35 U.S.C. § 203; Arti Rai & Rebecca Eisenberg, *Bayh-Dole Reform and the Progress of Biomedicine*, 91 AM. SCIENTIST 52 (2003).

71. See Kuszler, *supra* note 1, at 118–22.

environment is significantly more “entrepreneurial.”⁷² In this period of increased commercialization, financially conflicted medical centers and investigators may be tempted to side-step research subject protection,⁷³ particularly regarding easily overlooked intangible hazards. Financial conflicts of interest may also exacerbate intangible harm by eroding trust in clinical research generally,⁷⁴ as well as engendering perceptions of subject betrayal and exploitation for other parties’ commercial aims.

2. IRB Workload Strain and Continuing Review Problems

The dramatic increase in the number of clinical trials presents an additional stress factor for the research system. The upswing in clinical trial activity means that the typical IRB has more work to do for approving and monitoring protocols.⁷⁵ An IRB review system with such capacity strain is bound to have serious errors and failures, particularly regarding easily overlooked intangible hazards.

IRBs face daunting time and resource constraints and will likely look to physical injury as a crude proxy for any problems with a study. The federal regulations lack specificity in instructing IRBs what to look for, and even what documents to examine, in performing the critical continuing review function.⁷⁶ Because of such vague and open-ended guidance, intangible harm may receive little attention. For example, one IRB member told HHS investigators that in performing continuing reviews he looks to see if a patient died on the protocol; if there is no subject death, the IRB member stated that he generally probes no further.⁷⁷ A further troubling aspect of IRB continuing review is that it involves minimal presence in the field.⁷⁸ Intangible harms may be very

72. See Karen A. Jordan, *Financial Conflicts of Interest in Human Subjects Research: Proposals For a More Effective Regulatory Scheme*, 60 WASH. & LEE L. REV. 15, 20–21 (2003).

73. See Karin Morin et al., *Managing Conflicts of Interest in the Conduct of Clinical Trials*, 287 JAMA 78, 81–83 (2002); Jordan J. Cohen, *Managing Financial Conflicts of Interest in Clinical Research*, 8 SCI. ENGINEERING ETHICS 401, 402–03 (2002); Ken Gatter, *Fixing Cracks: A Discourse Norm to Repair the Crumbling Regulatory Structure Supporting Clinical Research and Protecting Human Subjects*, 73 UMKC L. REV. 581, 621–24 (2005).

74. See T. Boddenheimer, *Uneasy Alliance-Clinical Investigators and the Pharmaceutical Industry*, 342 NEW ENG. J. MED. 1539 (2000); Miller, *supra* note 7; Robert Gatter, *Walking the Talk of Trust in Human Subjects Research: The Challenges of Regulating Financial Conflicts of Interest*, 52 EMORY L.J. 327 (2003).

75. See OFFICE OF INSPECTOR GEN., DEP’T OF HEALTH & HUMAN SERVS., INSTITUTIONAL REVIEW BOARDS: THEIR ROLE IN REVIEWING APPROVED RESEARCH 7 (1998); Saver, *supra* note 44, at 657–60.

76. See Hoffman, *supra* note 61, at 733.

77. See INSTITUTIONAL REVIEW BOARDS: A TIME FOR REFORM, *supra* note 11, at 6.

78. See *id.*; Hoffman, *supra* note 61, at 733.

hard to detect or understand from mere paper review of ongoing research protocols.

3. Increased Subject Demand for Research Access

Potential research subjects have become quite savvy and determined in demanding opportunities to participate in clinical trials. This results in part from the larger access problems confronting the U.S. health care system. Patients without adequate, and in some cases any, health insurance coverage may view participation in research as their only effective way for receiving care other than sporadic treatment in an emergency room.⁷⁹ Moreover, powerful research advocacy groups influence the views of potential subjects. Advocacy organizations for persons with illnesses such as HIV/AIDS and breast cancer have been politically effective in procuring research funding for their respective diseases. This success has come in part to portraying to the public that study participation is the best way to obtain state-of-the-art medical care.⁸⁰ These advocacy groups may be contributing to unrealistic expectations of benefit among seriously ill patients, encouraging subjects to enroll in clinical trials of increasing risk and uncertain benefit.⁸¹

Given the changing demands of potential subjects, monitoring bodies' attempts to provide rigorous review of proposed studies and to reduce risk of intangible harm may not always be welcome. Many subjects likely view such oversight as not protecting them, but blocking desired opportunities for receiving cutting-edge care.⁸² Concerns about protecting research subjects from intangible harm and potential exploitation do not fit well with a primarily access-focused model of

79. See Gina Kolata & Kurt Eichenwald, *For the Uninsured, Drug Trials Are Medicine*, N.Y. TIMES, June 22, 1999, at A1.

80. See generally REBECCA DRESSER, WHEN SCIENCE OFFERS SALVATION: PATIENT ADVOCACY AND RESEARCH ETHICS (2001). Understandably, potential subjects may view investigational trials as their only hope of obtaining access to cutting edge therapy. For example, for pediatric cancer patients, state-of-the-art therapies may be practiced to a large degree only within the confines of clinical trials. See Nancy M.P. King, *Defining and Describing Benefit Appropriately in Clinical Trials*, 28 J.L. MED. & ETHICS 332, 339 (2000) (noting that pediatric patients with advanced cancer have limited opportunities for interventions of any sort outside of experimental studies). With other diseases, however, researchers may contribute to subjects' seemingly uncritical access demands. In interacting with patients, investigators may discount or minimize alternative ways that individuals can access new technologies and procedures without enrolling in a trial. See Jerry Menikoff, *The Hidden Alternative: Getting Investigational Treatments Off-Study*, 361 LANCET 63 (2003).

81. See DRESSER, *supra* note 80.

82. See U.S. GEN. ACCOUNTING OFFICE, SCIENTIFIC RESEARCH: CONTINUED VIGILANCE CRITICAL TO PROTECTING HUMAN SUBJECTS (1996).

clinical research.⁸³

II. TRADITIONAL LIMITED LIABILITY FOR MEDICAL RESEARCH ACTIVITIES INVOLVING INTANGIBLE HARM

Research subjects encounter numerous difficulties in bringing claims for experimentation-related injury, hurdles above and beyond what any patient must navigate to recover for injuries arising during ordinary medical care. When research subjects seek redress for intangible harm, these difficulties are compounded. This Part examines some of the more likely types of claims available to subjects and reviews the many barriers complicating recovery for intangible hazards.

A. Battery

Battery claims provide redress for an offensive and unconsented touching.⁸⁴ Thus, a subject bringing a battery action technically does not have to allege physical injuries. Battery constitutes a legal harm not for any physical pain inflicted but for offending a reasonable sense of personal dignity.⁸⁵

Despite the historical origins of malpractice claims in battery,⁸⁶ the modern trend is to apply negligence principles to address harms arising in the doctor-patient relationship. Even cases alleging dignitary injuries because of offensive touching have been more often treated as negligence actions, involving informed consent rules, rather than cognizable battery claims.⁸⁷ Battery actions in regular medical care

83. Cf. Lori A. Alvino, *Who's Watching the Watchdogs? Responding to the Erosion of Research Ethics by Enforcing Promises*, 103 COLUM. L. REV. 893, 905–06 (2003).

84. See RESTATEMENT (SECOND) OF TORTS §§ 13, 18 (1965).

85. See *id.* § 19; *Cruzan v. Dir., Mo. Dep't of Health*, 497 U.S. 261, 269 (1990).

86. Interestingly, the early common law cases involving research subjects did not distinguish the disputes from ordinary malpractice actions. Experimental therapy that differed from standard care was often presumed careless or reckless and physician-investigators faced quasi-strict liability for any damages the patient experienced. See generally Jesse A. Goldner, *An Overview of Legal Controls on Human Experimentation and the Regulatory Implications of Taking Professor Katz Seriously*, 38 ST. LOUIS U. L.J. 63, 71–74 (1993) (providing a thorough overview of the early research harm cases). A good many of these earlier cases applied the tort doctrine of battery. See *id.*

87. See, e.g., *Lugenbuhl v. Dowling*, 701 So. 2d 447, 453, 455–56 (La. 1997). In *Lugenbuhl*, a patient sued a physician who allegedly agreed to use a surgical mesh in repairing the patient's hernia, but proceeded to operate on the patient without the surgical mesh. No strong evidence was presented that the physician breached the standard of care in not using a surgical mesh or that the physician's actions caused a substandard medical outcome. The case seemingly presented a favorable situation for asserting battery because of the unconsented touching resulting from a clear disregard of the patient's wishes. But the court rejected battery-based liability. It instead found an informed consent violation and awarded five thousand dollars in damages based not on physical injury but on harm involving

remain limited today, confined to egregious situations of offensive, unconsented touching, such as when the alleged medical procedures differed significantly from what the patient consented to. Thus, battery currently offers few opportunities for research subjects seeking relief, save for the rare situations when subjects receive no disclosures regarding the research aspects of the encounter.⁸⁸

B. Negligent Design/Implementation of Protocol

To bring a successful malpractice claim of ordinary negligence, a patient must prove that the physician owed him a duty and breached that duty by providing treatment below the applicable standard of care, thus causing compensable damages. The analogous claim in the research context is negligent design or negligent implementation of the experimental protocol. This presents many challenges for the plaintiff, including difficulty in identifying what the relevant standard of care should be.⁸⁹ While custom helps define the standard of care for ordinary malpractice cases, it becomes more difficult to establish in the research setting. Because research activities often involve cutting-edge interventions that in fact represent a departure from therapeutic custom, generalizations from one setting to the other may not be appropriate and require considerable speculation. Considerable good-faith differences of opinion exist within the research community and different practices are followed, evidenced, for example, by the considerable variability in IRB determinations of acceptable risk/benefit ratios for study protocols.⁹⁰

Accordingly, subjects' chances of a successful claim improve greatly not by centering claims on intangible harm but by pointing to obvious, glaring missteps by researchers, such as a failure to follow the study protocol itself that results in physical injury. Representative of this

intangible concepts of dignity and privacy. *See id.* at 455–56.

88. *See, e.g.,* *Mink v. Univ. of Chi.*, 460 F. Supp. 713 (N.D. Ill. 1978). In *Mink*, the plaintiffs were pregnant patients given DES during their prenatal care as part of a study testing the drug's efficacy for preventing miscarriages. The plaintiffs sued under both negligence and battery theories, alleging injury from increased risk of cancer to their daughters and resulting emotional distress. The court allowed the battery claim. *See id.* at 717–18. Although not expressly stated in the opinion, the nonconsensual aspects of the research seem to have motivated the court to depart from traditional negligence principles. *See id.* at 716–18. *See also* E. Haavi Morreim, *Litigation in Clinical Research: Malpractice Doctrines Versus Research Realities*, 32 J.L. MED. & ETHICS 474, 478–79 (2004).

89. *See* E. Haavi Morreim, *Medical Research Litigation and Malpractice Tort Doctrines: Courts on a Learning Curve*, 4 HOUS. J. HEALTH L. & POL'Y 1, 38 (2003) (“In contrast [to medical practice], research cannot be judged by its conformity to standard practice since it is, by definition, a deviation from these routines.”).

90. *See, e.g.,* Henry Silverman et al., *Variability Among Institutional Review Boards' Decisions Within the Context of a Multicenter Trial*, 29 CRITICAL CARE MED. 235 (2001).

limited line of cases is the recent litigation arising from an experimental leukemia therapy trial at the University of Washington's Fred Hutchison Cancer Center.⁹¹ The jury awarded damages for the mishandling of specimens that damaged bone marrow donated for a particular transplant, but determined the medical center and physicians were not negligent in conducting the overall study.⁹² Thus, liability arose because of a rare misstep, and not because of the essential research activity of attempting the risky experimental transplant.

C. Informed Consent

Alternatively, a research subject may allege negligence due to failure to obtain her informed consent for the experimental intervention.⁹³ However, despite the general acknowledgment of numerous, serious informed consent problems in clinical trials,⁹⁴ research subjects still encounter considerable difficulty in recovering for informed consent violations. Plaintiff-friendly disclosure standards from certain jurisdictions in ordinary malpractice cases, such as whether information was disclosed that the reasonable patient would want to know,⁹⁵ may not work as well in the research setting. Subjects volunteer for experimental studies because of multiple, complex considerations that extend beyond immediate clinical needs. They participate in research for intensely personal and often highly subjective reasons, including altruism, a sense of having no hope, uncritical belief in medical innovation and new technology, a desire for access to perceived life-saving therapy, and a seeming need to do something and take direct action rather than pursue comfort, care, or passive monitoring.⁹⁶ More so than for the hypothetical reasonable patient offered conventional treatment, it becomes difficult to attribute what information is material to the

91. See Complaint, *Wright v. Fred Hutchison Cancer Ctr.*, No. 01-2-008376 (Kitsap County Super. Ct., Wash. Mar. 29, 2001), available at <http://www.sskrplaw.com/gene/wright/complaint1.html>

92. See Tracy Johnson, *Jury Sides With Hutch, Doctors in Deaths of 5*, SEATTLE POST-INTELLIGENCER, Apr. 9, 2004, at A1.

93. See generally JESSICA BERG ET AL., *INFORMED CONSENT: LEGAL THEORY AND CLINICAL PRACTICE* 249–303 (2d ed. 2001).

94. See *infra* notes 210–14 and accompanying text.

95. See, e.g., *Canterbury v. Spence*, 464 F.2d 772 (D.C. Cir. 1972).

96. It is too idealistic to presume that research subjects volunteer for studies primarily to benefit others from the knowledge gained. Research subject motivations are more complex and may involve a degree of self-interest. Nonetheless, altruistic impulses play a role in motivating many subjects to participate. For a more comprehensive discussion of research subject motivations, see Nancy E. Kass et al., *Trust: The Fragile Foundation of Contemporary Biomedical Research*, HASTINGS CTR. REP., Sept.-Oct. 1996, at 25; David T. Stern, *Future Challenges From the U.S. Perspective: Trust as the Key to Clinical Research*, 15 J. CLINICAL ETHICS 87, 88–89 (2004).

hypothetical reasonable research subject, given the multifaceted, highly individualistic reasons for research participation.⁹⁷

Also, informed consent actions based on inadequate disclosure of risk generally require that the plaintiff show that the undisclosed risk was the injury that actually materialized.⁹⁸ In research settings, the technology under study is often so new that the full appreciation of what risks actually existed and later developed may still be evolving in the clinical community. Even highly skilled, cutting-edge investigators cannot confidently predict what risks will materialize in many studies.⁹⁹

More importantly, a serious causation problem underlies many research subjects' informed consent claims. To maintain an informed consent action, the subject must prove the causation element. In other words, the subject must prove that, with proper disclosure, she would have opted not to enroll or continue in the trial and, further, by so choosing, would not have been physically injured. These threshold causation criteria are not easily established.¹⁰⁰ Even though informed consent actions theoretically protect a patient's interests in autonomy and self-determination, injuries to these interests alone, when not linked to corresponding treatment choice differences and adverse health outcomes, rarely become cognizable and therefore compensable in regular malpractice actions.¹⁰¹ Indeed, the award of dignitary-type damages remains rare in the absence of accompanying physical injury causally linked to the health care provider's malpractice.¹⁰² Among other issues, courts remain concerned that loosening traditional causation requirements for informed consent may lead to a flood of suits in which it would be difficult to discern credible claims for relief from

97. See Saver, *supra* note 50, at 232; Morreim, *supra* note 89, at 64–66.

98. See, e.g., Clark v. Miller, 378 N.W.2d 838, 845–46 (Minn. Ct. App. 1986); Alan Meisel, *A "Dignitary Tort" as a Bridge Between the Idea of Informed Consent and the Law of Informed Consent*, 16 L. MED. & HEALTH CARE 210, 215 (1988).

99. See Richard Delgado & Helen Leskovic, *Informed Consent in Human Experimentation: Bridging the Gap Between Ethical Thought and Current Practice*, 34 UCLA L. REV. 67, 69, 88–92 (1986) (explaining that in experimentation the full range of risks are truly not known in advance by either the subject or the researcher); Noah, *supra* note 4, at 384 ("In many cases, however, the investigators know so little about an experimental therapy that, even if they have fully disclosed all that they know . . . some commentators have wondered whether it even makes sense to speak of 'informed' consent in the research setting.").

100. Cf. Mary Crossley, *Infected Judgment: Legal Responses to Physician Bias*, 48 VILL. L. REV. 195, 248–49 (2003) (describing the similar problems in using informed consent claims to combat physician bias, such as failure to disclose treatment options to patients belonging to certain ethnic or racial groups).

101. See Barbara A. Noah, *The Invisible Patient*, 2002 U. ILL. L. REV. 121, 146–48. But see Lugenbuhl v. Dowling, 701 So. 2d 447 (La. 1997), discussed further at *supra* note 87 and *infra* note 263.

102. See generally Marjorie Maguire Shultz, *From Informed Consent to Patient Choice: A New Protected Interest*, 95 YALE L.J. 219 (1985).

ordinary disappointments and frustrations accompanying any period of illness.¹⁰³ These same concerns apply to the research setting, perhaps with even more force, given the considerable complexities, previously noted, in understanding how and why subjects choose to enroll in a clinical trial.

D. Other Causation/Damages Issues

Apart from the causation problems regarding choice inherent in informed consent claims (i.e., proving the research subject would have chosen differently and not enrolled in the trial), subjects also experience difficulty establishing other aspects of causation and damages in research harm cases. For a negligent design/implementation of the protocol claim, the subject must show that the experimental intervention actually and proximately caused her harm. If the thrust of the complaint instead is informed consent, the subject must show not only that she would have chosen differently, but that she would have experienced a different clinical outcome by choosing not to enroll in the trial.

Under either theory, linking causation to compensable damage becomes quite arduous to establish when, as with many clinical trials, the subjects begin a study protocol already ill and generally failing on conventional therapy. The recent litigation against the University of Washington/Fred Hutchison Cancer Center illustrates this trend. Although the jury agreed that the research conduct had been problematic, limited liability still resulted. An initially proposed damage award of five million dollars was significantly reduced because of the determination that the subject's chances of surviving his leukemia with or without the experimental transplant were not very high.¹⁰⁴ Indeed, subjects often enroll in a trial precisely because they are looking for new options when seriously ill and unresponsive to conventional treatment. In such situations, it may be impossible to distinguish between poor outcomes due to the research-related interventions and those due to natural progression of the underlying disease.¹⁰⁵

103. See, e.g., *Afentakis v. Mem'l Hosp.*, 667 N.Y.S.2d 602, 604 (N.Y. App. Div. 1997) (“[A] certain unavoidable loss of dignity attends most illnesses, terminal and otherwise An unsuitable expansion of liability would certainly result should courts attempt to distinguish between the ordinary assaults upon a patient's dignity which stem from the loss of power and control which is all too often the corollary to illness, and the loss of autonomy produced by even a short hospitalization, from those occasioned by the failure of a hospital and its staff to maintain a certain level of caring, respect and consideration for the feelings of its charges.”).

104. See *Johnson*, *supra* note 92, at A1.

105. See, e.g., *ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS*, *supra* note 32, at v (“For those who endure harm while participating in research, it is often very difficult

Finally, additional defendants, one level removed from directly enrolling the subjects in the study and administering the experimental procedures, such as the drug company sponsoring the clinical trial, likely enjoy additional limited liability because of proximate cause issues associated with their indirect status.

E. Emotional Distress Claims

Research subjects having difficulty proving causal links to physical damages might alternatively try to seek relief for negligent infliction of emotional distress. However, most jurisdictions have limited recovery rules for pure emotional harm in the absence of tangible physical injury. These rules require, for example, that the plaintiff endure some sort of physical impact, occupy a zone of danger where physical injury was likely, or experience distress so severe that it is followed by actual physical manifestation of the mental anguish.¹⁰⁶

This general approach disfavors a research subject's possibility of recovery. For example, it may be difficult, given an individual's initial ill state of health to deem that a zone of danger existed in which the experimentation further significantly threatened the subject's physical health. Moreover, the idea that subjects experience special mental distress because of the experimentation context should not be automatically assumed. Some commentators skeptically question whether the emotional distress arising from research is significant at all and whether it can be accurately identified.¹⁰⁷ A subject's knowledge that she was used as an experimental object, or that the goals of the

to separate injuries traceable to the research from those that stem from the underlying disease or social condition being studied."'). Some commentators question whether research subjects really face more difficult causation/damage problems than ordinary malpractice patients. See Lars Noah, *Deputizing Institutional Review Boards To Police (Audit?) Biomedical Research*, 25 J. LEGAL MED. 267, 275-76 (2004). After all, conventional patients alleging ordinary malpractice often have serious pre-existing illnesses and nonetheless must show a causal link between the health care provider's actions and the actual injury that they experience. *Id.* However, while research subjects may not face qualitatively different causation/damage problems of this type than ordinary patients, they have to navigate this barrier to a greater degree. Many subjects likely think about research enrollment after their disease states have significantly progressed, and they have nearly exhausted conventional approaches. The sicker they are at the time of the research intervention, the more difficult it becomes to establish injury caused by the experimental intervention or lost treatment opportunities.

106. See generally DAN B. DOBBS, THE LAW OF TORTS § 3.08, at 835-39, § 3.11, at 847-48 (2000); Andrew L. Merritt, *Damages For Emotional Distress in Fraud Litigation: Dignitary Torts in a Commercial Society*, 42 VAND. L. REV. 1, 21-23 (1989).

107. See Hamburger, *supra* note 20, at 341 ("In calculating the value of IRBs, one could take into account their prevention of the harms of offense, embarrassment, or other mental discomfort arising from research. Yet from a legal perspective, these are so trivial, immeasurable, or subjective as to be not typically cognizable at common law.").

experimental protocol potentially supplanted concerns for individually tailored treatment, while troubling as an ethical matter and raising questions of dignity, abandonment, and exploitation, does not lead inevitably to emotional distress. A subject can develop cruelly disappointed, starkly negative impressions of research participation while maintaining a level of emotional detachment from the experience so as not to endure severe mental anguish.

As opposed to actions sounding in negligence, intentional infliction of emotional distress claims do not require that the plaintiff show physical harm to recover.¹⁰⁸ While this tort theoretically is available to subjects unable to demonstrate a causal link to physical injury, courts recognize the claim in rare instances. The requirements that the defendant's actions be extreme and outrageous and that the defendant have intended or acted recklessly with regard to severe emotional distress¹⁰⁹ likely do not apply to the conduct of most research defendants, as they can usually plausibly contend that they thought subjects could benefit from the experimentation. Further, subjects have difficulty meeting the intentional tort's strict requirements of severity. Research encounters raising concerns of exploitation or abuse of trust may develop episodically and lead to longer-term emotional responses that harden over time into anger, despair, or disappointment, compared with the immediate, jarring, completely altering mental disturbance contemplated for recovery in the limited line of intentional infliction of emotional distress cases.

F. Fiduciary Duty and Related Theories

In theory, fiduciary duty theories seem a more promising avenue for aggrieved research subjects experiencing primarily intangible hazards. The remedy courts apply in many breach of fiduciary duty cases is disgorgement of profits and related restitutionary relief. This focuses the damages question less on a plaintiff's tangible physical injuries and more on the extent that the defendant, by breaching the fiduciary obligation, unjustly enriched himself.¹¹⁰

However, fiduciary duty claims must overcome certain obstacles. Even in regular treatment settings, courts have been willing to find health care provider liability for fiduciary breaches in only limited instances, such as failure to secure informed consent or to maintain

108. See generally DOBBS, *supra* note 106, § 3.03, at 826.

109. See RESTATEMENT (SECOND) OF TORTS § 46 (1965).

110. See D. Gordon Smith, *The Critical Resource Theory of Fiduciary Duty*, 55 VAND. L. REV. 1399, 1493–96 (2002); DAN B. DOBBS, *THE LAW OF REMEDIES* § 10.4, at 722–23 (2d. ed. 1993).

patient confidentiality.¹¹¹ Other courts have been reluctant to recognize distinct claims for fiduciary duty breach that arguably duplicate claims for ordinary malpractice that the plaintiff might bring on the same facts.¹¹²

A more basic difficulty with fiduciary duty claims stems, however, from the threshold question whether a fiduciary duty is owed by an investigator to a research subject. In ordinary medical care cases, finding the existence of a duty is much simpler. The law generally recognizes the physician-patient relationship as fiduciary in nature.¹¹³ As a fiduciary, the physician is generally required to act for the patient's benefit, provide individually appropriate treatment, and avoid elevating other interests above the patient's welfare unless there has been appropriate disclosure.¹¹⁴

Whether a similar fiduciary relationship exists between investigator and research subject remains subject to vigorous debate. Clinical protocols demand that the investigator follow consistent study procedures with some level of inflexibility, including when to initiate and stop therapy and what dosage of medication to prescribe, in order to develop generalizable data that will stand up to scientific review. Such actions are undertaken to benefit the study more than the immediate research subject and may, at times, be at odds with the treatment preferences and clinical needs of the individual subject.¹¹⁵

Thus, fiduciary duty theories apply awkwardly, if at all, to the research setting. Deviation from the subject's best medical interests,

111. See Maxwell Mehlman, *Fiduciary Contracting Limitations on Bargaining Between Patients and Health Care Providers*, 51 U. PITT. L. REV. 365, 389-90 (1990) (finding inconsistency in how courts have applied fiduciary principles to different health care arrangements). See also Marc A. Rodwin, *Strains in the Fiduciary Metaphor: Divided Physician Loyalties and Obligations in a Changing Health Care System*, 21 AM. J.L. & MED. 241, 247-48 (1995); Michelle Oberman, *Mothers and Doctors' Orders: Unmasking the Doctor's Fiduciary Role in Maternal-Fetal Conflicts*, 94 NW. U. L. REV. 451, 459 (2000) (noting limited application of fiduciary principles to physicians and observing how the law has not sufficiently acknowledged fiduciary breach problems arising in maternal-doctor conflicts).

112. See *Neade v. Portes*, 739 N.E.2d 496 (Ill. 2000) (refusing to recognize a distinct claim for breach of fiduciary duty, where physician allegedly failed to order an angiogram for the patient because of financial conflicts, because such a claim would involve the same operative facts and address the same basic injury as plaintiff's ordinary malpractice action). See also Crossley, *supra* note 100, at 252 ("[T]he courts' willing characterizations of physicians as fiduciaries has not been matched by an enthusiasm for holding physicians legally accountable.").

113. See Mehlman, *supra* note 111, at 389-90. Courts determine the fiduciary character not as automatic but more on a case by case basis, and limited to certain aspects of the relationship, responding to factors such as expertise of the physician, the patient's vulnerability and dependency, and some notion of entrustment. See Rodwin, *supra* note 111, at 243-44.

114. See Crossley, *supra* note 100, at 251-52.

115. See LEVINE, *supra* note 19, at 10.

presumed to be an unacceptable activity by a physician owing a fiduciary duty to her patient, may in fact be an inherent part of what any investigator does.¹¹⁶ Under this view, the experimental nature of the researcher's activity precludes any finding of a fiduciary relationship because the researcher does not act solely to benefit the individual subject.¹¹⁷

While case law features lofty rhetoric about the fiduciary's strict obligations to the principal, however, the law as pragmatically applied has rarely required that fiduciaries avoid any form of self-benefit arising from the fiduciary-principal relationship.¹¹⁸ Thus, the fact that researchers have a separate duty to the clinical trial and cannot act solely for the benefit of individual subjects may not definitively resolve the issue of whether fiduciary-like obligations exist in the research setting. Indeed, some commentators conclude that the duty investigators owe a research subject largely mirrors the fiduciary obligations in the doctor-patient relationship.¹¹⁹ The researcher-subject connection shares key aspects with relationships, including the doctor-patient relationship, where the law imposes fiduciary duties. The interactions between investigators and subjects feature power and informational asymmetries, the vulnerability and potential for exploitation of one party, conflicts of interest affecting the more powerful party, and significant levels of trust and expectations of confidence that one party places in the other, all common elements of fiduciary-like relationships.¹²⁰ These factors combined arguably support application of fiduciary-like obligations in the research setting, even if investigators and subjects do not enter into a technically full-fledged fiduciary relationship.

Unfortunately, there is a dearth of case law answering clearly whether a researcher owes fiduciary-like duties to a research subject and, if so, when these duties are breached. In *Moore v. Regents of the University of California*, the California Supreme Court held that physicians who

116. See Coleman, *supra* note 14.

117. See Morreim, *supra* note 89, at 41–46. It may not even be the researcher's goal to help the individual subject. The investigator aims more to help future patients through completion of a successful study that will provide generalizable information for future clinical use. When the investigator "cannot in good faith promise fidelity to doing what is best medically for the patient-subject," one must question whether a fiduciary relationship exists. See Howard Brody & Franklin G. Miller, *The Clinician Investigator: Unavoidable But Manageable Tension*, 13 KENNEDY INST. ETHICS J. 329, 336 (2003).

118. See Richard S. Saver, *Squandering the Gain: Gainsharing and the Continuing Dilemma of Physician Financial Incentives*, 98 NW. U. L. REV. 145, 220–21 (2003).

119. See, e.g., Angela R. Holder, *Do Researchers and Subjects Have a Fiduciary Relationship?*, IRB, Jan. 1982, at 6; Delgado & Leskovac, *supra* note 99, at 109–10.

120. See Coleman, *supra* note 14.

surgically removed a patient's spleen in the course of regular treatment had an obligation to inform the patient of ancillary research activity involving the extracted bodily material.¹²¹ The court applied heightened informed consent requirements in part because of the fiduciary obligations the physician owed the patient.¹²² However, the case's applicability to numerous clinical trial settings is unclear.¹²³ The Maryland Court of Appeals in *Grimes v. Kennedy Krieger Institute* held that the researcher-subject relationship imposes heightened obligations on investigators to protect subjects.¹²⁴ The breadth and scope of this holding, however, remains unclear. The court discussed several possible sources for finding that a duty existed, including a common law "special relationship" that might exist between a researcher and subject, the special quasi-contract established between the parties by the informed consent document, duties derived from the federal research regulations, and duties implied from international ethics standards such as the Nuremberg Code.¹²⁵ *Grimes* thus does not provide clear support for finding investigator obligations based solely on fiduciary/special relationship theories—nor has *Grimes* been widely followed to date.

Indeed, the difficulties in broadly applying the fiduciary duty label are illustrated by the more recent case of *Suthers v. Amgen, Inc.*¹²⁶ In *Suthers*, a federal district court declined to find that a pharmaceutical company sponsoring a clinical trial owed a fiduciary duty to the subjects. The plaintiffs sued to compel drugmaker Amgen to continue giving them an experimental drug used in a Parkinson's Disease study

121. 793 P.2d 479 (Cal. 1990).

122. The court reasoned that "a physician who is seeking a patient's consent for a medical procedure must, in order to satisfy his fiduciary duty and to obtain the patient's informed consent, disclose personal interests unrelated to the patient's health, whether research or economic, that may affect his medical judgment." *Id.* at 485.

123. Because the patient in *Moore* was not enrolled in a clinical trial, and the research aims of the physician were unrelated to any possible therapeutic treatment for the patient, the case's applicability is unclear as to numerous clinical trial settings where the investigator applies an experimental intervention with the hopes of patient benefit and to advance the study. Similarly, in *Greenberg v. Miami Children's Hospital Research Institute*, 264 F. Supp. 2d 1064 (S.D. Fla. 2003), the court considered a breach of fiduciary duty claim brought by subjects who had donated tissue to genetic researchers studying Canavan Disease. The tissue donors contested the researchers' plans to restrict public access through obtaining a patent to Canavan Disease testing technologies developed with the donated tissue. The court dismissed the breach of fiduciary duty claim, finding that an acceptance of trust by the defendants had not been well alleged. *See id.* Also, the donors were not receiving experimental interventions that might benefit them directly, as occurs in more ordinary clinical trial settings. *See id.*

124. 782 A.2d 807 (Md. 2001).

125. *Id.* at 818. *See also* Diane E. Hoffman & Karen H. Rothenberg, *Whose Duty Is It Anyway? The Kennedy Krieger Opinion and Its Implications for Public Health Research*, 6 J. HEALTH CARE L. & POL'Y 109 (2002).

126. 372 F. Supp. 2d 416 (S.D.N.Y. 2005).

conducted at New York University Medical Center. The clinical trial had later been discontinued. The court found that Amgen, which did not have direct contact or form a privity relationship with the subjects, stood in a position too far removed to have a fiduciary relationship with the subjects. The court further questioned, without disposing of the issue directly, whether the researchers or medical center with direct contact with the subjects assumed fiduciary duties, given their loyalties to the experimental protocol and not solely to the subjects.¹²⁷

Thus, some question remains whether researchers and subjects are in a common law special relationship, a fiduciary-like relationship, a full fiduciary relationship, or something altogether different. This makes unclear the corresponding obligations of investigators to protect subjects from any intangible harm. Some level of ambiguity is perhaps unavoidable given the lack of clear precedent regarding fiduciary law in the research context. But this lack of precision illustrates the numerous problems research subjects have getting a fiduciary-like duty standard practically applied to intangible harm actions.

G. Common Law Fraud

Research subjects have increasingly asserted common law fraud claims.¹²⁸ This likely reflects efforts to avoid statutes of limitation problems, damage caps, and other restrictions associated with ordinary malpractice claims. However, these claims are not easy for subjects to prevail upon. To sustain an action in medical cases alleging common law fraud, a plaintiff must ordinarily prove that: (1) the defendant made a false, material misrepresentation; (2) the defendant knew it was false or acted in reckless disregard of its truthfulness; (3) the defendant intended that the misrepresentation be acted upon by the plaintiff; (4) the plaintiff acted in reliance on the misrepresentation; and (5) damages.¹²⁹ But even in the usual medical context, courts have been reluctant to recognize a common law fraud action if it appears inseparable from a potential malpractice claim.¹³⁰ Common law fraud claims turning on the

127. *Id.* at 427–28 & n.9.

128. In the University of Pennsylvania gene therapy trial litigation, *see supra* note 9, the plaintiffs alleged fraud among other claims. *See* Complaint, Count VI, *Gelsinger v. Univ. of Pa.*, (Phila. Ct. of C.P. 2000), available at <http://www.sskrplaw.com/links/healthcare2.html>. The case eventually settled on undisclosed terms but terms understood to be favorable to the plaintiff. *See* Huntly Collins, *Penn. Family Settle Suit in Gene-Therapy Death: The Pact's Terms Included a Substantial Sum*, PHILA. INQUIRER, Nov. 4, 2000, at A1.

129. *See* *Gomez v. Diaz*, 57 S.W.3d 573, 580 (Tex. Ct. App. 2001); *Atamian v. Gorkin*, No. 97C-08-001, 1999 Del. Super. LEXIS 666 (Del. Super. Ct. Aug. 13, 1999).

130. *See, e.g.,* *Coopersmith v. Gold*, 568 N.Y.S.2d 250, 251–52 (N.Y. App. Div. 1991) (holding

same operative facts as potential malpractice claims may be consigned to malpractice counts alone, where, as noted, subjects face many obstacles in obtaining relief for intangible hazards.¹³¹ Also, courts evaluating common law fraud claims against health care providers often apply the causation and reliance elements strictly against the plaintiff.¹³² Thus, subjects will still face problems showing they would have chosen not to enroll in a trial, or would have experienced a different therapeutic outcome, if fraudulent representations about the research had not been made. Further, damages in the absence of physical harm or other direct economic loss, such as damages for emotional distress and other intangible hazards, are not easily recovered in fraud actions.¹³³

H. Contract

Contract claims do not offer research subjects a much better opportunity to recover for intangible harm. Notwithstanding the fact that most subjects sign written consent documents to enroll in a study, courts have displayed reluctance to find binding contractual obligations in the research setting. Many courts prefer to treat the disputes involving aggrieved subjects under traditional malpractice theories of ordinary negligence and informed consent and treat the written forms as merely notice of the subject's consent rather than an enforceable contract.¹³⁴

that a patient's fraud claims, asserted against a psychiatrist with whom she had an affair, were inseparable from patient's malpractice claims because the alleged sexualization of the doctor-patient relationship and the damages caused by any alleged fraud were the same as caused by the alleged malpractice). *See also* Trevino v. Christus Santa Rosa Healthcare, No. 04-01-00764-CV, 2002 Tex. App. LEXIS 7697, *1, **16-17 (Tex. Ct. App. Oct. 30, 2002) (Marion, J., concurring) (explaining how courts will not allow plaintiffs to re-cast negligence claims as fraud claims simply to evade the damage and procedural limitations of the state statute governing malpractice actions).

131. *See supra* notes 88-105 and accompanying text.

132. *See, e.g.,* Greene v. Thomas, 662 P.2d 491, 494-95 (Colo. Ct. App. 1982). The plaintiff asserted fraud claims against a plastic surgeon for allegedly telling the patient inaccurate information that a growth on his scalp had been completely excised. The court found the patient did not prove reliance. The court reasoned that the patient's delay in seeking treatment when a new tumor was later discovered related to a number of reasons other than the alleged misrepresentation—he was in his first year of college, his father needed surgery, and he was needed home—that could explain why the patient delayed seeking further treatment. *See id.*

133. *See* Merritt, *supra* note 106, at 3-5.

134. For example, in *Harden v. University of Cincinnati Medical Center*, No. 04AP-154, 2004 WL 2341713 (Ohio Ct. App. Oct. 19, 2004), the court rejected a subject's contract-based claims that defendants had promised, through the informed consent document, to provide the subject with medical care for life. The informed consent document, the court reasoned, merely served as notice of the subject's consent to the experimental procedure. It did not constitute a legally binding contract between the parties involving bargained for promises with sufficient consideration. *Id.* at **7-8. The lower court's opinion developed this point further. *See* *Harden v. Univ. of Cincinnati Med. Ctr.*, No. 98-

Even if a subject succeeds in characterizing the informed consent document, related study paperwork, and general understandings between the parties as evidence of a contract,¹³⁵ the ability to recover for intangible harms remains limited. The ordinary relief awarded in contract claims, the expectations damages that attempt to put the party in the position it would have been in had the contract been performed,¹³⁶ does not necessarily provide a subject with a clear opportunity to recover for intangible harms arising from a contract breach. Further, the consequential damages component of an expectation-based recovery must be proven with a reasonable degree of certainty and must have been contemplated by the parties at the time of contracting.¹³⁷ This presents difficulties for obtaining contract relief for intangible hazards, which, because of their intangible nature, may not have been highly foreseeable or readily proven with firm evidence.

To the extent that contract law primarily bases remedies on objective economic loss, relief for intangible harms such as mental anguish or loss of reputation is ordinarily not available unless the contract breach also amounts to tortious conduct or unless highly personal interests are at stake in the contractual promise.¹³⁸ Subjects could argue that research participation does implicate highly personal interests in an attempt to avoid the limitation of damages as occurs with commercial contracts. However, courts display reluctance to deviate from the general approach of confining contract damages to the value of the performance.¹³⁹ In any event, limited precedent exists regarding contract claims of research subjects because, as noted, not all courts even recognize contract rights as ordinarily emanating from research participation. Accordingly, subjects' claims for intangible harm remedy based on contract theories are highly tenuous at best.

11405, 2004 WL 119446, *1, **11–12 (Ohio Ct. Cl. Jan. 12, 2004). For further discussion of the case, see *infra* Part III.B.2.

135. See, e.g., *Dahl v. HEM Pharms. Corp.*, 7 F.3d 1399 (9th Cir. 1993) (characterizing the informed consent form and other study documents as a unilateral contract that could not be changed by the sponsor once subjects had materially performed their end of the bargain by enrolling in the experiment); *Grimes v. Kennedy-Krieger Institute*, 782 A.2d 807 (Md. 2001) (holding that researchers have special duties to the subjects based, in part, on the court's finding that a quasi-contract was formed between the parties by the informed consent document).

136. See DOBBS, *supra* note 110, § 12.1(1), at 752.

137. See *id.*

138. See *Lane v. Kindercare Learning Ctrs.*, 588 N.W.2d 715, 716–18 (Mich. Ct. App. 1998); DOBBS, *supra* note 110, § 12.1(1), at 753, § 12.5(1), at 789.

139. See, e.g., *Parks v. Wells Fargo Home Mortgage, Inc. f/k/a Norwest Mortgage Inc.*, 398 F.3d 937, 941–42 (7th Cir. 2005).

III. THE NEW WAVE OF RESEARCH LITIGATION

While traditionally there was a dearth of medical research litigation, this trend may be turning. The frequency of lawsuits against researchers, institutions, and trial sponsors appears to be on the upswing.¹⁴⁰ Whether the new wave of litigation will provide subjects better relief for intangible hazards remains to be seen. In the most recent round of litigation, plaintiffs asserting novel claims of intangible harm have met with limited success. Other recent cases have raised compelling concerns of intangible harm, such as frustrated access to experimental technology and early termination of a protocol in glaring disregard of the reasonable expectations and legitimate needs of subjects already then enrolled. Yet in these disputes, subjects have largely failed in recovering even conventional damages. These cases demonstrate the need for new approaches, as the law currently struggles to find an optimal response to intangible harm in medical research.

A. *Novel Dignitary Harm Claims*1. *Robertson v. McGee*

Representative of the recent litigation wave is *Robertson v. McGee*.¹⁴¹ The subjects, participants in a clinical trial of an investigational melanoma vaccine at the University of Oklahoma Health Science Center, sued the investigator, the University IRB, and the pharmaceutical company sponsoring the study. Among other allegations, the subjects contended that the sponsor manufactured and distributed the vaccine in an unsafe manner, investigators enrolled patients at remote sites without local IRB approval, pregnant patients were allowed to continue in the trial even though the protocol called for exclusion of pregnant subjects, other subjects did not meet protocol eligibility criteria, and the investigators changed the protocol without IRB approval.¹⁴²

Study nurse Cherlynn Mathias, who coordinated the clinical trial, turned whistleblower and helped uncover many of the improprieties.¹⁴³ Concerned about the University's entire system of oversight, the federal

140. See Michelle M. Mello et al., *The Rise of Litigation in Human Subjects Research*, 139 ANNALS INTERNAL MED. 40, 40–41 (2003).

141. No. 01-CV-60-C, 2002 U.S. Dist. LEXIS 4072 (N.D. Okla. Jan. 28, 2002).

142. See Complaint, *Robertson v. McGee* (N.D. Okla. 2002), available at <http://www.sskrplaw.com/gene/robertson/complaint-new.html> [hereinafter *Robertson Complaint*].

143. See Omer Gillham, *Cancer Study Case Still Alive*, TULSA WORLD, Mar 16, 2003, at A17; Lemonick & Goldstein, *supra* note 6, at 46.

OHRP temporarily suspended all government-sponsored studies involving human subjects at the University of Oklahoma.¹⁴⁴ The University eventually agreed to settle the case, and it also fired the lead researcher, Dr. J. Michael McGee.¹⁴⁵ Meanwhile, the plaintiffs' claims against Dr. McGee and several other defendants are still in litigation.¹⁴⁶

While the subjects obtained a partial settlement, the federal district court rejected their attempt to recover directly for affronts to dignity. The subjects' initial complaint had asserted that the common law recognized such a claim, consistent with the ethical standards of the Nuremberg Code and the Declaration of Helsinki.¹⁴⁷ Yet the court granted a motion to dismiss plaintiffs' first amended complaint. Although the ruling turned on Section 1983 civil rights jurisprudence, the court displayed skepticism about an independent legal right of subjects to be treated with dignity, reasoning that "such vague claims have no support in federal law."¹⁴⁸

The initial complaint alleged numerous other causes of action independent of the dignitary counts, ranging from common law fraud to lack of informed consent to ordinary negligence.¹⁴⁹ Although the full facts of the case remain to be developed, one can reasonably speculate that the plaintiffs would have some difficulty establishing causation and the requisite damages elements common to many of these types of claims. For example, the full clinical effect of the investigational vaccine was not well understood at the time of the study. It had only been recently tested for toxicity with a limited number of human subjects under Phase 1 testing, with the Oklahoma study representing the next step to combined Phase 1/2 testing for safety and efficacy.¹⁵⁰ Also, the subjects for the most part were patients with varying degrees of melanoma, including many late-stage disease sufferers¹⁵¹ who presumably were not responding to more conventional treatment. It would be difficult to show that any serious injuries for these subjects

144. See Rick Weiss & Deborah Nelson, *U.S. Halts Cancer Tests in Oklahoma*, WASH. POST, July 11, 2000, at A1; Fred Charatan, *US Halts University of Oklahoma Research*, 321 BRIT. MED. J. 195 (2000).

145. See Omer Gillham, *OU Settles Melanoma Research Suit*, TULSA WORLD, Aug. 28, 2002, at A13.

146. See Gillham, *supra* note 143, at A17.

147. See Robertson Complaint, *supra* note 142, ¶¶ 146–52.

148. No. 01-CV-60-C, 2002 U.S. Dist. LEXIS 4072, *1, *8 (N.D. Okla. Jan. 28, 2002).

149. See Robertson Complaint, *supra* note 142.

150. See *id.* For further discussion of the various FDA testing phases, see *supra* note 21 and accompanying text.

151. See Omer Gillham, *Coming to a Last Shot*, TULSA WORLD, July 15, 2002 (indicating that at least ninety-two late-stage melanoma patients were involved in the study when it began).

resulted from the vaccine and not from their natural disease progression. For other plaintiffs, the extent of physical injuries did not appear great. Some subjects simply alleged that they developed rashes, swelling, headaches, pain, nausea, and depression.¹⁵² While these are hardly trivial injuries, they do not seem substantial enough to generate damages large enough to sustain expensive litigation of this scale, especially considering that many of these same risks can be associated with the underlying melanoma itself.

Although plaintiffs convinced the University to settle, the award amount was for only approximately \$312,000, to be divided among eighteen research subjects and their families.¹⁵³ While not a paltry sum for each plaintiff, it is not a very sizable award, particularly in light of intangible hazards, such as loss of trust in the research process that likely resulted given the defendants' apparent disregard of basic practices for conducting ethical research.

The *Robertson* case also illustrates the paramount concern for treatment access among many research subjects. Notwithstanding revelations of improprieties with the study, and the fact that it was discontinued in 2000 because of safety concerns,¹⁵⁴ several subjects, convinced that the vaccine worked for them, still wanted treatment with it. Although the FDA had been concerned about safety issues, it granted a special exception allowing the discontinued study to extend two more years for twelve late-stage melanoma patients.¹⁵⁵ The case serves as a reminder of subjects' desperation in seeking cutting-edge health care access through clinical trials, underscoring their need for protection from exploitation given their indiscriminate and easily manipulated access demands.

2. *Diaz v. Hillsborough County Hospital Authority*

In at least one reported case, research subjects succeeded in recovering for novel dignitary claims. In *Diaz v. Hillsborough County Hospital Authority*, the plaintiffs comprised a class of approximately

152. See *Robertson Complaint*, *supra* note 142, ¶ 238.

153. See Gillham, *supra* note 143, at A17. However, a part of the settlement also apparently included \$90,000 to be put in a trust fund for a child born to a melanoma patient while enrolled in the study. The plaintiffs alleged that the researchers failed to disclose the risks of the vaccine for a subject's unborn fetus. See Gillham, *supra* note 145, at A13.

154. See Omer Gillham, *OU Admits to Flaws in Melanoma Study*, TULSA WORLD, Jan. 6, 2002.

155. See Gillham, *supra* note 151. A representative subject was Rosemarie Whisman. She had survived surgery to remove a stage-four tumor—indicating an advanced stage of the disease—in 1994 and became convinced that the vaccine presented her only chance at preventing melanoma reoccurrence. See *id.*

five thousand pregnant women who had been enrolled in randomized studies at Tampa General Hospital, allegedly without their consent, while receiving prenatal care.¹⁵⁶ The subjects initially alleged not only lack of informed consent, but also breach of fiduciary duty, battery, and violations of the federal research laws.¹⁵⁷ However, the essence of the claim upon which the case settled was invasion of dignity, based in part on constitutional rights.

Lead plaintiff Flora Diaz enrolled in a study examining treatments for respiratory distress syndrome resulting from fetal lung immaturity. The study randomized subjects between standard treatment with corticosteroids compared to the experimental treatment of corticosteroids combined with thyroid hormones. The investigation exposed subjects to multiple amniocentesis procedures for gathering data essential to the research, not for clinical treatment purposes.¹⁵⁸ Although investigators presented Diaz with a consent form for the research, her counsel alleged that the consent process was seriously deficient. They argued that the presentation of a complex, English-only consent form to a low-income, high-risk pregnant woman, after she had been given morphine and Demerol, represented a coercive and confusing enrollment process, meaning that Diaz never truly appreciated that many procedures applied were research in nature.¹⁵⁹

Plaintiffs argued that their constitutional due process interests in liberty afforded them dignitary rights, consistent with the liberty interest in bodily integrity.¹⁶⁰ Advancement of the dignitary harm count was critical to the subjects' success because the plaintiffs could not demonstrate that the research physically harmed them or their babies. Also, they could not produce credible evidence that the physicians had materially changed the standard of care for their pregnancies because of the ancillary research activities. Thus, ordinary informed consent and negligence claims would likely fail. Indeed, the defendants vociferously argued that not only were no subjects harmed, but that some subjects actually benefited therapeutically from enrollment in the studies.¹⁶¹

156. No. 8:90-CV-120-T-25B, 2000 U.S. Dist. LEXIS 14061, at **1-2 (M.D. Fla. Aug. 7, 2000). See also Stephen F. Hanlon & Robyn S. Shapiro, *Ethical Issues in Biomedical Research: Diaz v. Hillsborough County Hospital Authority*, 30 HUM. RTS. 16 (2003).

157. See *Informed Consent: Class Status Granted to Suit Over Unwilling Participation in Experiments*, 5 Health L. Rep. (BNA), No. 1, at 14 (Jan. 4, 1996).

158. See Kathryn A. Tuthill, *Protecting Patient Autonomy Through Informed Consent*, 18 J. LEGAL MED. 221, 235 (1997).

159. See Hanlon & Shapiro, *supra* note 156, at 16.

160. *Diaz*, 2000 U.S. Dist. LEXIS 14061, **6-7.

161. Defendants contended that many of the experimental treatments studied were proven effective and have now, in fact, become the standard of care for prenatal therapy. See *Informed*

Nonetheless, the medical center agreed to create a settlement fund of \$3,800,000 in addition to taking equitable steps to correct the institutional research practices going forward.¹⁶² In approving the consent decree, the court noted that it represented relatively uncharted territory in research subject litigation. This was likely the first time research subjects recovered substantial monetary awards in the absence of credible physical injury claims.¹⁶³

Some commentators claim that the court's decision in *Diaz* sends a signal that the standard defense in research litigation of "no harm, no foul"¹⁶⁴ will no longer work because even plaintiffs lacking credible physical harm allegations can still bring actionable dignitary harm claims. However, whether *Diaz* represents a launching pad for other dignity harm cases remains to be seen. The facts were unusual and the governmental defendants were no doubt encouraged to settle because negative publicity and mistrust in the community could imperil future research activities. Further, the court's decision in *Diaz* may be distinguishable as a rare case involving near-complete lack of informed consent and closer on the spectrum to battery, in which recovery does not turn on the presence or extent of physical injury.

B. Subject Abandonment

Other recent research litigation has involved subjects alleging improper conduct by the defendants in terminating a study prematurely or denying the subjects continued access to care that the subjects can obtain only through the study protocol. While these cases implicate the informed consent doctrine, they also raise a separate range of issues regarding the proper reasons for terminating a study and how to account for the expectations, needs, and personal investments of subjects already then enrolled in the clinical trial. Although plaintiffs in these disputes did not necessarily expressly plead theories of intangible harm, the cases share a recurring, underlying theme of the intangible hazards associated with subject abandonment.

1. Pollack v. Rosalind Franklin University

Representative of this line of cases is *Pollack v. Rosalind Franklin*

Consent: Class Status Granted to Suit Over Unwilling Participation in Experiments, *supra* note 157.

162. *Diaz*, 2000 U.S. Dist. LEXIS 14061, **6-7.

163. *Id.*

164. See Hanlon & Shapiro, *supra* note 156, at 16.

*University f/k/a Finch University Chicago Medical School.*¹⁶⁵ A certified class of approximately fifty breast cancer patients sued Rosalind Franklin University of Medicine and Science, alleging that the medical school wrongfully terminated a vaccine study in which they were enrolled. Dr. Georg Springer, the study's initial investigator, died in 1998 leaving a large bequest to Chicago Medical School. The subjects contended that he intended the donations for supporting continuation of the breast cancer vaccine research program.¹⁶⁶ However, in 2004, the University terminated the experiment after its IRB allegedly determined that the vaccine had not yet proven effective, and that it was not in the subjects' best interests to continue with unproven therapy.¹⁶⁷ The subjects opposed the study's discontinuation, as many felt that they were benefiting from the vaccine.¹⁶⁸

The plaintiffs contended that the consent forms, as well as oral representations made by the researchers, stated that the vaccine treatment would be continued "ad infinitum."¹⁶⁹ The subjects alleged breach of fiduciary duty, breach of contract, unjust enrichment, common law fraud, and negligence, among other counts.¹⁷⁰ They sought remedies including disgorgement of Dr. Springer's donated funds to the medical school, release of the available vaccines for scheduled injections, as well as actual and compensatory monetary damages.¹⁷¹

Although the plaintiffs did not expressly plead intangible harm counts such as an affront to dignitary rights, the case raises important concerns of intangible hazards in study termination disputes. In these termination situations, subjects can experience great difficulty in demonstrating any direct physical harm linked to the study discontinuation. Researchers and trial sponsors may claim that the experimental procedures have not yet been demonstrated to work and that any study withdrawal impact on an individual subject's therapeutic care is too wildly speculative to support a finding of proximate cause of physical harm.¹⁷² Indeed, the

165. See Complaint, *Pollack v. Rosalind Franklin University f/k/a Finch University Chicago Medical School*, No. 04CH12098 (Cir. Ct. Cook County, Ill., July 27, 2004) [hereinafter *Pollack Complaint*].

166. See Maurice Possley, *North Chicago Med School Sued on Closed Cancer Plan*, CHI. TRIB., July 29, 2004, at 1.; Abdon Pallasch, *Cancer Patients Sue After Med School Cuts Treatment*, CHI. SUN-TIMES, July 29, 2004.

167. See Pallasch, *supra* note 166.

168. See *Pollack Complaint*, *supra* note 165, ¶ 17.

169. See *id.* ¶¶ 2, 17, 50.

170. See *id.*

171. See *id.*

172. As bioethicist Arthur Caplan noted, the subjects' allegations were weakened by the fact that it was an unproven, experimental vaccine and that "[t]here are fewer obligations to continue a research

IRB apparently concluded that the study lacked scientific validity and that it was not proving the vaccine as effective,¹⁷³ thus offering the medical school a clear justification for shutting down the trial. Subjects in such termination situations might alternatively claim physical risk because of lost treatment opportunities, to the extent that they had been persuaded to follow the study protocol rather than alternate therapies. But such lost-chance claims are very speculative. For example, the medical school IRB apparently found the data simply inconclusive as to whether the vaccine was working, and the subjects' advanced disease states potentially precluded them from enrolling in other clinical trials.¹⁷⁴

Thus, intangible harm seems the real injury at issue in *Pollack*. Underlying many of the subjects' allegations was that the medical school simply abandoned the subjects by terminating the study as it did, with few plans for transitioning the subjects post-study. Clearly, informed consent problems may have also occurred. If investigators did tell the subjects that they would be entitled to the study vaccine ad infinitum, and this was never intended, then investigators failed to describe the study procedures accurately. However, the plaintiffs' complaint did not state a simple count for basic informed consent violations,¹⁷⁵ possibly in recognition of the problems of recovering under informed consent with the inconclusive evidence of physical harm. Instead, the plaintiffs alleged alternative theories of relief, including ordinary negligence based on the manner in which the trial was conducted, breach of fiduciary duty, and common law fraud,¹⁷⁶ all of which described a disturbing problem of subject abandonment.

For example, serious questions surround the design of the trial and the post-study plans for subjects. Some subjects were allegedly told that they could continue receiving conventional cancer treatment while also receiving the experimental vaccine.¹⁷⁷ Meanwhile, the protocol apparently did not call for comparison of the subjects to a control group of patients with similar clinical conditions who did not receive the

trial than there would be to continue a therapy. . . . You really can't prove there's a benefit." Pallasch, *supra* note 166.

173. See Pollack Complaint, *supra* note 165, ¶ 68; *Survivors Take Breast Cancer Fight to Court*, Oct. 25, 2004, <http://www.nbc5.com/health/3849161/detail.html>.

174. For example, several of the women had stage three breast cancer, representing an advanced stage of the disease, with standard treatment not necessarily offering a more promising outcome. See Pollack Complaint, *supra* note 165, ¶¶ 23, 38; see also Stages of Breast Cancer, http://www.breastcancer.org/dia_pict_staging.html.

175. See Pollack Complaint, *supra* note 165.

176. See *id.* Counts II, VI, VII.

177. See *Survivors Take Breast Cancer Fight to Court*, *supra* note 173.

vaccine.¹⁷⁸ Under such conditions, any effects seen in the subjects would be hard to attribute to the vaccine alone, to the conventional treatments that may have been partially pursued as well, or to some combination of the two. Thus, data emerging from the trial had to be suspect from the start. This is not to say that clinical trials need always use rigid randomization and control groups to provide generalizable data. But such trial designs often require careful consideration and planning to address the absence of a control group, including designing the trial so that high-quality metaanalysis can be applied to it, allowing statistical combination of the study results with data from other trials to determine the magnitude of the effect of the experimental intervention.¹⁷⁹ Apparently, this was not done. Indeed, in 1997 the FDA had disallowed investigators from enrolling new subjects because of the agency's concerns about the lack of control groups and, therefore, the conclusiveness of any of the emerging study data.¹⁸⁰

The defendants likely did not think through the implications of allegedly making promises of "ad infinitum" access to the vaccine. More concerning, the defendants' actions put the subjects in an untenable situation of not understanding whether their research participation mattered for future patients and whether the treatment was working or not, thus exacerbating the uncertainties and disturbance surrounding any decision to terminate the study early. It seems highly inappropriate to ask subjects to participate in a trial of such flawed design with insufficient plans for dealing with study discontinuation and emerging trial data that might be inconclusive, especially when intentions for continued post-study access to the vaccine were muddled and confused at best. The subjects were arguably treated no more charitably than discarded specimens of a botched experiment, simply thrown away with little regard for their personal investments in the research and their current desires and goals.

Notwithstanding the unclear nature of any tangible harm inflicted, the University eventually agreed to settle the case.¹⁸¹ This was likely because of concerns about continuing negative publicity surrounding the suit, the thorny issues surrounding the monetary donations to the University by the vaccine's creator, and the costs of defense, as well as

178. *See id.*

179. *See generally* Raymond Lam & Sidney Kennedy, *Using Metaanalysis to Evaluate Evidence: Practical Tips*, 50 CANADIAN J. PSYCHIATRY 167 (2005).

180. *See* Natasha Korecki, *Women Go To Court for Breast Cancer Vaccine*, CHI. SUN-TIMES, Oct. 26, 2004, at 12; *Survivors Take Breast Cancer Fight to Court*, *supra* note 173.

181. *See* Natasha Korecki, *Breast Cancer Vaccines Return With Settlement; University Was Sued After Experimental Program Came to Halt*, CHI. SUN-TIMES, Oct. 30, 2004, at 6.

other tactical reasons. Although the settlement terms were confidential, the University apparently agreed to fund a new anti-vaccine program for the women at another institution. This provided opportunities for subjects to have continued access to the investigational vaccine and the chance for the subjects to obtain full FDA approval for the treatment.¹⁸²

While *Pollack* seemingly resulted in a deserved settlement for the subjects, the case also demonstrates the practical difficulty of ordering appropriate relief for intangible hazards. In study discontinuation cases, even symbolic monetary awards are less likely to help redress plaintiffs' grievances. What subjects often want, above all else, is treatment access. When the settlement was announced, one plaintiff told the press, "we wanted our vaccine, that was our main thing."¹⁸³ Indeed, even the *Pollack* settlement's equitable relief provisions, under which the University agreed to partially fund continuation of the vaccine study at another institution, did not guarantee the plaintiffs the essential remedy of treatment access that they desired. The money is to be transferred to a yet-to-be-named institution.¹⁸⁴ Not surprisingly, the parties were unable to readily locate another institution willing to take over administration of a study conducted for so many years without more promising results, particularly with little promise of commercialization opportunities for the sponsoring institution.¹⁸⁵ Moreover, there is some question whether one of the key ingredients for the vaccine is still produced in the United States,¹⁸⁶ further complicating any efforts to restart the vaccine program at a different institution. *Pollack* demonstrates that even when research subjects can extract a settlement or partial ruling on the merits, they may find their remedies incomplete, with underlying problems of subject abandonment and its associated intangible hazards not sufficiently addressed.

2. *Harden v. University of Cincinnati Medical Center*

If the informed consent exchange appropriately advises the subject about a risk of physical injury and the subject experiences that hazard, should the subject nonetheless deserve some form of remedy?

182. See *id.*; Matt O'Connor, *University, Cancer Survivors Settle; Med School OKs Vaccine At New Site*, CHI. TRIB., Oct. 30, 2004, at 26.

183. See Korecki, *supra* note 181, at 6.

184. See *id.*

185. As the University's attorney noted, if the study data was more promising and indicated that the vaccine clearly was working, then "[e]veryone would be on board because it would be a billion-dollar product." Korecki, *supra* note 180, at 12.

186. See *Survivors Take Breast Cancer Fight to Court*, *supra* note 173.

Abandonment and associated intangible hazard concerns factor heavily in such situations, arguably deserving greater legal recognition.

The recent case of *Harden v. University of Cincinnati Medical Center*¹⁸⁷ illustrates this issue. The plaintiff suffered from an aneurysm behind her eye.¹⁸⁸ Her physicians recommended a balloon occlusion procedure, an experimental technique studied as part of a research investigation of cerebral aneurysms.¹⁸⁹ A few days after undergoing the procedure, the subject suffered a stroke and required emergency surgery.¹⁹⁰ However, the surgery failed to correct the problems, and she experienced permanent damage from lack of blood flow to the brain.¹⁹¹ As a result of the stroke complications, she required constant nursing and medical care for the rest of her life.¹⁹²

The subject sued the investigator and medical center, alleging ordinary negligence (medical malpractice), loss of consortium, and breach of contract.¹⁹³ She did not allege a separate count for an informed consent violation. In fact, the consent process had been quite clear about the possible risk of stroke complication. The informed consent document actually listed stroke first among a list of possible adverse consequences from the procedure.¹⁹⁴

Rather than argue that the stroke complication risk had not been disclosed, the plaintiff instead contended that the researchers had promised lifetime medical care if an experimental injury developed. The informed consent document did state, in the paragraph labeled "Objectives of the Study," that "[p]articipation in the study will include one year of follow-up, although long-term care will be offered for an indefinite period."¹⁹⁵ The subject argued that this amounted to a contractual promise to provide indefinite medical care for research-related injury.

This case illustrates the difficulties subjects face in successfully prevailing on breach of contract claims.¹⁹⁶ Both the lower court and appeals court ruled that the informed consent document did not

187. No. 04AP-154, 2004 WL 2341713 (Ohio Ct. App. Oct. 19, 2004).

188. *Id.* at *1.

189. *See Consent Statement Did Not Promise Lifetime Care, Ohio Appeals Court Says*, 3 Med. Res. L. & Pol'y Rep. (BNA), No. 21, at 829 (Nov. 3, 2004).

190. *Harden*, 2004 WL 2341713, at *1.

191. *Id.*

192. *Id.*

193. *See Complaint, Harden v. Univ. of Cincinnati Med. Ctr.*, No. 98-11405, 2004 WL 119446, (Ohio Ct. Cl. Dec. 11, 1998).

194. *See id.* at Exhibit 1, Section IV.

195. *See id.* at Exhibit 1, Section II.

196. *See supra* Part II.H.

constitute a legally binding contract between the parties with regard to any follow-up medical care.¹⁹⁷ Both courts concluded that the informed consent document was, at most, notice of the subject's consent to the experimental procedure, not a meeting of the minds and bargained for exchange between the parties.¹⁹⁸ The appeals court further ruled that even if the consent document did represent a binding contract, the terms were not clear enough regarding follow-up care to have required the defendants to provide for the subject's medical treatment.¹⁹⁹ The appellate court affirmed the lower court's finding that an ordinary malpractice claim could not be sustained because of insufficient evidence of failure to follow the standard of care.²⁰⁰

The plaintiff in *Harden* thus recovered nothing. At first blush, this is not a controversial or surprising result. A real and disclosed physical risk of the experimental procedure did in fact materialize, and the plaintiff did not produce strong evidence of breach of any standard of care in the performance of the balloon occlusion procedure. It is not clear that subjects should recover anything in these situations. Certainly, it would be hard to argue for recovery if this had occurred in an ordinary clinical setting. Further, the federal research regulations do not require institutions or investigators to compensate subjects for research-related injuries or even to reimburse their associated medical care expenses.

Despite these considerations, one could argue that a subject's status as a research participant, not as a patient in the clinic, should be treated as a distinct factor requiring a more flexible approach to remedy. In other words, once the patient has volunteered to become a research subject, it may be inappropriate to abandon the subject in his or her time of need when injuries develop, even if these risks were disclosed. The failure to assist the subject in these situations may create loss of trust, feelings of abandonment, ethical tensions, and other intangible harm beyond any physical injuries developed.

Numerous commentators, including the influential President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, have asserted that it is simply unethical to set up research studies with no adequate plans for compensating subjects for research-related injuries, even if such risks are disclosed in advance.²⁰¹ Reasons given include that the persons who

197. See *Harden*, 2004 WL 2341713, at *5.

198. See *Harden v. Univ. of Cincinnati Med. Ctr.*, No. 98-11405, 2004 WL 119446, at **12-13 (Ohio Ct. Cl. Oct. 19, 2004); *Harden*, 2004 WL 2341713, at * 7.

199. *Id.* at **7-8.

200. See *Harden*, 2004 WL 119446, at **9-11; *Harden*, 2004 WL 2341713, at **8-12.

201. See, e.g., 1 PRESIDENT'S COMM'N FOR THE STUDY OF ETHICAL PROBLEMS IN MED. &

benefit from the research (investigators and sponsors) should bear some portion of the costs of research-related injuries since the subjects risked injury on these other parties' behalf,²⁰² and the fact that research subjects volunteer to further larger societal goals and, thus, their injuries should not be ignored or dismissed simply because they were warned about them.²⁰³ Also, because society benefits from the knowledge gained by research and sanctions its conduct, principles of fairness support spreading the costs of subject injury to others.²⁰⁴ Even if the subject cares little about contributing to medical knowledge through research participation and is principally concerned with therapeutic improvement, this does not diminish the arguable obligations of others to assist with research-related injuries because the subject's participation nonetheless helps generate experimental data and advances medical progress.²⁰⁵

While providing no compensation for research-related injury may be common practice currently, the unique status and moral claims of research subjects may require reconsideration of this approach. At the very least, this practice raises troubling questions when the study presents more than a moderate risk of foreseeable injury and it involves particularly vulnerable subjects. Enrolling subjects in studies with no adequate planning or concern for their likely post-injury treatment costs approaches some form of abandonment. Such conduct creates a risk of intangible harm, including exploitation, loss of trust in the research enterprise, and failure to acknowledge subjects as deserving both respect as persons and support in a critical time of need.

IV. SHOULD THERE BE GREATER RECOGNITION OF INTANGIBLE HARM CLAIMS IN MEDICAL RESEARCH?

Is the time ripe for a different approach to remedies in medical research? Change seems warranted, given the importance of research subject protection and the inadequately addressed recurring problems of intangible harm in medical experiments. However, the issue is difficult

BIOMEDICAL & BEHAVIORAL RESEARCH, COMPENSATING FOR RESEARCH INJURIES: THE ETHICAL AND LEGAL IMPLICATIONS OF PROGRAMS TO REDRESS INJURED SUBJECTS 4 (1982); ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS, *supra* note 32, at 125; James Childress, *Compensating Injured Research Subjects: The Moral Argument*, HASTINGS CTR. REP., Dec. 1976, at 21.

202. See ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS, *supra* note 32, at 125.

203. See COMPENSATING FOR RESEARCH INJURIES: THE ETHICAL AND LEGAL IMPLICATIONS OF PROGRAMS TO REDRESS INJURED SUBJECTS, *supra* note 201, at 59–60.

204. See Childress, *supra* note 201.

205. See Hazel Beh, *Compensation for Research Injuries*, IRB: ETHICS & HUM. RES., May-June 2005, at 11, 12.

on many levels. A more open-ended approach to remedies for intangible hazards also presents significant downsides. This Part considers some of the general arguments in favor of and against greater recognition of subjects' intangible harm claims.

A. Reasons for Expanding Available Intangible Harm Remedies

1. Advancing the Principle of Respect for Persons

A common view is that medical research cannot be conducted in an ethical fashion without maintaining respect for subjects as persons.²⁰⁶ Of course, the very nature of the research enterprise involves some inherent degree of using research subjects as objects. Fidelity to the experimental goals of the clinical trial—ordinarily to generate experimental data through systematic procedures that demonstrate, under accepted scientific standards, whether the investigational technology is safe and effective—will at some level always be a prime driver of investigator, institutional, and sponsor behavior. It therefore becomes tempting to subordinate consideration of the individual subject's interests to what is best for the success of the experimental protocol.

Because of this concern, one that has persisted through decades of medical research, perhaps the law needs to do more to require that subjects be treated as individuals with intrinsic worth and dignity. Greater recognition of intangible harm claims would at least send the message, for deterrence purposes, that at some level, concern for individual subjects' needs and interests must always be present to justify research activity. What may seem most objectionable about certain research may have little to do with how the subject fared therapeutically. Instead, it will have everything to do with whether the investigators treated the subject with respect and solicitude as an autonomous person, by addressing the subject's capacity for independent action and recognizing that a subject has important preferences and values at stake in many research activities. Indeed, for the typical research subject, the "most salient injury is not [physical injury] . . . it is the fact that [the subject] was exploited and used . . . for another's gain."²⁰⁷

Apart from deterrence issues, greater flexibility regarding intangible harm claims would also make better use of the law's expressive function to promote the respect-for- persons-principle. Often, laws can have

206. See, e.g., BELMONT REPORT, *supra* note 8; *supra* Part I.A (discussing Helsinki Declaration and Nuremberg Code, both of which strive to acknowledge the subject as an independent, moral agent).

207. Morreim, *supra* note 24, at 908–09.

symbolic meaning, convey social messages, and influence attitudes and norms in a far more powerful way than their threat of legal sanctions.²⁰⁸ Currently, the law is sending a mixed message regarding the importance of the respect-for-persons principle in medical research. This ideal becomes seriously compromised when experimental goals can be zealously followed so that the design and implementation of the protocol or the procedures followed upon study termination blatantly disregard subjects' foreseeable value preferences, therapeutic aims, and concerns for access to therapy. A disturbing sense of exploitation and abandonment develops as subjects end up crudely subordinated to the protocol's objectives, losing sight of each subject's individuality, extra-protocol interests, and legitimate claims to societal support.²⁰⁹ The fact that the law so rarely recognizes this harm, unless accompanied by physical injury or severe mental anguish, may exacerbate the problem, as it implicitly sends the message that such hazards are not sufficiently important. A change in direction may be needed, awarding greater remedy for subjects facing such intangible harm, in order to provide social support and to develop medical research norms more attuned to the respect-for-persons principle.

2. Addressing Problematic Informed Consent in Research

More flexible recognition of intangible harms could strengthen and ensure a better informed consent process for research subjects. Currently, informed consent in research settings has largely disappointed for a number of reasons. Investigators have inherent conflicts of interest because of study aims divergent from individually tailored treatment for patients, potentially compromising investigators' ability to provide material information to subjects.²¹⁰ Also, patients of advanced age, limited education, and poor health—which describes a sizable number of potential research subjects—remain especially at-risk for poorly comprehending the research process and standard study consent forms.²¹¹ The time allocated for subjects to make enrollment decisions,

208. See, e.g., Cass R. Sunstein, *Social Norms and Social Roles*, 96 COLUM. L. REV. 903 (1996); Richard H. McAdams, *A Focal Point Theory of Expressive Law*, 86 VA. L. REV. 1649 (2000).

209. Cf. *In re Cincinnati Radiation Litig.*, 874 F. Supp. 796, 812 (S.D. Ohio 1995) ("To manipulate men, to propel them toward goals which we can see but they may not, is to deny their human essence, to treat them as objects without wills of their own, and therefore to degrade them." (quoting ISAIAH BERLIN, *FOUR ESSAYS ON LIBERTY* 136–37 (1969))).

210. See Christopher K. Daugherty, *Impact of Therapeutic Research on Informed Consent and the Ethics of Clinical Trials: A Medical Oncology Perspective*, 17 J. CLINICAL ONCOLOGY 1601 (1999).

211. See Holly A. Taylor, *Barriers to Informed Consent*, 15 SEMINARS ONCOLOGY NURSING 89, 90–91 (1999).

the timing in which research enrollment discussions are initiated, and the readability and length of study consent forms further contribute to problematic informed consent encounters.²¹²

Even more disturbing is the well-documented phenomenon of “therapeutic misconception.” Empirical investigations reveal that subjects often confuse research activities with ordinary therapeutic care. They fail to understand the degree to which individually tailored care is not offered as part of a standard study protocol. Some studies have shown that subjects, even after completing the informed consent process, failed to understand that they were participating in an actual experiment.²¹³ As a result of therapeutic misconception, subjects likely overstate the benefits of research, do not understand basic research procedures such as randomization and endpoints, and assume, incorrectly, that an untested therapy would not be offered in a study unless it clearly promised direct benefit.²¹⁴

In light of these serious informed consent difficulties, it is quite likely that many subjects enroll in clinical trials with an insufficient understanding of the degree to which individually tailored treatment is not available under standard study protocols. Also, they likely do not appreciate other significant aspects of research, such as what happens regarding access to the experimental technology when a study is discontinued at the sponsor’s discretion. For a sizable number of these subjects, after-the-fact attempts to seek redress for insufficient informed consent will run into the traditional barriers discussed previously, such as failure to prove causation and physical harm. Thus, a large number of problematic informed consent encounters likely occur in the research setting, but are not sufficiently deterred because of the limited ability of subjects to bring informed consent claims principally centered on intangible harm. If problematic research consent episodes creating intangible harm were actionable or triggered administrative sanctions more readily, researchers, institutions, and sponsors would have a stronger incentive to devote the time and resources necessary for improving the poor state of informed consent in research.

Commentators and case law suggest that informed consent

212. See *id.* at 92–94; Daugherty, *supra* note 210, at 1604–06; ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS, *supra* note 32, at 99 (summarizing several studies detailing problematic comprehension of research consent forms).

213. See generally Paul S. Appelbaum, Charles W. Lidz & Thomas Grisso, *Therapeutic Misconception in Clinical Research: Frequency and Risk Factors*, IRB: ETHICS & HUM. RES., Mar.-Apr. 2004, at 1; Sam Horng & Christine Grady, *Misunderstanding in Clinical Research: Distinguishing Therapeutic Misconception, Therapeutic Misestimation, & Therapeutic Optimism*, IRB: ETHICS & HUM. RES., Jan.-Feb. 2003, at 11–13.

214. See Appelbaum et al., *supra* note 213, at 2; King, *supra* note 80, at 334.

requirements, however necessary in regular clinical care, should apply more strictly in the research setting. Informed consent takes on increased importance in medical experimentation because, among other reasons, study interventions may have no therapeutic effect, research involves conduct beyond the ordinary physician-patient relationship, subjects are vulnerable to exploitation and objectification as experimental data, and investigators and subjects have a divergence of interests between individually tailored treatment and the study aims of the protocol.²¹⁵ If investigators have heightened informed consent duties for research, this arguably justifies as a doctrinal matter the need to loosen causation and damage requirements for research consent claims. A pragmatic way to ensure that such informed consent duties are discharged regularly and with appropriate solemnity would be to recognize to a greater degree subjects' informed consent claims centered on intangible harm.

Many patients in regular clinical care could likewise claim that flawed informed consent procedures deprive them of meaningful choice about use of their body, how to confront illness, and other dignitary aspects of their lives, causing them intangible harm. But the reason to focus first on the intangible harm arising in flawed research consent is the qualitatively different nature of acting as a research subject as compared with a regular patient. In ordinary medical encounters, the therapy provided by a health care professional, even if not properly consented to, at least may be partly justified for the patient's benefit. But the same justification does not apply to many study protocols as "research does not propose to benefit any specific enrollee . . ."²¹⁶ Further, experimental procedures cannot be easily justified as meeting the standard of care because of their investigational nature,²¹⁷ meaning that without proper consent, experimental interventions stand on particularly tenuous ground. Flawed informed consent in research settings thus presents significant concerns, perhaps calling for a more flexible approach to consent claims centered on intangible harm.

Of course, informed consent in research is already highly regulated. The informed consent requirements for research subjects via the federal

215. See e.g., Delgado & Leskovac, *supra* note 99, at 68–69, 92–107; John Luce, *Ethical Principles in Clinical Care*, 263 JAMA 696, 697 (1990); Halushka v. Univ. of Sask., [1965] D.L.R. 2d 436, 443–44 (“[T]he duty imposed upon those engaged in medical research . . . is at least as great as, if not greater than, the duty owed by the ordinary physician or surgeon to his patient.”).

216. Morreim, *supra* note 89, at 69. Professor Morreim contends that “[w]hen inadequacies of information have inappropriately steered a patient’s decisions about whether to participate in research, courts should be willing in at least some instances to see this as an injury itself.” *Id.* at 79.

217. See Coleman, *supra* note 14.

research regulations and the mechanism of IRB review of proposed consent forms²¹⁸ ensure far greater scrutiny of informed consent procedures with research subjects than with patients in regular clinical care. It may be questioned whether greater common law and regulatory recognition of intangible hazards in experimentation consent cases would really add much. However, it need not be an either-or proposition. Expanded litigation remedies and regulatory oversight need not be mutually exclusive, in that private litigation can supplement the efforts of regulators to ensure appropriate consent procedures to protect subjects from intangible harm. Litigation may also offer more opportunities for retrospective review of intangible hazards arising in clinical trials, whereas regulatory oversight currently focuses more on prospective review.²¹⁹

3. Consistent with Special Obligations of Investigators

The investigator-subject relationship remains hard to characterize legally, as previously discussed, with views differing whether it is a classic fiduciary relationship, fiduciary-like, or an otherwise special relationship under common law.²²⁰ Regardless of the precise label used, most would agree that special obligations of investigators should exist both legally and ethically because the researcher-subject relationship involves significant degrees of power imbalance, vulnerability, and trust and dependence by subjects.²²¹ At a minimum, these heightened obligations would include a requirement that investigators act with candor and respect and avoid opportunistic conduct and exploitation of the subject.²²²

Recognizing intangible harm claims centered on abuse of the investigator's position or on other trust-eroding conduct of the researcher would be consistent with valuing the investigator's special obligations. Fiduciary-like responsibilities tend to be imposed on a party in a position of trust, power, and confidence. The relief most often awarded for fiduciary breach in commercial settings is the fiduciary's disgorgement of profits to the principal.²²³ Although such awards may

218. See *supra* Part I.C.

219. See Sharona Hoffman & Jessica Berg, *The Suitability of IRB Liability*, 67 U. PITT. L. REV. (forthcoming).

220. See *supra* Part II.F.

221. See Coleman, *supra* note 14.

222. See, e.g., Franklin G. Miller & Howard Brody, *A Critique of Clinical Equipoise: Therapeutic Misconception in the Ethics of Clinical Trials*, HASTINGS CTR. REP., May-June 2003, at 26-27.

223. See RESTATEMENT (THIRD) OF RESTITUTION AND UNJUST ENRICHMENT § 3 CMT. C.

be criticized as a windfall to the principal, a strong deterrence rationale supports allowing such relief. This type of recovery sets clear incentives for fiduciaries to refrain from exploiting the relationship with the principal.²²⁴ The restitutionary remedy helps to strengthen the bonds between fiduciaries and their principals by providing remedies for a broader range of activity than ordinary compensatory damages. Such restitution awards reinforce fiduciary ties by indicating that damage to the fiduciary relationship itself, through opportunistic conduct, causes harm as a recognizable, intrinsic wrong.

Similarly, a more expansive approach to intangible harms claims by research subjects would help police opportunistic conduct in the investigator-subject relationship and generally strengthen the investigator's special obligations to subjects. Just as fiduciary-like remedies recognize and honor the principal's reasonable expectation of loyalty and trust when interacting with the fiduciary,²²⁵ the law should try to vindicate research subjects' reasonable expectations of solicitude and trust when dealing with investigators. A more flexible approach regarding the cognizability of subjects' intangible harm claims would help by recognizing injuries to the investigator-subject relationship itself as meriting redress.²²⁶

4. Promoting Trust-Enhancing Conduct and Recognizing Process Values in Medical Research

A related, instrumental concern supports expanded remedies for intangible harm. For the research system to function effectively, the fragile level of trust subjects currently have in medical experiments must not become further eroded. Trust remains essential to many aspects of a well-functioning health care system,²²⁷ and it is especially fundamental for ensuring the continued participation of subjects in clinical trials.²²⁸ When deciding to volunteer for a study, often at a time of critical illness and confounding medical uncertainty regarding their best therapeutic options, subjects ordinarily need to develop strong faith in investigators.

(Discussion Draft 2000).

224. See Smith, *supra* note 110, at 1494–96.

225. The restitution remedy in fiduciary law “vindicates some value other than the material well-being of the beneficiary.” *Id.* at 1495.

226. Cf. Oberman, *supra* note 111, at 489 (arguing that the physician's breach of fiduciary duty in doctor-maternal conflicts with patients should be actionable regardless of whether medical malpractice occurred because betrayal of trust resulting from such a breach is a harm independent of medical malpractice).

227. See generally Mark Hall, *Law, Medicine, and Trust*, 55 STAN. L. REV. 463 (2002).

228. See Gatter, *supra* note 74; Miller, *supra* note 7.

A subject's trust in physician-investigators and the research process may also contribute to better experimentation results, whether because of placebo effects, more genuine commitment by the subjects to follow the study protocol procedures diligently, or numerous other, unappreciated ways in which trust activates healing by subjects.²²⁹ On the other hand, loss of faith in medical research jeopardizes the cooperation of current subjects with protocol procedures, the ability to accrue future subjects, and the willingness to fund and support the research system.²³⁰ Therefore, actions that abuse the special trust aspects of the investigator-subject relationship, even if not leading to physical injury, should be recognized as creating significant harm both for the subjects involved²³¹ and for the research enterprise generally because of their trust-corrosive impact.

In particular, actions that contribute to a climate of distrust by undermining basic process values in medical research may need greater regulatory attention or sanctioning through the common law. Medical research law might learn from analogous civil rights disputes where damages may be awarded without evidence of a plaintiff's actual loss of money, property, or other tangible items of value. For example, in voting rights cases, damages can be awarded even if the votes allegedly interfered with would not have changed the election outcome. The law recognizes that individuals value the right to vote to such a degree that any deprivation of that right can lead to damages, with the appropriate amount to be determined by a jury.²³² Additionally, other civil rights actions provide for at least nominal damages, in the absence of proof of other damages, to address larger process concerns, such as recognizing seemingly non-harmful infringements on the right to free speech in order to protect the integrity of the decisionmaking process generally.²³³

Similarly, valuing the inherent worth of research subject decisionmaking, as well as the special trust aspects of the researcher-subject relationship,²³⁴ supports the award of intangible harm damages in select cases. When actions jeopardize such important foundations and

229. Cf. Hall, *supra* note 227, at 478–83 (discussing the therapeutic effects of trust in regular patient care).

230. See Goldner, *supra* note 9, at 381.

231. Cf. Stern, *supra* note 96, at 89 (describing how exaggerated perceptions of trust by subjects in the physician-researcher can lead to profound feelings of betrayal when the trust is broken).

232. See *Memphis Comm. Sch. Dist. v. Stachura*, 477 U.S. 299, 311 n.14 (1986).

233. See Aaron D. Twerski & Neil B. Cohen, *Informed Decision Making and the Law of Torts: The Myth of Justifiable Causation*, 1988 U. ILL. L. REV. 607, 649–52.

234. Cf. Hall, *supra* note 227, at 485 (examining the nature of medical trust and observing that “there is an emotional component in all trust-based relationships, which potentially gives them intrinsic value or unique instrumental worth”).

process components of the research system, the law needs to recognize the intrinsic worth of the interests affected and to better address the harm created.²³⁵ Of course, allowing more lawsuits or increasing regulatory remedies for intangible harm does not automatically help address trust concerns. Rather than supporting trust, such actions may merely be punitive and highlight the problematic features of clinical trials so as to further undermine subject confidence in medical research.²³⁶ Therefore, while instrumental concerns of supporting trust in research suggest the need for greater recognition of intangible harm claims, flexibility and subtlety in this approach are also necessary. It becomes critically important to anticipate the expressive effects of such claims and how they would coordinate with regulatory mechanisms, in order to adopt selective approaches to the remedies most likely to be trust enhancing when applied to the actual experience of subjects in the clinic.

B. Potential Drawbacks

A more flexible approach to intangible harm claims, while offering many benefits, nonetheless also presents drawbacks meriting further consideration. An open-ended remedy for intangible harm seems hard to reconcile with existing case law and regulatory approaches and could lead to over-deterrence. Also, pragmatic problems exist in defining limits for such claims, and greater remedies in this area may force the research system into a compensation scheme for subject injury that lacks legislative authorization.

1. Doctrinal Consistency Issues: Why Only for Research?

As a doctrinal matter, broader recognition of subjects' intangible harm claims may be hard to justify without a more dramatic reworking of informed consent, fraud, fiduciary duty, and other doctrines. Consider informed consent as a representative example. Many commentators have long complained that informed consent does not sufficiently protect the medical choice of patients in ordinary clinical settings. Thus, they have urged that the doctrine be more flexible in

235. *Cf.* Twerski & Cohen, *supra* note 233, at 648–49 (arguing for a similar approach to informed consent claims in regular clinical care). Twerski and Cohen question whether nominal damage awards will be sufficient to produce a desired deterrence effect and advocate for more than nominal damages to address informed consent process concerns. *Id.* at 648. This suggests that intangible harm awards in the research setting might have to be more than nominal to see real deterrence.

236. *Cf.* Hall, *supra* note 227, at 490–93 (examining similar complicating effects on patients' trust in physicians arising from patients' ability to sue for malpractice).

application and treat patient choice as an independent interest in order to better protect patient autonomy.²³⁷ Under such an approach, conduct that deprives the patient of choice would be actionable because of the ethical and policy reasons for protecting choice and control over medical decisionmaking, an interest distinct from safeguarding the patient from physical harm. The idea would be to respect purely dignitary aspects of patient choice by awarding nominal or general damages when the interest has been invaded even if the violations produced little tangible harm.²³⁸ Similarly, other commentators urge that informed consent be treated as a process right, where invasion of the process right becomes actionable because the patient's participation in decisionmaking has independent value and benefits irrespective of the medical decision outcome.²³⁹ A more flexible informed consent doctrine consistent with these approaches has been suggested to combat serious problems confronting ordinary patients, such as lack of understanding of treatment alternatives due to managed care cost containment strategies,²⁴⁰ as well as bias and health care disparities in the treatment of minority patients.²⁴¹

Yet to date, courts have exhibited little enthusiasm for extending informed consent doctrine to this degree. Thus, notwithstanding the merits of applying informed consent doctrine more flexibly, the critical question is how to reconcile existing law and regulation with greater cognition of intangible hazards arising in medical experimentation? Assuming no radical overhaul of informed consent doctrine or major regulatory change, why follow a different approach to intangible harm recovery for research subjects under informed consent theories but not for patients receiving regular clinical care?

As previously noted, one view is that informed consent requirements should apply more strictly in research settings,²⁴² perhaps justifying a different remedy approach that would independently value the dignitary aspects of subject choice in medical experiments. However, the research-versus-ordinary-care difference should not be overly relied upon. The exact source of dignitary rights for subjects remains unclear

237. Professor Marjorie Maguire Shultz was one of the first and leading proponents of this view. See Shultz, *supra* note 102.

238. See, e.g., *id.* at 290–91 (1985); Meisel, *supra* note 98, at 214–16.

239. See Twerski & Cohen, *supra* note 233, at 649–55.

240. See Joan H. Krause, *Reconceptualizing Informed Consent in an Era of Health Care Cost Containment*, 85 IOWA L. REV. 261, 364–68 (1999).

241. See Noah, *supra* note 101, at 146–47; Crossley, *supra* note 100, at 256–57.

242. See *supra* note 215 and accompanying text.

as a matter of law,²⁴³ and this may be too tenuous a legal concept to justify recognizing affronts to research subject dignity but not similar affronts to patient dignity. Any claims to special treatment of research subjects along such lines would, by necessity, diminish and marginalize the value of protecting the dignitary aspects of choice for ordinary patients. Such patients confront economic incentives to limit care, systematic racial and ethnic bias, and other serious threats to autonomous control over medical decisionmaking.²⁴⁴ It may be splitting hairs to say which group's dignitary interests deserve greater protection.

Likewise, while fiduciary doctrine and related theories, through the restitution remedy, may be more flexible for dealing with intangible harm,²⁴⁵ they do not necessarily justify focusing on intangible hazards consistently for research subjects but not for regular patients. First, the fiduciary nature of the researcher-subject relationship remains subject to reasonable dispute.²⁴⁶ Second, the notion that research subjects as a class have unique vulnerabilities, even compared to ordinary patients, and therefore deserve special legal rules for intangible harm recovery, likely oversimplifies things. It is far too easy to apply the "vulnerability" label as a catch-all for many complicated issues arising with patients experiencing advanced illness.²⁴⁷ Yes, research subjects often must decide to enroll in a clinical trial at a time when ill health, desperation, and anxiety may cloud their judgment. But the fact that many subjects face limited, suboptimal therapeutic options because of their health conditions does not make them automatically subject to coercion or inherently vulnerable as a group compared to other patients. Individuals with terminal cancer, for example, regularly must make complicated decisions besides research participation, such as executing advance directives for withdrawal of life-sustaining treatment or considering organ donation, yet they do not exhibit as a group the incapacity to make informed decisions on such matters.²⁴⁸

Finally, and perhaps most importantly, there remains the problem of the unclear distinction between research and regular clinical care. Ordinary medical treatment and experimental interventions lay along a continuum, with few distinguishing characteristics. Most non-research medical care involves some degree of tailoring and experimentation with

243. See *supra* Part I.D.

244. See *supra* notes 240–41 and accompanying text.

245. See *supra* Part II.F.

246. *Id.*

247. See Mansih Agrawal & Ezekiel Emanuel, *Ethics of Phase I Oncology Studies: Reexamining the Arguments and Data*, 290 JAMA 1075, 1081 (2003).

248. See *id.*

treatment modalities, many medical encounters in the regular clinical setting involve situations of great uncertainty, and regular medical treatments can involve great degrees of risk and injury.²⁴⁹ Thus, different doctrinal approaches to intangible harm for research subjects will inherently raise consistency issues when considering the experience of ordinary patients.

2. Opening the Floodgates

Greater recognition of intangible harm claims also raises concerns that courts will be flooded with additional litigation. If traditional causation and damage limitations are removed from informed consent actions in research, how can courts avoid having to decide an overwhelming number of complaints brought by subjects, whether truly aggrieved or not? Once the proverbial floodgates are opened to intangible harm claims, they may not be easily controlled and managed at socially optimal levels. This could lead to over-deterrence of useful research activities.

Consider how this would work for informed consent claims. If failure to secure the subject's informed consent to the material risks and benefits of a clinical trial becomes actionable as an intangible harm, without requiring further proof of physical injury or applying a strict causation element, then presumably many subjects could readily allege such claims. If informed consent problems are as pervasive in the research setting as the therapeutic misconception data suggests,²⁵⁰ then likely a great number of subjects would have some actionable claim for intangible hazards, potentially turning the system into one of quasi-strict liability. This could chill socially useful medical innovation. Additionally, heightened liability would not necessarily lead to better consent processes in research settings. Individuals' expectations and devotion of trust toward physicians remain so deeply engrained, and arise for such complex reasons, that subjects readily confuse research with ordinary care.²⁵¹ Incentivizing investigators through increased liability to implement "more" and "better" consent procedures will not clearly help address the root causes of therapeutic misconception.

249. See generally Noah, *supra* note 4. As Professor Noah observes, urging that heightened informed consent standards apply for research subjects may set up a false dichotomy. "If one believes that securing informed consent represents the most profound imperative when engaging in research with human subjects then why be any less dramatic about the issue in other medical encounters?" *Id.* at 407.

250. See *supra* notes 213–14 and accompanying text.

251. See Coleman, *supra* note 14; RESPONSIBLE RESEARCH: A SYSTEMS APPROACH TO PROTECTING RESEARCH PARTICIPANTS, *supra* note 11, at 125–26.

Meanwhile, intangible hazards claims, if not properly bounded, could lead to excessive damage awards and to over-deterrence of necessary risk-taking in medical innovation. At the very least, more litigation risk through intangible harm claims could increase the cost of engaging in medical research. The cost pressures could hinder the pace of needed medical innovation or lead to higher prices passed on to patients and payors when experimental technology reaches the market, exacerbating current health care cost and access problems. Of course, if courts limit damages for intangible hazards to nominal amounts and if juries are properly instructed, a reworking of doctrine in this area should not invite a flood of claims or dramatically increase the cost for engaging in research. Because of the cost to plaintiffs to litigate, not all subjects would rationally pursue claims based on such harm alone.²⁵² However, this assumes that courts and juries will be willing and able to enforce a consistent limitation on intangible harm damages.

The imprecise nature of intangible harm claims leads to considerable doubt about applying such limitations successfully. Expansion of intangible harm claims could allow subjects to conflate claims. Once subjects allege an actionable claim for intangible hazards, they could seek to augment their recovery amount with claims seeking compensation for various physical injuries, even if such injuries are not directly traceable to the research study but follow instead from the subjects' advanced stage of illness. The experience from regular medical malpractice cases indicates that juries often arrive at a holistic total amount of damages they think fair and then manipulate the categories to reach that amount.²⁵³ For example, a "crossover effect" has been identified in jurisdictions that have imposed caps on noneconomic damages in regular malpractice cases. Juries in jurisdictions with such damage caps nonetheless awarded very large total damage amounts, with economic damages a significantly high component of the total awarded. This suggests that juries viewed the damages as highly malleable, allowing some portion of the noneconomic damages that were supposedly capped to spill into the economic damages category, which remained uncapped, in order to arrive at what they thought was the fair total amount.²⁵⁴

Attempts to cabin intangible harm damages in research subject litigation may likewise fail because of an analogous crossover problem. A sick subject with a credible claim for intangible harm will likely

252. See Meisel, *supra* note 98, at 216.

253. See Sharkey, *supra* note 15.

254. See *id.*

attract sympathy and concern for the subject's state of ill health, even if the subject's physical difficulties arise from the disease's progression and not anything inappropriate about the research study. However, once the intangible harm becomes actionable, it becomes tempting to compensate the subject further for the poor therapeutic experience.

3. End-Run Around Lack of Research Injury Compensation Schemes

Potential crossover problems of this sort illustrate a more general concern about strategic gamesmanship by subjects seeking intangible harm recovery. Expanded litigation opportunities for intangible hazards would offer an attractive end-run for subjects facing a current lack of compensation schemes for many research-related injuries. Subjects not able to recover under ordinary informed consent claims for physical injuries, when the risks were properly disclosed, as occurred in *Harden v. University of Cincinnati Medical Center*,²⁵⁵ might instead seek compensation for the same physical injuries through the indirect route of intangible harm recovery, where spillover of damages may occur.

This would amount to a major change in research policy through the back door. Currently, federal research regulations do not require that institutions, sponsors, or investigators provide any compensation to subjects injured in research; common law claims also are unlikely to succeed when the risks of physical injury were disclosed in advance. Whether to develop more comprehensive research subject compensation, such as no-fault administrative programs to help subjects with health-related claims, has been the subject of recurring policy debate. Blue ribbon national panels and other interested parties have, over many years, advocated the establishment of a more systematic compensation program for research subjects, funded either federally, through insurance purchased by the research institutions and sponsors, or through other financing mechanisms.²⁵⁶

Despite meritorious and ethically compelling reasons to develop such a compensation program as a matter of ordinary research practice,²⁵⁷ lawmakers and regulators have until now resisted taking this step in the face of repeated calls for action. In light of this history, common law reforms that risk radically shifting the costs for subjects' physical

255. No. 04AP-154, 2004 WL 2341713 (Ohio Ct. App. 2004). See also *supra* Part III.B.2.

256. See, e.g., COMPENSATING FOR RESEARCH INJURIES: THE ETHICAL AND LEGAL IMPLICATIONS OF PROGRAMS TO REDRESS INJURED SUBJECTS, *supra* note 201; ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT (1995); ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS, *supra* note 32, at 123–26.

257. See *supra* notes 201–05 and accompanying text.

injuries should be viewed warily. The reasons for developing research subject compensation schemes, and the development of parameters for how they should be financed, crafted, and implemented without creating too costly an environment for institutions and sponsors to conduct clinical trials, need more political debate and scrutiny to gain public acceptance. Potential end-runs around ordinary legislative and regulatory channels, therefore, present considerable legitimacy problems.

V. REPRESENTATIVE SITUATIONS MERITING A NEW APPROACH TO INTANGIBLE HARM

The doctrinal consistency tensions, the floodgate problems, and end-run concerns suggest a need to proceed cautiously in reshaping research subjects' available remedies for intangible hazards. Equally important, some intangible harm concerns might be better addressed through more consistent, vigorous enforcement by the oversight agencies of existing laws and regulations rather than through judicial recognition of new types of claims.

Nonetheless, because intangible harm concerns in research remain significant, at least some change seems warranted. A serious commitment to research subject protection means that intangible hazards cannot continue to be ignored by simply hoping for improved agency enforcement under the current environment. To balance the competing considerations, an incremental reform approach is the best option. Broader relief for intangible harm should optimally occur, in the first instance, when it addresses compelling hazards faced by subjects, when it benefits the research enterprise, when it does not pose a significant risk of overdeterrence of valuable experimentation, and when it does not raise significant doctrinal consistency problems. Additionally, to coordinate common law and regulatory approaches, intangible harm remedies are best expanded when a regulatory vacuum exists, in which the agencies currently seem ill-equipped to address the hazards involved. This Article concludes with a discussion of representative situations meeting these criteria.

A. Fundamental Informed Consent Problems Regarding Near-Complete Ignorance About the Research or Its Impact on Treatment

While the source and extent of research subjects' dignitary rights

remains unclear,²⁵⁸ many commentators agree that, when informed consent is flagrantly lacking, experimentation raises particularly strong dignitary concerns deserving greater legal recognition.²⁵⁹ In these situations of complete or near-complete lack of proper consent, intangible harm remedies based on dignitary interests become urgently necessary and are also capable of limited application. *Diaz v. Hillsborough County Hospital Authority*, as discussed previously, represents such a scenario.²⁶⁰ In that case, the court appropriately adopted a more flexible approach to recognizing dignitary harm, as many women in the class of plaintiffs, even those not physically harmed, apparently failed to understand that they were part of a research study.²⁶¹

Research where the subjects lack even basic understanding that they are to be used as subjects, or do not appreciate at all how standard experimental objectives and procedures of the study protocol may compromise the delivery of individually tailored treatment, represents an especially problematic affront to the dignity of the participants. When research consent becomes so clouded and suspect at its most fundamental level, the subject's tacit agreement can no longer justify changing the ordinary physician-patient relationship into an investigator-subject relationship thereby subsuming the interests of the patient to the study aims of the research. Experimental interventions ordinarily cannot be independently justified as meeting the standard of care, nor are they offered to benefit a specific subject.²⁶² Thus, when the basic research consent breaks down at the highest levels, so that subjects fail to appreciate key research aspects of the activity, there is little support for enrolling them in a study. This is a qualitatively different type of problem than failure to disclose some risk or other routine informed consent violations. Experimentation activity in the face of near-complete misunderstanding by subjects of what research participation means risks objectifying subjects as mere specimens or pieces of data.

258. See *supra* Part I.D.

259. Professor Morreim, for example, urges a circumspect approach to recognizing subject claims based on affront to dignitary interests alone, suggesting that this type of action should "apply to cases in which the investigator failed utterly to inform a patient that he or she was being enrolled in research" as contrasted from "routine lapses [in informed consent], such as failure to identify a particular known risk." Morreim, *supra* note 24, at 908, 910. Similarly, Professor Coleman suggests that subjects have a dignitary harm remedy available in particular problematic informed consent situations, namely where the investigators fail to identify the activity's research aspects in a sufficient manner that apprises the subject that her individual interests may be potentially compromised by the research aims of the study. See Coleman, *supra* note 14.

260. See *supra* Part III.A.2.

261. See *id.*

262. See *supra* notes 216–17 and accompanying text.

Further, it sends the problematic message that potential exploitation and abuse of trust in relationships with subjects becomes seemingly acceptable so long as the individuals are not clearly made any physically worse off from the encounter.

Doctrinally, a cause of action for intangible harm in such situations could be justified as an incremental extension of informed consent law.²⁶³ Some form of nominal or presumed damages remedy is needed in such situations to address larger process concerns regarding the integrity of consent in research. Also, battery-like theories might support the award of intangible harm damages for near-complete lack of consent because of injury to intrinsic interests through offensive contacts. Alternatively, an intangible harm remedy arguably could flow from the special relationship obligations owed by investigators to subjects, analogous to the restitution remedy for fiduciary duty breaches. If consistently limited to instances of consent breakdown at the highest levels, such causes of action for intangible harm should not present end-run and flood concerns. As a practical matter, given the heightened regulatory attention already devoted to research consent, cases with fundamental informed consent breakdowns of this type should not occur frequently. Certainly, these lapses should not occur as often as more garden-variety informed consent problems, such as failure to disclose certain risks. Further, cases like *Diaz v. Hillsborough County Hospital Authority*²⁶⁴ indicate that the current regulatory environment fails to address adequately these informed consent breakdowns on a prospective review level, thus justifying an expanded retrospective remedy approach when such violations do occur.

263. For example, the Louisiana Supreme Court extended the informed consent doctrine in a similar manner by awarding damages for pure intangible harm in *Lugenbuhl v. Dowling*, 701 So. 2d 447 (La. 1997). The court found that the physician's use of surgical procedures that the patient had objected to, even if not leading to a poor therapeutic outcome, had caused intangible hazards meriting relief. The court essentially applied battery-like damages to an informed consent action.

Here, the doctor's failure to inform the patient adequately did not cause the patient to undergo a risk that materialized and caused physical damages. Rather, the doctor's breach of duty caused plaintiff to undergo a medical procedure to which the patient expressly objected and for which the doctor failed to provide adequate information in response to the patient's request, thereby causing damages to plaintiff's dignity, privacy and emotional well-being. The doctor, rather than explaining the advantages and disadvantages of the patient's express request, patronized his patient and mentally reserved the right to decide to disregard the patient's expressed wishes.

Id. at 455.

264. *See supra* Part III.A.2.

*B. Other Possible Areas for Cognizable Intangible Harm:
Subject Abandonment*

Subjects face significant intangible harm from conduct that occurs beyond the informed consent/enrollment stage. Specifically, subjects need relief from abandonment hazards. In operating and managing a study protocol, investigators, institutions, and sponsors can readily disregard, frustrate, and potentially exploit already enrolled subjects' legitimate interests, reasonable expectations, and personal investments in clinical trials. These abandonment harms can occur wholly independent of protection from physical injury and raise serious concerns for the affected subjects and for the research enterprise generally.

1. Termination of a Study

Abrupt termination of a study, including failure to account for how to transition subjects to other treatment options when the study ends, can significantly wrong a subject even in the absence of physical harm and even if properly informed consent procedures were followed during enrollment. When a clinical trial reaches conclusion, a subject will likely lose access to important monitoring procedures associated with the study, as well as access to the experimental technology, either because it is unavailable outside study protocols or because the subject will not be able to afford the technology once it is released on the commercial market. As demonstrated in recent research litigation such as *Pollack v. Rosalind Franklin University*²⁶⁵ and *Suthers v. Amgen*,²⁶⁶ subjects desperately want post-trial access to innovative therapies. How and when to conclude a clinical trial represents a particularly difficult conflict between the research aims of the protocol, the business interests of the trial sponsor, and the individual preferences of subjects. At such critical junctures, sponsors' business objectives and investigators' research goals can easily overwhelm all other considerations, crowding out a sufficient accounting for subjects' access preferences and for subjects' legitimate desire to see clinical trials, in which they have made considerable personal investment, carried out to a reasonable conclusion.

It remains critically important that investigators, institutions, and trial sponsors be afforded some deference in the review of their decisions to terminate a study. It would be counterproductive and set flawed

265. Pollack Complaint, *supra* note 165. See also *supra* Part III.B.1.

266. 372 F. Supp. 2d 416 (S.D.N.Y. 2005). See also *supra* notes 126–27 and accompanying text.

incentives to allow subjects to compel the continuation of clinical trials that investigators have legitimately lost confidence in, or that, based on preliminary trial results, the investigators reasonably deem to be unsafe. After all, subjects' access demands may be based on uncritical confidence in research as representing the best care, may reflect an unrealistic estimation of the risks and benefits involved, and may reflect their lack of better options.²⁶⁷ Responding to the desperation of individual subjects does not serve the long-term welfare of research subjects if flawed or dangerous experimentation is allowed to continue ad infinitum. Similarly, while investigators and sponsors may have some obligation to let subjects down easy at the conclusion of a study—perhaps counseling subjects about other treatment opportunities and making transition arrangements if reasonably feasible—this does not mean an obligation exists to provide subjects continued access to health care at levels more generous than the subjects enjoyed before enrolling in the research. Therefore, the ruling in *Suthers v. Amgen*²⁶⁸ seems appropriate, denying subjects' attempts to compel drugmaker Amgen to continue giving them an experimental drug for Parkinson's Disease. The trial sponsor presented evidence that a reasonable number in the research community believed the drug was not proven effective. Also, the subjects had not received an unconditional promise of uninterrupted access to the study drug.²⁶⁹

Yet in other study termination disputes, subjects' legitimate access interests and preferences apart from physical health receive such short shrift that the clinical trial interruption presents troubling intangible harm concerns. For example, purely commercial aims of the sponsor can dominate the decision to end a study prematurely. In a recent randomized trial of the experimental drug verapamil, a medication used for treatment of hypertension, the pharmaceutical company sponsoring the study ended the trial primarily for business reasons as opposed to safety concerns two years earlier than intended after less than one-third of the originally estimated required number of subjects had been enrolled.²⁷⁰

Such early trial discontinuation is not an isolated incident. Sponsors and institutions have stopped a number of other trials for primarily financial reasons, not necessarily related to poor results of the study, but because of lack of funding and resource commitment to continue the

267. See *supra* Part I.E.3.

268. See *Suthers*, 372 F. Supp. 2d 416. See also notes *supra* 126–27 and accompanying text.

269. *Id.*

270. See Bruce Psaty & Drummond Rennie, *Stopping Medical Research to Save Money: A Broken Pact With Researchers and Patients*, 289 JAMA 2128 (2003).

investigation.²⁷¹ Meanwhile, other clinical trials have denied research participants access to study vaccines proven beneficial because poor planning and design by the investigators and sponsor meant that the study simply ran out of enough vaccine to distribute when the clinical trial ended.²⁷² In these situations, one must question whether subjects adequately understood that after making the personal investment and commitment to a trial for months and even years, the study could be discontinued primarily because of the sponsor's changed financial outlook, even if the experimental technology was not yet proven ineffective, or that access to investigational technology actually proven beneficial could end so readily.

Such conduct generates considerable intangible harm by playing with subjects' easily manipulated desires regarding access to experimental technology and by frustrating their inaccurate assumptions regarding when and how a clinical trial may be stopped. Understandably, subjects expect that, unless safety concerns arise, investigators and sponsors will continue a trial until data is gathered to answer the experimental question at the heart of the investigation. While subjects should not rationally anticipate that sponsors and investigators will throw money away on testing ineffective technologies, subjects should expect that sponsors behind a study will devote appropriate resources to see the trial conducted to a legitimate stopping point; otherwise, the subject should not have been approached in the first place. Enrolling subjects in a study lacking sufficient resources and commitment to reach a reasonable end point, or with insufficient post-study transition plans for subjects, risks undermining the respect for persons principle. Such actions treat subjects as mere experimental pawns, inconvenient things that can be thrown away when no longer suiting newly revised research and business goals. It seems patently cruel to seek out subjects, ask for their enrollment, and allow them to invest significant personal resources in a trial, without sufficiently accounting for the likely disruption impact certain subjects will endure if the study is terminated before their course of treatment has concluded. Moreover, an early termination may hinder

271. See, e.g., A. Langer & G. Hopf, *Early Stopping of Trials*, 350 LANCET 890-91 (1997).

272. In a recent clinical trial of an experimental vaccine to treat shingles, more than eighteen thousand participants received a placebo instead of the study vaccine. The trial proved that other subjects who received the study vaccine were far less likely to develop shingles or to experience long-lasting pain from the condition. The subjects treated with the placebo allegedly had been promised that, if the study proved the vaccine effective, they would get it at the end of the trial. However, Merck, the drug company sponsor, did not have enough vaccine available and was unable to provide vaccine to many of the placebo subjects. When the subjects will get the vaccine remains unclear, pending Merck's receiving full FDA approval for the technology, which is not expected until at least early 2006. See Todd Ackerman, *Promising Drug Test, Unfulfilled Promise*, HOUS. CHRON., June 15, 2005, at A1.

the ability of the trial to generate sufficient data to contribute to the state of medical knowledge, thus undermining one of the basic reasons all subjects could rely upon in enrolling in the study in the first place.²⁷³

Of course, the complex consent forms used in clinical trials today may often warn subjects that studies may be discontinued for a variety of reasons. However, an action seeking recovery for the intangible hazards endured by early study termination could be doctrinally based on ordinary negligence rather than informed consent. Blanket statements in consent forms that the trial “may be discontinued at any time” should not override claims that sponsors, investigators, and institutions have a duty to design and operate a protocol in a non-negligent manner. Inviting subjects into a study without reserving necessary funds and making adequate financial plans to see the study to a reasonable conclusion as well as a failure to engage in adequate transition planning for subjects’ post-study access demands falls below a reasonable research standard of care. Just because a consent form may apprise a subject of the possibility of early termination, this conduct still should be undertaken in a reasonable, non-arbitrary manner that is respectful of subjects’ highly foreseeable access preferences and desires for studies to reach a reasonable conclusion.

Alternatively, intangible harm relief might be offered in such situations in recognition of the obligations arising in the special relationship between investigators and subjects.²⁷⁴ Allowing a study to terminate without properly planning for continued access claims by subjects, after a special relationship with the subjects has formed, could be considered an act of abandonment by investigators. To strengthen the relationship bonds between investigators and subjects, a more flexible approach to remedy, analogous to and consistent with restitution remedies for fiduciary breaches, would prove useful. If investigators have heightened, fiduciary-like obligations in dealing with subjects, then the burden should be placed on the investigator to justify premature trial terminations or otherwise risk paying intangible harm damages.²⁷⁵

Providing a remedy for problematic study termination, either based on special relationship theories or ordinary negligence, would help deter

273. See K. Boyd, *Commentary: Early Discontinuation Violates Helsinki Principles*, 322 *BRIT. MED. J.* 605, 605–06 (2001).

274. Whether the same special fiduciary-like obligations exist for trial sponsors, as opposed to investigators, remains an open question. See *Suthers v. Amgen*, 372 F. Supp. 2d 416 (S.D.N.Y. 2005); see also *supra* notes 126–27 and accompanying text. Often the trial sponsors, not the investigators, determine when a study will be discontinued.

275. Cf. Crossley, *supra* note 100, at 256–57 (arguing that damages for dignitary harm should be available in a fiduciary duty breach claim against a physician when personal bias influences the physician’s treatment choice).

opportunistic conduct in dealings with subjects. This supports the research enterprise overall. Otherwise, problematic study termination disputes will engender additional concerns of distrust and abandonment, potentially undermining future subject enrollment and public support for clinical trials generally.

Moreover, new remedy approaches seem needed to supplement the currently inadequate regulatory provisions dealing with study terminations. The federal regulations largely fail to address the many possible adverse implications of inappropriately terminating a study.²⁷⁶ The federal rules also have little to say regarding a sponsor's minimal resource commitment to see a study to a reasonable conclusion. When prospectively reviewing protocols, IRBs may ask about post-study transition plans for subjects, but this review is neither consistent nor clearly required by the current regulations. More importantly, once a study is underway, IRBs acting on behalf of aggrieved subjects have little authority to compel sponsors and investigators to continue a study to a reasonable stopping point, other than the indirect threat of not approving their future protocols, which may not be a sufficient deterrence when many trials can be moved to other institutions.

2. Failure to Disseminate Trial Results

Other conduct that approaches abandonment of subjects and significantly wrongs them even in the absence of physical injury occurs when data gathered from a study is obscured. Investigators and sponsors are understandably wary of widely publicizing negative trial results, as this may jeopardize commercialization opportunities, continued funding sources, and ongoing research subject recruitment. Unfortunately, withholding trial data has the potential to result in an inaccurate flow of information to the larger medical community. A sizable number of clinical trials involving human subjects never result in published articles. Further, the smaller number of published studies reflects a bias in favor of positive results; investigations with negative results tend to be published less frequently and with less speed.²⁷⁷

The desire of researchers and sponsors to spin trial results in the best positive light or to avoid disseminating disappointing trial results that legitimately may be premature is both understandable and not easily regulated or deterred. However, at times this conduct goes even further,

276. See Goldner, *supra* note 86, at 131–32.

277. See Kay Dickersin & Drummond Rennie, *Registering Clinical Trials*, 290 JAMA 516, 517 (2003); An-Wen Chan et al., *Empirical Evidence for Selective Reporting of Outcomes in Randomized Trials*, 291 JAMA 2457 (2004).

involving more aggressive attempts to withhold negative trial data from the larger medical community. Recent controversies surrounding a clinical trial conducted at the University of Toronto and the Hospital for Sick Children exemplify this disturbing trend. The study tested an experimental iron chelation drug on transfusion-dependent thalassemia patients. When investigators identified unexpected risks associated with the drug, the trial sponsor and drug manufacturer, Apotex, Inc., terminated the clinical trial before full subject enrollment had accrued. Apotex then sought to prevent the lead researcher from disclosing the risks to patients or publishing the findings, relying upon a confidentiality clause in its research agreement with the investigator.²⁷⁸

The public outcry over Apotex's maneuvers led the University of Toronto and its affiliated teaching hospitals to implement a new policy prohibiting contract clauses that could be used to restrict disclosure of such risks to research subjects.²⁷⁹ However, not all trial data obfuscation is as visible and receives the same degree of public scrutiny.²⁸⁰ Delays in publication or failure to write up negative research results can be more subtle, indirect ways of withholding negative trial results from the public. These actions become much harder to regulate. Subjects may not even realize that study data from the trial they participated in has not been disseminated through standard research channels, such as peer-reviewed medical journals and conference presentations, and they are unlikely to ask about data dissemination plans during the enrollment process.

A reasonable expectation of subjects, deserving vindication, is that the experiment they participate in will contribute to improving the state of medical knowledge. Imposing an obligation to disseminate trial results in good faith would not represent a significant change in legal doctrine. This duty likely arises from the special relationship between investigators and subjects. A common feature of the relationship is the subject's participation as a partner, or "co-adventurer," with the investigator in what was assumed to be a common goal of advancing scientific knowledge.²⁸¹ In other words, a minimum, although hardly

278. See generally Patricia Baird et al., *Clinical Trials and Industry*, 297 SCIENCE 2211 (2002).

279. See *id.*

280. Cf. Snigdha Prakash, *Did Merck Try To Censor Vioxx Critics?* (Nat'l Pub. Radio broadcast June 9, 2005), available at www.npr.org/templates/story/story.php?storyId=4696711 (discussing alleged attempts by the drug company Merck to exert its influence within academic medical centers in order to suppress safety concerns about its painkiller drug Vioxx).

281. See Dickersin & Rennie, *supra* note 277, at 517; Alexander M. Capron, *Protection of Research Subjects: Do Special Rules Apply in Epidemiology?*, 19 L. MED. & HEALTH CARE 184, 185-86 (1991). Cf. Jay Katz, *Am I My Brother's Keeper*, 3 J. CLINICAL GASTROENTEROLOGY 141, 141-46 (1981) (urging that research be viewed as a joint undertaking between investigator and subject in which

sufficient, condition for establishing the researcher-subject relationship is that the subject is asked to volunteer for a study that will actually matter. The trial itself should have a reasonable likelihood of generating and disseminating generalizable data to help advance confidence levels for clinicians in choosing between therapies. Further, the success of many clinical trials critically depends upon subject effort and adherence to protocol procedures, however unpleasant for the subject, regardless of the skills of the investigator and sponsor.²⁸² Thus, it seems only fair that subjects should enjoy a reward for their efforts—by honoring their expectations of contributing to medical knowledge.

When trial data obfuscation breaches such implied understandings of the investigator-subject relationship, intangible harm arises. A remedy for such breach would be analogous to the restitution remedy under fiduciary law. It may also force physician-investigators to address on a more regular basis the ongoing conflict they have between loyalties to the study and doing what is best for individual patients, particularly when they are forced to disseminate poor trial results.²⁸³

Further, making failure to disseminate trial results an actionable claim could be justified as an incremental, yet warranted, expansion of an ordinary negligence claim. Conducting a study in which subjects are asked to make considerable personal investments, without ensuring the dissemination of trial data in good faith, arguably falls below a reasonable research standard of care because it flagrantly disrupts settled custom and ordinary expectations that clinical trials contribute to medical progress.

Ensuring a cause of action when trial data obfuscation occurs also helps advance respect for subjects as persons. Withholding of trial data treats subjects no better than discarded specimens of a botched experiment. Valuing the subject's legitimate interest and expectation of trial result dissemination acknowledges that the subject's decision to participate in research was likely motivated in part by the desire to contribute to medical knowledge.²⁸⁴ Of course, one should resist the

they engage in advance dialogue that acknowledges the uncertainty of medical opinion so that both can understand why an experiment is underway).

282. Cf. E. Haavi Morreim, *Result-Based Compensation in Health Care: A Good, But Limited, Idea*, 29 J.L. MED. & ETHICS 174, 177 (2001) (noting that clinical outcomes depend to a large degree on patient effort, regardless of the skill of the treating medical providers).

283. See Ann Partridge & Eric Winer, *Informing Clinical Trial Participants About Study Results*, 288 JAMA 363, 365 (2002).

284. Indeed, one of the basic ethical requirements of the Nuremberg Code is that "[t]he experiment should be such as to yield fruitful results for the good of society" Nuremberg Code, *supra* note 30, ¶ 2. See also Rebecca Dresser, *A New Era in Drug Regulation?*, HASTINGS CTR. REP., May-June 2005, at 10.

inclination to paint subjects in too generous a light. Empirical investigations of subject preferences show that they do not volunteer for trials for purely selfless, altruistic reasons of helping others.²⁸⁵ Indeed, access concerns dominate many subjects' enrollment decisions.²⁸⁶ Nonetheless, empirical studies suggest that a good number of subjects believe that participating in a clinical trial will help advance medical progress, and this understanding partly motivates subjects to volunteer for research.²⁸⁷ Delay or concealment of study results disturbs these reasonable expectations and undermines the subject's perceived value of participation, thereby making the experiment itself less socially useful overall. Also, such conduct becomes trust-corroding, as it can cause subjects to lose faith in the research process and jeopardize future subject enrollment and continued public support for human subject trials. Ensuring that both negative and positive results are shared more openly may also help counter therapeutic misconception problems and the common over-estimation about research's direct benefits.²⁸⁸ Moreover, failure to disseminate trial data results runs the risk of wasteful, duplicative experimentation, as new studies are attempted for previously performed, undisclosed research.²⁸⁹

Finally, a more flexible approach to intangible hazards remedies would supplement the woefully inadequate regulatory and statutory provisions addressing trial results dissemination. Currently, a wide gap exists, as the federal regulations do not clearly require research results to be widely publicized. The regulations do provide that "significant findings" developed during the course of the experiment that would affect an individual's willingness to continue should be shared with subjects.²⁹⁰ But this requirement is limited to whether the data would affect the decision to continue as a subject; it does not necessarily extend to informing the subjects about the general research results at the trial's conclusion or even reporting back to subjects that the clinical trial data was inconclusive or negative if this data does not directly affect the

285. See Jeremy Sugarman et al., *What Patients Say About Medical Research*, IRB: ETHICS & HUM. RES., July-Aug. 1998, at 1, 4.

286. See *supra* Part I.E.3.

287. Empirical investigations indicate that few subjects volunteer for purely altruistic reasons. The majority of subjects have a mix of altruistic and self-interested motivations for volunteering. They may believe the research offers the better treatment option, and they also simultaneously hope to help advance medical science or to help others. For a thorough analysis of research subject motivations, see Sugarman et al., *supra* note 285, at 4. See also *supra* note 96.

288. See Conrad Fernandez et al., *Informing Study Participants of Research Results: An Ethical Imperative*, IRB: ETHICS & HUM. RES., May-June 2003, at 12, 13; Dresser, *supra* note 284, at 11.

289. See Dickersin & Rennie, *supra* note 277, at 517.

290. 45 C.F.R. § 46.116(b)(5) (2005), 21 C.F.R. § 50.25(b)(5)

subject's remaining treatment options and individualized plan of care.²⁹¹ Current medical custom does not support the sharing of trial results with subjects where their immediate treatment options are not affected. Indeed, very few IRB-approved consent forms even notify subjects about the right to receive summary results from the trial.²⁹²

Previous statutory reform attempts have been of limited help. The FDA Modernization Act of 1997 requires registration of certain drug trials in a publicly available database that contains basic information about each study.²⁹³ Because posting information about the actual results of the studies requires the consent of the sponsors,²⁹⁴ and because the database provisions apply only to testing of drugs used for life-threatening and serious illnesses,²⁹⁵ therefore not including many clinical trials, enforcement of the statute has been weak and the law has had limited impact.²⁹⁶

Recent developments indicate greater attention to the problem. For example, New York Attorney General Eliot Spitzer reached a novel settlement with drug company GlaxoSmithKline (GSK) in recent fraud litigation concerning GSK's promotion of its anti-depression drug Paxil. The lawsuit accused GSK of suppressing negative results from studies of Paxil in children, including burying results that suggested an increased risk of suicidal thinking among pediatric patients. In the settlement, GSK agreed to establish a "Clinical Trials Registry" summarizing the results of all GSK-sponsored drug studies and to make the information available on the World Wide Web within specific time frames after study completion.²⁹⁷ Meanwhile, the American Medical Association has endorsed the concept of a comprehensive, publicly available clinical trial registry.²⁹⁸ Additional pending legislative and regulatory proposals, as well as developing policies for medical journals and attempts at self-regulation by pharmaceutical companies, also seek to broaden clinical trial registration requirements.²⁹⁹

291. See Fernandez et al., *supra* note 288, at 12; Partridge & Winer, *supra* note 283.

292. See Conrad Fernandez et al., *Disclosure of the Right of Research Participants to Receive Research Results*, 97 CANCER 2904 (2003).

293. 42 U.S.C. § 282(j) (2005).

294. 42 U.S.C. § 282(j)(3)(B)(ii).

295. 42 U.S.C. § 282(j).

296. See Robert Steinbrook, *Public Registration of Clinical Trials*, 351 NEW ENG. J. MED. 315, 315-16 (2004).

297. See Order, *New York v. GlaxoSmithKline*, No. 04-CV-5304 MGC (S.D.N.Y., Aug. 26, 2004), available at www.oag.state.ny.us/press/2004/aug/aug26a_04_attach1.pdf.

298. See Barry Meier, *A.M.A. Adds Its Voice to Call For Disclosure On Drug Trials*, N.Y. TIMES, June 16, 2004, at C1.

299. See, e.g., Fair Access To Clinical Trials Act, H.R. 5252, 108th Cong. (2d Sess. 2004); Barry

However, notwithstanding future developments in this area, trial sponsors and investigators currently do not register a large number of studies, and they face understandable pressures to withhold certain trial results from general dissemination. Subjects are rarely told about trial result data or plans to share the results with the larger research community, unless the information affects their direct future treatment options or willingness to continue participating in a study. Providing subjects some form of retrospective relief for the intangible harm caused by failure to disseminate trial results would thus prove particularly useful and not likely run afoul of current regulatory mechanisms. This approach may even spur on better regulatory responses for dealing with such intangible research hazards prospectively.

C. Conclusion

It is tempting and far too easy to call for new causes of action to correct every perceived wrong. However, some wrongs simply cannot be addressed through legal claims. The law has often had to live with an imperfect harmonization between harm and remedy,³⁰⁰ and intangible hazards have frequently been neglected in many settings, not just research. Moreover, some of the dilemmas and otherwise adverse experiences of research subjects may be intractable and an inherent part of medical experimentation, given the desperate states of therapeutic uncertainty and limited access to care many subjects face. Providing research subjects with broader relief for intangible hazards is therefore not simple to justify doctrinally. It also threatens to add unpredictable costs to research activities, perhaps resulting in over-deterrence, while possibly doing very little to improve the regular disappointments, frustrations, and affronts to dignity that inevitably follow from the poor starting position of becoming a research subject. Further, a broader approach to an intangible harm remedy will raise many difficult implementation problems not easily resolved, including whether to recognize such claims through common law actions or regulatory

Meier, *Plan Would Require Full Disclosure of Drug Trials*, INT'L HERALD TRIB., June 16, 2004, at 13 (describing consideration by a group of top medical journals of a new policy requiring sponsors to register clinical trials in a public database in order for the results to be considered for later publication in the journals); Catherine De Angelis et al., *Is This Clinical Trial Fully Registered?*, 143 ANNALS INTERNAL MED. 146 (2005) (statement from the International Committee of Medical Journal editors on same policy); *Site to List Select Drug Tests*, WASH. POST, Sept. 8, 2004, at E2 (reporting that Pharmaceutical Research and Manufacturers of America to launch web site for drug companies to summarize results from selected trials).

300. See Anita Bernstein, *How to Make a New Tort: Three Paradoxes*, 75 TEX. LAW REV. 1539 (1997).

channels, the materiality threshold for when intangible harm claims are cognizable, and who has standing to bring claims centered less on individual injury and more on harm to the research enterprise and to subjects generally. Similarly, how to calculate optimal damage amounts raises many challenges, such as whether to use nominal, presumed, or other imprecise damage awards. Perhaps some form of “memorial” damages should be explored, as this could provide a mechanism to honor the contributions of the affected research subjects, provide some level of deterrence, promote corrective justice, and allocate damages in a way that benefits participating subjects and the research enterprise as a whole.³⁰¹

Notwithstanding these issues and implementation challenges, it must be recognized that medical research presents significant intangible hazards. The risk of intangible harm is at least as great as the likelihood of subjects experiencing any physical dangers. Given the high priority of research subject protection as a matter of health law and medical ethics, the special obligations flowing from the investigator-subject relationship, and the importance of trust to the research system, intangible harm concerns should not continue to be overlooked and marginalized. Some legal experimentation with new remedy approaches seems needed to improve the general state of medical experimentation. Recognition of intangible harm claims, where doing so amounts to an incremental, limited extension of existing case law and regulatory approaches, would be a welcome initial step. Hopefully, such an approach will offer help and solicitude to subjects deserving support and respect, deter opportunistic conduct in dealings with subjects, and promote trust and confidence in medical experimentation generally to ensure a better functioning research enterprise. The time has come to recognize, value, and better address the very real harm, even if intangible, that arises in medical research.

301. Cf. McClurg, *supra* note 28, at 34–40 (arguing for a new type of “lost life” damages and advocating that the damages principally be used to establish memorials honoring the deceased tort victims rather than awarding such recovery to the decedent’s estate or to the survivors).