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Learning from the Mistakes of the Past: Disclosure of Financial Conflicts of Interest and Genetic Research

Christopher Jackson *

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I. INTRODUCTION

[1] “Every human being of adult years and sound mind has a right to determine what shall be done with his own body”¹ From Benjamin Cardozo’s early expression of the principle of patient autonomy emerged the doctrine of informed consent, defined by both contract and fiduciary laws and elaborated upon by courts, state and federal legislatures, and professional associations. Later, as the world sought to reassemble itself following the horrors of World War II, the promulgation of the Nuremberg Code established an international standard for the treatment of human research subjects.² The experiences of the Nazi atrocities, together with America’s own unfortunate history in human experimentation, provided informal precedent for the courts in their interpretation of informed consent requirements.³

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¹ *Schloendorff v. Soc’y of the N.Y. Hosp.*, 105 N.E. 92, 93 (N.Y. 1914).

² See 2 TRIALS OF WAR CRIMINALS BEFORE THE NUERNBERG MILITARY TRIBUNALS UNDER CONTROL COUNCIL LAW NO. 10, at 181-82 (1949), available at <http://www1.umn.edu/humanrts/instree/nuremberg.html> (last visited Sept. 17, 2004) [hereinafter NUREMBERG CODE]. The Nuremberg Code uses natural law to describe a broad theory of human rights.

³ See Larry I. Palmer, *Genes and Disability: Defining Health and the Goals of Medicine: Genetic Health and Eugenics Precedents: A Voice of Caution*, 30 FLA. ST. U. L. REV. 237, 257 (2003). Palmer discusses the unique impact of the Nazi doctors’ trials at Nuremberg and the Tuskegee syphilis experiments on American courts. See *id.* at 258-61. Although not formally binding precedents, the philosophical and moral lessons from these “eugenics precedents” are often referenced in human experimentation cases. See

[2] The courts, federal statutory requirements, and international agreements draw on these unfortunate episodes in efforts to protect the autonomy and well-being of human subjects. The ethical requirements governing medical practitioners further supplement these protections.⁴ Today, with the decoding of the human genome and recent explosive growth in biotechnology research, medicine and the profit-motive intersect as never before.⁵ The resulting leaps in technological advancement and quality of care are remarkable, but the impact on human subjects research, especially the vulnerable populations that participate in such studies, raises serious ethical questions. The doctrine of informed consent requires thorough reevaluation, both in the therapeutic and non-therapeutic contexts, particularly where the disclosure of financial conflicts of interest is concerned.⁶

generally George J. Annas, *Mengele's Birthmark: The Nuremberg Code in United States Courts*, 7 J. CONTEMP. HEALTH L. & POL'Y 17 (1991) (discussing the United States' ambivalence towards human experimentation).

⁴ See generally CODE OF MEDICAL ETHICS: CURRENT OPINIONS WITH ANNOTATIONS (Am. Med. Ass'n Council on Ethical and Judicial Affairs 2002), available at <http://www.ama-assn.org/ama/pub/category/8288.html> (last updated Jan. 24, 2003) [hereinafter CODE OF MEDICAL ETHICS].

⁵ See, e.g., Jennifer A. Henderson & John J. Smith, *Financial Conflict of Interest in Medical Research: Overview and Analysis of Federal and State Controls*, 57 FOOD & DRUG L.J. 445, 446-47 (2002) ("Each [financial conflict of interest] regulation differs in its focus and definition of what constitutes a financial conflict, thus creating a patchwork of regulations—some designed to protect the integrity of research results and others designed for the safety of human research participants.").

⁶ See *Grimes v. Kennedy Krieger Inst., Inc.*, 782 A.2d 807, 812 n.2 (Md. 2001). The *Grimes* court offers a concise distinction between therapeutic and non-therapeutic research:

[a]t least to the extent that commercial profit motives are not implicated, therapeutic research's purpose is to directly help or aid a patient who is suffering from a health condition the objectives of the research are designed to address—hopefully by the alleviation, or potential alleviation, of the health condition.

Non-therapeutic research generally utilizes subjects who are not known to have the condition the objectives of the research are designed to address, and/or is not designed to directly benefit the subjects utilized in the research, but, rather, is designed to achieve beneficial results for the public at large (or, under some circumstances, for profit).

Id.

[3] Observers often point to the unique characteristics of biotechnology research as creating a need for higher scrutiny of the informed consent process.⁷ Biotechnology research in academic facilities involves a great deal of competition for funding, often from private sources, which creates a decidedly more entrepreneurial environment.⁸

[4] The result of this commercialization is that research of human subjects becomes “laced with more tangible financial conflicts of interest arising at multiple points throughout the research process.”⁹ Additionally, the now generally accepted proposition that researchers can obtain patent protection for genetic sequences greatly enhances the economic payoff and marketability of important discoveries.¹⁰ The sophisticated nature of both the science itself and of attending financial interests creates special concerns when explaining research to subjects, particularly where study populations may include indigenous or otherwise specially-situated individuals.¹¹

[5] The diverse roots of the informed consent doctrine, emerging as they did in the contexts of both medical treatment and scientific research, have fostered a number of ambiguities as each field evolves and changes over time. Strong financial incentives call the objectivity of institutional review practices into question,¹² and the need for clearly drawn ethical principles to govern these practices grows stronger as we move into the Human Genome Era.¹³

⁷ See, e.g., Karen A. Jordan, *Financial Conflicts of Interest in Human Subjects Research: Proposals for a More Effective Regulatory Scheme*, 60 WASH. & LEE L. REV. 15, 18 (2003).

⁸ See *id.*

⁹ *Id.*

¹⁰ See, e.g., *Diamond v. Chakrabarty*, 447 U.S. 303, 312-13 (1980) (holding that living organisms are not per se violations of the product of nature doctrine); *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991) (holding that conception of an invention involving a genetic sequence occurs when some level of reduction to practice is achieved).

¹¹ See generally Kara H. Ching, *Indigenous Self-Determination in an Age of Genetic Patenting: Recognizing an Emerging Human Rights Norm*, 66 FORDHAM L. REV. 687 (1997) (discussing how the law may aid indigenous peoples in securing meaningful control over their genetic material).

¹² See Henderson & Smith, *supra* note 5, at 446.

¹³ This era is characterized as “a period in which biomedical research will be dominated by the assumption that genetic knowledge will improve health care delivery and presumably overall health status.” Larry I. Palmer, *Disease Management and Liability in the Human Genome Era*, 47 VILL. L. REV. 1, 2 (2002). In essence, scientific progress and experimentation will dominate much of the health care system. See *id.* at 2-

[6] Complicating these concerns is the distinction created by both courts and legislatures between the duties of those engaging in “therapeutic” research and those engaging in “non-therapeutic” research.¹⁴ Some courts maintain that the non-therapeutic context does not trigger a doctor-patient style fiduciary relationship, and that researchers owe no duty to disclose otherwise relevant financial information in such situations.¹⁵ If this trend continues to develop, the negative impact on the relationship of trust between researchers and subjects will far outweigh any benefits to be gained from nondisclosure.

[7] This article addresses the issues arising from genetic human subjects research and recommends that researchers follow stricter requirements for the disclosure of financial conflicts of interest. Part II focuses on historical precedents providing a framework for the regulation of human subjects research. Part III lays out the relevant standards for informed consent. Part IV discusses a number of cases with implications for genetic research. Part V analyzes some of the unique characteristics of genetic research that raise ethical concerns. Finally, Part VI proposes stricter requirements for the disclosure of financial conflicts of interest during the informed consent process.

II. THE NECESSITY OF CONSENT

[8] In light of the troubling history of human subjects research, a number of international agreements and professional edicts have emerged discussing the ideal ethical requirements that should govern such practices. American courts make regular reference to these statements,

3. Writing before the *Greenberg* decision was reached, Palmer argued that researchers “must . . . disclose, without the plaintiffs’ asking, their intentions regarding the patenting of genetic knowledge and other data they obtain.” *Id.* at 28.

¹⁴ See Victoria Orlowski, Note, *Promising Protection Through Internationally Derived Duties*, 36 CORNELL INT’L L.J. 381, 393 (2003) (“The ‘therapeutic/non-therapeutic’ distinction . . . opens the possibility for deception because it encourages [institutional review boards] and researchers to cast their experiments as beneficial in some way because subjects are less likely to participate in research which will harm or not benefit them.”).

¹⁵ See *Greenberg v. Miami Children’s Hosp. Research Inst., Inc.*, 264 F. Supp. 2d 1064, 1070 (S.D. Fla. 2003) (holding that the duty of informed consent does not extend to economic interests in a non-therapeutic relationship). *But see* *Grimes v. Kennedy Krieger Inst., Inc.*, 782 A.2d 807, 845-46 (Md. 2001) (describing special relationships that may exist even in a non-therapeutic context).

although the exact nature of the legal obligations they create is, at best, unclear.¹⁶

[9] Following the Nazi doctors' trials, the Nuremberg court echoed Cardozo's early sentiments in its promulgation of the Nuremberg Code, declaring that "[t]he voluntary consent of the human subject is absolutely essential."¹⁷ The Nuremberg court used natural law theory to expand upon Cardozo's insistence on autonomy, emphasizing that subjects must have the legal capacity to consent, the right to refuse continuation in any study, and a demonstration of knowledge and comprehension of all risks associated with participation.¹⁸ The Code, although widely accepted and relied upon by the international scientific community, met with some criticism and resistance, primarily from researchers who felt its requirements were too legalistic and impracticable for everyday implementation.¹⁹

[10] In response to calls for a more flexible formulation of informed consent requirements, the World Medical Association issued the Declaration of Helsinki in 1964.²⁰ The Declaration placed the well-being of human subjects above "the interests of science and society,"²¹ and called for special protections for vulnerable research populations, particularly the "economically and medically disadvantaged."²²

[11] Many of these principles are reflected in what has come to be known as the "Common Rule" governing federally funded human subjects

¹⁶ For example, the Nuremberg Code has been cited only once by the Supreme Court, in a dissent by Justice O'Connor. *See United States v. Stanley*, 483 U.S. 669, 710 (1987) (O'Connor, J., dissenting). The majority denied relief to a former soldier alleging injury following military testing of LSD, finding that the Code's principles did not apply to the military context. *Id.* at 686.

¹⁷ NUREMBERG CODE, *supra* note 2, at 181.

¹⁸ *Id.*

¹⁹ *See Orłowski, supra* note 14, at 396.

²⁰ *See George J. Annas, The Changing Landscape of Human Experimentation: Nuremberg, Helsinki, and Beyond*, 2 HEALTH MATRIX 119, 122-23 (1992).

²¹ DECLARATION OF HELSINKI: ETHICAL PRINCIPLES FOR MED. RESEARCH INVOLVING HUMAN SUBJECTS § A.5 (World Med. Ass'n 2002), <http://www.wma.net/e/policy/b3.htm> (last visited Sept. 14, 2004) [hereinafter DECLARATION OF HELSINKI].

²² *Id.* § A.8.

research in the United States.²³ The provisions of the Common Rule are scattered throughout the regulations of several agencies and include the requirement of institutional review board (“IRB”) approval of protocols for the protection of the rights and safety of study participants.²⁴

[12] The American Medical Association’s (“AMA”) Code of Medical Ethics confers decision-making responsibility on the patient.²⁵ Further, it requires informed consent before the commercial use of human tissue, stressing the fact that financial interests must not influence medical decision-making.²⁶ The text of the AMA’s requirements dealing with the commercial use of human tissue bears repeating:

The rapid growth of the biotechnology industry has resulted in the commercial availability of numerous therapeutic and other products developed from human tissue. Physicians contemplating the commercial use of human tissue should abide by the following guidelines:

- (1) Informed consent must be obtained from patients for the use of organs or tissues in clinical research.
- (2) Potential commercial applications must be disclosed to the patient before a profit is realized on products developed from biological materials.
- (3) Human tissue and its products may not be used for commercial purposes without the informed consent of the patient who provided the original cellular material.
- (4) Profits from the commercial use of human tissue and its products may be shared with patients, in accordance with lawful contractual agreements.
- (5) The diagnostic and therapeutic alternatives offered to patients by their physicians should conform to standards of good medical practice and should not be influenced in any way by the commercial potential of the patient’s tissue.²⁷

²³ See Lori A. Alvino, Note, *Who’s Watching the Watchdogs? Responding to the Erosion of Research Ethics by Enforcing Promises*, 103 COLUM. L. REV. 893, 898-99 (2003).

²⁴ *Id.* at 898-900.

²⁵ See CODE OF MEDICAL ETHICS, *supra* note 4, § 10.01.

²⁶ See *id.* § 2.08.

²⁷ *Id.*

III. STANDARDS FOR DISCLOSURE

[13] From the earliest articulation of the patient's right of informed consent, courts have worked at defining a practicable standard with the influence of tort doctrine playing a large role in this evolution.²⁸ Stricter formulations of informed consent require the physician to disclose information that his patients might consider material to the course of treatment, while less rigorous applications of the doctrine utilize a more flexible standard requiring compliance with industry norms in the medical field.²⁹

[14] The informed consent doctrine requires general disclosure of the diagnosis and possible treatment alternatives, as well as the nature, risks, and likelihood of success of a given treatment or procedure.³⁰ In a slight majority of jurisdictions, courts rely on the physician-oriented standard to determine what information must be disclosed, applying an industry practice standard similar to that used for medical negligence generally.³¹ Other jurisdictions utilize the more stringent patient-oriented standard.³²

[15] The touchstone for the patient-oriented approach comes from *Canterbury v. Spence*, which assembled a variety of earlier holdings into a coherent standard.³³ The court held that the appropriate measure of disclosure is not what the reasonable physician would consider relevant, but what the reasonable patient would want to know before making a decision.³⁴ Relying heavily on Cardozo's opinion in *Schloendorff v. Society of the New York Hospital*, the *Canterbury* court defined the standard of care:

[d]ue care may require a physician perceiving symptoms of bodily abnormality to alert the patient to the condition. It may call upon the physician confronting an ailment which does not respond to his ministrations to inform the patient thereof. It may command the physician to instruct the patient as to any limitations to be presently observed for his

²⁸ See MARK A. HALL ET AL., HEALTH CARE LAW AND ETHICS IN A NUTSHELL 132 (2d ed. 1999).

²⁹ See *id.* at 134-35.

³⁰ *Id.* at 133.

³¹ *Id.* at 134.

³² *Id.* at 135.

³³ *Canterbury v. Spence*, 464 F.2d 772 (D.C. Cir. 1972).

³⁴ See *id.* at 786-87.

own welfare, and as to any precautionary therapy he should seek in the future. It may oblige the physician to advise the patient of the need for or desirability of any alternative treatment promising greater benefit than that being pursued. Just as plainly, due care normally demands that the physician warn the patient of any risks to his well-being which contemplated therapy may involve.³⁵

[16] This sentiment was echoed by other jurisdictions.³⁶ Still, the less-restrictive physician-oriented standard, which limits the informed consent requirement “to those disclosures which a reasonable medical practitioner would make under the same or similar circumstances,” became dominant.³⁷ The application of these two doctrines would trouble courts and commentators as new developments in biotechnology and medicine brought the worlds of treatment, research, and business closer together.

IV. INFORMED CONSENT IN GENETIC RESEARCH

[17] There are three important cases that have implications for informed consent in genetic research and that discuss both the patient-oriented and the physician-oriented standards for disclosure. These cases provide a good picture of the spectrum along which courts lie in their applications of the informed consent standards, and show where the courts may go when confronted with future disputes arising from genetic research.

[18] The eugenics precedents discussed above deal primarily with non-therapeutic research, where no direct benefit is conferred on the subject. This contrasts with therapeutic research, where subjects are also considered the patients of researchers, engaged in the type of relationship envisioned by the Code of Medical Ethics.³⁸ Although some jurisdictions maintain that the non-therapeutic context does not trigger a doctor-patient style fiduciary relationship,³⁹ this typically is not the approach taken by

³⁵ *Id.* at 781 (citations omitted).

³⁶ *See, e.g.,* Powers v. United States, 589 F. Supp. 1084, 1097-98 (2d Cir. 1984) (finding that the defendant’s conduct failed to satisfy the “lay” standard enunciated in *Canterbury*).

³⁷ Natanson v. Kline, 350 P.2d 1093, 1106 (Kan. 1960).

³⁸ *See* Orlovski, *supra* note 14, at 393. Interestingly, the Code of Medical Ethics refers to those involved in medical studies as “patients,” whereas the Nuremberg Code and most statutes regulating research refer to them as “subjects.” *Compare* CODE OF MEDICAL ETHICS, *supra* note 4, § 2.08, *with* NUREMBERG CODE, *supra* note 2, at 181.

³⁹ *Supra* note 15.

medical researchers or their subjects.⁴⁰ The cases below address situations arising from both therapeutic and non-therapeutic types of research, and illustrate how the blurred distinction between the two can create confusion for researchers and subjects alike.

[19] *Greenberg v. Miami Children's Hospital Research Institute, Inc.* is the most recent and perhaps most troubling case on this issue.⁴¹ In *Greenberg*, a United States district court in Florida held that a physician had no duty to obtain informed consent prior to his commercial use of donated tissues while researching the cause of Canavan disease, and further, that there was no fiduciary duty requiring disclosure of financial conflicts of interest.⁴² The court reasoned that no therapeutic relationship existed between the physician/researcher and his subjects.⁴³ It even went so far as to conclude that the plaintiffs were more akin to donors, or even co-researchers, than research subjects *per se*.⁴⁴

[20] The individual plaintiffs in *Greenberg* were parents of children with Canavan disease. Canavan disease interferes with brain fiber growth in children of Ashkenazi or Eastern European Jewish descent; it is usually fatal.⁴⁵ In 1987, plaintiff Daniel Greenberg approached Dr. Rueben Matalon requesting help in the search for the genetic cause of the disease and the development of a prenatal screening test to identify potential carriers.⁴⁶ Greenberg and one of the organizational plaintiffs, the Chicago Chapter of the National Tay-Sachs and Allied Disease Association, Inc., sought out other Canavan families to provide tissue (such as blood, urine, and autopsy samples), health histories, and financial support.⁴⁷ The plaintiffs alleged an understanding that any results from the research would remain in the public domain, on the basis of prior experience in community testing for Tay-Sachs disease.⁴⁸

⁴⁰ See Interview with Jim Evans, M.D., Ph.D, Department of Genetics, University of North Carolina at Chapel Hill, in Chapel Hill, N.C. (Feb. 18, 2004) (on file with Richmond Journal of Law and Technology) [hereinafter Evans Interview].

⁴¹ *Greenberg v. Miami Children's Hosp. Research Inst., Inc.*, 264 F. Supp. 2d 1064 (S.D. Fla. 2003).

⁴² *Id.* at 1070-72.

⁴³ *Id.* at 1070.

⁴⁴ *Id.* at 1071.

⁴⁵ Palmer, *supra* note 3, at 261-62.

⁴⁶ *Greenberg*, 264 F. Supp. 2d at 1066.

⁴⁷ *Id.* at 1067.

⁴⁸ *Id.*

[21] Following a breakthrough in 1993, however, Dr. Matalon obtained a patent for forty-four claims, including:

nucleic acid sequences, genes, polypeptides, antibodies, vectors containing the gene, host cells transformed with vectors containing the gene, animal models for the disease, methods for expressing the polypeptide, genetic screening methods and kits, diagnostic methods and kits, methods of treating Canavan disease and methods of genetic therapy for the disease.⁴⁹

[22] The plaintiffs further alleged that they had no knowledge of the patent, or of Matalon's commercial intentions, until 1998, when Miami Children's Hospital began threatening and imposing royalty fees on health providers using the Canavan test.⁵⁰ The plaintiffs brought suit for six claims, including lack of informed consent, breach of fiduciary duty, unjust enrichment, fraudulent concealment, conversion, and misappropriation of trade secrets.⁵¹ The court dismissed with prejudice all but the unjust enrichment claim.⁵²

[23] In dismissing the informed consent claim, the court reasoned that imposing such a duty would "chill medical research as . . . [researchers] constantly evaluate whether a discloseable event has occurred."⁵³ It also portrayed this "extra duty" as creating "dead-hand control that research subjects could hold because they would be able to dictate how medical research progresses."⁵⁴ The court dismissed the plaintiffs' contention that the Code of Medical Ethics required informed consent prior to commercial use of human tissue, finding that its 1994 promulgation occurred too late to bind the parties.⁵⁵

⁴⁹ U.S. Patent No. 5,679,635 (issued Oct. 21, 1997).

⁵⁰ Mary R. Anderlik & Mark A. Rothstein, *Currents in Contemporary Ethics: Canavan Decision Favors Researchers over Families*, 31 J.L. MED. & ETHICS 450, 451 (2003).

⁵¹ *Greenberg*, 264 F. Supp. 2d at 1068.

⁵² *Id.* at 1077-78.

⁵³ *Id.* at 1070.

⁵⁴ *Id.* at 1071.

⁵⁵ *Id.* at 1071 n.2. Although the Code of Medical Ethics does not confer a formal legal obligation on physicians, its provisions are often used to establish the standard of due care in the medical industry in tort claims. *See, e.g., Ketchup v. Howard*, 543 S.E.2d 371, 377 (Ga. Ct. App. 2000) (stating that "[w]e are not the first court to recognize that the Code of Medical Ethics sets forth the medical profession's standard on informed consent").

[24] The holding of the *Greenberg* court has dangerous ethical implications and creates opportunities for the exploitation of vulnerable study populations. Fortunately, alternative approaches taken by other jurisdictions provide more effective and ethical protections of patient autonomy, while simultaneously taking into account the interests of scientific progress.

[25] For example, in the widely-discussed case of *Moore v. Regents of the University of California*, the Supreme Court of California held that:

(1) a physician must disclose personal interests unrelated to the patient's health, whether research or economic, that may affect the physician's professional judgment; and

(2) a physician's failure to disclose such interests may give rise to a cause of action for performing medical procedures without informed consent or breach of fiduciary duty.⁵⁶

[26] In reaching this decision, the court relied on California's patient-oriented standard of disclosure,⁵⁷ and took the standard even further by recognizing that a reasonable patient would wish to be informed of potential profit motives or economic incentives.⁵⁸

[27] The plaintiff in *Moore* was diagnosed with hairy-cell leukemia in 1976 by defendant Golde, a physician at UCLA Medical Center.⁵⁹ The complaint alleged that at the time of the diagnosis, the defendants "were aware that 'certain blood products and blood components were of great

⁵⁶ *Moore v. Regents of the Univ. of Cal.*, 793 P.2d 479, 483 (Cal. 1990). The court upheld the defendants' motion to dismiss on the count of conversion, providing the other significant wing of the *Moore* decision. *See id.* at 480.

⁵⁷ *See Cobbs v. Grant*, 502 P.2d 1, 9-10 (Cal. 1972) (holding that the scope of communications must be determined by materiality with respect to the patient's needs).

⁵⁸ *Moore*, 793 P.2d at 483 (citing *Magan Med. Clinic v. Cal. State Bd. of Med. Exam'rs*, 57 Cal. Rptr. 256, 262 (Cal. Ct. App. 1967)). Concerns over the influence of financial considerations on medical decision-making have created a wealth of literature, particularly in the context of the managed care industry. *See generally, e.g.*, Mark A. Hall, *Rationing Health Care at the Bedside*, 69 N.Y.U. L. REV. 693, 693 (1994) (arguing "for lifting the ethical taboo against physician bedside rationing").

⁵⁹ *Moore*, 793 P.2d at 481.

value in a number of commercial and scientific efforts.”⁶⁰ Golde, who determined that Moore’s life was threatened by the condition, obtained consent to remove Moore’s spleen in 1976.⁶¹ From this time until 1983, Moore made several trips to UCLA Medical Center at Golde’s direction, where Golde drew samples of “blood, blood serum, skin, bone marrow aspirate, and sperm.”⁶² Moore alleged that he did so based upon Golde’s representations that such samples were necessary for his continued medical treatment and “the trust inherent in and by virtue of the physician-patient relationship.”⁶³

[28] Unbeknownst to Moore, Golde established a cell-line from Moore’s T-lymphocytes,⁶⁴ and obtained a patent for twenty-two claims, including the cell line and numerous procedures for the production of bone marrow proteins.⁶⁵ Based upon biotechnology industry reports, Moore alleged that the potential market for such procedures exceeded three billion dollars.⁶⁶

[29] *Moore* involved a clear case of a therapeutic, doctor/patient relationship, and is thus distinguishable from the situation in *Greenberg*. At least this was the rationale employed by the *Greenberg* court in its ruling.⁶⁷ Drawing this distinction too finely, however, invites troubling behavior if the IRBs charged with protecting patient safety misunderstand or misinterpret requirements, as was the case in *Grimes v. Kennedy Krieger Institute, Inc.*⁶⁸

[30] *Grimes* arose outside the field of genetic research, but its facts make concerns over the mishandling of the therapeutic/non-therapeutic distinction all the more clear. The Kennedy Krieger Institute (“Institute”), associated with Johns Hopkins University in Baltimore, initiated a non-therapeutic research project studying the relative efficacy of various levels

⁶⁰ *Id.*

⁶¹ *Id.*

⁶² *Id.*

⁶³ *Id.*

⁶⁴ *Id.* at 480-81. As explained by the court, T-lymphocytes are white blood cells that produce regulatory proteins essential to the immune system. *Id.* at 482 n.2. Moore’s T-lymphocytes overproduced certain proteins, or lymphokines, making it easier to identify the corresponding genetic code responsible for their production. *Id.*

⁶⁵ *Id.* at 482; see U.S. Patent No. 4,438,032 (issued Mar. 20, 1984).

⁶⁶ *Moore*, 793 P.2d at 482.

⁶⁷ *Greenberg v. Miami Children’s Hosp. Research Inst., Inc.*, 264 F. Supp. 2d 1064, 1070 (S.D. Fla. 2003).

⁶⁸ See *Grimes v. Kennedy Krieger Inst., Inc.*, 782 A.2d 807, 813-14 (Md. 2001).

of lead abatement in residential homes.⁶⁹ The Institute arranged with a local non-profit corporation administering low-income housing and a group of landlords to effect partial lead abatement modifications in certain homes, and to give priority to families with young, healthy children.⁷⁰ Over a two-year period, the study would measure the levels of lead dust present in the homes, as well as the levels of lead contamination present in the (previously) healthy children residing there.⁷¹ Prior studies had already indicated that lead dust would remain in the houses over a period of time.⁷²

[31] The court likened the children used in the study to “canaries in the mines,” and determined that there had been no adequate explanation during the consent process of how the lead dust in the homes related to either the lead abatement modifications or to the actual lead contamination in the children’s blood.⁷³ It further suggested that the IRB actually tried to assist researchers in avoiding stringent federal regulations governing non-therapeutic research on children by rephrasing its description of possible benefits to the control group, and that the IRB failed to grasp the distinction between therapeutic and non-therapeutic research.⁷⁴

[32] In finding a special relationship between the researchers and their subjects, the *Grimes* court relied on eugenics precedents such as the Tuskegee Syphilis Study and the Nazi doctors’ trials, as well as experiments conducted on prisoners, soldiers, and charity hospital patients.⁷⁵ Drawing on these experiences, it similarly characterized low-income children as a vulnerable research population, due to their youth and their poverty.⁷⁶ From this analysis, and specifically referencing the Nuremberg Code, the court held that the informed consent research agreements can act as contracts, or may create “special relationships” from

⁶⁹ *Id.* at 811-12.

⁷⁰ *Id.* at 812.

⁷¹ *Id.*

⁷² *Id.*

⁷³ *Id.* at 813.

⁷⁴ *See id.* at 813-14. Federal regulations include special protections for children, pregnant women, fetuses, and prisoners involved in medical research. *See* 45 C.F.R. §§ 46.201(a), 46.301(a), 46.401(a) (2003). The regulations make it extraordinarily difficult to conduct research involving greater than minimal risk of harm with no potential for benefit where children are involved. *See* 45 C.F.R. § 46.404 (2003).

⁷⁵ *See Grimes*, 782 A.2d at 816-17.

⁷⁶ *Id.* at 817.

which duties arise.⁷⁷ It further held that “normally, such special relationships are created between researchers and the human subjects used by the researchers.”⁷⁸

[33] In dicta, the court engaged in a lengthy discussion of financial conflicts of interest, but it eventually declared that the record did not sufficiently indicate the extent to which commercial interests may have interfered with the Institute’s research interests, and what effect these interests might have had on the researchers’ motivations.⁷⁹ The court worried, however, that potentially commercialized research involving vulnerable subjects might place obstacles between the researchers’ goals and the health of the subjects, thus creating a need for “full and continuous disclosure” of conflicts.⁸⁰

V. GENETIC SCIENCE AND HUMAN RESEARCH SUBJECTS

[34] The exploding market for biotechnology-related products creates large financial incentives for researchers working with human populations in the genetic science field. The disclosure of potential conflicts between research and commercial interests, and protection of the informed consent process generally, is often difficult because of frequent utilization of what one scholar refers to as “[t]he [q]uestionable [d]emographics of [m]edical [r]esearch.”⁸¹ Populations studied often include low-income or ethnic minority groups. Thus, the eugenics precedents are commonly cited as parallels to modern genetic research, in terms of subject characteristics.⁸² Discovery of these potential conflicts may be further complicated by the fact that genetic material of interest to researchers is frequently found in discrete or isolated indigenous populations.⁸³

[35] A number of recent incidents illustrate these “questionable demographics” in the field of cell line research, which authors frequently use to emphasize divergence between the cultural beliefs and social institutions of indigenous societies and the profit-seeking, “industrialized intellectual property systems.”⁸⁴ For example, a patent submission on the

⁷⁷ *Id.* at 857-58.

⁷⁸ *Id.* at 858.

⁷⁹ *Id.* at 840.

⁸⁰ *Id.* at 850-51.

⁸¹ Orłowski, *supra* note 14, at 394-95.

⁸² *See id.* at 395-96.

⁸³ *See Ching, supra* note 11, at 687.

⁸⁴ *Id.* at 700.

cell line of a member of the Guaymi people in Panama was protested by a tribal leader as being “contrary to the Guaymi view of nature, and our place in it.”⁸⁵ The tribe was not informed of the patent, nor of the establishment of a cell line, until the patent application was found by a rural development non-profit organization, who then contacted members of the tribe.⁸⁶

[36] Other recent examples of controversial research on indigenous populations include that on residents of the Solomon Islands and the Hagahai tribe of Papua New Guinea.⁸⁷ Due to cultural differences, it is not always easy for researchers to understand how risks and benefits might factor into the decision-making matrices of indigenous populations; the application of Western conceptions of the “reasonable patient” or the “reasonable physician” may be even more difficult.

[37] The Declaration of Helsinki took particular notice of what it deemed “vulnerable” research populations, including not only unsophisticated or uneducated populations, but also those that are economically disadvantaged.⁸⁸ It is with regard to these populations that researchers must tread most carefully, for in the absence of full disclosure, the risk of exploitation or mistreatment runs the highest. Even the mildest risk of harm can be amplified if researchers fail to satisfactorily explain all relevant dangers.⁸⁹

VI. DEFINING A NEW STANDARD FOR THE HUMAN GENOME ERA

[38] A commonly referenced tension surrounding legal requirements of informed consent and the medical realities facing practitioners is that between the principles of autonomy and beneficence.⁹⁰ Informed consent is rooted in autonomy. As reflected in Cardozo’s statement in *Schloendorff*, the doctrine seeks to place as much relevant information as

⁸⁵ *Id.*

⁸⁶ *Id.*

⁸⁷ *Id.* at 700-01.

⁸⁸ DECLARATION OF HELSINKI, *supra* note 21, § A.8.

⁸⁹ See Associated Press, *Study: Low “Health Literacy” Widespread*, <http://www.allhealthnews.net/news.html?view=4990> (Apr. 9, 2004) (discussing a recent study conducted by the Institute of Medicine, which found that nearly ninety-million adults have “limited health literacy,” and that this often leads to increased risks and generally less healthy lifestyles as a result of their failure to grasp even the most fundamental procedures relating to their treatments).

⁹⁰ HALL, *supra* note 28, at 131-32.

possible in the hands of the decision-maker: the patient.⁹¹ This goal conflicts, however, with the principle of beneficence, which is the idea that doctors are experts trained in the field who seek to provide their patients with the best possible care, and who will use their judgment and expertise to do so.⁹² Some limitation of patient autonomy might be necessary, for example, if the physician believes the patient's best interests are at stake.⁹³ To this extent, the law recognizes some compromises in the ideals of informed consent, allowing for implied or bundled consent in certain scenarios, or by the substitution of an objective reasonable person standard to satisfy the tort elements of causation and materiality of risk, rather than a subjective individual patient standard.⁹⁴ The instances, however, are few and far between, and are not likely to be the case during the course of a genetic research program, particularly when a researcher is contemplating the disclosure of financial conflicts.

[39] Although many jurisdictions utilize strict standards for human subjects research, and many IRBs apply closer scrutiny to research protocols than the law requires, the goal of patient autonomy is best fulfilled by a rigorous application of the informed consent principles.⁹⁵ A strict standard for the disclosure of financial conflicts of interest, without respect to the distinction between therapeutic and non-therapeutic research, is fundamental to the achievement of the goals of the informed consent doctrine. The disclosure requirements found in the Code of

⁹¹ *See id.* at 131.

⁹² *See id.* at 323.

⁹³ *See id.* This might occur, for example, when a patient is deemed too emotionally unstable to cope with a full disclosure of his present diagnosis.

⁹⁴ *See* Mark A. Hall, *A Theory of Economic Informed Consent*, 31 GA. L. REV. 511, 553-54 (1997). Implied and bundled consent occurs where a patient is said to have consented to a number of different treatments or procedures by consenting to participate generally. *Id.* at 553. For example, consent to have one's blood drawn entails consent to physical touching, as well as to disposal of the blood itself.

⁹⁵ The University of North Carolina School of Medicine IRB has rigorous disclosure standards for physicians participating in medical experiments, particularly where financial conflicts are concerned. For example, an annual reporting of potential conflicts, including sponsor compensation arrangements, licensing opportunities, and research funding applications is required for each project in which the researcher is involved. *See* POLICY ON CONFLICTS OF INTEREST AND COMMITMENT (Univ. of N.C. 2004), <http://www.unc.edu/campus/policies/coi.html> (last visited Sept. 17, 2004); INSTRUCTIONS FOR SUBMITTING IRB APPLICATIONS FOR RESEARCH THAT INCLUDES THE COLLECTION OF HUMAN BIOLOGIC SPECIMENS (Univ. of N.C.), http://research.unc.edu/ohre/forms_new/Consent/Biomedical/CFsampad.doc (last visited Sept. 17, 2004).

Medical Ethics that govern researchers who anticipate commercial use of human tissue come much closer to achieving these goals.⁹⁶

[40] Additionally, the “full and continuous disclosure” of conflicts discussed in *Grimes* greatly contributes to these ideals.⁹⁷ More complete disclosure reinforces the idea of patient autonomy in decision-making, and it further protects against exploitation of vulnerable subjects or any increased risk of harm arising from a potential financial conflict of interest.⁹⁸

[41] In addition, the Common Rule already requires the disclosure of any risks or benefits which may apply to the subject *or to third parties*.⁹⁹ A potential fortune a physician or his financial backers stand to make seems to fall within the scope of this requirement.

[42] Within the medical profession, there is little reason to think that physician-researchers distinguish between therapeutic and non-therapeutic work; they also do not consider the duties owed to subjects to be significantly different between the two contexts.¹⁰⁰ With reference to the Hippocratic principles governing such relationships, the idea that a researcher operating in a non-therapeutic context “cannot do harm to people, and cannot be influenced by [financial] conflicts is silly.”¹⁰¹

[43] The difference between therapeutic and non-therapeutic research is not self-evident; it is perhaps even counter-intuitive. As mentioned, the *Grimes* court determined that the Johns Hopkins IRB itself failed to grasp

⁹⁶ The National Human Research Protections Advisory Committee, which provided recommendations to the Department of Health and Human Services and the Office for Human Research Protections, supports disclosure of potential financial conflicts of interest during the consent process. *See* FIN. RELATIONSHIPS IN CLINICAL RESEARCH: ISSUES FOR INSTS., CLINICAL INVESTIGATORS, AND IRBS TO CONSIDER WHEN DEALING WITH ISSUES OF FIN. INTERESTS AND HUMAN SUBJECT PROT. § 5.3 (Nat’l Human Research Prots. Advisory Comm. 2001), <http://www.hhs.gov/ohrp/nhrpac/mtg12-00/finguid.htm> (last updated Jan. 13, 2003). In addition, it recommends that IRBs and researchers work very closely to identify and manage these conflicts. *See, e.g., id.* §§ 1.2, 2.2.

⁹⁷ *Grimes v. Kennedy Krieger Inst., Inc.*, 782 A.2d 807, 851 (Md. 2001).

⁹⁸ *See* Robert Gatter, *Walking the Talk of Trust in Human Subjects Research: The Challenge of Regulating Financial Conflicts of Interest*, 52 EMORY L.J. 327, 355 (2003).

⁹⁹ Alvino, *supra* note 23, at 901.

¹⁰⁰ *See* Evans Interview, *supra* note 40.

¹⁰¹ *Id.*

the distinction.¹⁰² If the IRB at a sophisticated research institution has difficulty distinguishing between the two, clearly a less sophisticated patient/subject might also misunderstand the distinction.¹⁰³ For the purpose of disclosure, courts should not hold researchers in the non-therapeutic context to a less-stringent standard of care; such an approach does not accurately reflect the expectations of patients or subjects—however they are characterized—nor does it do justice to the ethical principles governing the medical profession.

[44] As genetic research becomes increasingly commercialized and profit-driven, and if the *Greenberg* court's limitation on the scope of disclosure in the non-therapeutic context is followed, the danger of harm to human research subjects via undisclosed financial influence on medical decisions is significant. This kind of harm is to be taken as seriously and is to be avoided as conscientiously as the risk of physical injury, particularly if the ethical goals of preserving patient autonomy and fostering an atmosphere of trust between researchers and subjects is to be realized.¹⁰⁴

[45] The *Greenberg* court's warnings of a chilling effect on research certainly should be considered, but not at the expense of the trust inherent in the relationship between doctors and patients, or between researchers and subjects.¹⁰⁵ Indeed, the "chilling" that may occur in a regime of tight-lipped, profit-seeking researchers may be on the willingness of subjects to enroll in such studies, greatly hampering technological progress. The interests of science in general, and genetic research in particular, can only benefit by the cultivation of this trust through the free, full, and continuous disclosure of potential financial conflicts of interest.

¹⁰² See *Grimes*, 782 A.2d at 814.

¹⁰³ See Orłowski, *supra* note 14, at 394.

¹⁰⁴ See Evans Interview, *supra* note 40.

¹⁰⁵ See *Greenberg v. Miami Children's Hosp. Research Inst., Inc.*, 264 F. Supp. 2d 1064, 1070 (S.D. Fla. 2003).