RATIONALIZING RISK ASSESSMENT IN HUMAN SUBJECT RESEARCH

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I. INTRODUCTION

Americans are deeply suspicious of medical research.[1] Some of this suspicion stems from the legacy of events like the Tuskegee syphilis study,[2] the Willowbrook hepatitis experiments,[3] and the government's testing of LSD on unsuspecting soldiers.[4] These and other instances of unethical conduct by medical researchers have made many Americans fearful of being experimented upon without their consent. Much of the trepidation, however, has its origins in more recent research scandals, in which problems with consent were not the primary concern. In 1996, for example, a healthy 19-year-old student at the University of Rochester died while participating in a study designed to determine how lungs defend themselves against pollutants.[5] In 2001, another healthy college student died during a study at Johns Hopkins University that sought to determine how healthy lungs respond to asthma triggers.[6] Like numerous other research-related incidents that have resulted in investigations and lawsuits,[7] these events occurred at prestigious universities generally regarded as centers of excellence. More alarming than the specific tragedies that galvanized public attention is that these deaths turned out to be symptoms of deep and pervasive problems. Investigations at Johns Hopkins, for example, uncovered widespread deficiencies in the university's system for protecting human subjects, prompting federal authorities to shut down most federally financed research at the university for several days.[8]

Few would deny that our system of protecting human subjects faces an unprecedented crisis. What is less clear is how to improve the system to avoid problems in the future and to begin restoring the public's trust. However, there is

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1. Giselle Corbie-Smith et al., *Distrust, Race, and Research*, 162 ARCHIVES INTERNAL MED. 2458–59 (2002) (finding that nearly 80 percent of African Americans and 52 percent of Caucasian Americans believed that they or "people like them" could be used as "guinea pigs" for medical research without their consent).

2. In the Tuskegee studies, researchers observed hundreds of poor African American men with syphilis over several decades to determine the natural course of the disease. Not only did the researchers fail to offer treatment to the men, even when penicillin became widely available, but they also actively sought to prevent the men from obtaining treatment from other sources. *See* Allan M. Brandt, *Racism and Research: The Case of the Tuskegee Syphilis Study*, HASTINGS CTR. REP., Dec. 1978, at 21.

3. From 1956 to 1971, researchers gave live hepatitis viruses to mentally retarded children at the Willowbrook State School as part of an effort to study the disease and ultimately develop a vaccine for it. *See* DAVID J. ROTHMAN & SHEILA M. ROTHMAN, THE WILLOWBROOK WARS (1984).

4. United States v. Stanley, 483 U.S. 669 (1987) (rejecting a claim brought by a former servicemember who was given LSD without his knowledge in secret Army experiments in the 1950s, on the ground that any injuries arose out of or were in the course of activity incident to service).

5. Elisabeth Rosenthal, *New York Seeks to Tighten Rules on Medical Research*, N.Y. TIMES, Sept. 27, 1996, at B4.

6. Lawrence K. Altman, *F.D.A. Faults Johns Hopkins over Process in Fatal Study*, N.Y. TIMES, July 3, 2001, at A12.

7. *See infra* text accompanying notes 41–44.

8. Associated Press, *Report on Research Death Faults Review Board*, N.Y. TIMES, Aug. 31, 2001, at A16.

widespread consensus that any effective reform program must do something to improve the existing system of institutional review boards ("IRBs"), the committees within research institutions that decide which protocols can go forward and under what conditions.[9] IRBs have exercised primary oversight responsibility for human subject research for the past three decades, but they continue to be overburdened, underfunded, and often incapable of reviewing complex research protocols effectively.[10]

Unfortunately, most of the current discussion about IRB reform has focused on questions about the basic structure of the IRB system, ignoring important process-oriented questions about how IRBs actually decide which protocols to accept, reject, or revise.[11] For example, many commentators have emphasized the need for greater resources and training for IRB members,[12] as well as the importance of managing the conflicts of interest that increasingly exist throughout the IRB system.[13] However, even if we create well funded, knowledgeable, and conflict-free IRBs, we cannot simply assume that they will be able to identify those protocols that should be rejected or modified. The effectiveness of IRB review also depends on the underlying methodology IRBs employ in making decisions. In other words, we must ask how IRBs actually go about reviewing proposals to use human subjects in research, and whether this approach is likely to protect human subjects from unjustifiable risk.

Examining IRBs' decision-making methodology is important for two interrelated reasons. First, the way any organization makes its decisions necessarily influences how at least some of those decisions are ultimately resolved. Thus, if we are not comfortable with the decisions that IRBs are making, we must consider whether they are going about making their decisions in an appropriate way. Second, continued progress in biomedical research depends on maintaining the public's trust in the integrity of the oversight system, both to ensure an adequate supply of individuals willing to be research subjects and to preserve public support for research funding.[14] Because the process by which decisions are

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9. *See infra* text accompanying notes 26–30. As of 1998, there were an estimated 3,000 to 5,000 IRBs in the United States. Robert Steinbrook, *Improving Protection for Research Subjects*, 346 NEW. ENG. J. MED. 1425, 1425 (2002).

10. *See infra*, text accompanying notes 62–65.

11. This distinction between structure and process draws on Avedis Donabedian's categorization of mechanisms for evaluating health care quality. Under this framework, structural questions would include those related to IRBs' composition, organization, and capacity to carry out their underlying mission, while process-oriented questions are those concerning the manner in which IRBs engage in the enterprise of protocol review. *See* Avedis Donabedian, *Criteria and Standards for Quality Assessment and Monitoring*, 12 QUALITY REV. BULL. 99 (1986).

12. *See infra* text accompanying notes 62–63.

13. *See infra* text accompanying note 39.

14. 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, 381 (2000) (arguing that the loss of public trust in research "has implications for the willingness of individuals to participate as subjects in research, for the public to financially support research efforts, and ultimately for our very ability to continue to alleviate suffering, conquer disease, and treat painful medical conditions").

made ultimately affects the legitimacy of those decisions,[15] it is important that decisions to approve the use of human subjects in research are not based on a process likely to be perceived as irrational or arbitrary.

Accordingly, this Article takes a critical look at the process IRBs use to review research protocols, focusing specifically on risk assessment, one of the most important, and least understood, elements of protocol review.[16] In evaluating IRBs' decision-making process, this Article begins with the premise that IRBs are engaged in a process of *legal* decision-making, insofar as they interpret specific regulatory requirements pursuant to authority that has been delegated to them by administrative agencies.[17] Thus, it compares the process IRBs employ with that used by other institutions responsible for interpreting and enforcing legal requirements, particularly juries, judges, and administrative agencies. The Article concludes that IRBs have embraced a decision-making model that is ill-suited to the underlying goal of protecting human subjects, and suggests alternative mechanisms designed to transform the way IRBs work.

Part II of this Article provides a brief background about human subject research and the IRB system. Part III examines the risk assessment process IRBs currently employ. It argues that IRBs' current approach to risk assessment closely mirrors the deliberative process used by common-law juries, and that in both juries and IRBs this process suffers from considerable flaws. After examining the limitations of a jury approach to risk assessment determinations, Part III explains why our willingness to tolerate these limitations in the context of jury deliberations does not mean they also should be accepted in IRB review. Part IV examines alternative decision-making mechanisms used by courts and administrative agencies. Like IRBs, courts and administrative agencies make decisions that prospectively regulate future behavior, as opposed to the retrospective responsibility-allocating decisions with which juries are concerned. Part IV specifically focuses on four decision-making methods employed by courts and/or agencies: (1) reasoning by analogy; (2) the use of written opinions; (3) appellate review and precedent; and (4) notice-and-comment rulemaking. It shows how IRBs could incorporate these strategies into the protocol review process, and evaluates the advantages and drawbacks of these different approaches. Part V outlines an agenda for reforming IRB deliberations along the lines suggested in this Article, focusing on some practical considerations the proposed changes are likely to raise.

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15. William N. Eskridge, Jr. & Philip P. Frickey, *The Making of the Legal Process*, 107 HARV. L. REV. 2031, 2044 (1994) ("[P]rocess is critical to law's legitimacy.").

16. Thus, the Article does not address how IRBs evaluate researchers' plans for obtaining subjects' informed consent, the other major component of IRBs' responsibilities. *See infra* text accompanying note 27.

17. *See* LARS NOAH & BARBARA A. NOAH, LAW, MEDICINE, AND MEDICAL TECHNOLOGY 155 (2002) (noting that the Food and Drug Administration has "delegated quasi-regulatory functions" to IRBs).

II. BACKGROUND

A. Overview of the Existing Regulatory Framework

Federal regulation of human subject research dates back to 1974, when the Department of Health, Education, and Welfare ("DHEW") promulgated regulations requiring institutionally-based ethics review of research supported by the Public Health Service.[18] That same year, Congress passed the National Research Act[19] in response to widespread public concerns about ethical abuses in medical experimentation.[20] The Act directed the Secretary of DHEW to issue additional regulations on research with human subjects, and it established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research to develop ethical principles to guide the regulatory scheme.[21] The final regulations were put into effect in 1981 and were based largely on the framework set forth in the National Commission's still-influential *Belmont Report*.[22] Ten years later, they were made applicable to research supported by most other federal agencies, and since that time they have been known as the "Common Rule."[23] In addition to the Common Rule, the Food and Drug Administration ("FDA") has its own regulations on human subject protection, which in most respects parallel the Common Rule requirements.[24] Taken together, the Common Rule and the FDA regulations govern most, although not all, research involving human subjects in the United States.[25]

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18. 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, 95 (1993).

19. Pub. L. No. 93-348, 88 Stat. 342 (1974).

20. Goldner, *supra* note 18, at 96 (noting that public disclosure of events like the Tuskegee and Wilowbrook studies led to the congressional hearings that resulted in the National Research Act); ALBERT R. JONSEN, THE BIRTH OF BIOETHICS 98 (1998) (discussing the importance of public concerns about fetal research in stimulating congressional action).

21. Goldner, *supra* note 18, at 96–99.

22. NAT'L COMM'N FOR THE PROT. OF HUMAN SUBJECTS OF BIOMEDICAL & BEHAVIORAL RESEARCH, U.S. DEP'T OF HEALTH, EDUC., AND WELFARE, PUB. NO. (OS) 78-0012, THE BELMONT REPORT: ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH (1978).

23. NAT'L BIOETHICS ADVISORY COMM'N, 1 ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS 156, (2001), *available at* http://govinfo.library.unt.edu/nbac/human/overvol1.pdf (noting that the Common Rule covers 18 federal agencies).

24. FDA Institutional Review Boards, 21 C.F.R. § 56 (2003).

25. The regulations apply to all research conducted or supported by the federal government, as well as to all research related to the development of drugs or medical devices, regardless of whether federal funding is involved. In addition, most institutions that conduct federally-funded research have signed "assurances" with the federal government, in which they agree to comply with the federal regulations in all of their research with human subjects. Goldner, *supra* note 18, at 99. However, "[a]n unknown amount of nonfederally funded research is completed unregulated under the federal system." NAT'L BIOETHICS ADVISORY COMM'N, *supra* note 23, at 12 (observing that unregulated research "may include experimental surgical techniques, research on reproductive technologies, some uses of approved drugs and medical devices, and research use of private, identifiable data").

The centerpiece of the federal regulations is the requirement that investigators obtain IRB approval[26] and the informed consent of individuals who enroll in a study.[27] The provisions concerning IRBs provide that, before approving a protocol, the IRB must determine that risks to subjects have been minimized[28] and that the risks "are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result."[29] In addition, IRBs are responsible for ensuring the adequacy of investigators' plans for obtaining informed consent, as well as their proposed methods for selecting subjects, monitoring the data, and addressing issues related to privacy and confidentiality.[30]

In addition to the federal regulations, some states have their own statutes or regulations governing human subject research,[31] although these laws do not appear to be regularly enforced. In addition, investigators and institutions engaged in research with human subjects can be subject to damages under general principles of negligence law if they cause harm to subjects as a result of deviating from the applicable standard of care.[32] Until recently, there have been surprisingly few tort cases brought by injured research subjects, but in the past few years plaintiffs' lawyers have become more aggressive in pursuing these claims.[33] Nonetheless, tort law's potential effectiveness as a mechanism for overseeing human subject research is inherently limited, because it requires not only an injured plaintiff who is willing to sue, but also someone who can prove all the elements of a negligence claim. In many cases, even if the plaintiff is able to prove a deviation from the standard of care, it may be difficult to establish a causal link between the researchers' actions and the ultimate injuries. This is particularly true for individuals who enter into research already suffering from debilitating illnesses, whose injuries also might result from their underlying disease.

Proposals to require IRB review of all research involving human subjects are now pending in Congress. Elizabeth White, *Sen. Kennedy Proposes Legislation to Tighten Research Subject Safeguards*, 1 MED. RES. L. & POL'Y REP. 453 (2002).

26. HHS Protection of Human Subjects, 45 C.F.R. § 46.109 (2003). Certain categories of minimal risk research are exempt from the regulations. *See id.* § 46.101(b).

27. *Id.* §§ 46.116–117. In limited circumstances, IRBs may waive or alter the usual consent requirements, or waive the obligation to obtain a signed consent form. *Id.* §§ 46.116(c)–(d), 46.117(c).

28. *Id.* § 46.111(a)(1).

29. *Id.* § 46.111(a)(2).

30. *Id.* § 46.111 (a)(3)–(7).

31. *See, e.g.*, CAL. HEALTH & SAFETY CODE §§ 24170–24179.5 (West 2003); N.Y. PUB. HEALTH LAW §§ 2440–2446 (McKinney 2003); VA. CODE ANN. §§ 32.1-162.16–32.1-162.20 (Michey 2003).

32. Goldner, *supra* note 18, at 87–88.

33. Alice Dembner, *Lawsuits Target Medical Research: Patient Safeguards, Oversight Key Issues*, BOSTON GLOBE, Aug. 12, 2002, at A1 (noting that, "[f]or years medical researchers were largely immune from lawsuits," but that a new upsurge in suits "is sending shivers through the research community").

B. A System in Crisis

While a variety of factors have contributed to the current crisis in human subject protection,[34] two developments have been especially significant. The first is the rapid growth in the amount of research being conducted. Federal expenditures on biomedical research almost doubled between 1986 and 1995, and expenditures by private industry tripled during that same period.[35] Within the pharmaceutical industry alone, research expenditures rose fourteen-fold between 1980 and 2000.[36] The sheer amount of research now being conducted has placed a severe burden on an oversight system that has always operated under significant resource constraints.

The second factor is the changing context in which much biomedical research now takes place. Existing federal regulations were developed at a time when most research was funded by the federal government and conducted in major academic medical centers.[37] Today, the majority of research is supported by private industry, particularly pharmaceutical companies, and much of it takes place in nonacademic settings, including private physicians' offices.[38] The increasing influence of commercial interests on the conduct of research has generated serious conflicts of interest throughout the research enterprise, including among IRB members.[39] In addition, the shift away from academic medical centers has complicated the effectiveness of an institutionally-based oversight system, particularly in large studies involving multiple sites.[40]

Two dimensions of the current crisis in research have received particular attention: (1) deficiencies in the process of obtaining subjects' informed consent; and (2) the ineffectiveness of the IRB system. A variety of initiatives are underway to address both problems, and additional reform proposals are actively being considered. The remainder of this Part will examine the promises and limitations of these measures, before turning to the methodological problems surrounding the process of protocol review.

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34. For a general discussion of these factors, see NAT'L BIOETHICS ADVISORY COMM'N, *supra* note 23, at 2–16.

35. *See id.* at 4.

36. *See id.*

37. Erica Heath, *The History, Function and Future of Independent Institutional Review Boards*, *in* NAT'L BIOETHICS ADVISORY COMM'N, 2 ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS E8, (2001), *available at* http://www.georgetown.edu/research/nrcbl/nbac/human/overvol2.pdf.

38. Thomas Bodenheimer, *Uneasy Alliance: Clinical Investigators and the Pharmaceutical Industry*, 342 NEW ENG. J. MED. 1539 (2000).

39. *See id.*; *see also* Mark Barnes & Patrick S. Florencio, *Investigator, IRB and Institutional Financial Conflicts of Interest in Human Subjects Research: Past, Present, and Future*, 32 SETON HALL L. REV. 525 (2002); Mark Barnes, *Financial Conflicts of Interest in Human Subjects Research: The Problem of Institutional Conflicts*, 30 J.L. MED. & ETHICS 390 (2002); Goldner, *supra* note 18.

40. *See* NAT'L BIOETHICS ADVISORY COMM'N, *supra* note 23, at 14 (noting that "local IRBs are sometimes poorly situated to review multi-site research").

1. Informed Consent: Problems and Limitations

One manifestation of the current crisis in human subject protection is the growing number of publicized cases involving individuals who were enrolled in protocols without receiving sufficient information about the benefits and risks. For example, after 18-year-old Jesse Gelsinger died in a gene transfer study at the University of Pennsylvania, his father testified before Congress that he and his son were never clearly informed that the study offered no possibility of benefiting Jesse's own medical condition.[41] In addition, subjects in the study were allegedly not told that previous participants had suffered significant adverse reactions.[42] Serious problems with informed consent also have led to lawsuits against the prestigious Fred Hutchinson Cancer Center in Seattle.[43] These suits claim that subjects who were given experimental bone marrow transplants were told that if the transplants did not work they would be eligible to receive a conventional bone marrow transplant, despite the fact that the likelihood of a second transplant working was less than five percent.[44]

In response to these problems, a variety of initiatives have been undertaken to improve the process of obtaining informed consent to research.[45] However, while improving informed consent is unquestionably important, informed consent will never provide a complete solution to the ethical complexities of human subject research.[46] One reason it is necessary to look beyond informed consent is that prospective subjects often approach research with fundamental misconceptions about the nature of the research enterprise, which can be extremely resistant to correction through the process of informed consent. Studies have shown that, even after receiving accurate information about the purposes of research, many subjects have difficulty appreciating that the *raison d'être* of research is the production of generalizable knowledge, not the provision of medical care best suited to each subject's individualized needs.[47] Thus, subjects often fail to grasp the significance of common research techniques like randomization,[48] masking,[49] and the use of placebos,[50] all of which disregard the

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41. Sheryl Gay Stolberg, *Teenager's Death Is Shaking Up Field of Human Gene-Therapy Experiments*, N.Y. TIMES, Jan. 27, 2000, at A20.

42. *Id.*

43. Duff Wilson & David Heath, *The Blood-Cancer Experiment: Patients Never Knew the Full Danger of Trials They Staked Their Lives On*, SEATTLE TIMES, Mar. 11, 2001, at A1.

44. *Id.*

45. *See* COMM. ON ASSESSING THE SYS. FOR PROTECTING HUMAN RESEARCH PARTICIPANTS, INST. OF MED., RESPONSIBLE RESEARCH: A SYSTEMS APPROACH TO PROTECTING RESEARCH PARTICIPANTS 119–27 (Daniel D. Federman et al. eds., 2003) (describing previous efforts to improve the informed consent process and setting forth additional recommendations).

46. On the insufficiency of informed consent as an ethical safeguard in research, see Richard W. Garnett, *Why Informed Consent? Human Experimentation and the Ethics of Autonomy*, 36 CATH. LAW. 455 (1996).

47. *See* JESSICA BERG ET AL., INFORMED CONSENT: LEGAL THEORY AND CLINICAL PRACTICE, 288–90 (2d ed. 2001).

48. Randomization refers to the "[a]ssignment of subjects to different treatments, interventions, or conditions according to chance rather than systematically." It is an

individual subject's therapeutic best interests to ensure that the study results are statistically valid.[51]

This inability to differentiate research and treatment, a phenomenon known as the "therapeutic misconception,"[52] is particularly pronounced in Phase I clinical trials, small-scale studies designed to evaluate a drug's toxicity before commencing larger studies testing the drug's effectiveness. In one study of participants in Phase I cancer trials, over 85 percent of subjects reported that they participated in part because they believed the investigational drugs would improve their conditions, despite having been told that Phase I studies are not expected to produce any therapeutic effect.[53] While it may be possible to reduce the impact of the therapeutic misconception by developing better ways of communicating information to prospective research subjects,[54] it is unlikely that the problem will ever disappear. As Paul Applebaum notes, the subject's "lifetime of experience in clinical settings has often rather firmly entrenched the notion that physicians ought to be single-mindedly devoted to advancing one's health."[55]

In addition to overestimating the likelihood that they will benefit from the research, many subjects underestimate the significance of research-related risks. Subjects often assume that physicians would not offer them interventions that pose significant health risks, and therefore may discount the information about risks the investigators have disclosed.[56] For example, when the Advisory Committee on Human Radiation Experiments interviewed individuals who had been subjects in

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important technique in research "because it makes more likely the probability that differences observed between subject groups are the result of the experimental intervention." OFFICE FOR HUMAN RESEARCH PROTECTIONS, *Considerations of Research Design, in* INST'L REVIEW BD. GUIDEBOOK, *available at* http://ohrp.osophs.dhhs.gov/irb/irb.chapter4.htm (last visited Mar. 7, 2003).

49. A "masked" study design (sometimes also called a "blind" design) "compar[es] two or more interventions in which either the investigators, the subjects, or some combination thereof do not know the treatment group assignments of individual subjects." *Id.*

50. A placebo is "[a] chemically inert substance given in the guise of medicine for its psychologically suggestive effect." In research, placebos are sometimes given to a subset of subjects "to determine whether improvement and side effects may reflect imagination or anticipation rather than actual power of a drug." *Id.*

51. *See* BERG ET AL., *supra* note 47, at 280–83 (explaining how these and other features of research result in an inherent conflict of interest between researchers and subjects).

52. *See id.* at 288.

53. Christopher Daugherty et al., *Perceptions of Cancer Patients and Their Physicians Involved in Phase I Trials*, 13 J. CLINICAL ONCOLOGY 1062, 1064 (1995).

54. For suggestions on dispelling the therapeutic misconception, see BERG ET AL., *supra* note 47, at 291–97; *see also* Nancy M. P. King, *Defining and Describing Benefit Appropriately in Clinical Trials*, 28 J.L. MED. & ETHICS 332, 334 (2000) (suggesting that, in early-stage clinical trials, investigators should be asked to justify any language about potential benefits that offers more hope than the statement, "'You will not benefit'").

55. Paul S. Applebaum, *Clarifying the Ethics of Clinical Research: A Path Toward Avoiding the Therapeutic Misconception*, AM. J. BIOETHICS, Spring, 2002, at 22, 23.

56. *See* BERG ET AL., *supra* note 47, at 289.

government-sponsored radiation studies, many respondents expressed the belief "that hospitals would never permit research to be conducted that was not good for the patient-subjects."[57]

Even when it is possible to obtain genuine informed consent to participation in research, an individual's willingness to accept a particular risk does not, in and of itself, justify the imposition of that risk. In some situations, imposing risks on human subjects may have significant social consequences, in addition to the specific burdens they impose on subjects themselves. Permitting physicians to perform dangerous or painful interventions, for example, might undermine the public's trust in the medical profession, or offend deeply-rooted societal norms against torture or exploitation.[58] These consequences may well impose costs that would outweigh even the most promising medical advances. Thus, the Nuremberg Code, a set of ethical guidelines that emerged from the trials of Nazi physicians, explicitly recognizes that certain types of risks will almost always be unjustifiable, despite the Code's overall embrace of a balancing approach to the assessment of risk.[59] In particular, the Code states that "[n]o experiment should be conducted where there is an *a priori* reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects."[60] This language would preclude, for example, a study involving the amputation of healthy limbs to test a new procedure for treating accident victims, even if the process of informed consent is perfectly adequate and even if the study might produce valuable information unavailable through other means.[61]

2. Beyond Informed Consent: Reforming the System of IRB Review

The insufficiency of informed consent as a safeguard for subjects underscores the importance of IRBs' independent assessment of the benefits and risks of research protocols. Unfortunately, the IRB system suffers from serious

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57. ADVISORY COMM. ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT OF THE ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS 761 (1995).

58. In addition to the potential impact of research on broad societal values, some types of research may pose risks for particular segments of society. For example, studies investigating the genetic basis of diseases may result in discrimination or stigmatization if they identify mutations associated with particular racial or ethnic groups. *See* Richard R. Sharpe & Morris W. Foster, *Involving Study Populations in the Review of Genetic Research*, 28 J.L. MED. & ETHICS 41, 41 (2000).

59. NUREMBERG CODE § 5, *available at* http://ohsr.od.nih.gov/nuremberg.php3 (last visited Oct. 29, 2003).

60. *Id.*

61. Examples like this demonstrate that, even though the risk assessment standard in the federal regulations does not explicitly set an upper limit on risk, it is unlikely that certain risks to subjects could ever be justified, regardless of the benefits a study is likely to achieve. More generally, it suggests that, in extreme cases, it does not matter whether one adopts a deontological or utilitarian approach to research ethics. Whether one believes that certain risks are inappropriate because they violate basic moral values (as a Kantian might argue), or that they are inappropriate because they will lead to harmful social consequences (as a utilitarian would claim), the end result is the same—those risks cannot be justified regardless of the study's potential contribution to knowledge.

limitations. A 1996 General Accounting Office study found that IRBs are overburdened, underfunded, insufficiently prepared, and often too willing to rely on investigators' good intentions as the primary method for protecting subjects.[62] Two years later, a report issued by the Office of the Inspector General of the Department of Health and Human Services ("DHHS") reached essentially the same conclusions.[63] Beginning in October 1998, federal regulators temporarily shut down research programs at several prominent institutions, based on a variety of deficiencies in those institutions' IRB processes.[64] Among other concerns, the investigators noted that "little substantive review takes place at convened meetings," and that there was "scant evidence that IRB approval of research is consistently based on consideration of the determinations required under HHS regulations."[65]

Certainly, inadequate IRB review is not the only explanation for unreasonably risky research. For example, the death of the student at the University of Rochester[66] was at least partly attributable to decisions by the investigators performing the procedures, who increased the amount of anesthetic to dangerous levels in response to the student's complaints of discomfort.[67] A workgroup convened by the New York State Department of Health following the Rochester incident emphasized that researchers have an independent obligation to monitor subjects during the course of interventions, and to terminate interventions that appear to be causing unacceptable harm.[68]

However, even if IRBs are not the sole source of problems in research, they will be critical to the success of any reforms. In addition to their authority to reject protocols whose risks are disproportionate to the benefits, IRBs can set

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62. GEN. ACCOUNTING OFFICE, SCIENTIFIC RESEARCH: CONTINUED VIGILANCE CRITICAL TO PROTECTING HUMAN SUBJECTS, HEHS-96-72 (1996).

63. OFFICE OF THE INSPECTOR GEN., DEP'T OF HEALTH & HUMAN SERVS., INSTITUTIONAL REVIEW BOARDS: A TIME FOR REFORM (1998), *available at* http://www.washingtonfax.com/samples/docs/bioethics/patients/irbtest.pdf [hereinafter A TIME FOR REFORM]. A 2000 follow-up to the report concluded that only minimal progress had been achieved. OFFICE OF THE INSPECTOR GEN., DEP'T OF HEALTH & HUMAN SERVS., PROTECTING HUMAN RESEARCH SUBJECTS: STATUS OF RECOMMENDATIONS (2000), *available at* http://oig.hhs.gov/oei/reports/oei-01-97-00197.pdf.

64. Goldner, *supra* note 14, at 389 (describing the suspension of research activities at numerous research institutions).

65. OFFICE FOR HUMAN RESEARCH PROTS., OHRP COMPLIANCE ACTIVITIES: COMMON FINDINGS AND GUIDANCE, *available at* http://ohrp.osophs.dhhs.gov/references/findings.pdf (last visited Mar. 5, 2003).

66. *See supra* text accompanying note 5.

67. Press Release, State of New York, Dept. of Health, *Case Report on Death of University of Rochester Student Issued* (Sept. 26, 1996), *available at* http://www.health.state.ny.us/nysdoh/consumer/pressrel/96/wan.htm.

68. State of New York, Dept. of Health, *Workgroup on IRB Guidelines, Safeguarding Healthy Research Subjects: Protecting Volunteers from Harm*, *available at* http://www.health.state.ny.us/nysdoh/provider/volunteer/intro.htm (last visited Mar. 12, 2003).

conditions on the research to minimize risks to acceptable levels.[69] For example, they can impose eligibility requirements that exclude individuals at high risk of injury, set limits on the number of interventions performed on any particular subject, or require monitoring of subjects by independent clinicians. IRB oversight is particularly important in research that is not conducted or supported by federal agencies. While federally supported research goes through a rigorous process of peer review at the national level,[70] privately funded research is often not subject to any external oversight other than the process of IRB review.

As with informed consent, a variety of initiatives are underway to improve the effectiveness of IRB oversight. These efforts gained momentum in 1999, when the Office for Protection from Research Risks was moved from the National Institutes of Health to a more influential position in the Office of the Secretary of DHHS. Now known as the Office for Human Research Protections ("OHRP"), it has been active in promoting educational and quality improvement efforts for research institutions and IRBs.[71]

More recently, legislation has been proposed in Congress to expand the jurisdiction of federal research regulations and to address some of the conflicts of interest that undermine the oversight system's integrity. Under one proposal introduced by Senator Kennedy, all IRBs would be required to receive accreditation from either the OHRP or a private accreditation organization designated by the OHRP director.[72] In addition, in order to increase IRBs' access to necessary resources, Senator Kennedy's bill would permit IRB expenses to be charged as "direct costs" on federal grants.[73] This would enable investigators to include specific line items in their budgets for the costs associated with IRB review, rather than forcing institutions to dip into their general overhead budgets for such costs, as is currently required. The Kennedy bill also includes provisions addressing the problem of conflicts of interest, as do other pending initiatives designed to ensure the independence of IRB oversight.[74]

In addition to these legislative proposals, two private health care accreditation organizations recently formed a partnership to accredit human subject protection programs.[75] The draft accreditation standards are based in part on recommendations issued in 2001 by the Institute of Medicine.[76] While the

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69. *See* HHS Protection of Human Subjects, 45 C.F.R. § 46.109(a) (2003) (authorizing IRBs to require modifications to research proposals).

70. *See generally* Nat'l Insts. of Health, Ctr. for Scientific Review website, *at* http://www.drg.nih.gov/default.htm (last visited Mar. 12, 2003).

71. Jesse A. Goldner, *Symposium on Human Subjects Research: Redux*, 30 J.L. MED. & ETHICS 358 (2002).

72. White, *supra* note 25.

73. *Id.*

74. *See generally* Barnes & Florencio, *supra* note 39.

75. M. Alexander Otto, *JCAHO, NCQA Form Partnership to Inspect, Accredit Human Subject Protection Programs*, 2 MED. RES. L. & POL'Y REP. 87 (2003).

76. COMM. ON ASSESSING THE SYS. FOR PROTECTING HUMAN RESEARCH SUBJECTS, BD. OF HEALTH SCI. POL'Y, INST. OF MED., PRESERVING PUBLIC TRUST: ACCREDITATION AND HUMAN RESEARCH PARTICIPANT PROTECTION PROGRAMS (2001).

program is currently voluntary, it is expected to be adopted by most major research institutions in the country.[77]

These are all welcome developments, and they are a necessary element of systemic reform. However, we cannot simply assume that resources, education, and attention to conflicts of interest will guarantee effective IRB review. The quality of IRB oversight also depends on how IRBs actually go about the protocol review process. This Article now turns to that question.

III. HOW DO IRBS ASSESS RISKS? THE JURY MODEL AND ITS LIMITATIONS

A. The IRB Risk Assessment Process

The regulations do not specify any particular method IRBs must use to carry out their risk assessment responsibilities. Nonetheless, the process followed at many IRBs tends to follow a similar pattern.[78] Typically, when the IRB receives a protocol the staff circulates it among the members, often designating one or more members to serve as primary reviewers, and schedules the protocol for discussion at an upcoming meeting. At the meeting, the primary reviewers summarize the protocol and their assessment of it, other members are invited to make comments, and then a vote is taken. In many cases, recommendations of the primary reviewers are adopted without further discussion by the membership as a whole.[79] In particularly complicated cases, a subcommittee may be formed to study the protocol further or to consult with the principal investigator, and in rare cases the IRB may solicit the opinion of an outside expert. However, the use of subcommittees and outside experts is optional, and it is not common practice at many IRBs.[80]

IRBs' current approach to evaluating protocols has several distinctive characteristics. First, decisions are made by a relatively small group of people who tend to come from similar professional and institutional backgrounds.[81] In

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77. *See* Otto, *supra* note 75.

78. This description of IRBs' decision-making processes is based on information contained in governmental reports, *see supra* text accompanying notes 62–65, presentations at professional conferences, interviews with IRB members from different institutions, and the Author's own experience serving on an academic medical center's IRB. Obviously, some IRBs employ procedural mechanisms that differ from those described in this Article. For those IRBs, some of the concerns addressed in the text may be less relevant.

79. A TIME FOR REFORM, *supra* note 63, at 6.

80. Ezekiel J. Emanuel, Chief, Ctr. for Clinical Bioethics, Nat'l Insts. of Health, Testimony before the President's Council on Bioethics, Sept. 12, 2002, *available at* http://www.bioethics.gov/transcripts/sep02/session2.html.

81. The regulations require only one member "whose primary concerns are in nonscientific areas" and one member who is unaffiliated with the institution. HHS Protection of Human Subjects, 45 C.F.R. § 46.107 (2003). Concluding that one or two members are unlikely to be in a position to exert significant influence over IRB deliberations, the National Bioethics Advisory Commission recommended that that 25 percent of IRB members should be individuals whose interests are primarily in nonscientific

addition, deliberations are conducted behind closed doors,[82] and minutes of meetings are made available to outsiders only under limited circumstances.[83] In general, therefore, the process is both insular and secretive.[84]

Second, the risk assessment process is highly unstructured; essentially, the members are simply given a set of protocols and asked for their reactions. The only specific guidance the members receive for this exercise is the general regulatory standard for approving research—i.e., whether the risks are "reasonable" in relation to the study's anticipated benefits.[85] Each member is free to interpret this reasonableness standard as he or she sees fit.[86] Because the members are not required to state reasons for their decisions, the process encourages reliance on impressionistic judgments, or "gut reactions."[87]

Third, IRBs are rarely required to explain or justify their decisions. IRBs do not issue written opinions, and while they are required to keep minutes of meetings, these minutes often contain little substantive information about the basis of decisions, particularly when the IRB decides to approve a protocol.[88] In addition, while federal agencies conduct audits of IRBs, these audits are infrequent and tend to focus on matters like documentation and record-keeping, not the substance of decisions about particular protocols.[89] The prospect of a federal audit, therefore, creates little incentive for IRBs to develop articulable rationales for their

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areas, who are unaffiliated with the institution, or who represent the perspectives of research participants. *See* NAT'L BIOETHICS ADVISORY COMM'N, *supra* note 23, at xvi.

82. Goldner, *supra* note 18, at 109–10.

83. *Id.* at 110 (noting that IRB records are generally not covered by the Freedom of Information Act). *But cf.* M. Alexander Otto, *Human Research Protection Law to Affect Protocols Started Prior to Effective Date*, 1 MED. RES. L. & POL'Y REP. 290 (2002) (noting that Maryland's newly-enacted law governing human subject research provides for public access to IRB minutes).

84. The usual justifications for IRB secrecy are that public scrutiny might reduce the candor of IRB deliberations or force sponsors and investigators to disclose trade secrets or other proprietary information. However, as the National Commission recognized, these arguments do not compel IRBs to close their meetings in all circumstances. In fact, some IRBs at major institutions open all of their meetings to the public. Goldner, *supra* note 18, at 109–10.

85. *Supra* text accompanying note 29.

86. Peter C. Williams, *Why IRBs Falter in Reviewing Risks and Benefits*, IRB, May/June 1984, 1, at 1 (noting that the concepts of risk and benefit in the regulations are "wholly undefined," and that IRBs "are given no guidance on how to balance the interests of a particular subject against the interests of the collective").

87. *Cf.* H.E. Van Luijin et al., *Assessment of the Risk/Benefit Ratio of Phase II Cancer Clinical Trials by Institutional Review Board (IRB) Members*, 13 ANNALS ONCOLOGY 1307, 1307 (2002) ("Few IRB members reported weighing risks and benefits in a systematic manner, but rather relied on global impressions or preferred to leave such matters to the IRB as a whole or to their patients.").

88. *Infra* text accompanying note 229.

89. C.K. Gunsalus, *An Examination of Issues Presented by Proposals to Unify and Expand Federal Oversight of Human Subject Research*, *in* NAT'L BIOETHICS ADVISORY COMM'N, 2 ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS D-7 (2001), *available at* http://www.georgetown.edu/research/nrcbl/nbac/human/overvol2.pdf.

decisions. The only time most IRB decisions receive serious scrutiny is in the rare event that an investigation or lawsuit is initiated following a significant injury, at which point any damage caused by an inappropriate decision has already been done.[90]

Fourth, the system does not encourage IRBs to look beyond the specifics of particular protocols, or to develop general principles with applicability to more than one set of facts. In IRBs with longstanding memberships, customary ways of dealing with particular issues may develop informally,[91] but no formal mechanisms exist to standardize risk-benefit assessments by incorporating prior decisions into current evaluations. There also is no mechanism for IRBs to learn about deliberations that have taken place at other institutions, except when issues happen to be publicized at conferences or in professional journals, both of which are relatively uncommon occurrences. As a result, IRBs are regularly challenged by issues of first impression—not necessarily issues that are new to the world of research, but issues that have never previously come before the particular IRB.

Finally, IRBs' independence, combined with the fact that IRB decisions are not appealable to any higher authority, leads to widely varying approaches to similar issues at different institutions.[92] For example, commentators have noted widespread differences in how IRBs interpret the riskiness of common procedures like venipuncture, arterial puncture, gastric and intestinal intubation, and lumbar puncture.[93] This variation is one of the reasons some investigators engage in the

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90. Moreover, to the extent IRBs are thinking about the potential for litigation, there may actually be an incentive to document *less* information about the risk assessment process, given that juries tend to look unfavorably at defendants who engage in an explicit process of risk-benefit balancing. Reid Hastie & W. Kip Viscusi, *What Juries Can't Do Well: The Jury's Performance as Risk Manager*, 40 ARIZ. L. REV. 901, 914 (1998) (observing that "[p]ost-trial interviews with jurors provide evidence that the plaintiff's introduction of corporations' calculations and benefit-cost memos provokes hostility and punitive attitudes," despite the fact that "thinking about risks rigorously is exactly what organizations should do so that they can strike a reasonable balance between costs and benefits").

91. *See infra* text accompanying note 110.

92. For studies of IRB variability, see Jerry Goldman & Martin D. Katz, *Inconsistency and Institutional Review Boards*, 248 J. AM. MED. ASS'N 197 (1982); Rita McWilliams et al., *Problematic Variation in Local Institutional Review of a Multicenter Genetic Epidemiology Study*, 290 J. AM. MED. ASS'N 360 (2003); Henry Silverman et al., *Variability Among Institutional Review Boards' Decisions Within the Context of a Multicenter Trial*, 29 CRITICAL CARE MED. 235 (2001); Thomas O. Stair et al., *Variation in Institutional Review Board Responses to a Standard Protocol for a Multicenter Clinical Trial*, 8 ACAD. EMERGENCY MED. 636 (2001). While much of the variability discussed in these studies involved informed consent issues, there were several examples of differences related to risk assessment determinations.

93. Loretta M. Kopelman, *Pediatric Research Regulations Under Legal Scrutiny: Grimes Narrows Their Interpretation*, 30 J.L. MED. & ETHICS 38, 45 (2002); *see also* M. Alexander Otto, *Advance Directive, Minimal Risk Mandate Could Hamper Vulnerable Subject Research*, 1 MED. RES. L. & POL'Y REP. 352 (2002) (reporting survey of 200 IRB chairs that found widespread disagreement about whether procedures like magnetic resonance imaging and allergy skin testing constituted more than a "minimal risk" to research subjects).

practice of "IRB shopping," a term used to describe "submitting a research proposal disapproved by one IRB to a second IRB to see if the outcome is more favorable."[94] In response to this problem, the FDA has requested comments on a proposed rule that would require investigators to disclose to IRBs whether their protocol has previously been reviewed by an IRB at a different institution.[95] While adopting such a rule might diminish IRB shopping, it would not change the underlying variation in IRBs' standards that led to the problem of IRB shopping in the first place.

The virtually unfettered discretion that IRBs currently exercise is partly an intentional result of the system's commitment to localized research oversight, in which responsibility for reviewing protocols rests primarily on the institution in which the research will be carried out.[96] The justification for localized review is that knowledge of local conditions and the attitudes of the population from which subjects will be drawn is essential to assessing a study's risks and benefits, as well as to ensuring the adequacy of informed consent.[97] While there have been proposals to move towards a more centralized system, at least for certain studies,[98] the emphasis on localism remains deeply ingrained in the current regulatory structure.

B. IRBs and Juries

Many of the characteristics of IRB review outlined above could just as easily describe another prominent decision-making body, the common-law jury. Juries face many of the same analytical challenges that confront IRBs, particularly juries in negligence cases, where the reasonableness of the defendant's risk-taking

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94. David G. Foster, *Independent Institutional Review Boards*, 32 SETON HALL L. REV. 513, 521 (2002); *see also* GEN. ACCOUNTING OFFICE, *supra* note 62 (citing incidents in which corporate sponsors "shifted projects away from institutions where local institutions raised concerns about the sponsor's study").

95. Institutional Review Boards: Requiring Sponsors and Investigators to Inform IRBs of Any Prior IRB Reviews, 67 Fed. Reg. 10115 (Mar. 6, 2002) (to be codified at C.F.R. pt. 56) (advance notice of proposed rulemaking).

96. *See* NAT'L COMM'N FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL & BEHAVIORAL RESEARCH, U.S. DEPT. OF HEALTH, EDUC., AND WELFARE, PUB. NO. (OS) 78-0008, INSTITUTIONAL REVIEW BOARDS: REPORT AND RECOMMENDATION 1–2 ("Compared to the possible alternatives of a regional or national review process, local committees have the advantage of greater familiarity with the actual conditions surrounding the conduct of research.").

97. *See* Steven Peckman, *Local Institutional Review Boards*, *in* NAT'L BIOETHICS ADVISORY COMM'N, 2 ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS K9–K10, (2001), *available at* http://www.georgetown.edu/research/nrcbl/nbac/human/overvol2.pdf (noting that an important justification for local review is that it involves "'individuals who are in the best position to know the research at the site, the resources at the institution, the capabilities and the reputations of the investigators and staff, the prevailing attitudes and ethics of the community and most importantly, the likely subject population'") (quoting Gary Ellis, former director of the Office of Protection from Research Risks); *see also* Goldner, *supra* note 18, at 95 (noting that IRBs were originally designed to "serve as a surrogate for the community at large").

98. *See infra* text accompanying notes 243–46.

is the primary issue. In addition, the process of jury deliberations exhibits many of the same characteristics as IRB decision-making, including reliance on general, impressionistic judgments unsupported by specific reasons; the absence of any obligation to explain or justify decisions; a focus on individual cases rather than general principles or rules; and the potential for inconsistent determinations in similar situations. Juries are also justified by the same values of localism and community input that underlie the current system of IRB review.

1. IRBs and Negligence Juries Compared

The question at issue in negligence cases—whether the defendant exercised reasonable care under the circumstances[99]—requires the same sort of risk-benefit balancing that IRBs employ in determining the acceptability of research risks. Like an IRB, a negligence jury must (1) identify the foreseeable risks resulting from the conduct at issue, taking into account both the magnitude of those risks and their probability of occurring; (2) evaluate the expected benefits, or social utility, associated with the activity; and (3) balance foreseeable risks against expected benefits to determine the reasonableness of proceeding with the activity under the circumstances.[100] While juries, unlike IRBs, engage in this analysis after the risks of the relevant conduct have already materialized, they are expected to evaluate the defendant's actions from an *ex ante* perspective—i.e., based on the information available to the defendant before the injury occurred.

Juries and IRBs also engage in a similar sort of open-ended, unstructured deliberative process. While rules of evidence and procedure determine the information juries hear during the trial, there are virtually no rules governing the manner in which juries process this information once their deliberations begin.[101] As a practical matter, juries are free to review the evidence carefully or to ignore it completely, to discuss the arguments in favor of both parties or to vote as soon as they enter the room.[102]

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99. DAN B. DOBBS, THE LAW OF TORTS 275 (2000) ("[T]he emphasis in negligence cases is on unreasonably risky conduct.").

100. This formulation of the negligence standard reflects the approach set forth by Judge Learned Hand in *United States v. Carroll Towing Co.*, 159 F.2d 169 (1947). Judge Hand's approach "is recognized as authoritative by judicial opinions in a majority of states, by the leading torts treatises, and by most contemporary torts scholars." Stephen G. Gilles, *On Determining Negligence: Hand Formula Balancing, the Reasonable Person Standard, and the Jury*, 54 VAND. L. REV. 813, 815 (2001).

101. A few rules do exist. For example, jurors may not "agree to be bound by an average of their respective quantitative positions with respect to damages or percentages of fault." Bunnell v. Lucas, 126 N.H. 663, 669 (1985). However, the secrecy of jury deliberations makes these rules extremely difficult to enforce. *See infra* text accompanying note 103.

102. In some jurisdictions, rules governing juror behavior may further increase the likelihood that juries will engage in impressionistic decision-making. Prohibitions on note-taking or directing questions to witnesses, for example, make it difficult for jurors to become "active learners" of the issues at stake in a trial, thereby preventing them from engaging with the evidence during the deliberative process. Steven I. Friedland, *Legal*

Juries also do not give reasons for their decisions, and the secrecy of jury deliberations precludes any effective scrutiny of the decision-making process.[103] As a result, it is impossible to determine whether juries have even attempted to adhere to the governing law.[104] Juries have been described as a type of "black box" decision-making: "[T]he evidence and law are fed into one end of the box and the box sends a result 'without an opinion to explain or justify its decision.'"[105]

In addition, juries focus solely on the resolution of a particular controversy; like IRBs, they do not develop principles to apply to multiple cases. For this reason, decisions of previous juries in similar situations have no bearing on a jury's analysis; in fact, it is unlikely that juries will even be aware of how other juries have assessed similar facts.[106] It should not be surprising, therefore, that juries commonly reach inconsistent decisions in similar situations.[107]

Finally, juries are justified by the same appeal to local values and attitudes that underlies the IRB system. The most common justification for jury decision-making is the jury's ability to "bring[] the common wisdom of the community to bear on the resolution of the private dispute" and "to legitimize that

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Institutions: The Competency and Responsibility of Jurors in Deciding Cases, 85 NW. U. L. REV. 190 (1990).

103. Graham C. Lilley, *The Decline of the American Jury*, 72 U. COLO. L. REV. 53, 69 (2001) ("A faulty performance is often obscured by the rules providing for jury secrecy and allowing only the most limited judicial interrogation of jurors concerning their verdict."); *see also* FED. R. EVID. 606(b) (precluding jurors from testifying about their reasons for reaching a verdict or indictment).

104. Special verdicts and jury interrogatories represent a limited exception to this rule. *See* FED. R. CIV. P. 49. However, "when the device is used, the 'special' questions typically posed are broad in form, mingling elements of law and fact in a manner similar to the general verdict." Mark S. Brodin, *Accuracy, Efficiency, and Accountability in the Litigation Process—The Case for the Fact Verdict*, 59 U. CIN. L. REV. 15, 22 (1990).

105. Brodin, *supra* note 104, at 34 (quoting *In re* Japanese Elec. Prod. Antitrust Litig., 631 F.2d 1069, 1085 (3d Cir. 1980)).

106. *Cf.* D. C. Barett, *Propriety and Prejudicial Effect of Reference by Counsel in Civil Case to Amount of Verdict in Similar Cases*, 15 A.L.R.3D 1144 (1967 & 1999 Supp.) (noting that lawyers are generally prohibited from informing the jury about the amount of damages other juries have awarded in similar cases).

107. Kenneth S. Abraham, *The Trouble with Negligence*, 54 VAND. L. REV. 1187, 1197 (2001) ("[U]nlike administrative rulemaking, in negligence cases, a new rule is made again for each case, and the rule may differ from case to case even when the facts do not."); *see also* L. Harold Levinson, *The Legitimate Expectation that Public Officials Will Act Consistently*, 46 AM. J. COMP. L. 549, 559 (1998) ("The guarantee of a jury trial retains an unpredictable element in the administration of justice, producing a constant possibility of inconsistent treatment."); *see also* John E. Coons, *Consistency*, 75 CAL. L. REV. 59, 79 (1987) (asserting that, because they are comprised of unique groupings of individuals, "juries can scarcely be expected to produce symmetry").

resolution in the eyes of that community."[108] These justifications mirror the emphasis on localism in the system of IRB review.[109]

Of course, juries and IRBs are not identical in all respects. For example, in contrast to juries, IRBs are continuous bodies whose members decide multiple issues over an extended period. This makes it possible for IRBs to at least *try* to render decisions that are internally consistent, even if they cannot ensure consistency across different IRBs. The institutional setting of IRBs may further contribute to the internal consistency of IRB decisions, to the extent inconsistent decisions provoke discussion or complaints by the members' institutional colleagues.[110]

In other respects, however, the jury system may do a better job than IRBs at weighing risks and benefits. While the extent to which juries actually represent the community is subject to debate,[111] they are certainly more representative than IRBs, which tend to be dominated by institutional insiders with similar backgrounds.[112] Jury decision-making also includes safeguards that do not exist in the IRB system. For example, judges can take cases away from the jury if the reasonableness of the defendant's activities is susceptible to only one interpretation as a matter of law.[113] In addition, appellate courts can reverse jury verdicts if they find that the jury acted unreasonably in evaluating the evidence.[114] While these solutions still leave considerable room for jury variability, they set outer limits on jury discretion. There is no comparable oversight process in the IRB system. While there are some mechanisms for the retrospective review of IRB decisions,[115] the IRB has the final say on whether the risks are reasonable when making the critical determination about whether the study should proceed.

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108. Brodin, *supra* note 104, at 15; *see also* LAWRENCE M. FRIEDMAN, LAW IN AMERICA: A SHORT HISTORY 89 (2002) (arguing that the jury "*is* the voice of the community—a voice harsher at times, more lenient at times, than the voice of the formal law") (emphasis in original).

109. *See supra* text accompanying notes 96–97.

110. At the same time, however, the potential for IRBs to be influenced by comments from colleagues may skew IRB decisions toward the preferences of investigators. IRB members undoubtedly hear more complaints from investigators whose protocols are rejected or modified than when inconsistencies result in an investigator's study being approved.

111. Brodin, *supra* note 104, at 106 (arguing that, after jurors have "passed the careful scrutiny of highly partisan attorneys" during the voir dire process, "[t]he resulting panel of six or twelve, the so-called conscience of the community, is far too small to satisfy any pollster's requirements for a representative sample of that community").

112. *See supra* text accompanying note 81.

113. DOBBS, *supra* note 99, at 355. Judges also can order new trials or alter the amount of damages the defendant is required to pay. *See* FED. R. CIV. P. 59.

114. For a discussion of the potential applicability of these mechanisms to IRBs, see *infra* text accompanying notes 248–49.

115. *See supra* text accompanying note 89.

2. Limitations of a Jury Approach to Risk Assessment

If IRBs share significant similarities with common-law juries, many of the problems with the jury deliberation process are also likely to apply to IRBs' review of research protocols. This section explores some of the limitations of a jury approach to risk-benefit analysis. The next section considers whether our willingness to tolerate these limitations in negligence litigation means that they also should be accepted in IRB review.

One limitation of any system that relies on unstructured group deliberations is that it leaves enormous discretion to the individuals entrusted with making the decisions. This is especially true when decisions are subject to an inherently amorphous standard like "reasonable risk," a concept that is susceptible to a virtually limitless range of possible interpretations.[116] Granting decision-makers some degree of discretion is often a necessary part of a regulatory system, but the more extensive the discretion the greater the potential for arbitrariness and inconsistency.[117] This potential is exacerbated when the decision-makers are neither required to state reasons for their decisions nor to apply standards consistently to different situations involving similar facts. As Lawrence Friedman notes, "although juries are not supposed to be 'lawless,' not supposed to toss a coin or decide cases on the basis of prejudice or sympathy, there is absolutely nothing to prevent the jury from doing any or all of these things."[118]

A system that relies on the discretionary judgments of a small group of people also risks overemphasizing the values and attitudes of those particular individuals.[119] The decision-makers' perspectives are likely to play an especially influential role in risk assessment determinations, given the highly variable way that people identify, value, and justify risks. In addition to the inevitable impact of

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116. The definition of a "favorable" risk-benefit ratio proposed by Robert Levine, one of the leading authorities on research ethics, underscores the amorphous nature of the IRB's inquiry: "'Favorable,'" Levine argues, "is a term used to suggest to reasonable persons that there is something about the balance of harms and benefits that other reasonable persons are likely to find felicitous." ROBERT J. LEVINE, ETHICS AND REGULATION OF CLINICAL RESEARCH, 63 (2D ED. 1986); *see also* Douglas K. Martin et al., *The Incommensurability of Research Risks and Benefits: Practical Help for Ethics Committees*, IRB, Mar.–Apr. 1995, at 8 (noting that assessing the reasonableness of research risks is particularly challenging because the risks and benefits of research often affect different people or "different domains of health status").

117. *See, e.g.*, Ashutosh Bhagwat, *Modes of Regulatory Enforcement and the Problem of Administrative Discretion*, 50 HASTINGS L.J. 1275, 1320 (1999) (observing that "unfettered discretion . . . creates the potential for arbitrariness or 'rogue lawmaking'"). The problem of inconsistency is discussed further *infra* text accompanying note 133.

118. Lawrence M. Friedman, *Some Notes on the Civil Jury in Historical Perspective*, 48 DEPAUL L. REV. 201, 209 (1998).

119. As Kenneth Abraham argues:

> A negligence decision that reflects only the distinctive point of view of the particular individuals who serve on the jury also is a mere contingency because the decision would not necessarily be the same if the same case were tried to a different jury. Such contingency lacks the legitimacy that uniformity of decision would provide.

Abraham, *supra* note 107, at 1205–06.

personal history and experiences, risk perceptions tend to vary according to individuals' professional and demographic backgrounds.[120] Factors like race, gender, and social status also appear to affect individuals' perceptions of the risks associated with different activities.[121] If risk perceptions depend on the particular decision-makers' background and attitudes, an insular process of small-group deliberations has the potential to yield unbalanced and idiosyncratic results.

Indeed, a jury-like process of risk-benefit assessment may not even accurately reflect the values and attitudes of the individuals participating in the deliberative process. This apparent anomaly may arise because perceptions of risk are frequently distorted by a variety of cognitive biases, which are likely to be fueled by a decision-making system that relies on general impressions and case-by-case determinations.[122] For example, the manner in which risk information is presented, or "framed," can significantly influence individuals' perceptions of the magnitude of a risk. In one study examining the significance of framing, two groups were asked to imagine that they had lung cancer and were then presented with the option of surgery or radiation. The first group was given statistical information about the chances of surviving with surgery ("68 percent of patients who undergo surgery will survive"), while the second group was presented with information about the chances of dying ("32 percent of patients who undergo surgery will die"). Of the group that was told their chances of dying from surgery, 44 percent opted for radiation. By contrast, only 18 percent of the group that was presented with their chances of surviving from surgery chose radiation—even though the information each group received was substantively identical.[123]

Numerous other cognitive biases have been shown to affect individuals' ability to make judgments about probabilistic information. For example, individuals "tend to think that risks are more serious when an incident is readily

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120. *See, e.g.*, Nancy Kraus et al., *Intuitive Toxicology: Expert and Lay Judgments of Chemical Risks*, *in* THE PERCEPTION OF RISK 285 (Paul Slovic ed., 2000) (demonstrating differences in risk perceptions between toxicologists and the lay public).

121. For example, one survey found that white men generally perceive environmental risks as much lower than either white women or nonwhite persons of either gender. James Flynn et al., *Gender, Race, and Perception of Environmental Health Risks*, 14 RISK ANALYSIS 1101 (1994). According to one of the authors of this study, the influence of race and gender on risk perceptions suggests that "sociopolitical factors," including individuals' sense of power and status in the world, play a significant role in how people identify and value risks. The reason a majority of white men do not view technology as particularly risky may be that white men disproportionately "create, manage, control, and benefit from many of the major technologies and activities" in the world. Paul Slovic, *Trust, Emotion, Sex, Politics, and Science: Surveying the Risk Assessment Battlefield*, 1997 U. CHI. LEGAL F. 59, 76. Women and nonwhite men, by contrast, may perceive greater risks in comparable activities "because in many ways they are more vulnerable, because they benefit less from many of [the world's] technologies and institutions, and because they have less power and control over what happens in their communities and their lives." *Id.*

122. Cass R. Sunstein et al., *Predictably Incoherent Judgments*, 54 STAN. L. REV. 1153, 1153 (2002) (suggesting that decision-makers who assess problems in isolation "produce a pattern of outcomes that they would themselves reject, if only they could see that pattern as a whole").

123. Slovic, *supra* note 121, at 65.

called to mind or 'available,'"[124] regardless of the risks' actual significance. Described as the "availability heuristic," this phenomenon leads people to pay greater attention to risk information they have learned recently than information they learned a long time ago, and to trust "detailed, concrete reports" about risk more than "abstract though arguably more relevant ones."[125] At the same time, the phenomenon of "anchoring" suggests that, once individuals have reached preliminary estimates of an activity's risks, they tend to hold on to them, discounting subsequent information that, although relevant, is contrary to their initial judgment.[126] The underlying value an individual attaches to a particular activity also affects perceptions of the activity's risks. As the perceived benefit of an activity increases, the perception of its risks tends to decline, despite the fact that the benefits and risks of technologies are often positively correlated.[127]

Studies of mock jurors suggest that these cognitive biases commonly distort jurors' ability to rationally assess evidence.[128] Given the similarities between IRB review and jury deliberations, it is reasonable to believe that these cognitive biases have a similar effect on IRBs. In fact, some of these biases are likely to have a greater impact on IRB review than on jury decision-making. In litigation, each of the parties has an opportunity to frame the evidence in a manner that supports its particular position, and to introduce evidence that will be readily "available" to the jury when a decision is made. IRBs, however, rely largely on the information submitted by the investigator, which may present a one-sided view of relevant risks. While IRB members, unlike jurors, generally have scientific expertise, expert risk perceptions are also affected by cognitive biases, particularly when experts "are forced to go beyond their data and rely on judgment."[129] Moreover, experts tend to be unduly confident in judgments that stem from cognitive distortions.[130] According to many commentators, tragedies like the Three Mile Island nuclear accident and the Challenger space shuttle crash were due in

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124. Cass Sunstein, *Which Risks First?* 1997 U. CHI. LEGAL F. 101, 118.

125. Clayotn P. Gillette & James E. Krier, *Risk, Courts, and Agencies*, 138 U. PA. L. REV. 1027, 1092 (1990).

126. *Id.*

127. Melissa L. Finucane et al., *The Affect Heuristic in Judgments of Risks and Benefits*, *in* THE PERCEPTION OF RISK, *supra* note 120, at 413, 416 ("If an activity was 'liked,' people tended to judge its risks as low and its benefits as high. If the activity was 'disliked,' the judgments were opposite—high risk and low benefit.").

128. In the negligence context, jurors are particularly influenced by the "fundamental attribution error," the view that "if an accident has occurred, someone deserves blame for it." Neil R. Feigenson, *The Rhetoric of Torts: How Advocates Help Jurors Think About Causation, Reasonableness, and Responsibility*, 47 HASTINGS L.J. 61, 126 (1995). This phenomenon leads juries "to allocate . . . blame based on the sorts of people they perceive the parties to be," a tendency that undoubtedly explains at least some of the variation in jury decisions in comparable factual situations. *Id.*

129. Paul Slovic et al., *Fact Versus Fears: Understanding Perceived Risk*, *in* JUDGMENT UNDER UNCERTAINTY: HEURISTICS AND BIASES 463, 475 (D. Kahneman et al. ed., 1982).

130. *Id.* at 472.

large part to experts' overconfidence in risk assessments based on limited information.[131]

The influence of idiosyncratic perspectives and cognitive biases on the decision-making process helps explain why juries and IRBs often reach inconsistent decisions in similar situations. Of course, it is not necessarily inappropriate for different decision-makers to react differently to comparable situations, especially since risk assessment involves opinions rather than objectively determinable facts. Moreover, some variation in outcome can be attributed to genuine differences in local conditions and attitudes, factors that both IRBs and juries are supposed to take into account.[132]

However, the fact that risk assessments are inherently subjective does not mean that any decision is as good as any other. Whether because of aberrational perspectives, cognitive distortions, or simply bad judgment, some decision-makers may grossly underestimate the individual or societal costs associated with particular activities, or overestimate the likelihood and significance of the benefits those activities are expected to achieve. Ultimately, the judgment that a risk is "reasonable" must mean more than a particular group of people happen to conclude that the risk is acceptable—otherwise, risk assessment would be nothing more than a tautological process in which a decision's legitimacy would depend solely on the fact that a decision has been made. At some point, a risk assessment determination may fall outside the range of approaches the broader community is willing to accept as legitimate. In such situations, it is possible to say that the process has yielded an invalid determination—i.e., an unreasonable interpretation of the meaning of "reasonable risk."

Unfortunately, a jury-like deliberative process is inherently incapable of identifying such "unreasonable reasonableness determinations." If the individuals participating in the process themselves believe that the balance between risks and benefits is perfectly acceptable, how can they be expected to realize that members of the larger community are unlikely to share that view? This problem is exacerbated by the secrecy and insularity of jury deliberations, which prevent decision-makers from learning how others identify, value, and weigh comparable risks and benefits. Without this information, they have no way of knowing where their determinations fit in the spectrum of societal opinion. It is unrealistic to expect individuals to recognize aberrational decisions without knowing what sort of decisions constitute the norm.

In addition to the potential for juries to reach unreasonable decisions, the inconsistency of jury determinations can be problematic even if each decision seems appropriate when viewed in isolation. The danger is that widely differing outcomes in similar situations can create the impression that important decisions are being made on an arbitrary basis. Perceptions of arbitrariness are most likely when a single deliberative body renders internally inconsistent decisions, such as when an IRB at a single institution interprets similar situations differently from meeting to meeting. At some point, however, even inconsistency among different

131. Gillette & Krier, *supra* note 125, at 1093–94.

132. *See supra* text accompanying notes 97 (IRBs) and 108 (juries).

decision-makers can raise problems of legitimacy, as outcomes come to be seen as depending more on the particular decision-makers' identity than the merits of the issues under consideration.[133] This is especially true when inconsistencies stem from nonsubstantive factors like varying access to information, differences in how information is presented, or the diversity of perspectives incorporated into the deliberative process. In such circumstances, inconsistent decisions can undermine the public's confidence in the integrity of the process, regardless of whether individual decisions might seem acceptable when standing alone.

3. The Reasons Juries Are Used in Negligence Litigation Are Not Relevant to IRB Review

One possible conclusion from the above observations is that jury deliberations are an inherently inappropriate way to assess risks and benefits, whether in negligence litigation or IRB review. Arguments about the perceived defects of the common-law jury have a long and distinguished history. In *The Common Law*, for example, Oliver Wendell Holmes argued that juries are inherently inferior decision-makers to judges, as judges can base decisions on repeated exposure to similar situations and can articulate reasons for their decisions in order to guide future behavior.[134] Francis Bohlen, writing in 1924, argued that juries are unreliable decision-makers because they are likely to be unduly swayed by sympathy to the plaintiff and insufficiently attentive to the social utility of risky activities.[135]

One need not agree with these critics of the common-law jury, however, to question the appropriateness of a jury approach to risk assessment in IRB review. While both juries and IRBs are justified by similar appeals to community values, they each serve different social functions. Therefore, the reasons we tolerate the limitations of jury deliberations in negligence litigation do not necessarily apply to decision-making by IRBs. The primary difference between juries and IRBs is that juries are concerned with apportioning responsibility for risks that have already materialized, while IRBs determine whether researchers should be permitted to expose individuals to future risks, which are, by definition, still avoidable. In fact, juries are not authorized to prospectively regulate future behavior. Thus, only judges, not juries, have the power to issue injunctions, a type of remedy that directly determines the range of activities individuals may perform in the future.[136]

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133. Ernest D. Prentice & Dean L. Antonson, *A Protocol Review Guide to Reduce IRB Inconsistency*, IRB, Jan./Feb. 1987, at 9, 11 ("Inconsistency in its most serious context suggests that the welfare of subjects may be at the mercy or whim of a semirandomized IRB decision-making process. In a broader context subjects may be placed at greater risk simply because of their institutional affiliation.").

134. OLIVER WENDELL HOLMES, JR., THE COMMON LAW 123–24 (1881).

135. Gilles, *supra* note 100, at 837.

136. Some scholars believe that these restrictions on juries' authority developed in part because of concerns about jurors' limited abilities to rationally assess evidence. Ann Woolhandler & Michael G. Collins, *The Article III Jury*, 87 VA. L. REV. 587, 657 (2001) ("[W]hile some scholars have doubted whether functional considerations as to whether

It is true, of course, that jury decisions can indirectly influence future behavior by signaling to others the liability risks associated with particular conduct.[137] However, given the inconsistency of jury decisions, the deterrent effect of negligence judgments is often quite minimal.[138] Moreover, even assuming that jury verdicts, over time, collectively influence individuals' willingness to engage in particular activities, juries are not supposed to decide individual cases based primarily on their perception of the message a particular decision will send.[139] Instead, they are expected to evaluate the responsibility of the particular parties before the court, an obligation that sometimes requires juries to exonerate defendants even when imposing liability might produce an appropriate deterrent effect.

The most persuasive justifications for negligence juries, therefore, have focused not on juries' power to guide people's behavior through the rational application of legal standards, but on their ability to render decisions in individual cases that represent a fair apportionment of responsibility between the particular parties before the court. Catherine Pierce Wells, for example, contends that juries' legitimacy depends on their ability to achieve corrective justice in individual cases—i.e., to determine "whether, all things considered, it is fair to require this defendant to pay for this plaintiff's injuries."[140] Wells argues that the jury system is a fair method for apportioning responsibility because it provides a mechanism for transcending the "viewpoint-dependent narratives" advanced by each of the parties.[141] It does this by relying on procedures that give both parties ample opportunities to present their perspectives[142] and requiring a decision that reflects a

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judges or juries were better at deciding certain fact issues played much of a role in determining the scope of jury trial rights, the inherent limitations of juries were sometimes cited as reasons for extensions of equity.").

137. Indeed, the deterrent effect of liability determinations is frequently cited as one of the primary advantages of the system of negligence law, particularly among law and economics scholars. Christine Jolls et al., *A Behavioral Approach to Law and Economics*, 50 STAN. L. REV. 1471, 1525 (1998).

138. *See supra* text accompanying note 107; *see also* Feigenson, *supra* note 128, at 165 (arguing that we cannot reasonably expect deterrence to result from "such a wide-open and unarticulated process as decision-making by nonprofessional, discontinuous bodies that need not give the public reasons for their decisions"). One example of jury decisions' ineffectiveness in encouraging appropriate behavior is the limited impact of malpractice decisions on the reduction of medical errors. Michelle M. Mello & Troyen A. Brennan, *Deterrence of Medical Errors: Theory and Evidence for Malpractice Reform*, 80 TEX. L. REV. 1595, 1607 (2002) ("There is little evidence of true error deterrence stemming from medical malpractice liability.").

139. The exception, of course, is when juries award punitive damages, which are expressly designed to send a message to individuals not before the court. City of Newport v. Fact Concerts, Inc., 453 U.S. 247, 266–67 (1981) (noting that one purpose of punitive damages is to deter persons other than the defendant from engaging in wrongful activities).

140. Catherine Pierce Wells, *Tort Law as Corrective Justice: A Pragmatic Justification for Jury Adjudication*, 88 MICH. L. REV. 2348, 2360 (1990).

141. *Id.* at 2395.

142. As Wells argues, "[t]he dominant consideration is that all relevant information should be admitted so long as it is possible through the technique of cross examination or otherwise to place the information in its proper perspective." *Id.* at 2404.

consensus among individuals "with varying normative viewpoints."[143] She argues that such a system is legitimate because it is fair to the litigants, each of whom has been given an equal opportunity to persuade the jury of his or her point of view.[144]

If the primary purpose of negligence litigation is to provide a process for resolving disputes that is fair to the parties, it does not necessarily matter whether jury decisions yield a rational framework for guiding the behavior of individuals not before the court.[145] Indeed, tort law is generally skeptical of the possibility of making reasonableness judgments that apply beyond the circumstances of a particular situation. As stated by the drafters of the *Restatement (Third) of Torts*, tort law "'has accepted an ethics of particularism, which tends to doubt the viability of general rules capable of producing determinate results, and which requires that actual moral judgments be based on the circumstances of each individual situation.'"[146] This particularistic focus of negligence law, Mark Gergen argues, is one of the primary reasons that negligence decisions are generally entrusted to juries, despite the fact that normative questions in most other legal contexts are decided by judges.[147] If no two negligence cases are ever the same, the potential for jury inconsistency is not really relevant. Consistency means treating like cases alike,[148] a principle that has no application to a system in which every case is genuinely unique.

IRBs are therefore characterized by a curious contradiction: They rely on a decision-making process that resembles that of common-law juries, but they do so in pursuit of functions that juries were never intended to perform. Unlike juries, IRBs are not engaged in a retrospective exercise in corrective justice; rather, their deliberations occur before any injury requiring correction has even occurred. Nor are IRBs evaluating competing normative positions advanced by disputing parties. Thus, their legitimacy cannot be based on the extent to which they are fair to the particular individuals involved in the process. Indeed, the individuals with the greatest stake in IRB decisions—the prospective research subjects—do not even participate in the process of IRB review. Instead, research subjects make individual decisions about participation as part of the informed consent process, which does not take place until after the IRB has already determined that the study

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143. *Id.* at 2409 (arguing that the jury's ability to reach consensus "is a significant part of the reason why tort adjudication is an acceptable and justifiable normative practice").

144. *Id.* at 2410.

145. *Id.* at 2408.

146. Gilles, *supra* note 100, at 855 (quoting RESTATEMENT (THIRD) OF TORTS: GENERAL PRINCIPLES § 5 cmt. d (Discussion Draft Apr. 5, 1999)).

147. Mark P. Gergen, *The Jury's Role in Deciding Normative Issues in the American Common Law*, 68 FORD. L. REV. 407 (1999). Gergen argues that two considerations determine how power is allocated between judge and jury: "the values of popular judgment," and the need for consistency and predictability in law. In most legal contexts, the interest in consistency and predictability is so important that it "will always swamp the value of popular judgment" and lead judges to make most important decisions. In negligence cases, however, developing generalizable principles is usually not possible, given the importance of a particularized analysis of the specific situation. *Id.* at 438.

148. Coons, *supra* note 107, at 59 (noting that this understanding of consistency derives from Aristotle).

should be permitted to proceed. In this sense, the relationship between the IRB and research subjects is exactly the opposite of the relationship between juries and the parties to a lawsuit: In litigation, the parties have the opportunity to influence the outcome of the jury's deliberations, but in research, the subjects are more likely to be influenced *by* the IRB's deliberations, insofar as subjects' perceptions are shaped by the imprimatur of the IRB's decision to approve the study, as well as its guidance to investigators about the process of informed consent.[149]

IRBs are also in a better position than juries to base decisions on generalizable principles, as opposed to the case-specific focus that characterizes negligence determinations. The uniqueness of negligence cases is integrally linked to the retrospective nature of the jury's inquiry. Because the jury must evaluate the facts as they actually transpired, and because events will never unfold precisely the same way again, negligence cases are necessarily *sui generis*. By contrast, IRBs review general blueprints for future behavior, not irreproducible sets of historical events. IRBs also have the power to alter the risks to which subjects will be exposed by requiring the investigators to make revisions to protocols.[150] This power can be used to minimize the number of situations involving truly unprecedented risks.

If jury deliberations are an inappropriate model for IRB risk assessment, what other decision-making mechanisms might work better? To answer that question, the next Part considers some decision-making mechanisms employed by other institutions involved in the prospective regulation of future behavior, particularly courts and administrative agencies. In contrast to the unstructured and secretive process of jury deliberations, both judges and agencies have developed a variety of techniques to avoid arbitrariness, promote consistency, and incorporate multiple perspectives into the process of interpreting and enforcing the law.

IV. ALTERNATIVE DECISION-MAKING MODELS: LESSONS FROM JUDGES AND ADMINISTRATIVE AGENCIES

Both judges and administrative agencies regularly make decisions designed to regulate future behavior, as opposed to the retrospective allocation of responsibility that characterizes jury decision-making. Some of these decisions directly determine what particular individuals may or may not do in the future, as when a judge issues an injunction to enjoin a prospective nuisance,[151] or when the FDA authorizes a company to begin marketing a new drug.[152] Other decisions establish rules for broad categories of situations, such as when the Environmental Protection Agency adopts regulations on toxic waste,[153] or when the Occupational Health and Safety Administration promulgates rules for avoiding

149. *See supra* text accompanying note 57 (noting subjects' tendency to assume that research would not be conducted if it involved significant risks).

150. HHS Protection of Human Subjects, 45 C.F.R. § 46.109(a) (2003).

151. *See infra* text accompanying notes 164–65.

152. FDA Applications for FDA Approval to Market a New Drug, 21 C.F.R. § 314 (2003).

153. EPA Standards Applicable to Generators of Hazardous Waste, 40 C.F.R. § 262 (2003).

exposure to potentially infectious materials in the workplace.[154] Some future-oriented decisions may relate to controversies about events that transpired in the past, but the resolution of these controversies establishes general principles that guide the behavior of individuals not involved in the dispute—for example, judicial determinations about the meaning of "due process of law."

The manner in which judges and agencies make these prospective legal interpretations differs markedly from jury deliberations. This Part considers the potential relevance to IRBs of four decision-making mechanisms used by judges and agencies. It begins with a close look at an aspect of judicial decision-making with significant potential for transforming the manner in which IRBs review protocols—the process of reasoning by analogy. It then turns to other methods used by judges and/or agencies, including written opinions, the systems of appellate review and precedent, and notice-and-comment rulemaking.

A. Analogical Reasoning

Deciding cases by comparing the issues presented with those that have been addressed in previous decisions is the primary characteristic of common-law reasoning. The process involves identifying relevant features of the case under consideration, finding prior cases in which those features also exist, and then evaluating similarities and differences between the cases to determine whether the approach taken in prior cases should also be applied to the issue currently under consideration.[155] Because no two cases are ever alike in all respects, analogical reasoning usually does not point to any single, obviously correct conclusion.[156] Rather, the decision-maker must determine whether the case under consideration is "'relevantly' similar" to the prior cases, "and that there are not 'relevant' differences between them."[157]

1. Uses of Analogical Reasoning in Law

Reasoning by analogy is used for a variety of purposes in the law. Often, courts compare cases to prior decisions to determine the meaning of an imprecise legal standard or term. For example, in *California v. Ciraolo*,[158] the Supreme Court was asked whether the police conducted a "search" within the meaning of the

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154. OSHA Occupational Safety and Health Standards, 29 C.F.R. § 1910 (2003).

155. Cass Sunstein has identified four steps to the process of analogical reasoning: (1) Some fact pattern *A* has a certain characteristic *X*, or characteristics *X*, *Y*, and *Z*; (2) Fact pattern *B* differs from *A* in some respects but shares characteristics *X*, or characteristics *X*, *Y*, and *Z*; (3) The law treats *A* in a certain way; (4) Because *B* shares certain characteristics with *A*, the law should treat *B* the same way.

Cass R. Sunstein, *On Analogical Reasoning*, 106 HARV. L. REV. 741, 745 (1993).

156. In this respect, reasoning by analogy differs from deductive reasoning, a process in which "the truth of the premises guarantees the truth of the conclusion." Scott Brewer, *Exemplary Reasoning: Semantics, Pragmatics, and the Rational Force of Legal Argument by Analogy*, 109 HARV. L. REV. 925, 942 (1996).

157. Sunstein, *supra* note 155, at 745.

158. 476 U.S. 207 (1986).

Fourth Amendment when they flew over the defendant's house to determine if the defendant was growing marijuana in his backyard. In considering whether the police had intruded on a "reasonable expectation of privacy"—the undisputed standard for determining whether a search had occurred[159]—the Court looked to prior cases involving governmental observation of arguably private activities. Finding that a common theme of those decisions was that individuals have no reasonable expectation of privacy in activities that can be viewed from public vantage points, the Court concluded that aerial surveillance did not constitute a search because the police observed the defendant's backyard while flying in public airspace.[160] In this case, by bringing to light characteristics of activities that had previously been deemed to constitute "searches," the prior decisions helped give content to an otherwise ambiguous legal term.

Analogical reasoning also may be used to determine the scope of a previously announced decision or rule. For example, in *Thompson v. County of Alameda*,[161] the issue was whether a county that released a violent juvenile offender into his mother's custody had a duty to warn the public, the police, or the boy's mother that the boy had threatened to kill a child in the neighborhood. In considering whether to recognize such a duty, the court compared the situation to its previous decision in *Tarasoff v. Regents of the University of California*,[162] which had recognized a therapist's duty to disclose his patient's threat of violence against a certain third party. The court concluded that the duty recognized in *Tarasoff* did not apply to the county's release of the juvenile offender, given that the boy had not identified a specific victim and that warnings to the public, the police, or the boy's mother would probably not have been effective at protecting the potential victim. Comparing the situation at hand with the prior decision in *Tarasoff* helped the court identify legally significant aspects of the controversy, while also clarifying the scope of the previously announced *Tarasoff* rule.

Courts also rely on analogies when balancing the risks and benefits of particular activities. Some of these evaluations arise in connection with litigation seeking damages for injuries that have already occurred. For example, in determining whether the transportation of gasoline is "abnormally dangerous," and hence subject to strict liability, the court in *Siegler v. Kuhlman*[163] compared it with activities that had already been deemed to be subject to strict liability (impounding water) as well as to activities for which strict liability had been rejected (maintaining an underground water main). In other cases, courts evaluate risks when reviewing petitions to enjoin activities prospectively. For example, in *Miniat*

159. *Id.* at 211.

160. *See id.* at 213–14.

161. 614 P.2d 728 (Cal. 1980).

162. 17 Cal.3d 425 (1976).

163. 81 Wn.2d 448, 454–60 (1972) (concluding that strict liability should be applied to the transportation of gasoline). Similarly, in *Gallick v. Barto*, 828 F. Supp. 1168 (M.D. Pa. 1993), the court held that owners of ferrets should be subject to strict liability because ferrets are more like wild animals, whose owners are subject to strict liability, than domesticated dogs, whose owners are subject to a negligence standard. *See id.* at 1174 (contrasting ferrets, "a wild animal with domestic propensities," with pit bulls, "a domestic animal with dangerous propensities").

v. McGinnis,[164] property owners sought an injunction prohibiting the construction of a long-term care facility for mentally ill and disabled individuals on the ground that the facility would be a private nuisance, a claim that depended in part on establishing that the construction would cause unreasonable harm to the property owners. In rejecting the petition, the court compared the proposed facility to activities like "the construction of a jail or gas station in an essentially residential area," both of which had previously been considered to be reasonable despite their potential to depress local property values.[165]

Scholars have offered a variety of theories to explain the process judges employ when they engage in analogical reasoning. Cass Sunstein, for example, argues that reasoning by analogy depends on the development of "governing principles,"[166] which he describes as rationales for explaining prior decisions that are less developed than full-blown jurisprudential theories but sufficiently broad to provide a coherent basis for explaining the result in more than one case.[167] For example, in *California v. Ciraolo*,[168] the governing principle would be that it is unreasonable to expect privacy in activities that can be viewed from public vantage points. Scott Brewer suggests that judges develop these principles (or, to use Brewer's term, "analogy-warranting rules"[169]) through "abductive inference," a method of reasoning similar to the process of scientific discovery.[170] After developing tentative explanations that would justify adopting these rules, the judge tests the validity of the rules and explanations by applying them to additional cases to determine whether they would lead to acceptable results. Finally, once the judge confirms the rules' validity, she applies them to the particular issues presented in her case.[171]

As both Sunstein and Brewer's descriptions suggest, analogical reasoning does more than simply produce appropriate decisions in individual controversies. It also contributes to the development of coherent legal principles with implications not only for the specific case being decided, but also for future cases. It is an ideal method for giving content to open-ended legal standards, as each decision further clarifies the standard's meaning by applying it to a new situation according to principles implicit in decisions that have already been made. As

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164. 26 Ark. App. 157 (1988).

165. *Id.* at 160. Countless other examples of analogical reasoning in law exist. *See, e.g.*, Brewer, *supra* note 156, at 936–38 (offering additional examples).

166. Sunstein, *supra* note 155, at 745.

167. *Id.* at 747 (arguing that "analogical reasoning produces principles that operate at a low or intermediate level of abstraction," and that "[a]nalogical reasoning usually operates without express reliance on any general principles about the right or the good").

168. *See* 476 U.S. at 213–14.

169. Brewer, *supra* note 156, at 962; *see also id.* at 974 ("[N]o example can serve as an example without a rule to specify what about it is exemplary.").

170. *Id.* at 945–49. The process involves the following steps: First, the judge "notices some phenomenon that calls for explanation." Second, she "notices that the existence of some other factor or set of factors could explain the given phenomenon." Finally, she "settles on the hypothesis (H) as the tentatively correct explanation of the phenomenon (P)." *Id.* at 947–48.

171. *Id.* at 963, 1023.

Sunstein suggests, this process of incremental decision-making enhances the legitimacy of the ultimate interpretation of the standard. "[S]ometimes there may be no criteria for truth in law," he argues, "except for our considered judgments about particular cases, once those judgments have been made to cohere with each other."[172]

2. Applying Analogical Reasoning to IRB Review

IRBs encounter a number of issues whose resolution could be aided by analogical reasoning. Like courts, IRBs must sometimes interpret imprecise legal language—for example, the definition of "minimal risk" in the federal regulations, which affects issues ranging from the permissibility of using expedited review procedures[173] to the authority of parents to enroll their children in certain studies.[174] The regulations define "minimal risk" as those risks that are "ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests"[175]—a definition that raises almost as many questions as it purports to answer. For example, whose daily life should be considered?[176] What are the risks that this person "ordinarily" encounters, and what magnitude and probability of harm do those risks involve? Evaluating prior minimal risk determinations could help IRBs develop a coherent approach to these questions, by revealing any common characteristics of interventions that already have been deemed to satisfy (or not to satisfy) the definition of minimal risk.

IRBs also confront situations that raise questions about the scope of generally applicable principles or rules. For example, while it is often argued that physicians have an ethical obligation to offer patients optimal therapeutic interventions, commentators disagree about the extent to which this principle precludes enrolling individuals in studies involving placebo controls.[177] Some believe that the use of placebos is unethical whenever an effective intervention exists for a particular condition;[178] others maintain that prohibiting the use of placebos in all such situations would unnecessarily prevent valuable research from taking place.[179] By considering a variety of actual situations in which placebos have been used, IRBs might be able to identify factors to consider in determining whether to approve a study involving the use of placebo controls. For example, an

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172. Sunstein, *supra* note 155, at 777; *see also* Emily Sherwin, *A Defense of Analogical Reasoning in Law*, 66 U. CHI. L. REV. 1179, 1189 (1999) (arguing that one benefit of the common-law process of analogical reasoning is that it produces principles that "represent the collective reasoning of a number of judges over time").

173. HHS Protection of Human Subjects, 45 C.F.R. § 46.110 (2003).

174. *Id.* §§ 46.404–406. The concept of minimal risk also is relevant to IRBs' authority to waive or modify informed consent requirements. *Id.* §§ 46.116(d)(1), 46.117(c)(2).

175. *Id.* § 46.102(i).

176. Kopelman, *supra* note 92, at 41 ("The problem is that the federal regulations do not state whose daily life researchers should consider.").

177. *See generally* Franklin G. Miller & Howard Brody, *What Makes Placebo-Controlled Trials Unethical?*, AM. J. BIOETHICS, Spring 2002, at 3.

178. *Id.* at 3.

179. *Id.* at 4.

analysis of prior situations might suggest that a different approach would be appropriate in protocols involving treatments for minor conditions for which individuals might rationally decide to forego available treatment (such as a placebo-controlled trial of a new drug for treating mild allergies or baldness), as opposed to situations where withholding treatment would cause subjects significant pain (for example, a placebo-controlled trial of palliative care interventions for chemotherapy patients).[180]

Finally, in some cases analogies could help IRBs evaluate the overall balance between particular risks and benefits, much like courts sometimes rely on previous cases in tort or property disputes.[181] In fact, it is likely that IRBs already engage in such a comparative process, at least implicitly, when prior decisions known to the members suggest a framework for thinking about particular risks. For example, in considering a protocol involving the deception of subjects, most IRBs would probably start by comparing the protocol to the infamous Milgram experiments, an example of deception research that has been widely condemned. In those studies, subjects were asked to administer what appeared to be painful electrical shocks to people who were posing as "learners," purportedly to determine the effect of punishment on learning. In reality, no shocks were actually administered; instead, the purpose of the study was to determine whether the subjects would continue to follow the investigators' instructions even when the "learners" appeared to be experiencing severe pain.[182] The study's findings produced valuable insights on the extent to which individuals will engage in sadistic behavior upon instructions from authority figures. In so doing, however, it caused significant psychological damage to many subjects, who were tricked into discovering aspects of their personality they might rather not have known.[183] Comparing the Milgram study to deception studies that seem harmless[184] can help

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180. *Cf.* Marc L. Citron, *Placebos and Principles: A Trial of Ondansetron*, 118 ANNALS INTERNAL MED. 470 (1993) (criticizing a placebo-controlled trial of a method for reducing the pain associated with chemotherapy).

181. *See supra* text accompanying notes 163–65.

182. LEVINE, *supra* note 116, at 217–18.

183. *Id.* at 218 (noting that "during the debriefing many of these subjects learned that they were capable of egregious cruelty," and that "[u]pon learning this about themselves, many of the subjects experienced severe and, in some cases, prolonged anxiety reactions").

184. Consider the following example:

> The researcher plans to determine how mood and perception of one's body image may be related. Initially, student subjects complete a series of written questionnaires and scales about their body image. After the subjects are presented with visual images intended to evoke a negative mood, the subjects are asked to complete the same questionnaires and scales. The effect of evoking a negative mood is evaluated.

Marianne M. Elliott, *Research Without Consent or Documentation Thereof*, *in* INSTITUTIONAL REVIEW BOARD: MANAGEMENT AND FUNCTION 250, 251 (Robert Amdur & Elizabeth Bankert eds., 2002) [hereinafter INSTITUTIONAL REVIEW BOARD].

The author of this example suggests that the IRB could waive the requirement to disclose the purpose of this study to prospective subjects, given that the risks of the study are minimal and that disclosing the purpose of the study would necessarily impair the validity of the results. *Id.*

IRBs identify factors that distinguish appropriate and inappropriate uses of deception in research.

This type of reasoning process should not be alien to those engaged in bioethical decision-making. In recent years, increasing dissatisfaction with principle-driven approaches to moral analysis has led to renewed interest among bioethicists in "casuistic," or case-based, modes of reasoning. Casuistry rejects the effort to decide hard cases by appealing to broad philosophical theories. Instead, it approaches controversies by comparing the salient issues with those raised in prior cases whose outcome seems clear.[185]

For example, Albert Jonsen uses a casuistic analysis to analyze the ethical implications of a resident's decision to administer lethal medications to an unfamiliar terminally ill patient in response to the patient's statement, "Let's get this over."[186] He argues that the process of case comparison can not only help the decision-maker identify the factors to consider in evaluating the resident's actions, but it also can suggest how those factors should be balanced to the extent they conflict.[187] Thus, an examination of other cases involving killing would reveal a variety of factors relevant to an ethical analysis of life-ending actions, including the actor's motivations, the extent to which the actions were consensual, and the physical condition of the person whose life was ended. By identifying "paradigm cases" in which some of these considerations clearly appear to outweigh all the others, the decision-maker can better assess how the considerations should be balanced in the resident's case.[188] Based on such an analysis, Jonsen concludes that the resident's case "is resolved casuistically with ease," as the circumstances are dramatically different from paradigm cases in which killing can be justified, given the lack of clarity about the patient's capacity and the resident's limited knowledge of the patient's medical condition.[189]

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185. *See, e.g.*, Mark G. Kuczewski, *Casuistry and Its Communitarian Critics*, 4 KENNEDY INST. ETHICS J. 99, 100 (1994).

> The casuist observes that proper actions are obvious in certain cases, and our clearest moral perceptions can be used as paradigms to fix the limits of right action. Particular, increasingly complicated cases then must be examined for elements of competing paradigms contained within them. Finally, actions should be based upon the paradigm that is most closely resembled.

Id.

186. Albert R. Jonsen, *Casuistry as Methodology in Clinical Ethics*, 12 THEORETICAL MED. 295, 298 (1991). The case is taken from a story that appeared in the *Journal of the American Medical Association*. *See* Anonymous, *It's Over, Debbie*, 259 J. AM. MED. ASS'N. 272 (1988).

187. Jonsen, *supra* note 186, at 306.

188. *Id.* ("Casuistry will be able to locate the case in a taxonomy of cases, recognize the similarities and differences and appreciate the shift from moral certainty to moral doubt."); *see also* Carson Strong, *Justification in Ethics*, *in* MORAL THEORY AND MORAL JUDGMENTS IN MEDICAL ETHICS 193, 206 (Baruch A. Brody ed., 1988) (arguing that paradigm cases are those in which particular morally relevant factors are clearly weightier than others, and that considering such cases can suggest how to balance competing factors in situations that are less clear).

189. Jonsen, *supra* note 186, at 305.

Obviously, reasoning by analogy cannot eliminate the discretionary element of IRB decision-making. On the contrary, at every stage of the process of analogical reasoning, the decision-maker is faced with discretionary judgments that analogies alone cannot resolve—from identifying the universe of relevant prior situations, to elucidating a lesson from these situations that has some bearing on the current controversy, to applying that lesson to resolve the particular issue at hand. In many situations there are likely to be multiple ways to approach all these determinations, each with vastly different implications for the final result.

Rather, the potential benefit to IRBs of considering prior decisions—including decisions rendered by IRBs at different institutions—is that it could provide a mechanism for structuring IRBs' exercise of discretion, potentially yielding judgments that are more carefully reasoned and less prone to the idiosyncratic reactions of a particular group. First, requiring IRBs to consider decisions that have been rendered by different decision-makers would necessarily broaden the range of perspectives incorporated into the IRB's analysis. As Mark Kuczewski argues, one benefit of a casuistic approach to ethical reasoning is that, by focusing the decision-maker's attention on a broad range of real-world considerations, it can provide "a series of perspectives from which to criticize too narrow a focus on tradition-as-it-happens-to-be within an institution or practice."[190] Considering decisions from other institutions also could act as a counterweight to the influence currently exercised by the primary reviewers: If a prior decision in a similar situation conflicts with the primary reviewer's recommendations, the other members are likely to approach those recommendations with a more critical eye. Similarly, prior decisions could be useful sources of support for members who otherwise might be reluctant to express their opinions, such as members unaffiliated with the institution,[191] members without scientific expertise, or members whose views conflict with those of the IRB chair or other people in positions of authority in the institution.

Second, by forcing the IRB to look beyond the particular situation it is currently reviewing, analogical reasoning can help reveal deficiencies in what otherwise might appear to be an appropriate approach. Through what Brewer refers to as the process of "reflective adjustment," analogical reasoning encourages the decision-maker to test tentative approaches to issues by considering whether they would lead to appropriate results in the other situations to which the current case is being compared.[192] Thus, a seemingly acceptable basis for resolving a controversy "might be rejected because, although it may be an attractive solution in some ways, it does not, as applied to some particular cases, cohere sufficiently with explanatory or justificatory rationales that the reasoner is unwilling to amend."[193] Similarly, a tentative decision might "turn[]out to yield particular results that are, at least prima facie, unacceptable to the reasoner."[194] While it might also be possible to engage in this process by considering hypothetical

190. Kuczewski, *supra* note 185, at 112.

191. *See* NAT'L BIOETHICS ADVISORY COMM'N, *supra* note 23, at 62 (noting that unaffiliated members may be reluctant to "mention concerns or challenge the group").

192. *See supra* text accompanying note 171.

193. Brewer, *supra* note 156, at 1023.

194. *Id.*

variations of the circumstances currently under consideration, the value of hypotheticals is necessarily limited by the imagination of their creator. There is no substitute for what John Arras refers to as the "messy reality of cases,"[195] which will inevitably raise considerations that abstract speculation would not reveal.

Third, encouraging IRBs to consider prior decisions is likely to reduce the inconsistency of IRB determinations. One reason is simply that few people prefer inconsistency; all things being equal, most decision-makers will favor results that can be reconciled with what others have done before. Thus, if an IRB knows that a comparable situation has already been resolved in a particular manner, those who wish to reach a contrary decision will have the burden, at least implicitly, of justifying why the approach already taken should not be followed. This is particularly true when it appears that a consensus has emerged supporting a particular resolution of an issue. When the weight of prior decisions suggests that a norm has developed, decision-makers are likely to think especially carefully before adopting a different approach.

Even when there are no prior determinations directly on point, an analogical reasoning process can suggest the parameters in which a particular issue should be analyzed. For example, in deciding whether a particular procedure should be considered a "minimal risk" intervention, an IRB could compare the procedure's characteristics with other interventions previously found to involve minimal risks. Thus, it might consider whether the procedure involves a comparable likelihood of short- or long-term complications, or whether it is more or less likely to involve considerable pain. In other words, instead of trying to determine the risk level of interventions in the abstract, IRBs would engage in a comparative evaluation, asking whether an intervention is "as risky," "less risky," or "more risky" than interventions that have already been analyzed. Using prior decisions as reference points in this manner can help give content to the otherwise amorphous standard of minimal risk.

Fourth, a system in which IRBs review prior decisions from different institutions could function as a method for sharing innovative strategies about risk reduction methods. For example, an IRB might discover that another IRB reviewing a similar protocol required the investigators to incorporate additional safeguards, such as monitoring of the subjects by independent clinicians on a regular basis. This information might lead the second IRB to consider imposing similar requirements. If IRBs share this type of information more frequently, "best practices" for risk-reduction methods might begin to emerge.

In addition, if IRBs share not only their initial decisions but also any significant information received after the protocol begins,[196] subsequent IRBs could also learn about risks they otherwise might not think to consider. The

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195. John D. Arras, *Getting Down to Cases: The Revival of Casuistry in Bioethics*, 16 J. MED. & PHIL. 29, 32 (1991); *see also id.* at 37 (arguing that, when using cases in the classroom, "the cases discussed should reflect the degree of complexity, uncertainty, and ambiguity encountered" in the real world).

196. IRBs should be aware of this information because investigators are required to inform the IRB of adverse events. *See* FDA Institutional Review Boards, 21 C.F.R. §§ 56.108, 312.66, 812.150 (2003).

aftermath of the UCLA schizophrenia studies provides an example of the potential benefits of greater sharing of information about study outcomes. In these experiments, patients with schizophrenia were taken off medications and put on placebos, as part of an effort to identify predictors of relapse among patients who stop taking their medications.[197] One patient put on a placebo committed suicide, while another hitchhiked to Washington, D.C. in an attempt to assassinate the President.[198] The publicity associated with this study has led some IRBs to insist that trials in which patients with schizophrenia will be taken off medications be limited to in-patient settings, in order to minimize the harm experienced by patients who relapse.[199] While this particular requirement arose because of public attention devoted to the UCLA experience, it provides an example of the potential benefits of broader information sharing by IRBs as a standard part of protocol review.

Whether incorporating analogical reasoning into the protocol review process would reduce the distorting influence of cognitive biases is difficult to determine.[200] As Dan Hunter observes in his examination of judicial decision-making, cognitive biases appear to play a considerable role in the process of drawing analogies.[201] Thus, in contrast to those commentators who characterize analogical reasoning as primarily a principle-driven process,[202] Hunter argues that principles are most influential in the context of *justifying* analogies, after the judge has already concluded that two cases are similar or different for other reasons.[203] At the initial stage of "discovering" an analogy, Hunter argues, judges are likely to rely less on principles than on impressionistic comparisons, which are subject to a variety of common cognitive constraints. For example, the "surface-level constraint" suggests that judges may place greater emphasis on superficial similarities and differences between cases than on more relevant jurisprudential or policy-based points of comparison.[204] Thus, two cases may seem similar because

197. Joy Horowitz, *For the Sake of Science*, L.A. TIMES MAG., Sept. 11, 1994.

198. *Id.*

199. Interview with Nancy N. Dubler, Director, Division of Bioethics, Montefiore Medical Center (Feb. 10, 2003).

200. *Cf.* William N. Eskridge, Jr. & John Ferejohn, *Structuring Lawmaking to Reduce Cognitive Bias: A Critical View*, 87 CORNELL L. REV. 616, 617 (2002) (suggesting that cognitive psychology "has not generated a sufficiently coherent body of empirically supported rules and meta-rules about human behavior in political institutional settings to serve as a basis for a model of decisionmaking").

201. Dan Hunter, *Reason Is Too Large: Analogy and Precedent in Law*, 50 EMORY L.J. 1197 (2001).

202. *See supra* text accompanying notes 166–71.

203. Hunter, *supra* note 201, at 1245–50.

204. *Id.* at 1215–16. This surface-level constraint is subject to manipulation by the parties, who can introduce additional surface-level factors into evidence to make some cases seem more analogous than others. *See id.* at 1218 ("The best trial lawyers are able to influence judicial assessments of similarity by a skillful manipulation of the context effect.").

they both involved car accidents, even if the cases otherwise have little to do with each other.[205]

Nonetheless, analogical reasoning should reduce some of the most common cognitive biases involved in risk assessment determinations, even if it does not eliminate them completely. The impact of the "framing bias,"[206] for example, might be mitigated if IRBs evaluate not only the risks as described in an individual protocol, but also descriptions of similar situations that have arisen at other IRBs. Similarly, to the extent the "availability heuristic"[207] causes individuals to place greater emphasis on readily available information, a system that encourages IRBs to incorporate multiple prior determinations into their analyses will broaden the information members are likely to recall. Recent research suggests that cognitive biases are most pronounced when individuals engage in rapid, intuitive types of decision-making, as opposed to methodologies that encourage a more reflective and self-aware approach.[208] Thus, to the extent that analogical reasoning would encourage a more self conscious and deliberate analytical process, it is likely that the impact of cognitive biases would be reduced.

A final advantage of incorporating analogical reasoning into IRB decision-making is that it might help individuals with different philosophical perspectives find a framework for analysis to which everyone can agree. Even on matters about which considerable disagreement exists, it should be possible to identify at least a few prior decisions whose outcome seems correct to most people,[209] or at least decisions whose outcomes the decision-makers are prepared to accept as binding. As Sunstein observes, individuals may often agree about certain low-level principles that can be generated from comparing a series of prior decisions, even if they disagree profoundly about larger questions of legal or political theory.[210] Thus, "reasoning by analogy may have the significant advantage of allowing people unable to reach anything like an accord on general principles to agree on particular outcomes."[211]

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205. Similarly, Loretta Kopelman suggests that the process of case comparison suffers from "problems of bias in describing, framing, comparing and using cases or paradigms." Loretta M. Kopelman, *Case Method and Casuistry: The Problem of Bias*, 15 THEORETICAL MED. 21, 23 (1994) (arguing that "we cannot identify what count as relevant features" of cases "unless we have general views about what is relevant; but some of our general views are biased, both in the sense of being unwarranted and in the sense that they may represent one-sided perspectives").

206. *See supra* text accompanying note 123.

207. *See supra* text accompanying notes 124–25.

208. Cass R. Sunstein, *Hazardous Heuristics* (unpublished manuscript), *available at* http://ssrn.com/abstract_id=344620, at 11–13 (last visited Mar. 9, 2003); *see also id.* at 13 (noting that "[f]requently, the legal system disregards this advice, relying on juries and hence on ordinary intuitions about probability and causation").

209. *See* Kuczewski, *supra* note 185, at 105 (suggesting that "thoughtful moral persons" are likely to agree on the outcome of certain cases even in the absence of an "elaborate vision of the good life or shared hierarchy of goods").

210. *See supra* note 155.

211. *Id.*

3. Limitations of Analogical Reasoning

Incorporating analogical reasoning into IRB deliberations also has potential drawbacks. One danger is that, if the decisions against which a situation is being compared are themselves the result of faulty analysis, an analogical reasoning process might simply replicate those initial mistakes. This problem of "bad beginnings"—the fact that, "almost surely, many of the legal materials in which the justifying legal principles are supposedly immanent will turn out to be morally mistaken"[212]—has led Larry Alexander to conclude that the process of analogical reasoning is either "impossible or perverse."[213] In a similar vein, some critics of casuistic reasoning in bioethics have argued that the process may inappropriately reinforce the ethical status quo, to the extent it relies on paradigm cases that may no longer reflect contemporary moral norms.[214]

The potential for analogical reasoning to reinforce initially bad decisions is a legitimate concern, but it does not mean that reasoning by analogy serves no useful purpose. It is important to differentiate analogical reasoning from the rote application of precedent. While analogical reasoning often is used in connection with authoritative precedents, it is not limited to that context. For example, courts often compare issues with cases decided in other jurisdictions, even though those prior cases do not have binding precedential effect. Such comparisons may suggest different ways of thinking about issues, or help the court recognize the full implications of a potential rationale. Even if the court ultimately rejects the approach taken in the other jurisdiction, the process of considering implications of competing approaches can help it reach a more informed result.

As long as IRB decisions continue to lack binding precedential value, the potential for analogical reasoning to reinforce initially bad decisions is less of a concern than it is in the judicial context. Even if the system is changed so that some IRB decisions are treated as binding authority,[215] all systems of precedent include methods for correcting manifest errors.[216] In some cases analogical reasoning may actually facilitate discovery of errors, as decision-makers test existing principles against new factual situations and evaluate previous factual situations in light of newly-developed norms.[217]

Another potential drawback of incorporating analogical reasoning into IRB decision-making is that the process can be difficult to apply to many of the open-ended problems that IRBs regularly encounter. Common-law analysis works best when prior determinations can be interpreted to yield a series of rule-like principles, which can then be deductively applied to resolve the particular issue at hand.[218] Deriving rule-like principles will sometimes be possible in the IRB context—for example, when IRBs rely on prior determinations to establish

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212. Larry Alexander, *Bad Beginnings*, 145 U. PA. L. REV. 57, 82 (1996).
213. *Id.* at 86.
214. *See, e.g.*, Arras, *supra* note 195, at 44–46.
215. *See infra* text accompanying notes 248–49.
216. *See* Planned Parenthood v. Casey, 505 U.S. 833, 854 (1992) (observing that "the rule of *stare decisis* is not an 'inexorable command'").
217. *See* Sunstein, *supra* note 155, at 768–69.
218. *See supra* text accompanying notes 166–71.

acceptable thresholds of pain or discomfort for minimal risk research, or when they look to prior decisions about interview or survey research to identify types of disclosures that could "be damaging to the subjects' financial standing, employability, or reputation."[219] However, most IRB decisions do not turn on such specific determinations; instead, they involve a more generalized risk-benefit balancing based on the totality of the circumstances. Brewer refers to such open-ended reasonableness determinations as "Gestaltist"-type judgments, a type of reasoning "that has the 'I can't say what it is, but I know it when I see it' structure."[220] He argues that, because such decisions are not easily translated into deductively-applicable rules, they are ill-suited to reasoning by analogy.[221]

Nonetheless, the fact that reasonableness determinations do not necessarily yield specific rule-like principles does not mean they are incapable of providing guidance for decision-makers. For example, prior risk assessments might suggest how much weight an IRB should give certain types of considerations, such as concerns about privacy risks associated with reviewing medical records,[222] or the uncertainty inherent in any investigation of an unproven drug. Similarly, they can suggest how to balance considerations that pull in different directions, such as the importance of enrolling an adequate number of subjects to generate sufficient statistical power, as compared to the danger that broad eligibility criteria will undermine the results' validity by introducing too many confounding variables.[223] While prior decisions may not provide specific rules for decision, they can help IRBs identify and valuevarious competing considerations.

This open-ended process of comparative evaluation is perhaps more similar to a casuistic model of moral analysis than to traditional common-law reasoning by courts. As Albert Jonsen suggests, casuistic decision-makers need not limit their focus to directly analogous prior situations. Instead, "[t]he ultimate view of the case and its appropriate resolution comes, not from a single principle, nor

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219. HHS Protection of Human Subjects, 45 C.F.R. § 46.101(b)(2)(ii) (2003). This determination is relevant to whether certain types of research, such as interview or survey procedures, can be exempted from IRB review.

220. Brewer, *supra* note 156, at 1000.

221. *Id.* at 992–93.

222. *See* David G. Forster, *Privacy and Confidentiality*, *in* INSTITUTIONAL REVIEW BOARD, *supra* note 184, at 169, 169–70.

223. *Cf.* Benjamin Freedman & Stanley H. Shapiro, *Ethics and Statistics in Clinical Research: Towards a More Comprehensive Examination*, 42 J. STATISTICAL PLANNING & INFERENCE 233 (1994) (discussing trade-offs between scientific validity and clinical generalizability). These methodological questions are an integral part of the risk assessment process, as studies that will produce no usable knowledge do not justify any level of risk to subjects, no matter how small. *See* Eran Bellin & Nancy Neveloff Dubler, *The Quality Improvement-Research Divide and the Need for External Oversight*, 91 AM. J. PUB. HEALTH 1512 (2002) (observing that "the IRB must evaluate scientific merit . . . since a protocol that will not produce useful data can support no risk").

from a dominant theory, but from the converging impression made by all of the relevant facts and arguments that appear in each of those spaces."[224]

In fact, Brewer's claim that analogical reasoning requires decisions that can be translated into deductively-applicable principles has more to do with specific characteristics of *judicial* analogies than with the relevance of open-ended determinations to analogical reasoning in general.[225] Thus, Brewer emphasizes that "the rule of law ideals of clarity, notice, and accountability presuppose that legal commands—including those embedded in legal analogies—are deductively applicable, and that vague norms—of the sort of which one is left if legal commands are not deductively applicable—are inconsistent with those basic values."[226] The importance of these "rule of law ideals" stems from the fact that individuals rely on the meaning of judicial decisions in determining what constitutes appropriate behavior; as Emily Sherwin notes, judicial analogies are "not only a judicial practice but an accepted tool of legal planning."[227] These concerns are not nearly as relevant in the context of IRBs' decisions about research protocols. Unlike judicial determinations, IRB decisions affect only the narrow question of whether a particular protocol may be conducted, not the rights and responsibilities of individuals throughout society. While investigators may rely on IRB decisions in structuring additional protocols, their ability to predict how the IRB will react in the future has few long-term consequences. If they misjudge the IRB's expected reaction, they can revise the protocol and resubmit it, or pursue different research. Thus, to the extent Brewer's concerns about "vague norms" relate to the reliance interest generated by judicial pronouncements, they have only limited application in the context of IRB review.

B. Written Opinions

As noted above, IRBs are generally under no obligation to specify reasons for their decisions.[228] While IRBs' final determinations must be recorded in the minutes, the minutes need not indicate the basis for decisions unless the IRB rejects or requests modifications of a protocol, or when there is a "discussion of controverted issues" in the course of a meeting.[229] Requiring IRBs to explain decisions to reject protocols but not to approve them is somewhat ironic, given that it is only when protocols are approved that the possibility of harming human subjects even arises. Moreover, the absence of "controverted issues" at a meeting is hardly a guarantee of a decision's appropriateness. On the contrary, it may simply be a sign that no one took the time to review the protocol carefully, or that

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224. Albert R. Jonsen, *Casuistry: An Alternative or Complement to Principles?*, 5 KENNEDY INST. ETHICS J. 237, 245 (1995).

225. Brewer quite explicitly limits his focus to the logical structure of judicial analogies. Brewer, *supra* note 156, at 990 ("The special institutional setting in which legal exemplary argument takes place should affect the theorist's interpretation of the logical form of the exemplary arguments that legal reasoners (especially judges) offer.").

226. *Id.* at 992–93.

227. Sherwin, *supra* note 172, at 1192.

228. *See supra* text accompanying note 88.

229. 45 C.F.R. § 46.115(a)(2) (2003).

the decision-making process did not include individuals with a sufficient diversity of perspectives to recognize potential problems with the study.

In contrast to IRBs, most judicial decisions involving significant legal questions are reported in formal written opinions. Unlike jury verdicts, which simply announce the jury's ultimate conclusion, judicial opinions typically include an extensive analysis of applicable issues and arguments. Many decisions are published, and even "unpublished" opinions are often accessible through on-line databases.[230]

Written opinions are also an important part of decision-making by administrative agencies. When agencies announce new regulations, for example, they must "provide a statement of basis and purpose that adequately explains the justifications, purposes, and legal authority for the rule and indicates compliance with regulatory analysis requirements imposed by statute."[231] In addition, decisions in formal adjudications before administrative law judges, while subject to less stringent requirements than agency rulemaking, must contain enough detail to enable a court to engage in meaningful judicial review.[232] If the decision departs from the agency's prior decisions in similar circumstances, it "must be accompanied by an explanation for that departure."[233]

In addition to written opinions announcing final determinations, both courts and agencies rely extensively on written evaluations at other stages of the decision-making process, albeit in a less formal sense. For example, a major part of a judicial law clerk's job is the preparation of "bench memos," which analyze issues in a case and arguments raised by the parties. These memos help provide a structure for the judge's analysis of the issues, and they are sometimes incorporated into the judge's final opinion. Decision-making within administrative agencies likewise relies on extensive written analyses. When the FDA reviews a new drug application, for example, members of interdisciplinary review teams set forth their conclusions in detailed written evaluations, each of which focuses on a specific aspect of the risk assessment process.[234]

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230. Kirt Shuldberg, Comment, *Digital Influence: Technology and Unpublished Opinions in the Federal Courts of Appeals*, 85 CAL. L. REV. 541, 566 (1997).

231. Section of Administrative Law and Regulatory Practice of the American Bar Association, *A Blackletter Statement of Federal Administrative Law*, 54 ADMIN. L. REV. 17, 35–36 (2002) [hereinafter *Blackletter Statement*] (noting that, although the Administrative Procedure states only that agencies must provide a "concise general statement of [the] basis and purpose" of rules, "courts have required that for rules likely to have major economic or other impacts the statement (a) must demonstrate that the agency fully considered significant alternatives to its final rule, important public comments, and relevant information and scientific data and (b) must explain the agency's rejection of any of the foregoing").

232. *Id.* at 28 ("It is sufficient if the bases of its decision are reasonably discernible and a reviewing court can satisfy itself that the agency took a 'hard look' at the relevant issues.").

233. *Id.*

234. Michelle Meadows, *The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective*, FDA CONSUMER, July–Aug. 2002, *available at* http://www.fda.gov/fdac/features/2002/402_drug.html.

Incorporating written evaluations into IRB decision-making could improve risk assessment in a number of ways. At a minimum, written opinions would provide the necessary information for decisions to serve as a basis for analysis in future cases, whether as binding authority[235] or simply a source of ideas. In addition, an obligation to write opinions would force IRBs to develop articulable reasons for their decisions, rather than simply relying on impressionistic judgments or gut reactions.[236] In this way, writing opinions could help mitigate the impact of cognitive biases on the risk assessment process.

Writing opinions also is likely to contribute to consistency and rationality in IRB risk assessments. As Frederick Schauer argues, giving reasons for a decision implicitly functions as a promise of consistency, limiting the likelihood that the decision-maker will arbitrarily change her mind in future situations.[237] Opinions also facilitate the development of generalizable principles, as the essence of giving a reason for a decision "is to include that decision within a principle of greater generality than the decision itself."[238] Thus, when decision-makers do not state reasons for their judgments, it is typically in contexts in which consistency and generalizability are not considered important values—for example, when juries announce verdicts, or when the Supreme Court denies *certiorari*.[239] If we believe that IRBs should strive to make principled decisions, encouraging them to provide reasons for decisions will go a long way toward promoting that goal.

Incorporating opinion writing into IRB decision-making would be valuable even if few people ever read the opinions, as the writing process itself would force IRB members to think more carefully about the issues they are considering.[240] As anyone who has ever written a paper or article is aware, one's views can change considerably in the process of putting them down on paper, as

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235. *See infra* text accompanying notes 248–49.

236. For similar reasons, Norman Daniels and James Sabin recommend that insurance companies employ a "case law" system when they make decisions about whether to cover particular health interventions. In addition to promoting more carefully reasoned decisions, a case law approach would "promote a deliberative process in which decision makers and affected persons determine over time what counts as acceptable reasons" for particular results. REBECCA DRESSER, WHEN SCIENCE OFFERS SALVATION: PATIENT ADVOCACY & RESEARCH ETHICS 86 (2001) (commenting on Norman Daniels and James Sabin, *Limits to Health Care: Fair Procedures, Democratic Deliberation, and the Legitimacy Problem for Insurers*, 26 PHIL. & PUB. AFFAIRS 303 (1997)).

237. Frederick Schauer, *Giving Reasons*, 47 STAN. L. REV. 633, 645 (1995) (arguing that giving reasons constitutes an implicit promise to apply those reasons consistently in future situations).

238. *Id.* at 641. As James Boyd White argues, when judges write opinions they say "not only 'This is the right outcome for this case,' but also, 'This is the right way to think and talk about this case, and others like it.'" James Boyd White, *What's an Opinion For?* 62 U. CHI. L. REV. 1363, 1366 (1995). The opinion is therefore the cornerstone of the law's effort to "explain[] and limit[] itself over time." *Id.* at 1367.

239. *See* Schauer, *supra* note 238, at 637 (discussing contexts in which decision-makers are not required to give reasons for decisions).

240. *See* United States v. Merz, 376 U.S. 192, 199 (1964) (observing that judges "will give more careful consideration to the problem if they are required to state not only the end result of their inquiry, but the process by which they reached it").

writing out an argument can expose its deficiencies or reveal unforeseen implications. Similarly, writing opinions can serve as a check against bias, self interest, or simply excessive haste.[241]

A final reason it is important for IRBs to document their decision-making process more carefully is to facilitate more effective external oversight of the IRB system. Without contemporaneous statements of the IRB's reasons for decisions, it is impossible to know whether decisions were based on adequate analysis. If federal auditors, private accreditation teams, and other external overseers are to do more than simply check the adequacy of record-keeping and other administrative matters, they need a means to assess the quality of IRBs' reasoning, not simply their compliance with procedural requirements related to protocol review.

C. Appellate Review and Precedent

Both appellate review and precedent are mechanisms that constrain the discretion of individual decision-makers by giving certain interpretations of the law priority over others. In a system of appellate review, decisions made by individuals or institutions at a higher level of the hierarchy trump decisions made by those at lower levels. In a system of precedent, decisions made in the past limit decision-makers' options in the future. While it would be possible to have appellate review without precedent, or precedent without appellate review, the two mechanisms usually function in tandem. As a result, they become mutually reinforcing mechanisms for constraining discretion—appellate review by ensuring that judgments that will have precedential effect have been adequately considered, and precedent by ensuring that lower-level decision-makers will adhere to the appellate court's approach in future cases.

As currently designed, the IRB system relies on neither appellate review nor precedent to limit individual IRBs' discretion. Instead, each IRB essentially operates as an independent jurisdiction, lacking direction from either a higher tribunal or past authoritative decisions. Few constraints therefore exist regarding how individual IRBs interpret regulatory standards. As noted above, the IRB system's radical localism reflects an intentional policy decision by the system's designers, who believed that the protocol review process must be entrusted to individuals familiar with local conditions and the attitudes of the population from which subjects are drawn.[242]

This emphasis on local autonomy, however, comes with significant costs. By insulating local IRBs from external scrutiny in all but the most egregious of situations (and even then, only after harm to the subjects has already occurred), the system does nothing to prevent arbitrary or irrational decision-making. A system that treats all IRB decisions as essentially unreviewable also makes it unlikely that coherent decision-making principles or guidelines will develop over time. In the judicial system, appellate court oversight is essential to the coherent evolution of the law: While lower courts may experiment with innovative approaches to novel situations, the appellate courts ensure the law's long-term coherence by

241. *See* Schauer, *supra* note 237, at 657.

242. *See supra* text accompanying notes 96–97.

overturning lower court decisions that depart too much from prevailing legal norms. Without this ongoing dialogue between lower courts and courts of appeals, there would be fewer constraints on innovation by lower court judges, but there also would be no one to synthesize disparate approaches, identify and enforce broad legal principles, or weed out inappropriate solutions adopted by particular lower court judges.

The system's emphasis on local decision-making is also difficult to reconcile with contemporary sociological reality. While different parts of the United States clearly have distinct local or regional characteristics, developments in communications and transportation have made these differences far less pronounced today than they were when the IRB system was first developed. Moreover, to the extent these differences continue to exist, they are more likely to be relevant to issues like subject recruitment or informed consent than to assessment of a protocol's underlying risks and benefits. For example, in a community with a large immigrant population, it would be important to take into account language and cultural barriers in determining the type of information that should be provided to prospective subjects, or the manner in which that information should be conveyed. However, it is unlikely that the perceived risk of, for example, developing a painful rash from a trial of a new psoriasis medication depends on factors that are specific to particular parts of the country.

In fact, the system's emphasis on localism is already beginning to give way, due largely to practical considerations raised by increasing use of multi-site studies. In some cases, investigators in multi-site studies are not affiliated with any research institution, making it impossible to obtain local review at all study sites. As a result, some reviews may be conducted by centralized IRBs, including "non-institutional IRBs" that are managed by private companies.[243] These IRBs attempt to balance consideration of issues common to all research sites, with attention to special considerations likely to confront researchers in particular locations.[244] Another example of the move away from purely local decision-making is the National Cancer Institute's newly-developed process of combined centralized and local review for large multi-site studies.[245] Developed in collaboration with the OHRP, the system relies on centralized review of major issues by a diverse national panel of experts and laypersons, followed by a more streamlined review of local considerations by local IRBs.[246]

These developments appropriately recognize that many issues surrounding research are not location-specific, and that attention to local considerations is not inconsistent with more centralized review. Accordingly, to

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243. NAT'L BIOETHICS ADVISORY COMM'N, *supra* note 23, at 117–18.

244. For example, the Western Institutional Review Board ("WIRB"), one of the most prominent and well regarded commercial IRBs, has a large network of regional representatives and local advisors. According to WIRB's website, "[t]he use of these consultants, as well as WIRB liaison with local IRBs when possible, allows WIRB to accurately gauge local attitudes and customs that could affect the research." WIRB website, *at* www.wirb.com (visited Mar. 9, 2003).

245. Michaele C. Christian et al., *A Central Institutional Review Board for Multi-Institutional Trials*, 346 NEW. ENG. J. MED. 1405 (2002).

246. *Id.*

the extent local IRBs continue to dominate the system of human subject protection,[247] there is no reason to insulate them from some form of centralized oversight. One issue that would have to be determined if an appellate system is developed is the circumstances that would trigger appellate review. In most situations, the only individuals with a sufficient stake in the process to request an appeal will be the investigators, who would obviously appeal only when the IRB rejects their proposed research. However, the purpose of appellate oversight should be to ensure the quality and consistency of IRB deliberations, not simply to give disgruntled investigators a second bite at the apple. As such, there also should be some process for appellate review of decisions to approve research—for example, by providing for review of any decision involving a specified number of dissenting votes, or any decision involving certain categories of sensitive determinations (e.g., decisions about protocols in which members of vulnerable populations will be exposed to greater-than-minimal risks with no prospect of direct benefit). Such a system might also include a mechanism for IRBs to petition the appellate panel for review of any study the IRB considers worthy of further scrutiny, even if it does not fit within a specified category automatically eligible for appellate review.[248]

If the IRB system is modified to incorporate appellate review, it would be appropriate to treat appellate decisions as binding on decision-makers of lesser authority, just as decisions of appellate courts are binding precedent for lower court judges. It would not make sense, however, to consider determinations by decision-makers at equivalent levels of authority as binding on one another, as doing so would arbitrarily grant priority to whichever board happened to confront a particular issue first. Instead, decisions of IRBs at co-equal levels of authority should be treated like decisions of district court judges—"persuasive authority" for subsequent decision-makers, but without any formal precedential effect.[249]

Whether IRBs should treat *their own* prior decisions as binding is a more difficult question. On the one hand, if IRBs knew that they would be obligated to follow whatever approach they adopt today in their deliberations tomorrow, they might apply more care to the decision-making process. Federal judges' increasing tendency to issue unpublished decisions has generated controversy in part because

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247. Some commentators have called for the complete elimination of local IRBs. *See, e.g.*, Emanuel, *supra* note 80 (proposing the establishment of regional ethics boards in place of the local IRB system); Harold Edgar & David J. Rothman, *The Institutional Review Board and Beyond: Future Challenges to the Ethics of Human Experimentation*, 73 MILBANK Q. 489 (1995) (suggesting the use of national, topic-specific advisory panels). Even under a regional or national system, an appellate process would remain important to ensure external oversight of decisions and to reconcile incompatible approaches adopted by different boards.

248. Alternatively, instead of (or in addition to) an appellate process, the agencies in charge of regulating human subject research could develop a process for IRBs to request written guidance on complicated or controversial protocols, much like the DHHS Inspector General issues advisory opinions interpreting the fraud and abuse laws. *See* HHS Advisory Opinions by the OIG, 42 C.F.R. § 1008 (2003).

249. *See* John Harrison, *The Power of Congress Over the Rules of Precedent*, 50 DUKE L.J. 503, 518 (2000) (noting that "the federal district courts regard their precedents as persuasive authority only").

of the concern that judges who write nonbinding opinions may be tempted to ignore important legal norms.[250] On the other hand, an obligation to treat prior determinations as binding precedents might be difficult to enforce, particularly for open-ended determinations whose resolution does not lead to deductively-applicable rules.[251] Moreover, treating every IRB decision as binding on future deliberations might inappropriately lock the IRB into an approach that, upon further reflection, turns out to be misguided. For issues that will never be appealed to a higher authority, the IRB should be free to change its mind if it decides that an approach taken in the past no longer seems correct.

Rather than treating IRB decisions as binding precedents, it therefore makes more sense to encourage IRBs to strive to render judgments that can be reconciled with one another whenever appropriate. Incorporating analogical reasoning into the process would be an important step in that direction. Like administrative law judges,[252] IRBs also should be required to indicate when they are departing from approaches they took in the past, and to explain their reasons for doing so.

D. Notice-and-Comment Rulemaking

Given that IRBs' authority to review and approve research protocols ultimately derives from powers that have been delegated to them by administrative agencies,[253] one way to promote greater rationality in IRB decision-making would be for these agencies to develop specific rules governing particular aspects of the risk assessment process.[254] Like a system of appellate review for particularly sensitive issues,[255] a regulatory approach to risk assessment would remove certain issues from local decision-makers' discretion, reducing the potential for outcomes to turn on the idiosyncratic perspectives of particular IRB members or other arbitrary or irrational considerations.[256]

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250. *See, e.g.*, Johanna S. Schiavoni, Comment, *Who's Afraid of Precedent? The Debate over the Precedential Value of Unpublished Opinions*, 49 UCLA L. REV. 1859, 1882 (2002) (arguing that the publication requirement promotes judicial accountability for decisions).

251. *See supra* text accompanying notes 218–21.

252. *See supra* text accompanying notes 232–33.

253. *See supra* text accompanying note 17.

254. The FDA and OHRP occasionally issue guidance statements to IRBs about specific issues. U.S. FOOD AND DRUG ADMIN., GUIDANCE AND INFORMATION SHEETS ON GOOD CLINICAL PRACTICE IN FDA-REGULATED CLINICAL TRIALS, *available at* http://www.fda.gov/oc/gcp/guidance.html (last visited Mar. 9, 2003); U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, OFFICE OF HUMAN RESEARCH PROTECTIONS, GUIDANCE TOPICS BY SUBJECT, *available at* http://ohrp.osophs.dhhs.gov/g-topics.htm (last visited Mar. 9, 2003). However, the guidance sheets do not have the legal status of regulations. Moreover, none of them directly addresses the process of risk assessment.

255. *See supra* text accompanying note 248.

256. By their very nature, rules leave less discretion to decision-makers than open-ended standards. Legal norms expressed as standards set forth general criteria for resolving certain questions, but they delegate the ultimate application of those criteria to subsequent decision-makers. Rules, by contrast, limit the discretion of subsequent decision-

A regulatory approach also would promote broader public participation in the decision-making process. Unlike the insular process of IRB deliberations, agencies considering a new rule must publish a notice in the Federal Register, and they must allow sufficient time for interested members of the public to provide written comments on the rule.[257] The agency must make all of these comments available to the public, as well as any written factual material, studies, and reports relied on or seriously consulted by agency personnel in formulating the rule.[258] In addition to encouraging the agency to consider multiple perspectives on the issues being considered, these requirements promote public scrutiny of the decision-making process by making the public aware of pending decisions and the information on which those decisions will be based.

A possible objection to adopting specific risk assessment rules is that they would be unduly rigid, incapable of taking into account the circumstances of individual situations or differences in local conditions and attitudes. While these are valid considerations, they suggest only that the regulatory approach should be limited to certain types of determinations, not that it should be rejected entirely. At a minimum, the rulemaking process should be limited to matters that (1) involve questions of significant public concern; (2) arise with sufficient regularity to make it worthwhile to undertake the burdens of the rulemaking process; and (3) raise issues whose resolution is unlikely to turn on case-specific factors, including factors related to particular local conditions or attitudes. Possible examples of such situations include applying the "minimal risk" definition to certain commonly-used procedures,[259] or developing policies regarding the appropriateness of controversial research techniques like placebo controls[260] or "washout" periods in which subjects are taken off medications prescribed to them outside the research.[261] To leave room for flexibility, the regulations could permit exceptions to generally applicable rules upon application to the agency.

Even without engaging in the complex notice-and-comment rulemaking process, agencies could draw on certain aspects of the process to encourage greater public participation in particular risk assessment questions. One model for such a system is the existing process for reviewing pediatric research protocols that do not meet the usual requirements for IRB approval (typically, because the study involves significant risks and no prospect of direct benefit to the children in the study).[262] In these situations, the Secretary of DHHS is authorized to approve the

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makers by specifying how particular issues should be resolved. HENRY M. HART, JR. & ALBERT M. SACKS, THE LEGAL PROCESS: BASIC PROBLEMS IN THE MAKING AND APPLICATION OF LAW 139–40 (William N. Eskridge, Jr. & Philip P. Frickey eds., 1994).

257. *Blackletter Statement*, *supra* note 231, at 34.

258. *Id.* at 34–35.

259. *See supra* text accompanying note 173–76.

260. *See* Sharona Hoffman, *The Use of Placebos in Clinical Trials: Responsible Research or Unethical Practice?* 33 CONN. L. REV. 449, 499 (2001) (arguing that rules governing the use of placebos in clinical trials should be incorporated into the federal research regulations).

261. *See supra* text accompanying notes 197–99.

262. *See* HHS Protection of Human Subjects, 45 C.F.R. § 46.407 (2003).

research after consultation with "a panel of experts in pertinent disciplines,"[263] based on a determination that the research "presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children" and that it "will be conducted in accordance with sound ethical principles."[264] In carrying out his responsibilities under these provisions, the Secretary of DHHS (along with the Secretary of the FDA) recently issued requests for public comment about two studies involving children, each of which raised issues that could not be resolved by local IRBs. One study involved the testing of Dryvax, a smallpox vaccine, on children two to five years of age;[265] the other involved a longitudinal study to determine precursors to diabetes among Japanese-American youth.[266] Both studies received extensive comments from interested members of the public.[267] Such protocol-specific notice-and-comment procedures could easily be extended to other risk assessment determinations raising unprecedented questions or significant public concerns.

A modified version of this process also could be adopted at the level of local IRBs, without requiring the direct involvement of regulatory agencies. For example, IRBs confronting novel issues for which analogies to prior determinations are unhelpful could be encouraged to solicit public input by requesting written submissions from interested individuals or organizations, or by holding public hearings or community forums. Such an approach could be modeled on the system for waiving informed consent in research involving incapacitated patients in emergency settings. Under FDA regulations adopted in 1996, IRBs may approve such waivers in certain circumstances, provided they first consult with members of the community from which subjects are likely to be drawn.[268] This process of community consultation is typically carried out by a combination of meetings with local leaders, solicitation of public comments, and

263. *Id.* § 46.407(b).

264. *Id.* § 46.407(b)(2)(i)–(ii). In its report on research involving persons with mental disorders, the National Bioethics Advisory Commission proposed a similar mechanism for certain categories of research involving individuals with mental disorders that impair decision-making capacity. NAT'L BIOETHICS ADVISORY COMM'N, *Moving Ahead in Research with Persons with Mental Disorders: Summary and Recommendations*, in 1 RESEARCH INVOLVING PERSONS WITH MENTAL DISORDERS THAT MAY AFFECT DECISION-MAKING CAPACITY 54 (1998).

265. Solicitation of Public Review and Comment on Research Protocol: "A Multicenter, Randomized Dose Response Study of the Safety, Clinical and Immune Responses of Dryvax Administered to Children 2 to 5 Years of Age," 67 Fed. Reg. 66,403 (HHS Oct. 31, 2002).

266. Proposed Research Protocol: Precursors of Diabetes in Japanese American Youth, 67 Fed. Reg. 77,495 (HHS, Dec. 18, 2002).

267. The Dryvax study was subsequently withdrawn, following changes in smallpox preparedness plans that made the investigation of Dryvax unnecessary. U.S. Department of Health and Human Services, Office of Human Research Protections web page, http://ohrp.osophs.dhhs.gov/dpanel/dpindex.htm (last visited Mar. 9, 2003). The comment period for the diabetes study is still open. *Id.* at http://ohrp.osophs.dhhs.gov/whatsnew.htm#PROTOCOL.

268. FDA Protection of Human Subjects, 21 C.F.R. § 50.24(a)(7) (2003).

community meetings,[269] strategies that could be extended to other types of protocols raising community-wide concerns.

V. AN AGENDA FOR REFORM

Transforming the process of IRB review along the lines described above will require the coordinated efforts of numerous actors, including federal agencies, researchers and research institutions, and IRBs themselves. For some of the proposed strategies, regulatory and/or legislative changes would be necessary—for example, in order to establish a system of appellate review, or to require IRBs to issue written opinions. All the proposed changes will require a fundamental shift in the way that IRBs conceive of their role. Of all the strategies discussed in this Article, incorporating the model of analogical reasoning into IRB decision-making raises the most far-reaching issues, as it strikes at the heart of the current jury-like model of protocol review. This Part therefore expands on some practical considerations such a transformation would raise.

Initially, it should be apparent that a system of protocol review modeled on common-law judging would require a much greater investment of time and resources than a jury-like deliberative process. Not only will someone have to prepare written opinions about particular decisions, but a system will have to be developed to track those opinions, and as new protocols are reviewed someone will have to search that system to identify relevant prior cases. It is unrealistic to expect unpaid IRB members to assume these responsibilities. Thus, the proposal will require a major infusion of resources to a system that already is severely underfunded,[270] at a time of shrinking federal budgets and cutbacks in spending by private philanthropy. Yet, if we are serious about reforming the human subject protection system, we must accept the fact that doing so will cost money. No other legal institution entrusted with life-or-death decisions is dependent almost entirely on the efforts of unpaid volunteers. Moreover, paying for a more rigorous IRB review process can be seen as an investment in the future of biomedical research, to the extent it will help regain public trust in the oversight system's integrity.[271]

Assuming sufficient staff to issue written opinions, another problem will be ensuring that those opinions say something meaningful, rather than simply reiterating what is already described in the protocol itself. As anyone who has ever read the minutes of a faculty meeting knows, it is all too easy to create an accurate record of a discussion without revealing anything interesting or useful to persons who were not in attendance. In contrast to judges, IRB staff are unlikely to be motivated to issue well-crafted decisions by a desire for fame or the possibility of being elevated to a more prestigious job. Moreover, other pressures may motivate them in the opposite direction, including time and resource constraints and concerns that their decisions will be used against them if a subject is injured and a lawsuit is brought. Accordingly, in addition to devoting resources to training and feedback, it will be important to develop incentives for IRB staff that reward good

269. Helen McGough, *Waiver of Consent in Emergency Medicine Research*, *in* INSTITUTIONAL REVIEW BOARD, *supra* note 184, at 132, 134–35.

270. *See supra* text accompanying notes 62–63.

271. *See supra* text accompanying note 14.

opinion writing. In addition, opinion quality should be a component of federal audits and inspections by accrediting agencies.

For opinions to be useful, they also will have to be compiled and made accessible to future decision-makers. The most sensible way to do this would be to create a computerized database of opinions, ideally one that is searchable by keywords and/or digested according to an indexing system like the West key numbers.[272] Creating such a database would obviously raise concerns about confidentiality. Some of these issues might be addressed by redacting sensitive information, or perhaps by delaying a study's inclusion until the results are published.[273] Ultimately, however, sponsors' and investigators' desire for confidentiality should not come at the expense of constructing an effective system for disseminating information that could facilitate better reviews. Confidentiality concerns also should not be used as a shield to limit the public's ability to participate in and oversee the decision-making process. Thus, barring exceptional reasons requiring the protection of particular information, both IRB deliberations and their written opinions should be open to the public.[274]

Even if the changes proposed in this Article are accepted in principle, implementing these changes will not happen overnight. In the meantime, there are several modest steps IRBs could take to lay the groundwork for a more systematized approach to the risk assessment process. For example, IRBs could voluntarily share more information about their decision-making process through listservs,[275] academic conferences, and professional journals. In addition, medical journals could ask researchers to include an "IRB deliberations" section as a standard element of a published research report.

The potential value of analogical reasoning for IRB deliberations also has implications for educational programs for IRB members. Instead of focusing exclusively on general principles of research ethics or specific federal regulatory

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272. On the impact of the key number system on the development of common-law reasoning, see Robert C. Berring, *Collapse of the Structure of the Legal Research Universe: The Imperative of Digital Information*, 69 WASH. L. REV. 9, 21 (1994) (arguing that the key number system was inherently conservative, as all decisions had to be classified into pre-existing categories established by the classification system). The potential for an indexing system to limit the manner in which IRBs analyze issues is less significant today, as it could be combined with more open-ended search features like those available on Lexis or Westlaw. *Id.* at 30–31 (noting that, with the advent of online databases that permit Boolean searching, "[i]nstead of a pre-coordinated index into which all data is funneled, the database now stands open for post-coordinated indexing by the searcher").

273. Of course, this option would not work for either long-term studies or for protocols that are rejected.

274. *See supra* text accompanying notes 83–84. A possible model for such a database is the Genetic Modification Clinical Research Information System ("GeMCRIS"), a database being developed by the federal Office of Biotechnology Activities for disseminating information about gene transfer research. The GeMCRIS will have different levels of access for different visitors, including the general public. *See* Nancy M.P. King, *RAC Oversight of Gene Transfer Research: A Model Worth Extending?* 30 J.L. MED. & ETHICS 381, 385–86 (2002).

275. An existing listserv where such discussions already take place is the "IRB Forum," *at* http://www.irbforum.org (last visited Mar. 9, 2003).

requirements, educational programs also should train IRB members in the process of case-based decision-making. Just as law students are trained by reading cases, discussing their nuances, and considering the implications of changes in the facts, the case method should become a standard part of IRB members' training and continuing education. The overall message to IRBs should be that good decision-making requires more than good ethical principles and a desire to do the right thing; it depends on careful application of specific analytical skills.

VI. CONCLUSION

Serving on an IRB is often a thankless task. IRB members assume difficult and time-consuming responsibilities for no compensation and with little support. Despite these constraints, many IRBs work hard to develop an ethically responsible and intellectually rigorous process for reviewing protocols. However, even if some IRBs work well, a responsible human subject protection system requires a decision-making process expressly designed to avoid arbitrariness, inconsistency, or otherwise inappropriate determinations. The current jury-like process of IRB deliberations is inherently incapable of achieving those goals.

Incorporating the decision-making mechanisms suggested in this Article will not prevent all excessively risky research from taking place. No decision-making process will result in correct determinations in every situation, and even research that is approved for good reasons may ultimately result in some harm. However, to the extent the mechanisms proposed in this Article will lead IRBs to be more careful and rigorous in decisions about risk assessment, they are likely to result in fewer decisions to approve research that involves unjustifiable risks. By reducing the system's perceived arbitrariness and irrationality, they should also go a long way toward restoring the public's trust.

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