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Critical Care Research and Informed Consent

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CRITICAL CARE RESEARCH AND INFORMED CONSENT

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The doctrine of informed consent severely limits the ability of medical researchers to develop, evaluate, and refine investigational technologies for the treatment of patients suffering from heart attacks, strokes, and other "critical care" conditions. In this Article, Mr. Saver examines the current doctrine of informed consent as applied to critical care research and its various deficiencies. In addition, he analyzes recent reforms proposed by the Food and Drug Administration, which are intended to remove certain obstacles to critical care research posed by informed consent. While the proposed reforms address several of the current deficiencies, he asserts that they lack the breadth and scope necessary to advance the progress of critical care research in an ethical and sensible manner. Mr. Saver proposes several complementary and alternative reforms that would better accomodate the interests of all affected parties: the patients, their families, the researchers, and the general public.

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INTRODUCTION

Approximately 350,000 people suffer sudden heart attacks in the United States each year. Most die. Bystanders resuscitate only a small percentage of persons experiencing cardiac arrest.[1] Of those who live long enough to be admitted to a hospital, less than twenty-

1. *See* Don Colburn, *CPR From Bystanders Often Not Done Right*, WASH. POST, Jan. 2, 1996 (Health Insert), at 5. When the cardiac arrest occurs outside the hospital, only about 20-30% of victims survive. *See* SHERWIN B. NULAND, HOW WE DIE 41 (1994). The likelihood of survival drops to near zero for patients who have not responded to cardiopulmonary resuscitation by the time of arrival at the hospital. *See id.*

five percent survive to leave. Among this group, many are often irreversibly impaired by brain damage, organ malfunctions, and other devastating complications.[2]

Given these grim statistics, researchers have questioned whether standard cardiopulmonary resuscitation (CPR) techniques can be improved in terms of better survival rates or quality of life factors for post-cardiac arrest victims. Because current CPR practices were developed on a mostly theoretical basis, few controlled studies of CPR techniques or other cardiac arrest treatments have been conducted.[3] Thus, much of what has become standard medical therapy for use in resuscitative clinical care has not been sufficiently evaluated by investigational trials that demonstrate safety or effectiveness. Research in this area has been impeded by the near impossibility of satisfying legal standards for informed consent. Until recent regulatory reforms, the applicable law, consisting primarily of federal regulations governing human subjects research, required that prospective informed consent be obtained from subjects before the administration of experimental therapies, with few available exceptions. For example, the Food and Drug Administration (FDA) recently halted clinical trials of the "Cardiopump" active compression-decompression cardiopulmonary resuscitation device, a plunger-like mechanism developed for the administration of new CPR techniques. FDA stopped the Cardiopump trials in part because subjects were unable to provide prospective consent to participate in the research.[4]

Obtaining the prospective informed consent from a patient under circumstances such as cardiac arrest is impossible. The patient is unable to communicate and/or lacks decisional capacity, but the experimental therapy must be applied before the patient stabilizes and regains the capability of providing legally effective consent. This Article refers to such situations as "critical care." In critical care settings, the patient's decisional or communicational incapacity may be temporary or permanent.[5] Typical conditions that impair the criti-

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2. *See Waiver of Informed Consent: A Critical Issue for Improving Treatment of Emergent Medical Conditions*, North American Society of Pacing and Electrophysiology Government Relations Committee Position Statement, Testimony presented at FDA/NIH Public Forum (1995) [hereinafter *FDA/NIH Public Forum Testimony*]; *see also* NULAND, *supra* note 1, at 40 (explaining that when the brain is starved of oxygen during a heart attack for longer than two to four minutes, brain damage becomes irreversible).

3. *See FDA/NIH Public Forum Testimony*, *supra* note 2.

4. *See* Carin M. Olson & Drummond Rennie, *Plungers and Polemics: Active Compression-Decompression CPR and Federal Policy*, 273 JAMA 1299, 1299 (1995).

5. What constitutes decisional incapacity is beyond the scope of this Article. In many critical care situations, patients are completely unconscious or unable to communi-

cal care patient include stroke, coma, seizure, cardiac arrest, senility, depression of mental faculties, drug overdose, head trauma, poisoning, hemorrhagic shock, acute asthma attacks, and pulmonary embolism.[6] The state of incapacity may be slowly progressive, as with the cognitive impairments arising from dementia or Alzheimer's disease,[7] or sudden and severe, such as can occur with head trauma or the onset of a coma. Satisfying the informed consent requirements proves problematic even with conscious critical care patients because they experience extreme duress and often cannot provide legally effective consent. Indeed, critical care patients able to respond to questions about research participation often later do not remember having consented to become subjects.[8]

The legal difficulties and controversy surrounding the Cardiopump trials demonstrate a fundamental problem common to critical care research. Although researchers have developed investigational technologies and techniques that can be applied to patients in critical care situations,[9] many such therapies require rapid application to be effective[10] and satisfying the informed consent requirement presents a

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cate. However, questions of patient competence and decisional capacity can be more difficult to judge, for example, in patients with certain neurological problems. *See generally* Morris Freedman et al., *Assessment of Competency: The Role of Neurobehavioral Deficits*, 115 ANNALS INTERNAL MED. 203 (1991) (proposing guidelines for assessing competency in patients with cognitive deficits due to neurological disorders); Edmund G. Howe et al., *Medical Determination (and Preservation) of Decision-Making Capacity*, 19 LAW MED. & HEALTH CARE 27 (1991) (contending that patients suffering from depression may not be equipped to make competent medical decisions).

6. *See* Charles R. McCarthy, *To Be or Not to Be: Waiving Informed Consent in Emergency Research*, 5 KENNEDY INST. ETHICS J. 155, 155 (1995); Paul B. Solnick, *Proxy Consent for Incompetent Non-Terminally Ill Adult Patients*, 6 J. LEGAL MED. 1, 2 (1985).

7. *See* Dallas M. High, *Research with Alzheimer's Disease Subjects: Informed Consent and Proxy Decision Making*, 40 J. AM. GERIATRICS SOC. 950, 950 (1992) (noting that persons afflicted with Alzheimer's disease are, by definition, on a path of declining capacity to consent to research); Dale L. Moore, *An IRB Member's Perspective on Access to Innovative Therapy*, 57 ALB. L. REV. 559, 578 (1994).

8. *See Researchers Seeking More Freedom for ER Experiments*, PHYSICIANS FIN. NEWS 16 (indicating that in a trial of heart-attack patients who went through the consent process only 48% of patients even remembered signing the consent form and only half remembered receiving the experimental therapy).

9. *See* William H. Spivey et al., *Informed Consent for Biomedical Research in Acute Care Medicine*, 20 ANNALS EMERGENCY MED. 1251, 1251 (1991).

10. *See* Carin M. Olson, *The Letter or the Spirit: Consent for Research in CPR*, 271 JAMA 1445, 1445 (1994). For example, irreversible organ damage may occur before the patient can be expected to regain consciousness. *See* Norman S. Abramson et al., *Deferred Consent: A New Approach for Resuscitation Research on Comatose Patients*, 255 JAMA 2466, 2467 (1986). Similarly, research into the benefits of thrombolytic therapy for heart attack victims shows that the timing of drug administration is crucial. *See* Pamela S. Grim et al., *Informed Consent in Emergency Research: Prehospital Thrombolytic Therapy for Acute Myocardial Infarction*, 262 JAMA 252, 254 (1989); *see also* National

significant obstacle to clinical investigations.[11] Apart from the Cardiopump trials, several other experimental investigations have grounded to a halt because of liability concerns related to waiving informed consent.[12] This occurs at a time of renewed concern about the ethical conduct of medical experimentation generally[13] and, as a

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Institute of Neurological Disorders and Stroke, *Tissue Plasminogen Activator for Acute Ischemic Stroke*, 333 NEW ENG. J. MED. 1581, 1581 (1995) (asserting that treatment of stroke with intravenous recombinant tissue plasminogen activator improves clinical outcomes if administered within three hours of onset of ischemic stroke).

11. *See* Protection of Human Subjects; Informed Consent, 60 Fed. Reg. 49,086, 49,090 (1995) (to be codified at 21 C.F.R. pt. 50) (proposed Sept. 21, 1995). At one academic medical center, a protocol for a randomized clinical trial of high dose versus standard dose epinephrine in cardiac arrest failed to receive necessary approvals, even though clinicians at the medical center were split on the merits and some used the high dose treatment as conventional therapy while others did not. *See id.* The research was not approved due to informed consent obstacles, with the result that no data was available from a controlled clinical trial to test which dosage schedule of the drug was truly more effective. *See id.*; *see also Problems in Securing Informed Consent of Subjects in Experimental Trials of Unapproved Drugs and Devices: Hearings Before the Subcomm. on Regulation, Bus. Opportunities, and Tech. of the House Comm. on Small Bus.*, 103rd Cong., 14-17, 111-16 (1994) (testimony of Jeffrey Koepsell, President, Cardiologic Systems, Inc.) [hereinafter *Problems in Securing Informed Consent*] (describing how obtaining prospective informed consent in a trial of a vest-CPR system, by seeking out potential cardiac arrest victims, would require approaching approximately 260,000 patients to enroll 400 at a cost of $1.4 million).

12. For example, a sponsor stopped a study at the University of Nebraska Medical Center involving closed head injury victims given an experimental drug to help control cerebrovascular damage. The sponsor reevaluated its position and stated that the trial could continue only with the prospective informed consent of subjects. This compromised the study's statistically valid sample and delayed enrollment, resulting in failure to evaluate the test drug under optimal conditions of rapid application. *See* Ernest D. Prentice et al., *IRB Review of a Phase II Randomized Clinical Trial Involving Incompetent Patients Suffering from Severe Closed Head Injury*, IRB, Sept.-Oct. 1993, at 1.

Dr. John Barrett, director of Cook County Hospital's trauma unit, proposed a new treatment to the hospital's research review committee involving administration of experimental treatment to unconscious, head-injury patients in the emergency room. The committee found the study promising but, concluding that the hospital would be at risk for potential liability, it postponed the investigation. *See* Lynne Markek, *Ethical Dilemma in the ER: Experiment on Patients?*, CHI. TRIB., May 23, 1994, at 1.

More recently, researchers at the University of Texas Health Sciences Center in Houston encountered problems completing an investigation involving use of cooling blankets to induce hypothermia in severe head injury patients. *See* McCarthy, *supra* note 6, at 156. The hypothermia study has been allowed to proceed without meeting prospective informed consent requirements only after the Department of Health and Human Services granted a special waiver. *See* Action Related to Emergency Research Activity, 60 Fed. Reg. 38,353 (1995).

13. Researchers at the University of California, Los Angeles recently revealed that they had enrolled schizophrenic patients in a clinical trial studying the effects of lowering doses of medication, with the reasonable belief that this could lead to disruptive psychiatric episodes, without having obtained full informed consent of the patients or their representatives. At Rhode Island Hospital, researchers denied food to drunken patients who were temporarily, but severely, impaired by the effects of alcohol, in an effort to

result, increased sensitivity towards the need for obtaining subjects' fully informed consent.

Numerous commentators criticize the informed consent doctrine as elevating ritual and form over substance because it requires procedures which do not advance the patient's understanding, are easily subject to manipulation, and impose burdensome information exchange costs.[14] Thus, there have been calls to change the informed consent standards and expressly require that investigators engage in frank and extended discussions with patients about the experimental nature of the proposed activity in order to ensure that subjects are not coerced or misled.[15] But in critical care situations, there simply is no time for an extended dialogue between investigator and subject about the nature of the experiment. In such settings, it is impossible to comply even with the minimum legal standards already criticized as deficient and inadequate.

The legal requirement for informed consent, although historically rooted in the protections against bodily injury under the battery doctrine, derives continued support from the ethical and common-law principle that patients should be respected as persons capable and entitled to control their own medical care decisions. If patients are to be treated as autonomous agents, they must be provided material information relating to the risks and benefits of a proposed medical treatment and its alternatives in order to effectively decide

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study blood glucose levels in alcoholics. *See* Jim Montague, *Balancing Caution and Courage: Physicians and Regulators Weigh Informed Consent Issues in Clinical Research*, HOSP. & HEALTH NETWORKS, Sept. 20, 1994, at 50; *Problems in Securing Informed Consent*, *supra* note 11, at 4-14.

14. Criticisms of the informed consent doctrine include that it promotes individualistic values at the expense of communitarian values, wastes valuable resources, undermines trust in the medical profession, and fails to recognize that some patients simply do not want to be informed. *See* Alan Meisel, *The "Exceptions" to the Informed Consent Doctrine: Striking a Balance Between Competing Values in Medical Decisionmaking*, 1979 WIS. L. REV. 413, 415-16 [hereinafter Meisel, *Striking a Balance*]; *see also* Alan Meisel, *More on Making Consent Forms More Readable*, IRB, Jan. 1982, at 8 (calling informed consent a "myth" because physicians provide whatever information is necessary to get the patient to go along with their recommendation); Alan Weisbard, *Informed Consent: The Law's Uneasy Compromise with Ethical Theory*, 65 NEB. L. REV. 749, 751 (1986) (arguing that the law has transformed the ideal of informed consent into little more than a duty to warn of medical risks which is not measured by actual informational needs of individual patients; the entire process has taught physicians more how to practice medicine defensively than to foster the physician-patient relationship). Professor Jay Katz has argued for a complete overhaul of the current legal framework, contending that the present legal standards and procedures are too easily subject to manipulation by physician investigators and do not satisfactorily protect the rights of subjects to individual autonomy, self-determination, and bodily integrity. *See* Jay Katz, *Human Experimentation and Human Rights*, 38 ST. LOUIS U. L.J. 7, 9 (1993).

15. *See, e.g.*, Katz, *supra* note 14, at 25.

whether to participate in the research. Validation of this broad underlying principle of the informed consent doctrine "requires that we deliberate before we decide."[16]

Consequently, nowhere is the gap between legal theory and the realities of medical practice more evident than in application of the traditional informed consent doctrine to critical care research. The reasoned deliberation of the patient contemplated by the informed consent doctrine is simply not feasible when the patient suffers decisional or communicational incapacity and there is a limited time window for administering an experimental treatment. Thus, rigid application of informed consent requirements in critical care settings severely limits medical researchers' ability to test and study new therapies, preventing the efficient diffusion of beneficial medical technologies.

In a significant new regulatory development, the FDA has proposed amendments to its informed consent regulations that would relax the informed consent requirements in the critical care setting.[17] In response to criticisms of the current obstacles to conducting critical care research, the FDA has proposed to revise its regulations to allow waiver of informed consent under limited circumstances.[18] Relaxing the informed consent requirement for critical care research raises difficult issues regarding the physician-patient relationship and biomedical research. At one end of the spectrum are firmly held be-

16. RONALD MUNSON, INTERVENTION AND REFLECTION: BASIC ISSUES IN MEDICAL ETHICS 337 (5th ed. 1996).

17. *See* Protection of Human Subjects; Informed Consent, 60 Fed. Reg. 49,086, 49,090 (1995) (to be codified at 21 C.F.R. pt. 50) (proposed Sept. 21, 1995).

18. In 1993, the National Institutes of Health's (NIH) Office of Protection from Research Risks (OPRR) sent a warning letter to academic medical centers in response to reports that certain institutions were conducting critical care research using "deferred consent" procedures, where patients were informed of their enrollment in the clinical investigation after the fact. *See infra* notes 157-59 and accompanying text. The warning letter reiterated the need for researchers to obtain prospective informed consent. *See* Letter from Gary Ellis, OPRR Director, to IRB Chairpersons, *Informed Consent—Legally Effective and Prospectively Obtained*, OPRR REP. NO. 93-3 (Aug. 12, 1993) [hereinafter *OPRR Letter*]. The medical research community responded in a series of articles, correspondence, and public meetings demanding reform of the informed consent rules. Industry representatives testified at a May 23, 1994 hearing of the Subcommittee on Regulation, Business Opportunities, and Technology, of the House Committee on Small Business. *See generally Problems in Securing Informed Consent*, *supra* note 11 (discussing the testimony). In addition, several professional organizations formed the Coalition of Acute Resuscitation and Critical Care Researchers to address the issue and in January 1995, the FDA and NIH cosponsored a public forum where the Coalition's recommendations were discussed and other testimony heard. *See* Protection of Human Subjects; Informed Consent, 60 Fed. Reg. at 49,090.

liefs about individualism and patient autonomy as well as underlying concerns for patient safety in light of the egregious medical experiments of previous decades. Countervailing considerations include the societal benefits gained by systematic testing of medical technologies and the professional commitment, and at times paternalistic impulse, of physicians to act in their patients' best interests, especially where the patients cannot act for themselves. At bottom, it seems a terrible choice between forcing patients to become mere experimental objects or protecting these same patients to death.

As explained in further detail below, the FDA has proposed to strike the balance in favor of increased experimentation. FDA's proposed rules permit waiver of informed consent where: (i) the subject is in a life-threatening situation; (ii) available treatments are unproven or unsatisfactory; (iii) the subject cannot consent because of the medical condition; (iv) the intervention must be administered before consent from the patient or a representative is feasible; and (v) the risk of the intervention is reasonable in light of what is known about the medical condition, the current therapy, and the proposed intervention.[19] Once the FDA rules are issued in final form, the Department of Health and Human Services (HHS) is expected to harmonize its separate informed consent regulations through amendment and/or waiver so that both agencies will permit waiver of consent for critical care research under the same circumstances.[20]

This Article acknowledges the merit of the FDA's proposed rules, which attempt to remove unnecessary obstacles to critical care research while preserving safeguards for patient safety and respect for individual autonomy, but concludes that the revised regulations are ultimately inadequate and unsatisfactory. The FDA's proposed reforms are underinclusive in that they are limited to "life-threatening" situations, thus leaving in place significant barriers to research involving rapid application of experimental therapies for patients who face intractable pain and/or permanent disability but who are not at risk of imminent death. In addition, the rules are ambiguous and unclear in certain key respects, such as failing to provide clear guidance as to when available treatments are considered sufficiently unproven or unsatisfactory to warrant application of experimental therapies to patients without their consent. This lack of

19. *See* Protection of Human Subjects; Informed Consent, 60 Fed. Reg. at 49,095-96.

20. *See* F. William Dommel, Jr., Senior Policy Advisor, Office for Protection From Research Risk, National Institutes of Health, Oral Remarks at the Conference Concerning Legal Issues Affecting Academic Medical Centers Sponsored by the American Academy of Healthcare Attorneys in Arlington, Virginia (Jan. 18, 1996).

clear standards will allow researchers and academic medical institutions too much leeway in neglecting patients' rights and avoiding consideration of their treatment preferences. Informed consent should be waived with critical care patients only if the research sponsors follow express procedures to demonstrate that the trial design, in light of what is known, maximizes likely benefits and minimizes likely harm. Moreover, the research sponsors should be required to demonstrate that the study can yield generalizable scientific results, so that, at a minimum, subjects' nonconsensual participation in the experiment has the potential to produce meaningful answers.

In addition, this Article argues that complementary to the reforms in the FDA proposed rules, regulatory and legislative change is needed to increase use of flexible surrogate consent procedures that approximate critical care patients' treatment preferences. This would require broadening and making more readily identifiable the class of persons who may have legal authorization to consent to research participation for the critical care patient. Researchers should be permitted to consult a standardized hierarchy of representatives who may act for the critical care patient and such surrogates should be directed to make research participation decisions using the substituted judgment standard, approximating what they think the patient would want. Only if all potential surrogates are unavailable should the research be allowed to proceed by waiving informed consent.

Although significant problems with surrogate consent are acknowledged, this Article maintains that increased use of readily available and commonly understood surrogate consent procedures represents the best practical compromise of competing concerns. Increased use of surrogate consent procedures advances the progress of critical care trials and yet accommodates to some degree the ethical and legal principle of respect for autonomy by requiring, wherever possible, that a surrogate be charged to act in accord with the patient's individual preferences. Also, increased use of surrogate consent mechanisms provides an additional level of review of the experiment and allows for a more critical examination of the risks and benefits of the proposed investigation by outside parties.

Part I of this Article reviews the law of informed consent in critical care research and the limitations placed on waiver of consent that existed before the recent FDA proposals.[21] Part II discusses the ethical issues raised by waiving informed consent in critical care research and analyzes the merits of various alternative approaches apart from

21. *See infra* notes 25-106 and accompanying text.

the new FDA rules, such as deferred consent and advance directives, that have been proposed for dealing with informed consent in the critical care setting.[22] Part III reviews in detail the FDA's reform proposal and argues that the new regulations are underinclusive, unfairly excluding injured critical care patients who do not face imminent death, and that the FDA has paid insufficient attention to autonomy concerns in justifying its new rules.[23] This section further argues that the Agency has failed to ensure that consent will be waived only when the likely risk/benefit comparison of the standard treatment and investigational therapy satisfies acceptable levels. Part IV concludes with recommendations and policy options to complement the FDA proposed reforms, emphasizing increased use of surrogate consent procedures that approximate critical care patients' preferences.[24] Also strongly recommended is that critical care trials depending on waiver of consent employ expert surrogate consent procedures that demonstrate the acceptability of an investigation to medical experts who are not affiliated with the principal researchers.

I. INFORMED CONSENT IN CRITICAL CARE RESEARCH: THE LEGAL BACKGROUND

To appreciate the problems the FDA has tried to address in its new rules, it is important to understand the nature and extent of the previous legal limitations affecting critical care research. This section summarizes and reviews the applicable law on informed consent and medical experimentation before the proposed FDA reforms. Principally, federal regulations govern the conduct of research involving human subjects. However, research in the critical care setting also implicates the common law, statutory, and constitutional rights of competent adult patients to accept or refuse proffered medical care. Pending final adoption of the new reforms proposed by the FDA, the applicable law allows research without the patient's prospective consent only under extremely narrow circumstances. In many jurisdictions, the law remains unclear as to who besides the patient may consent for participation in research. This uncertainty in the legal rules contributes to present problems.

A. Medical Experimentation Regulations

As a result of increasing public outrage at the discovery of egre-

22. *See infra* notes 107-75 and accompanying text.
23. *See infra* notes 176-206 and accompanying text.
24. *See infra* notes 207-40 and accompanying text.

gious violations of patient rights in the name of medical "research,"[25] Congress in 1974 enacted the National Research Act (NRA),[26] which authorized the creation of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (the Commission). The Commission issued the influential Belmont Report, a set of ethical principles and guidelines for the protection of human subjects in research.[27] Many of the regulatory recommendations of the Belmont Report were implemented by the federal agencies. In 1981 both the FDA and HHS relied upon the recommendations when revising their regulations concerning the protection of human subjects.

The FDA and HHS regulations have broad application, affecting most biomedical research activities conducted in the United States. Research subject to the regulations needs to be submitted to Institutional Review Boards (IRBs) for approval, which must ensure that clinical studies adhere to the informed consent requirements.[28] The FDA regulations apply to all clinical investigations regulated by the Agency, as well as clinical investigations that support applications for research or marketing permits for products regulated by the FDA.[29] HHS requires IRB review of research it conducts, funded in whole or

25. *See, e.g., In re* Hyman, 258 N.Y.S.2d 397 (1964) (live cancer cells were injected into elderly patients at the Jewish Chronic Disease Hospital in Brooklyn without the patients' knowledge or consent). In the federally sponsored Tuskegee Syphilis Study, poor African-American men suffering from syphilis were deliberately left untreated as part of a study investigating the natural history of the disease. The patients were not aware that they were in the study and several were not even told that they had syphilis. *See generally* JAMES H. JONES, BAD BLOOD: THE TUSKEGEE SYPHILIS EXPERIMENT (2d ed. 1993).

26. *See* National Research Act of 1974, Pub. L. No. 93-348, 88 Stat. 342 (codified as amended at 42 U.S.C. §§ 201 to 300aaa-13 (1994)).

27. *See National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, DHEW Publication No. (OS) 78-0012, Appendix Volume I, DHEW Publication No. (OS) 78-0013, Appendix Volume II, DHEW Publication No. (OS) 78-0014 (1978) [hereinafter *Belmont Report*].

28. IRBs are committees established in accord with the federal regulations to monitor and approve applications for individual investigations at different research institutions. *See* 45 C.F.R. §§ 46.102(g); 46.103(b)(4), (5); 46.108(a). IRB membership is required by the regulations to include persons of different backgrounds and professions, in an attempt to reflect the prevailing values of the community. *See* 45 C.F.R. § 46.107 (1995).

29. Before 1981, clinical research conducted in private physicians' offices was generally exempted from the IRB review requirement. The 1981 revision of FDA's regulations requires all research submitted to the agency to be reviewed by an IRB. Noninstitutional Review Boards have been formed to review research conducted outside research institutions. These boards function like IRBs and review proposals from outside researchers for a fee. *See* Angela Holder, *Regulation of Human Subjects Research*, *in* TREATISE ON HEALTH CARE LAW § 23.02[2], at 23-12 (Michael MacDonald et al. eds., 1995).

in part by an HHS grant, cooperative grant, or fellowship, or subject to regulation by a federal agency.[30] The HHS regulations are implemented under the direction of the Office for Protection from Research Risks (OPRR) at the National Institutes of Health (NIH). Many biomedical research institutions and academic medical centers file general assurances with OPRR,[31] and thus require IRB review of all research done on their premises, even if not federally funded. In addition, most private foundations and other research funding agencies require compliance with federal standards for any research funded by them because of governing ethical policies, as well as the desire to limit potential liability.[32]

Pending promulgation of final rules adopting the FDA proposed reforms, the federal regulations generally require that the "legally effective informed consent" of the subject be obtained before administration of the experimental therapy.[33] Investigators can seek consent of potential subjects only under circumstances that provide the prospective subject "sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence."[34] Clearly, the time demands and inherently stressful circumstances associated with critical care research are not contemplated.

The regulations provide that, in place of the subject, an investigator may seek and obtain consent from the patient's "legally authorized representative."[35] But it is not at all clear how to identify this potential surrogate. The regulations simply define a patient's legally authorized representative in circular fashion to mean "an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research."[36] Because federal law ultimately does not answer this question, investigators must look to state law to determine who is the subject's authorized representative.[37] Unfortunately, the law is unsettled in many jurisdictions and

30. *See* 45 C.F.R. § 46.101 (1995).

31. *See id.* at § 46.103.

32. *See* Holder, *supra* note 29, § 23.02[1], at 23-10; Moore, *supra* note 7, at 564; A. John Popp & Dale L. Moore, *Institutional Review Board Evaluation of Neuroscience Protocols Involving Human Subjects*, 41 SURGICAL NEUROLOGY 162, 163 (1994).

33. 21 C.F.R. § 50.20 (1996); 45 C.F.R. § 46.116 (1995).

34. 21 C.F.R. § 50.20; 45 C.F.R. § 46.116.

35. 21 C.F.R. § 50.20; 45 C.F.R. § 46.116.

36. 21 C.F.R. § 50.3(m); 45 C.F.R. § 46.102(c).

37. *See* Moore, *supra* note 7, at 580.

often a clear answer is not readily available. Despite the custom of hospitals and emergency room physicians to rely on next-of-kin consent in treating patients in critical care situations, relatives in several jurisdictions are not necessarily legally authorized to make health care decisions for a patient unless a durable power of attorney for health care has been executed or a guardianship proceeding has concluded.[38] In many states, the applicable laws and regulations are vague and confusing and fail to provide clear guidance as to who, beside the patient or court-appointed guardian, may consent.[39]

The previous FDA regulations diverge somewhat from the HHS regulations in certain critical respects. In particular, these regulations establish a different set of criteria for waiving the informed consent requirement than do the HHS rules.

1. HHS Waiver Requirements

Pending reform of its regulations to harmonize with the new FDA rules, HHS permits waiver of informed consent provided that:

> (1) [t]he research involves no more than minimal risk to the subjects; (2) [t]he waiver or alteration will not adversely affect the rights and welfare of the subjects; (3) [t]he research could not practicably be carried out without the waiver or alteration; and (4) [w]henever appropriate, the subjects will be provided with additional pertinent information after participation.[40]

The principal problem in applying the HHS standards to critical care research protocols is satisfying the criterion that the research involve no more than "minimal risk."[41] The HHS regulations define "minimal risk" as when "the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or

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38. *See, e.g.*, Prentice et al., *supra* note 12, at 3 (describing the approval of a study at the University of Nebraska Medical Center involving consent of next-of-kin for enrollment of closed head injury patients in an experimental trial despite the fact that, at the time, Nebraska law expressly gave only court appointed guardians and individuals named in durable powers of attorney authority to make health care decisions for incompetent persons).

39. *See, e.g.*, 28 PA. CODE. § 553.12(b)(10) (1995) (outlining Pennsylvania patient "bill of rights" regulation for licensed ambulatory surgery facilities and stating that "responsible person[s]" may give informed consent for participation in a research program for a patient unable to do so, but failing to indicate how to identify such persons).

40. 45 C.F.R. § 46.116(d) (1995).

41. *Id.* § 46.116(a)(1).

tests."[42] In most cases, the experimental therapy under investigation will not be able to meet this narrow definition. Arguably, a patient with a life-threatening illness such as AIDS, for which no standard therapy is recognized as ultimately effective, faces no more than "minimal risk" in receiving an experimental therapy because the conventional treatment itself carries certain risk and only limited benefit. However, in a typical clinical investigation the *comparative* risk of the treatments—the degree to which the experimental therapy may pose more dangers than the standard therapy—is unknown, which explains precisely why the experiment is being undertaken in the first place.[43] Certainly, most researchers expect that the investigational treatment will not put the patient at a disproportionate risk. Despite an investigator's good faith belief in the efficacy of the experimental therapy, the results of clinical investigations often prove otherwise.[44]

Others contend that a researcher can satisfy the "minimal risk" criterion so long as at the start of the investigation, the researcher has no reason to believe that patients with the standard treatment will fare better and that no known superior treatment is withheld.[45] However, this interpretation ignores the plain language of the regulation, which requires that the risk anticipated be no more than that encountered in ordinary life. Because of the uncertainties inherent in biomedical research, providing any assurances that this minimal risk threshold will not be crossed proves difficult.[46] This is especially true

42. *Id.* § 46.102(i).

43. *See* Olson, *supra* note 10, at 1446.

44. Randomized trials have discredited numerous technologies as ineffective, such as internal mammary artery ligation, long after their use has become widespread. *See* Byron W. Brown, Jr., *Statistical Controversies in the Design of Clinical Trials—Some Personal Views*, 1 CONTROLLED CLINICAL TRIALS 13, 15 (1980). Other technologies supported by anecdotal observations of clinicians, such as corticosteroids for chronic hepatitis B and cytosine arabinoside for disseminated herpes zoster, not only were proven ineffective, but were shown to be more harmful than a placebo when tested under controlled studies. *See* Douglas D. Richman, *Public Access to Experimental Drug Therapy: AIDS Raises Yet Another Conflict Between Freedom of the Individual and Welfare of the Individual and Public*, 159 J. INFECTIOUS DISEASES 412, 413 (1989); *see also* Lawrence K. Altman, *Fatal Drug Trial Raises Questions About "Informed Consent,"* N.Y. TIMES, Oct. 5, 1993, at C3 (stating that experimental hepatitis B drug, Fialuridine, caused unexpected deaths among trial participants, even though animal experiments and monitoring tests did not suggest the severe dangers).

45. *See* Robert J. Levine, *Research in Emergency Situations: The Role of Deferred Consent*, 273 JAMA 1300, 1301-02 (1995).

46. *But see* McCarthy, *supra* note 6, at 158-59 (arguing that regulatory history of the development of the minimal risk concept evidences intent that the regulations be interpreted in a flexible manner in light of the risks ordinarily encountered by research subjects, not the risks ordinarily encountered by healthy persons).

in many critical care circumstances where the investigational therapy may be studied under an "add-on" design, in which every patient receives the standard treatment in addition to the treatment being compared. Little is known about the interaction of different therapies and techniques under critical care conditions. In addition, the minimal risk standard cannot be applied consistently to a critically ill or injured patient, who already experiences risks beyond the ordinary.[47] A researcher's conclusion that the patient faces a desperate situation in which the unknown experimental therapy offers at least the same promise of benefit as the unsatisfactory standard treatment fails to provide sufficient justification for proceeding with the research. A fundamental purpose of the informed consent requirement is to guard against the dangers of a researcher's misguided expectations and overreaching paternalism.[48]

An alternative interpretation of the critical concept of minimal risk suggests that the analysis should focus on the circumstances of the individual patient, who because of the illness is already facing greater than common danger, and thus compare the *differential* risk between the standard and experimental therapy. Under this approach, the minimal risk criterion is satisfied if the difference is minimal between the dangers presented by the standard accepted therapy and the risk of an undesirable outcome with the experimental therapy.[49] However, this interpretation also ignores the clear regulatory language that the risk presented be no more than that "ordinarily encountered in daily life." Moreover, this interpretation assumes in circular fashion that the researcher can ensure, in advance, that the experimental therapy does not produce unaccepted risk, notwithstanding the fact that the therapy remains investigational. The emphasis on differential risk downplays the investigational nature of the activity, conveniently glossing over the fact that one of the critical unknown variables is how much risk is posed by application of the experimental therapy to the critical care condition.

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47. *See* Coalition Conference of Acute Resuscitation and Critical Care Researchers, *Informed Consent in Emergency Research*, 273 JAMA 1283, 1285 (1995).

48. *See, e.g.*, A.M. Capron, *Protection of Research Subjects: Do Special Rules Apply in Epidemiology?*, 19 LAW MED. & HEALTH CARE 184, 186-87 (1991); *infra* notes 123-43 and accompanying text (discussing the role of patient autonomy in medical decisionmaking).

49. *See, e.g.*, Abramson et al., *supra* note 10, at 2468.

2. Previous FDA Waiver Requirements

Before the additional circumstances provided for under the FDA's recent proposed regulatory changes, the FDA allowed waiver of informed consent only when each of the following conditions were met:

> (1) The human subject [was] confronted by a life-threatening situation necessitating the use of the test article.
>
> (2) Informed consent [could not] be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
>
> (3) Time [was] not sufficient to obtain consent from the subject's legal representative.
>
> (4) There [was] available no alternative method of approved or generally recognized therapy that provid[ed] an equal or greater likelihood of saving the life of the subject.[50]

These criteria contemplate waiver of informed consent only in life-threatening situations and even then under limited circumstances. For example, if the research involves randomization of patients between the experimental therapy and a placebo, it would be difficult to satisfy the first criterion, because use of a placebo is not "necessitated" by the subject's acute care condition.[51]

The principal obstacle to waiving informed consent under these narrow standards is satisfying the fourth criterion that no existing therapies provide an equal or greater chance of saving the patient's life. Such a requirement generally prevents waiver for an experiment comparing investigational therapy to a standard therapy with a recognized effectiveness, even if the standard therapy is considered to offer only modest benefits. Because an experimental therapy's effectiveness will be unknown, it will be virtually impossible to provide assurances that the experimental therapy provides the greater likelihood of saving the patient's life.[52] The subjects will of course benefit if the experimental therapy works as planned, but participation could expose subjects to grave unknown risks, evidencing the importance of obtaining their informed consent prospectively.

In addition, investigators waiving informed consent under these

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50. 21 C.F.R. § 50.23(a) (1996).

51. However, FDA regulations arguably permit a study which compares the standard treatment plus a placebo to the standard treatment plus the experimental article, because in this situation, administration of the placebo would not constitute nontreatment. *See* Prentice et al., *supra* note 12, at 4.

52. *See* Olson, *supra* note 10, at 1446.

provisions must submit documentation to the IRB within five days after administration of the investigational therapy.[53] The documentation requirement suggests that waiver is expected to occur on a case-by-case basis in emergency circumstances.[54] Accordingly, these provisions provide dubious authorization for research protocols involving a blanket waiver of informed consent for all potential subjects.

B. Statutory and Common Law

1. Informed Consent for Research

Apart from the federal regulations, the common law imposes certain duties and obligations on participants in clinical research. Scant case law exists concerning medical experimentation. Indeed, the early reported cases did not directly address the experimental aspects of therapeutic research and instead analyzed such situations as typical malpractice cases, with the experimental therapy considered evidence that a practitioner had deviated from standard practice. Courts generally assumed that such therapy was careless or reckless, and physicians could be held strictly liable for any damages resulting to the patient.[55]

Nevertheless, researchers today generally may apply experimental therapy without risk of common-law liability if they first obtain the subject's informed consent. The common-law duty for obtaining informed consent, which mirrors the informed consent requirements of the federal regulations, follows from the recognition of the physician-patient relationship as a fiduciary relationship. According to the basic laws of agency, a fiduciary must not only justify the reasonableness of a transaction, but also disclose it and seek the agreement of the principal-client.[56] As a fiduciary to the patient, the physician owes a certain deference to the patient's interests, which means that the physician must ascertain what the patient's preferences are in light of the risks presented by the proposed treatment and available

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53. *See* 21 C.F.R. § 50.23(c) (1996).

54. *See* Olson, *supra* note 10, at 1446. Indeed, because of the narrow case-by-case limitations, federal officials contrasted the HHS regulations as allowing waiver of informed consent while the FDA regulations did not. *See* Joan P. Porter, *Development of a Federal Policy for the Protection of Human Subjects of Research*, 45 FOOD DRUG COSM. L.J. 623, 628 (1990).

55. *See generally* Jesse A. Goldner, *An Overview of Legal Controls on Human Experimentation and the Regulatory Implications of Taking Professor Katz Seriously*, 38 ST. LOUIS U. L.J. 63, 71-74 (1993) (collecting cases and discussing history).

56. *See* RESTATEMENT (SECOND) OF AGENCY §§ 381, 383 (1994).

alternatives.[57] Although the case law has not specifically addressed the question, the medical researcher likely has a fiduciary relationship to the subject just as the doctor has to his or her patient.[58]

Moreover, the common law recognizes a person's right of "self-determination" to make medical decisions about his or her body.[59] The right to self-determination includes the right to make decisions regarding participation in medical research. To protect this right, the subject's informed consent must be obtained before the application of experimental treatment.[60]

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57. *See, e.g.*, Canterbury v. Spence, 464 F.2d 772, 782 (D.C. Cir. 1972).

58. *See* Holder, *supra* note 29, § 23.03[1], at 23-22. In many cases, the physician is also the researcher and the fiduciary relationship can be implied from the investigator's role as physician. Whether biomedical researchers who have not established a therapeutic relationship with their subjects are fiduciaries is less clear. *See* Angela R. Holder, *Do Researchers and Subjects Have a Fiduciary Relationship?*, IRB, Jan. 1982, at 6 (suggesting that there is such a relationship).

59. The seminal case articulating this concept of patient autonomy is *Schloendorff v. Society of New York Hospital*, 105 N.E. 92 (N.Y. 1914), *overruled on other grounds by* Bing v. Thunig, 143 N.E.2d 3 (N.Y. 1957), where Judge Cardozo stated that "[e]very human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient's consent, commits an assault...." *Schloendorff*, 105 N.E. at 93; *See also* Pratt v. Davis, 118 Ill. App. 161, 166 (1905) (holding that a patient has the right to the "inviolability of his person"), *aff'd*, 79 N.E.2d 562 (Ill. 1906).

60. Although the physician-patient relationship may be contractual in nature, tort law supplies the background legal rules that limit and regulate a physician's professional authority. Thus, the patient-subject's interest in autonomy and self-determination is analyzed mainly under tort doctrines. The notion of bodily integrity reflected in the common-law protections against battery is embodied in the requirement that a patient's informed consent must be obtained before the initiation of medical treatment. *See* Cruzan v. Director, Mo. Dep't of Health, 497 U.S. 261, 269 (1990).

However, the battery doctrine does not apply to many aspects of the physician-patient relationship because not every malpractice claim can be characterized as a nonconsensual touching. *See, e.g.*, Cobbs v. Grant, 502 P.2d 1, 7-8 (Cal. 1972) (distinguishing between claims constituting a battery and those sounding in negligence); Marjorie Maguire Shultz, *From Informed Consent to Patient Choice: A New Protected Interest*, 95 YALE L.J. 219, 225-26 (1985); Richard P. Dooling, Comment, *Damage Actions for Nonconsensual Life-Sustaining Medical Treatment*, 30 ST. LOUIS U. L.J. 895, 900-01 (1986). Accordingly, today the informed consent requirement is more commonly analyzed under the tort rubric of negligence. A physician is held to have a duty to provide sufficient information to a patient so that he or she may make an informed medical choice. The various jurisdictions follow two general standards for the extent of disclosure required to make a patient's consent a truly informed one. *See* Goldner, *supra* note 55, at 76-77. The majority rule is that a physician must disclose what a reasonable practitioner, practicing according to community standards, would disclose under the same circumstances. *See id.* Alternatively, slightly less than half of jurisdictions determine the scope of disclosure by what the reasonable patient would want to know under the circumstances in order to make an informed choice about medical treatment. *See id.* In the latter jurisdictions, the physician's duty to seek the patient's informed consent is based less on the fiduciary nature of the physician-patient relationship and more on the patient's right to self-

Accordingly, most commentators agree that the informed consent requirements for research are essentially the same as the informed consent requirements for standard medical practice.[61] Indeed, the informed consent doctrine may apply more rigorously in the research setting.[62] As part of the fiduciary nature of the physician-patient relationship, the physician is presumed to act in the best interests of the individual patient. However, clinical protocols demand that the investigator follow systematic procedures to develop generalizable knowledge, including when to initiate and stop therapy, that may end up benefiting future patients more than the immediate

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determination. *See, e.g.*, *Canterbury*, 464 F.2d at 786 ("[T]he patient's right of self-decision shapes the boundaries of the duty to reveal."). The informed consent provisions of the federal regulations follow the reasonable patient standard for determining the scope of disclosure. *See* 21 C.F.R. § 50.25 (1996); 45 C.F.R. § 46.116(a) (1995).

61. *See, e.g.*, Katz, *supra* note 14, at 13-14 & n.21 (noting the only significant distinction is that in therapy settings, physicians may still invoke the "therapeutic exception" to enable the physician to withhold certain information that is likely to cause psychological harm to the patient).

62. *See* Nancy M. King, *Consent to Treatment, in* HEALTHCARE FACILITIES LAW, §§ 7, 7.13 (Anne M. Dellinger ed., 1991); Richard Delgado & Helen Leskovac, *Informed Consent in Human Experimentation: Bridging the Gap Between Ethical Thought and Current Practice*, 34 UCLA L. REV. 67, 93-94 (1986); Nancy M. King & Gail Henderson, *Treatments of Last Resort: Informed Consent and the Diffusion of New Technology*, 42 MERCER L. REV. 1007, 1044 (1991); *see also* Estrada v. Jaques, 70 N.C. App. 627, 649, 321 S.E.2d 240, 254 (1984) (holding that a health care provider offering an experimental procedure has a duty to inform a patient of the *uncertainty* regarding risk associated with experimental procedures as well as the known or most likely projected risks); Clemens v. Regents of the Univ. of Cal., 87 Cal. Rptr. 108, 114 (Cal. Ct. App. 1970) (instructing the jury that a physician seeking consent to a new or experimental procedure should inform the patient that it is new or experimental when seeking consent). In *Halushka v. University of Saskatchewan*, [1965] D.L.R.2d 436, one of the few reported experimentation cases, the plaintiff volunteered to participate in a study involving circulatory responses under anesthesia. *See id.* at 437-39. The physician neither disclosed several of the risks associated with the procedure, nor that the new drug was an anesthetic. *See id.* at 444. The court stated that "the duty imposed upon those engaged in medical research . . . is at least as great as, if not greater than, the duty owed by the ordinary physician or surgeon to his patient." *Id.* at 443-44. In *Schwartz v. Boston Hospital for Women*, 422 F. Supp. 53 (S.D.N.Y. 1976), the plaintiff claimed that hospital physicians improperly performed a scraping of her uterus after her Caesarean section delivery as part of an experiment without her consent. *See id.* at 54. The district court denied the hospital's motion for summary judgment, stating that "if the [procedure] was performed in the aid of [a] study rather than for reasons personal to Mrs. Schwartz, and if she did not consent to its performance and it caused her injury, the hospital could be found liable." *Id.* at 56. Nevertheless, despite the differences between research and regular medical practice, some question remains as to whether the research subject should be informed to the same degree as the individual patient. *See, e.g.*, Thurstan B. Brewen, *Consent to Randomized Treatment*, 2 LANCET 919, 921 (1982) (characterizing as "illogical" the "idea that the mere fact of randomization [of treatment in a clinical trial] always requires special informed consent"). The subject, in volunteering for an experiment, recognizes that a scientific investigation lurks in the background and cannot reasonably expect the investigator to act like his family doctor. *See id.*

subjects.[63] Because research involves activities beyond the expected scope of the normal physician-patient relationship, the informed consent doctrine may require that more detailed information be disclosed about expected risks and alternative therapies in the experimentation context.[64] In addition, deference to medical expertise is less appropriate in the research setting, where many more variables remain unknown. Finally, informed consent standards may be more rigorous for investigational therapy because the researcher and subject have conflicting interests. The duty to maintain the scientific integrity of the study will necessarily limit an investigator's flexibility in tailoring treatments to the individual patient's specific needs.[65]

The distinction between research and standard therapy may be more useful in theory than in practical application. Increasingly, the difference is becoming blurred, making it all the more confusing for physician-investigators and patient-subjects to understand their re-

63. *See* ROBERT J. LEVINE, ETHICS AND REGULATION OF CLINICAL RESEARCH 10 (2d ed. 1986).

64. *See* John Luce, *Ethical Principles in Clinical Care*, 263 JAMA 696, 697 (1990). In *Moore v. Regents of the University of California*, 793 P.2d 479 (Cal. 1990), the well-publicized patented cell-line case, the Supreme Court of California recognized that research activities can affect the scope of disclosure required to obtain informed consent. *See id.* at 485. Moore had developed hairy cell leukemia and was treated by physicians at UCLA Medical Center. *See id.* at 480. The physicians applied the standard therapy and removed his spleen. *See id.* at 481. The treating physicians then used biological products extracted from Moore to develop a cell line capable of producing commercially valuable proteins. *See id.* at 481. Moore sued the physicians and UCLA Medical Center, seeking in part to recover a proprietary interest in products produced from his cells and the cell line. *See id.* at 487. Although the case is most often remembered for the court's holding that the cell line and protein products derived from Moore's spleen were not the patient's personal property, *see id.* at 492, the court also held that Moore's treating physician failed to obtain effective informed consent. *See id.* at 485. The court reasoned that "a physician who is seeking a patient's consent for a medical procedure must, in order to satisfy his fiduciary duty and to obtain the patient's informed consent, disclose personal interests unrelated to the patient's health, *whether research* or economic, that may affect his medical judgment." *Id.* (emphasis added) (footnote omitted).

65. *See* Delgado & Leskovac, *supra* note 62, at 68-69, 88-92. The authors identify the following reasons for heightened informed consent requirements in the experimental setting: (1) because the risks are not known in advance, only the subject can decide to undergo them; (2) deferral to medical expertise is inappropriate in the research setting; (3) the research subject may be unlikely to benefit directly from the research and cannot be presumed to consent to it; (4) the researcher and subject often have conflicting interests; (5) conscripting human subjects without their consent deprives their acts of moral meaning; (6) the researcher and the subject have "conflicts of value;" and (7) the researcher has a fiduciary relationship with the subject. *See id.* at 68-69, 92-107. The authors recognize that "conflicts of interest" between researcher and subject may not be stark and crystallized. Thus, they use the term "conflict of value" to describe the situation where, although both parties' interests may not be opposed, they may still have different ideas about the purposes and goals of the research. *See id.* at 100-01.

spective rights, obligations, and duties when "innovative" therapies are attempted during critical care situations. Medical practice often encompasses both research and therapeutic aspects.[66] However, significant differences remain. In therapeutic medical practice, individualized adjustments in treatment are more likely to occur as the physician attempts to address the distinct medical circumstances of the particular patient, including conditions not under investigation. Such innovative or novel therapies administered with the primary intent of benefitting the immediate patient will not yield much more than anecdotal evidence.[67] In contrast, clinical research decisions are made at a more generalizable level in order to test a hypothesis or develop new knowledge that is statistically significant. What treatment the patient receives is often the result of a predesigned mechanization, such as randomization, than individual clinical decisions of what is best for the patient. Thus, a patient in an investigational trial is deprived of the "experimentation ordinarily done to enhance the well-being of the patient" that is commonly found in clinical practice.[68] This distinction between innovative clinical practice and experimental research, which of course will vary in degree depending on the structure of the research protocol, is arguably the most compelling reason for requiring heightened informed consent in the research context.

There have been very few cases involving subjects suing researchers for injuries sustained because of negligent care while undergoing experimental therapy. Experimental subjects as a group do not appear to be harmed physically more than patients with similar diseases in therapeutic settings.[69] In most cases, "malresearch" claims involve allegations that a particular risk that has occurred had not been explained or that the treatment administered was not part of the agreed-upon research.[70] Because tort suits for malresearch

66. *See* Katz, *supra* note 14, at 8.

67. *See Belmont Report, supra* note 27, at 2-4.

68. *See* LEVINE, *supra* note 63, at 10.

69. The Advisory Committee on Human Radiation Experiments, which recently completed a review of randomly selected, federally-funded research projects, from both radiation and non-radiation related disciplines, concluded that most studies posed only minimal risk of harm. *See Research Ethics and the Medical Profession: Report of the Advisory Committee on Human Radiation Experiments*, 276 JAMA 403, 408 (1996) [hereinafter *Research Ethics and the Medical Profession*]. *See generally* Phillipe V. Cardon et al., *Injuries to Research Subjects*, 295 NEW ENG. J. MED. 650 (1976) (discussing a study conducted in order to determine the number of research related injuries with the aim of discovering the feasibility of compensating patients injured during such research).

70. *See* Holder, *supra* note 29, § 23.08[1], at 23-99. However, in one malresearch case involving a professional diver who sustained injuries while participating in studies of

generally must meet the technical requirements for maintaining a negligence or battery action, damages are a required element, which may be difficult to prove in the absence of physical harm. The dearth of malresearch suits alleging physical harm suggests that the primary purpose of the informed consent doctrine in the experimentation context is not so much to safeguard potential subjects from physical danger as to delineate limits on the physician's professional authority and to ensure respect for the personal autonomy of patients, regardless of whether they are exposed to physical harm.[71] Indeed, an underlying concern evident in the experimentation cases is that the investigator, however well-intentioned her reasons, has motivations that may differ from and may even be contrary to the patient's. Courts generally have been more receptive to patients' claims regarding improper medical treatment where the circumstances suggest that the physician's research objectives posed a conflict of interest.[72]

2. State Statutes

Several states have enacted statutes addressing human experimentation.[73] Such laws generally prohibit certain classes of incompetent persons, primarily involuntary patients in state mental

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deep-sea diving at Duke University, the court held that in rare circumstances the doctrine of assumption of risk may apply and bar plaintiffs' recovery. *See* Whitlock v. Duke Univ., 637 F. Supp. 1463, 1475 (M.D.N.C. 1986). The case had unique facts in that the subject knew more about the risks of deep-sea diving than the investigators. *See id.* at 1465-66.

71. *See Research Ethics and the Medical Profession, supra* note 69, at 408 (noting that the Advisory Committee on Human Radiation Experiments found that most current studies pose only minimal harm but that seriously ill patients are often confused about research activities and may not have realistic views of the likely benefits). Most commentators conclude that protection from physical harm lies at the heart of the informed consent requirement in the research context. *See, e.g.*, Capron, *supra* note 48, at 185. However, it is difficult to distinguish the protection of harm function from the function of promoting self-determination as the two objectives are intertwined and advancing one interest often helps further respect for the other. *See id.* at 186.

72. *See, e.g.*, Mink v. University of Chicago, 460 F. Supp. 713 (N.D. Ill. 1978). In *Mink*, the plaintiffs were pregnant women who were given DES during their prenatal care as participants in an experiment evaluating the efficacy of the drug at preventing miscarriages. *See id.* at 715. The plaintiffs sued under both negligence and battery theories, alleging injury from the increased risk of cancer to their daughters and for resulting emotional distress. *See id.* at 715-16. The court allowed the battery claim even though the classic situation of nonconsensual touching was not present. *See id.* at 717-18. Although not expressly stated in the opinion, the nature of the nonconsensual research seems to have motivated the court to depart from traditional tort principles. *See id.* at 716-18; *see also* Shultz, *supra* note 60, at 258-60, 274 (discussing the decision in *Mink* and concluding "that there need be no implication of wrongdoing in the narrow sense of that word to justify aggressive protection of patient choice").

73. *See, e.g.*, CAL. HEALTH & SAFETY CODE § 24175 (West 1992); 28 PA. CODE § 553.12 (1994).

hospitals, from participating in experimental research.[74] The state statutes usually permit experimentation with other incompetent persons if a legally effective surrogate consents or if a court order is obtained.[75] But these statutes do not directly address the problems of consent in the critical care research context by, for example, providing for waiver of informed consent if a patient's legal representative is not immediately available.[76] In addition, many state experimentation statutes contain automatic preemption language stating that they are intended to be preempted by the federal regulations with regard to federally-funded research.[77] Thus, the state laws that could be interpreted to permit relaxation of consent standards in critical care situations may not make a practical difference since most critical care research will be subject to the federal regulations because of their broad applicability.[78]

Nearly every state has professional licensing statutes governing the professional conduct of physicians.[79] In theory, a physician conducting research without proper consent procedures could be deemed to be engaged in unprofessional conduct under these laws and face

74. *See, e.g.*, MO. ANN. STAT. § 630.115(8) (West 1989).

75. *See* CAL. HEALTH & SAFETY CODE § 24175(b) (permitting conservator of patient adjudicated incompetent to consent where patient does not object to participation or where conservator acts in good faith during an emergency, but requiring conservator of patient who has not been adjudicated incompetent to obtain court order before being allowed to consent on patient's behalf where patient refuses to consent); 410 ILL. COMP. STAT. ANN. § 50/3.1 (West 1993) (permitting consent of patient's guardian, spouse, parent, or authorized agent for experimental procedures if patient is unable to consent); N.Y. PUB. HEALTH LAW § 2442 (McKinney 1993) (permitting experimentation with person unable to render consent if a party legally empowered to act for the patient consents in writing); 28 PA. CODE. § 553.12(b)(10) (patient bill of rights for patients at state-licensed ambulatory surgery centers provides that "responsible person" may give consent for enrolling patient in medical care research program where patient is unable to give informed consent); VA. CODE. ANN. §§ 32.1-162.16 to -162.18 (Michie 1992) (allowing consent to research of legally authorized representative of patient if patient not competent, but not defining clearly who the legally authorized representative is other than custodial parent or guardian).

76. Also, the statutes are often narrowly worded and in some instances have been interpreted to apply only when there is a clear research protocol, as opposed to when a clinician uses an innovative or experimental therapy in the course of regular treatment. *See, e.g.*, Trantafello v. Medical Ctr. of Tarzana, 227 Cal. Rptr. 84, 87 (Cal. Ct. App. 1986) (stating that California's experimentation statute did not apply because physician's use of new acrylic compound for bone graft was used not in the course of a research program, but in the course of therapeutic treatment).

77. *See, e.g.*, N.Y. PUB. HEALTH LAW § 2445 (McKinney 1993).

78. *See supra* notes 28-32 and accompanying text.

79. *See, e.g.*, CAL. BUS. & PROF. CODE § 2000-2099 (West 1990 & Supp. 1996) (outlining medical licensing requirements); N.C. GEN. STAT. §§ 90-2 to -21 (1993) (same); TEX. REV. CIV. STAT. ANN. art. 4495b (West Supp. 1996) (same).

losing his license. However, there have been few cases in which the medical licensing laws have been applied to suspend the licenses of physicians for conducting improper research.[80]

3. Surrogate Consent

A common practice of hospitals and emergency room physicians is to rely on next-of-kin or other surrogate consent to make medical decisions when a patient is unable to provide consent. Although this may be the recognized custom, few cases address the legality of such practices in the context of standard medical practice, let alone medical research.[81] Even fewer cases address who is authorized to act as the surrogate for the critical care patient (e.g., parent, spouse, close family friend, etc.).[82]

The legality of surrogate consent has been considered for the most part in the context of right-to-die cases. Several states allow surrogates to make health care decisions with drastic consequences, such as the decision to withdraw life-sustaining treatment.[83] In addition, certain of these states allow for the default appointment of a surrogate in the event that the health care provider is unable to locate a legally authorized representative. Maryland, for example, allows the spouse, adult child, parent, sibling, or even close friend of the patient to consent to the withdrawal of life-sustaining treatment if the patient is in a terminal condition, persistent vegetative state, or an advanced, progressive and irreversible debilitating condition.[84]

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80. *See* Goldner, *supra* note 55, at 67.

81. *See* Elaine B. Krasik, *The Role of the Family in Medical Decision-making For Incompetent Adult Patients: A Historical Perspective and Case Analysis*, 48 U. PITT. L. REV. 539, 548 (1987).

82. *See* Meisel, *Striking a Balance*, *supra* note 14, at 473. Some states have enacted laws authorizing surrogate consent for medical care that identify the possible surrogates who may consent for an incapacitated patient. *See, e.g.*, TEX. HEALTH & SAFETY CODE ANN. §§ 313.001 to .007 (West Supp. 1996) (identifying surrogates but not clearly authorizing surrogate consent for research).

83. *See, e.g.*, John F. Kennedy Mem'l Hosp. v. Bludworth, 452 So. 2d 921, 926 (Fla. 1984) ("[T]he right of a patient, who is in an irreversibly comatose and essentially vegetative state to refuse extraordinary life-sustaining measures, may be exercised either by his or her close family members or by a guardian of the patient appointed by the court."); Barber v. Superior Court, 195 Cal. Rptr. 484, 493 (Cal. Ct. App. 1983) (refusing to impose criminal liability upon physician for removing intravenous feeding line from vegetative comatose patient at family's request).

84. *See* MD. CODE ANN., HEALTH-GEN. II § 5-605 (1994). For examples of similar statutes, see D.C. CODE ANN. § 21-2210 (Supp. 1996); N.C. GEN. STAT. § 90-322 (1993); N.M. STAT. ANN. § 24-7-8.1 (Michie 1994); N.Y. PUB. HEALTH LAW §§ 2960-2978 (McKinney 1993); OR. REV. STAT. §§ 127.635, 127.640 (1995); TEX. HEALTH & SAFETY CODE ANN. §§ 313.001 to .007 (West Supp. 1996); VA. CODE ANN. § 54.1-2986 (Michie

Most states with such surrogacy statutes require that the surrogate use the "substituted judgment" standard and make the decision as the patient would have done.[85] A minority of states, either through legislation or case law, reject this standard and instead require that the decision be made in the "best interests" of the patient.[86] Some states combine the best interest and substituted judgment standards. One of the more detailed statutes, Illinois' Health Care Surrogate Act, allows for the appointment of surrogates for patients who lack decision-making capacity and have terminal conditions, are in a state of permanent unconsciousness, or in an incurable or irreversible condition causing severe pain or imposing significant burdens.[87] The possible surrogates, in order of priority as specified in the statute, have the right to consent to the withdrawal of life-sustaining treatment.[88] The surrogate is supposed to make the decision based on the patient's wishes under the circumstances or, if not known, by acting in the patient's best interests.[89] Yet, despite this progressive statute providing patients lacking decisional capacity a mechanism to implement their presumed choices, Illinois has not enacted similar detailed legislation directly applicable to critical care research.[90]

The related case law dealing with withdrawal of medical care provides some support for the practice of surrogates consenting to experimental medical treatment. Increasingly, courts have held that the common-law right to self-determination, which includes the right to refuse medical treatment, may be asserted by surrogates for incompetent patients.[91] However, these cases are distinguishable to the

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1994).

85. *See* Robert M. Portman, *Surrogate Decision-Making Legislation: The Next Frontier in Life-Sustaining Treatment Policy*, 24 J. HEALTH & HOSP. L. 311, 314 (1991).

86. *See id.; see also* CLAIRE C. OBADE, PATIENT CARE DECISION-MAKING: A LEGAL GUIDE FOR PROVIDERS §§ 9:2-9:4 (1995) (describing the distinctions between the "best interests" and "substituted judgment" standards).

87. *See* 755 ILL. COMP. STAT. ANN. 40/10 (West 1993).

88. *See id.* 40/25.

89. *See id.* 40/20.

90. *See* 410 ILL. COMP. STAT. ANN. 50/3.1. The Illinois Medical Patient Rights Act provides that if the patient is unable to consent to experimental therapy, a guardian, spouse, parent or "authorized agent" may consent for the patient. But the statute, in contrast to the Health Care Surrogate Act governing withdrawal of life-sustaining treatment, is silent on many key issues. *See id.* It does not indicate under what circumstances the patient may be presumed unable to consent, limits the number of surrogates, without indicating their relative priority, and does not provide guidance as to how the surrogate is supposed to make the decision. *See id.*

91. *See, e.g.*, Degrella v. Elston, 858 S.W.2d 698, 709 (Ky. 1993) (permitting a mother to employ "substituted judgment" in order to refuse artificial nutrition for daughter in persistent vegetative state); *In re* Martin, 504 N.W.2d 917, 922-23 (Mich. Ct. App. 1993) (permitting a surrogate to discontinue treatment of a brain-damaged but nonvegetative

extent that they concern treatment decisions involving application and withdrawal of standard therapy, as opposed to the special circumstances involved in consenting to experimentation. Medical research, as noted above, may require special vigilance with respect to obtaining the patient's consent because of the unknown risks involved and because the therapy has certain research goals that are beyond the needs and interests of the individual patient. In addition, the withdrawal of care cases often involve patients in persistent vegetative states, where there is time for reasoned deliberation about the patient's values and treatment preferences and the ultimate prognosis and where, practically speaking, the patient's opportunity for directly consenting or objecting is permanently lost. Indeed, courts have been less willing to recognize a patient's right to make medical decisions through a surrogate when the patient suffers a temporary neurological deficit and will not likely be deemed permanently incompetent.[92]

Accordingly, in the absence of specific authorizing legislation, researchers and medical institutions relying upon surrogate consent for application of experimental therapies face potential liability. This is especially true when the enrolled patient suffers only temporary decisional incapacity. Liability for negligent medical care is likely to be greater when informed consent is waived for an unconscious patient who may regain medical decision-making capacity than for a patient in a life-threatening situation who is unlikely to survive application of standard therapy.

4. Emergency Exception

All jurisdictions recognize an exception to informed consent for medical treatment in emergency care situations.[93] Some states have a statute expressly recognizing the emergency exception,[94] while in

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patient through either a "best interest" or "substituted judgment" approach depending on the circumstances); Delio v. Westchester County Med. Ctr., 516 N.Y.S.2d 677, 693-94 (N.Y. App. Div. 1987) (allowing surrogate to assert, on the behalf of a patient in persistent vegetative state, the patient's right to self-determination based on wishes expressed by the patient prior to losing cognizance).

92. *See* OBADE, *supra* note 86, § 8.13, at 8-28.

93. *See* Meisel, *Striking a Balance, supra* note 14, at 439 (recognizing the close relation between the emergency exception to the informed consent doctrine and the exception for incompetent patients).

94. *See, e.g.*, MD. CODE. ANN., HEALTH-GEN. II § 5-607 (1994) (allowing treatment without consent where treatment is of "an emergency medical nature" and physician determines that life or health of patient would be adversely affected by delaying treatment); 35 PA. CONS. STAT. ANN. § 6933 (West 1993) (eliminating civil liability for health professionals who fail to obtain consent in rendering emergency medical services where patient

other jurisdictions the exception has been developed through case law.[95] Under the exception, medical providers may render treatment to patients who are incapable of making an informed decision if a person authorized to give consent is not immediately available and there is an emergency situation requiring rapid medical treatment.

While the emergency exception contemplates application of accepted medical therapies, it is less clear whether experimental therapy falls within the exception. One view is that the emergency exception justifies waiving prospective informed consent of the critical care patient because if the physician does not know what therapy is best, he or she does all that can be done by enrolling the patient in an experiment with a predesigned protocol for random allocation.[96]

However, the basis for the emergency exception is that consent may be implied because a reasonable person would agree to such therapy under the circumstances if not suffering from decisional incapacity.[97] When the therapy applied is experimental, it is not as easy to imply patient preferences. First, the lack of knowledge about the experimental therapy makes the risk/benefit analysis much more complicated than when evaluating standard treatment in emergency situations.[98] For example, the Cardiopump holds out the promise of restoring circulatory function better than current CPR techniques for cardiac arrest victims. On the other hand, the device does not necessarily hold out the same promise of restoring neurological function,

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is unable to consent, no other authorized representative is available, and health professional acts in good faith).

95. *See, e.g.*, Dunham v. Wright, 423 F.2d 940, 941-42 (3d Cir. 1970); Estate of Leach v. Shapiro, 469 N.E.2d 1047, 1052 (Ohio Ct. App. 1984).

96. *See, e.g.*, Norman S. Abramson et al., *Informed Consent in Resuscitation Research*, 246 JAMA 2828, 2830 (1981).

97. *See, e.g.*, Ellen Covner Weiss, *The Effect of the Treatment Setting on the Decision-Making Process: Acute Care Hospitals and Emergency Services*, 19 LAW MED. & HEALTH CARE 66, 67 (1991).

98. For example, the drug-maker Upjohn recently suspended a clinical trial of the drug Freedox (tirilazad) administered to head-injury victims because of an unexpected number of high deaths in the experimental arm of the trial compared to the placebo arm. The research involved head-injury victims from whom obtaining informed consent was difficult. *See Institutional Review Boards Should Be Entrusted With Informed Consent Waiver*, HEALTH NEWS DAILY, Jan. 11, 1995, at 4-5. The history of internal carotid artery bypass surgery for the prevention of strokes also illustrates the dangers of relying on clinical intuition and faith in new procedures to waive informed consent. The bypass procedure initially generated positive reports from the field. Nearly a decade after it was introduced, an international randomized trial demonstrated that contrary to expectations, the procedure was related to an increased risk of death from strokes. *See* EC/IC Bypass Study Group, *Failure of Extracranial-Intracranial Arterial Bypass to Reduce the Risk of Ischemic Stroke: Results of an International Randomized Trial*, 313 NEW ENG. J. MED. 1191, 1191 (1985).

thus increasing the chance that a "rescued" patient would still have brain damage. Given these particular risks and benefits, some persons would opt for the experimental treatment but quite clearly others would decline, regardless of whether the Cardiopump is the best possible medical intervention for the emergency.[99]

More importantly, justifying waiver of consent in critical care research because, in the physician's judgment, the patient stands an equal chance of benefiting from the experimental therapy as the standard treatment greatly diminishes the principle of patient autonomy. Notwithstanding the physician's best intentions and judgment, this rationale ignores the fact that an actual experimental study is underway. Ordinarily, the patient must make the independent moral determination whether to become an experimental subject. Knowing that a therapy is experimental changes the nature and character of the patient's decision.[100] Patients may be either less willing to consent to therapy when they understand the research aspects or if they do consent, the reasons may be other than the prospect of direct medical benefit.[101] The research subject may be motivated by, for example, altruism or the sense of having no hope.[102] Thus, any characterization of the reasonable person's preferences must be suspect. Individual value systems can lead patients to decline experimental therapy even when there is no apparent difference between the risks of standard versus experimental therapy and the experimental therapy holds great promise of benefit.

C. *Constitutional Law*

Research involving critical care patients without prospective informed consent also raises thorny constitutional problems. Because the exact nature and contours of the constitutional right to control medical decisions is still evolving in medical jurisprudence, the scope and application of the right is unclear. Fully exploring and resolving the constitutional issues implicated by critical care research is beyond the intended scope of this Article. Indeed, research in the critical

99. A review of the limited Cardiopump studies to date shows that, on the whole, the plunger device improves intermediate outcomes. However, no study has demonstrated improvement in the critical measure of neurologically intact survival to hospital discharge. *See* Olson & Rennie, *supra* note 4, at 1299; *Problems in Securing Informed Consent, supra* note 11, at 18 (testimony of Arthur Caplan, Director, Center for Bioethics, University of Pennsylvania).

100. *See* King, *supra* note 62, § 7.13, at 510.

101. *See id.* at 510-11.

102. *See id.* at 511.

care setting likely raises issues of first impression concerning the constitutional right to accept or decline medical care. This subsection merely identifies the basic issues implicated as a reminder that there may be constitutional limits to efforts to relax or modify the informed consent requirement.

Whether articulated as part of the constitutional right to privacy or as part of the constitutionally protected liberty interest, patients clearly have some constitutional rights with respect to declining medical treatment. However, the constitutional parameters are not well articulated and the constitutional rights themselves can be counterbalanced by other interests.[103]

Constitutional privacy cases involving birth control, abortion, and the right to withhold life-saving treatment recognize the constitutional right of patients to maintain their privacy against unconsented-to medical treatment.[104] Courts also have held that incompetent pa-

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103. *See, e.g.*, Doe v. Sullivan, 756 F. Supp. 12, 17-18 (D.D.C.), *aff'd*, 938 F.2d 1370 (D.C. Cir. 1991). In *Sullivan*, the district court denied a motion to enjoin the Department of Defense from using unapproved drugs on troops taking part in Operation Desert Storm without first obtaining consent from individual military personnel. *See id.* at 13. The court recognized service members' constitutional liberty interest in receiving full information and the need to obtain their informed consent before administration of unapproved drugs. *See id.* at 14. But the court scrutinized the policy under the rational basis test and found a legitimate countervailing governmental interest in furthering the military goals of Operation Desert Storm. *See id.* at 17-18. The government contended that it needed to administer the drugs uniformly to prevent unnecessary danger to troops. *See id.* at 17.

104. *See, e.g.*, Planned Parenthood v. Casey, 505 U.S. 833, 851 (1992) (recognizing a long line of cases protecting personal decisions relating to marriage, procreation, contraception, family relationships, and education as including choices central to personal autonomy and dignity which are central to the liberty protected by the Fourteenth Amendment); Cruzan v. Director, Mo. Dep't of Health, 497 U.S. 261, 278-79 (1990) (assuming, for purposes of the decision, that the Fourteenth Amendment affords a liberty interest in refusing life-saving nutrition and hydration and recognizing a general liberty interest in refusing medical treatment); Compassion in Dying v. Washington, 79 F.3d 790, 816, 836-39 (9th Cir. 1996) (en banc) (declaring unconstitutional a Washington law prohibiting physicians from prescribing life-ending medications to terminally ill patients and finding a constitutionally-protected liberty interest in determining the time and manner of one's own death, which encompasses a liberty interest in refusing unwanted medical treatment), *stay granted sub. nom*, Washington v. Gluckberg, 116 S. Ct. 2494 (1996), *cert. granted*, 65 U.S.L.W. 3085 (U.S. Oct. 1, 1996) (No. 96-110); *cf.* Quill v. Vacco, 80 F.3d 716, 729-30 (2d Cir. 1996) (declaring unconstitutional on Equal Protection Clause grounds two New York statutes penalizing assistance in suicide as applied to physicians aiding the death of terminally ill patients), *cert. granted*, 64 U.S.L.W. 3795 (U.S. Oct. 1, 1996) (No. 95-1858). Often, state constitutions may provide the clearer source of authority for the right to accept or decline medical treatment. *See, e.g.*, Bouvia v. Superior Court of Los Angeles County, 225 Cal. Rptr. 297, 298 (Cal. Ct. App. 1986) (recognizing a privacy right under the California Constitution of a quadriplegic woman to seek removal of nasogastric tube inserted and maintained against her consent for purpose of keeping her alive through involuntary force feeding).

tients, despite the loss of decisional capacity, maintain a constitutional right to privacy regarding medical treatment and that the right, in order to be preserved, may be exercised by a surrogate when the patient is unable to consent.[105] Other courts, however, have determined that the right is "personal" and "peculiar to the individual" and can be invoked by the individual only "when that individual is a competent and alert adult."[106] Thus, conducting research with critical care patients without obtaining prospective informed consent, or relying on the consent of a surrogate, raises difficult constitutional issues. Pending a clearer resolution of the federal constitutional issues by the federal courts, the ability to use surrogates to consent to critical care research likely will depend in significant respects on differing state constitutional standards for protection of privacy.

II. LEADING PROPOSALS FOR CONDUCTING CRITICAL CARE RESEARCH

Because of the legal obstacles to conducting critical care research, clinical investigators and other commentators have advanced different approaches for modifying the informed consent requirements. This section reviews several leading proposals, apart from the new FDA reforms. Certain approaches have, of course, been proposed in combination with one another, but it is useful to examine each in isolation and identify its merits and weaknesses. This examination first requires, however, a threshold consideration of whether the informed consent requirements should be changed at all, in order to identify more clearly the implications of relaxing informed consent.

A. Why Allow Critical Care Research Without Prospective Consent?

The federal agencies regulating medical experimentation inter-

105. *See, e.g.*, Superintendent of Belchertown State Sch. v. Saikewicz, 370 N.E.2d 417, 424, 431-32 (Mass. 1977) (relying on constitutional privacy right and common-law right to informed consent to permit withholding of chemotherapy from a profoundly retarded 67-year-old man suffering from leukemia); *In re* Peter, 529 A.2d 419, 429-30 (N.J. 1987) (holding that surrogate, authorized by health care power of attorney, may elect to refuse life-sustaining treatment for 65-year-old nursing home patient in vegetative state); *In re* Quinlan, 355 A.2d 647, 671-72 (N.J. 1976) (recognizing right of incompetent patient to refuse medical treatment and that this right may be asserted on patient's behalf when patient is incapable of exercising it on her own).

106. *In re* Brown, 478 So. 2d 1033, 1041 (Miss. 1985). Such cases have generally involved refusal of life-sustaining medical treatment, which may explain some courts' heightened scrutiny regarding the need for informed consent and reluctance to allow the constitutional right to be asserted by a surrogate.

pret congressional intent as requiring that biomedical research be conducted in accord with the highest contemporary ethical standards.[107] Thus, the legal merits of any regulatory reforms stand, in part, on how well they address the ethical issues raised by critical care research. A full-fledged ethical analysis is beyond the intent and scope of this Article, but it is useful to examine briefly the theoretical ethical issues underlying the informed consent requirement as applied to critical care research. This subsection reviews the ethical implications of relaxing informed consent in critical care research under the three guiding principles of biomedical ethics: beneficence, justice, and autonomy. The Belmont Report, upon which the HHS and FDA regulations are based, noted that these three guiding principles are not capable of resolving biomedical ethical conflicts beyond dispute, nor are they always capable of consistent application.[108] Nevertheless, the principles provide an analytical framework to guide consideration of the ethical issues implicated by critical care research.[109]

1. Beneficence

The principle of beneficence requires the provision of benefits to help others in a manner that minimizes the imposition of risk.[110] Complementary to the principle of beneficence is the concept of nonmaleficence, or doing no harm.[111] In the research setting, this re-

107. *See, e.g.*, Protection of Human Subjects; Informed Consent, 60 Fed. Reg. 49,086, 49,090 (1995) (to be codified at 21 C.F.R. pt. 50) (proposed Sept. 21, 1995) (FDA noting that this congressional purpose reflected in both the Drug Amendments of 1962 and the Medical Device Amendments of 1976).

108. *See Belmont Report*, *supra* note 27, at 2.

109. *See id.* Alternative methods have been proposed for resolving bioethical issues which call for a more inductivist, contextual analysis, moving beyond reasoning at the level of abstract principles and universal norms and paying closer attention to the pragmatic impact of bioethical and legal rules, with special attention to differences associated with race, gender, ethnicity, and socioeconomic condition. *See, e.g.*, Susan M. Wolf, *Shifting Paradigms in Bioethics and Health Law: The Rise of a New Pragmatism*, 20 AM. J.L. & MED. 395, 395 (1994). The discussion of the guiding principles in this Article is not meant to diminish the importance of ethical analysis of critical care research by alternative methods. The principle-based approach can coexist with and be complemented by alternative paradigms. *See* Tom Beauchamp, *Principles and Other Emerging Paradigms in Bioethics*, 69 IND. L.J. 955, 961, 971-72 (1994). Indeed this Article calls for further attention to the pragmatic impact of changed informed consent requirements in an attempt to fill out and refine the application of the guiding principles. *See* text accompanying note 234.

110. *See* TOM BEAUCHAMP & JAMES CHILDRESS, PRINCIPLES OF BIOMEDICAL ETHICS 260 (4th ed. 1994).

111. *See id.* at 190-96.

quires that the risks associated with research be reasonable in light of the expected benefits, and that all possible benefits be maximized and the chance of harm minimized.[112] The Belmont Report also acknowledged that beneficence involves application at two different levels—within the particular study at hand and within the research enterprise in general.[113] While research should be designed so as to maximize benefits and reduce risks to particular subjects, ethical analysis may also account for the fact that research participation can benefit society as a whole.[114]

Thus, waiver of consent in critical care research is consistent with beneficence in circumstances where there is vigilant review of the study design to ensure that the likely benefits and harms meet acceptable levels. Also, as noted previously, much of what has been accepted as standard therapy in the critical care setting has not been systematically evaluated for safety and efficacy. Beneficence suggests, therefore, that critical care research be encouraged because further investigation will help other patients (and the subject in the future) by demonstrating the relative difference between investigational and standard interventions.[115]

2. Justice

The principle of justice requires that the distribution of societal benefits and burdens involves fairness of treatment.[116] With respect to medical experimentation, this means that the distribution of benefits and burdens of research should be equitable.[117] Researchers must ensure that subjects, especially vulnerable persons, are chosen because their condition is essential and relevant to what is being studied and not because of other reasons involving differential treatment.[118] In addition, subject selection should account for the potential bene-

112. *See* Larry Gostin, *Ethical Principles for the Conduct of Human Subject Research: Population-Based Research and Ethics*, 19 LAW MED. & HEALTH CARE 191, 192 (1991). In addition, consider the FDA's discussion of the ethical principles underlying its proposed rule included in Protection of Human Subjects; Informed Consent, 60 Fed. Reg. at 49,093-94.

113. *See Belmont Report, supra* note 27, at 7.

114. *See id.*

115. *See* Protection of Human Subjects; Informed Consent, 60 Fed. Reg. at 49,093-94.

116. *See* MUNSON, *supra* note 16, at 38.

117. *See id.*

118. For example, the infamous Tuskegee Syphilis Study violated the justice principle because primarily poor African-Americans were chosen as subjects and this racial and economic classification was not essential to the scientific merits of the investigation. *See generally* JONES, *supra* note 25 (discussing this experiment).

fits of experimental therapy by providing research participation opportunities in a fair and open manner.[119] Categorically excluding critical care patients from participation in clinical trials because of informed consent difficulties conflicts with the justice principle. This denies the opportunity of research participation to a vulnerable population, patients with diminished capacity, and directly withholds the potential benefits that may arise from research directed toward alleviating the conditions causing their diminished capacity.

Consistent with the principle of justice, IRBs are charged with ensuring that the selection of research subjects is "equitable."[120] The direction to ensure "equitable" selection of subjects can be interpreted as requiring the preservation of the critical care patient's opportunity to participate in research or refuse investigational treatment.[121] Waiving or modifying informed consent requirements for critical care research helps to ensure a more equitable distribution of research costs and benefits, assuming that safeguards are observed so that the critical care population does not disproportionately bear the burdens of research that could be carried out with other populations.[122] Research with vulnerable critical care patients that could be conducted as effectively with other populations would not satisfy the requirements of justice.

3. Respect for Patient Autonomy

The principle of respect for patient autonomy presents the most serious obstacle to relaxing informed consent requirements in critical care research. Autonomy recognizes people as independent moral agents whose choices should be respected and observed.[123] Autonomy involves "personal rule of the self" and the exercise of meaningful decisions that are not controlled by others. With regard to research, the autonomy principle suggests that persons with diminished capacity need to be protected or even excluded from the harms of unconsented-to research.[124] The ethical problems associated with forced enrollment in research arise not only from the threat of physical injury, but also from the moral wrong committed by using other persons merely as means (research object) to an end (the study conclusions). Autonomy generally would require that a patient pro-

119. *See* Gostin, *supra* note 112, at 191.
120. *See* 45 C.F.R. § 46.111(a)(3) (1995).
121. *See* Moore, *supra* note 7, at 571.
122. *See id.* at 573.
123. *See id.*
124. *See* Gostin, *supra* note 112, at 191, 194.

vide consent in order to become a co-adventurer with the investigator and willingly adopt the research objectives as his or her own.[125]

Some would argue that under critical care circumstances, the competing principles of beneficence and justice simply override autonomy concerns. Alternatively, others would insist that respect for autonomy means that the principle can never be compromised. Neither of these extreme positions proves satisfactory. Allowing beneficence and justice concerns to overwhelm autonomy concerns merely underscores the reason why respect for autonomy is needed as a guiding ethical principle in the first place. Biomedical ethicists have distinguished between "strong" and "weak" paternalism in medicine.[126] Strong paternalism occurs when the physician alone decides what is in the best interests of the patient.[127] Such practices clearly violate the ethical bases of informed consent.[128] Overriding a person's judgment shows lack of respect for the person as an autonomous agent and denies others the freedom to act as moral agents.[129] Indeed, the law's increasing focus on informed consent and the corresponding nascent patient-consumer movement developed in large part as responses to the medical profession's traditional paternalism, a system that failed to acknowledge the patient as the legitimate medical decision-maker. Allowing the physician-researcher to waive informed consent requirements and also make the substantive medical decisions tilts too far in favor of professional authority over the patient. The informed consent requirement generally serves as a check and counterbalance to the physician-investigator's natural enthusiasm for and advocacy of experimental technologies.[130]

In contrast, the "weak" form of medical paternalism recognizes that the patient has the prerogative to make self-governing decisions, but also that the physician remains obligated to make such decisions under circumstances where the patient cannot truly make an autonomous decision.[131] "Under these circumstances, the physician is obligated to act for the patient but always, if possible, to remove the obstacles to an autonomous decision and to empower the patient's

125. *See* Capron, *supra* note 48, at 185-86.

126. *See, e.g.*, Edmund Pellegrino, *Autonomy, Beneficence, and the Experimental Subject's Consent: A Response to Jay Katz*, 38 ST. LOUIS U. L.J. 55, 58-59 (1993).

127. *See id.*

128. *See id.* at 59.

129. *See* Gostin, *supra* note 112, at 193.

130. *See* King & Henderson, *supra* note 62, at 1032.

131. *See* Pellegrino, *supra* note 126, at 59.

decision-making capacity to the fullest extent possible."[132] For example, waiver of informed consent can be justified as respecting the patient's personal dignity if the patient, because of the stress of illness, desires waiver to avoid having to make a decision he or she does not want to make.[133] Thus, if informed consent is to be relaxed at all in the critical care setting, this should occur only under a weak paternalism framework and not through a full-fledged abandonment of autonomy concerns.

Too rigid a respect for autonomy, however, can lead to inflexible rules that fail to consider the importance of beneficence and justice. Biomedical ethicists generally do not recognize the autonomy principle as paramount to the other guiding principles.[134] At times, autonomy must give way to competing ethical concerns and the realities of medical practice.[135] Indeed, it is simply misleading to insist on prospective informed consent as the gold standard for critical care research. In reality, the consent provided by non-critical care patients enrolling in investigational trials is not truly informed because patient-subjects are rarely told, in terms they understand, the probabilities and uncertainties inherent in biomedical research.[136] Personal autonomy is already compromised in most medical settings. Patients are usually in vulnerable states and are prone to unwarranted or uncritical acceptance of a physician's or researcher's recommendations.[137] Moreover, the value of autonomy varies with the range of choices realistically available to the patient. Where the patient has few or no treatment options available that may offer likely benefit, meaningful choice is necessarily limited, and respecting

132. *Id.*

133. *See* Meisel, *Striking a Balance*, *supra* note 14, at 459.

134. *Cf.* MUNSON, *supra* note 16, at 43-45 (addressing philosophical principles that may be employed to justify restricting patient autonomy).

135. *Cf.* BEAUCHAMP & CHILDRESS, *supra* note 110, at 181.

136. Numerous studies have shown that patients illogically process the probability information provided to them under informed consent procedures. Common errors include underutilizing base rate information (giving disproportionate weight to an isolated, specific piece of information), inability to combine and assess multiple risks, and giving excess weight to memorable examples while undervaluing more abstract presentations of data. *See, e.g.*, Aaron D. Twerski & Neil B. Cohen, *Informed Decision Making and the Law of Torts: The Myth of Justiciable Causation*, 1988 U. ILL. L. REV. 607, 627-34. Other studies call into question whether patients understand the information provided or can recall that information accurately when a decision must be made. *See* Alan Meisel & Loren H. Roth, *Toward an Informed Discussion of Informed Consent: A Review and Critique of the Empirical Studies*, 25 ARIZ. L. REV. 265, 292-98 (1983).

137. See JAY KATZ, THE SILENT WORLD OF DOCTOR AND PATIENT chs. V-VI (1984).

autonomy becomes less paramount.[138]

Relaxation of consent requirements can be attempted while still ensuring a large degree of respect for autonomy. There are alternatives, admittedly imperfect, to individual consent. Consultation with peers representative of the subject or the use of surrogates can help approximate the subject's preferences and facilitate the self-determination process critical to the principle of autonomy.[139] In this manner, the subject's moral choices are acknowledged as meriting serious consideration by establishing procedures that approximate what such decisions would be under the circumstances. Approximation of the wishes of the patient lacking full autonomy is one condition, but not the only condition, that should be present before relaxing the consent requirement for impaired subjects. It is important that the research design be reviewed critically to ensure that subjects are protected from unwarranted potential harm. Strict study design criteria, including the thorough minimization of risk and the direct relevance of the investigation to the subject's condition, should apply before persons unable to consent are enrolled in an experiment.[140]

Of course, even if waiving informed consent can be defended under limited circumstances as consistent with autonomy by giving voice to the patient's presumed preferences, the question remains whether this provides sufficient justification. Many legal barriers prevent persons from having their intent effectuated. For example, in most states, the parol evidence rule forbids oral testimony regarding variation of the terms of a written contract.[141] Similarly, most states require that wills be in writing and refuse to enforce oral agreements to leave property by will.[142] These laws frustrate individual intent. But the critical care research setting may be distinguishable because of the inherently personal nature of the decision to undergo experimental medical treatment and the often drastic and immediate consequences involved. In addition, in the other situations there may exist alternate readily available legal mechanisms to express one's intent (e.g., amend a contract, draft a will)

138. *See* Peter H. Schuck, *Rethinking Informed Consent*, 103 YALE L.J. 899, 925 (1994).

139. *See* Capron, *supra* note 48, at 188.

140. *Cf.* Gostin, *supra* note 112, at 194 ("Traditional micro-ethical principles... require [that]... vulnerable subjects [be]... selected only if the research is directly relevant to the person or class of persons.").

141. *See* RESTATEMENT (SECOND) OF CONTRACTS § 213 (1981).

142. *See* RESTATEMENT (SECOND) OF PROPERTY (Donative Transfers) § 33.1 (1992).

before becoming incapacitated. Establishing legally effective proof of prior consent to experimental treatment remains difficult at best.[143]

In sum, a brief review of the ethical principles indicates that valid justifications exist for relaxing or waiving the informed consent requirement in the critical care setting, but the specific protections required and the manner in which the consent requirements may be waived are subject to reasonable disagreement. The best compromise of the difficult ethical considerations is to insist that critical care research accommodate personal autonomy in some fashion even if prospective informed consent is not feasible. This can be accomplished by approximating the patient's preferences through use of surrogate consent mechanisms, or limiting conduct of the research to situations where it may be legitimately assumed reasonable persons would consent, or both. In addition, the principles of autonomy and beneficence direct that critical care trials relaxing informed consent requirements be of especially rigorous design.

In light of these ethical considerations and the preceding discussion of the legal obstacles, the remainder of this section discusses several leading approaches, apart from the new FDA rules, for addressing the problems of informed consent in critical care research.

B. Waiver of Consent

One obvious approach to addressing the problems of informed consent in critical care research would be to waive the informed consent requirement altogether. Certain investigators have maintained that the emergency exception should be extended to critical care research.[144] The argument is that the physician is ethically bound to do what is best for the patient in a study, including providing experimental therapies. According to this view, if the physician believes that an investigational therapy may be better for the critical care patient, he or she must choose that for the patient.[145] Similarly, if the researcher truly does not know which therapy is better and has a predesigned protocol for assigning patients to standard and investigational therapies, the physician is still exercising his or her best clinical judgment by enrolling the patient in a randomized study.[146]

The inclination to override patient autonomy is understandable. Subjects in critical care research situations are suffering from deci-

143. *See infra* notes 168-75 and accompanying text.

144. *See* Abramson et al., *supra* note 96, at 2829.

145. *See id.*

146. *See id.* at 2829-30.

sional incapacity, and it is difficult for physicians operating on the front line and providing urgent care to dissociate the patient from the condition. As Sachs and Cassel observe:

> When writers emphasize the principle of autonomy in discussing informed consent, they have us envision a subject who is an active participant, even a partner, in the research endeavor. In contrast, when physicians and other investigators see demented subjects, they most often see people who have already formally or informally given over decision-making authority even for many of their simple daily activities to a family member or other caregiver.[147]

But, as discussed previously, the reasons for the emergency exception to the informed consent doctrine do not support waiving informed consent requirements where clinical investigations are involved.[148] The emergency exception reflects the societal judgment that providing medical care without a patient's consent in an emergency is permissible because reasonable persons would consent to such treatment if they were capable and the medical care provided is likely to benefit the patient. In experimental settings, where the benefits and risks are largely unknown and the treatment participation decisions more complicated, these factors cannot be presumed with the same level of confidence.[149]

Moreover, justifying waiver of informed consent solely on the premise that the investigator must and will act for the patient's benefit overemphasizes the principle of beneficence at the expense of valid, competing concerns. Presumably, most researchers believe that the experimental therapy under investigation will benefit the patient. But the reason the research is being done is to demonstrate whether this hypothesis is statistically valid by generalizable study results. The researcher's treatment preference, where experimental therapy is involved, cannot be used as the sole justification for enrolling the subject.

First, this inclination can be wrong and patients need to be protected against physical harm due to uncritical reception of new technologies.[150] Apart from patient safety concerns, allowing researcher-initiated waiver of informed consent invites disregard for the law by making the informed consent requirements easily subject

147. Greg A. Sachs & Christine K. Cassel, *Biomedical Research Involving Older Human Subjects*, 18 LAW MED. & HEALTH CARE 234, 237 (1990) (footnote omitted).

148. *See supra* notes 93-102 and accompanying text.

149. *See* Delgado & Leskovac, *supra* note 62, at 90-91.

150. *Cf. supra* notes 63-68 and accompanying text.

to manipulation or deliberate evasion. Too much emphasis on beneficence leads to dangerous paternalism.[151] A general waiver approach, with no other compensating safeguards, conceals the fact that the patient is being asked to participate in an experimental, unknown undertaking. In the modern era, medical uncertainty is pervasive and differences of opinion are resolved only on the basis of risk assessment and individual value preferences. Thus, "[m]edical choice increasingly depends on factors that transcend professional training and knowledge.... Health care choices involve profound questions that are not finally referable to professional expertise."[152]

C. *Pre-Critical Care Episode Prospective Consent*

An alternative approach to complete waiver is to seek consent from potential subjects well before they find themselves in critical care situations. In theory, experimental protocols could be designed that identify and seek consent from patients likely to need investigational therapies in the future because of their present medical conditions. Because certain medical episodes occur predictably in special populations, potential experimental subjects could be approached in advance. For example, recovering cardiac arrest patients could be asked if they would be willing to participate in clinical studies of experimental resuscitation techniques should they again become incapacitated during the recovery period.[153]

However, the prospective identification of subjects eligible for investigational treatments is possible only in a small subset of critical care situations. Because of the uncertainties inherent in medical research, it can prove extremely difficult to identify in advance the class of patients who will present the right conditions and circumstances for the experimental protocol.[154] For an experimental study design to have any rigor, certain constraints for participation must be established that cannot be predicted in advance of the immediate onset of the critical care condition. Furthermore, while prospective consent

151. *See generally* Pellegrino, *supra* note 126, at 361, 365-66 (revealing the moral dangers and potential conflict of interest in clinical research when the physician is both a caregiver and physician-scientist).

152. Shultz, *supra* note 60, at 222.

153. In its preamble notice, the FDA warns that it is not appropriate to invoke the regulation waiving informed consent when the research subjects can be identified and their consent sought in advance. *See* Protection of Human Subjects; Informed Consent, 60 Fed. Reg. 49,095 (1995) (to be codified at 21 C.F.R. pt. 50) (proposed Sept. 21, 1995).

154. *See Problems in Securing Informed Consent*, *supra* note 11, at 111-16 (discussing need to seek out prospective consent of disproportionately large number of patients in order to ensure valid sample size for study of vest-CPR therapy).

might be readily obtained from already hospitalized patients at risk for certain medical episodes or conditions, this would exclude non-hospitalized patients from the experimental protocol, which could significantly bias the research results. To be generalizable, a clinical study's subject pool must be selected according to entry criteria applicable to a well-defined population.[155] In addition, obtaining the prospective consent of the minimum number of patients needed to commence a study would likely be so time consuming that the available information about risks and benefits of the treatment under investigation could change after the initial period. Presumably, this would cause further delays because it would likely require the reconsenting of the initial patients who consented based on outdated information.[156] Finally, identification of eligible research subjects in advance is simply not possible for studies involving accident victims, persons suffering severe head trauma, poisoning, drug overdoses, or the numerous other critical care episodes not related to progressive medical conditions.

D. Deferred Consent

IRBs have in some cases approved investigations that employ "deferred consent."[157] Under this approach, the experimental therapy is administered without seeking prospective consent. Instead, the patient's representative, or the patient if she regains decisional capacity, is told as soon as possible that the therapy has been initiated. At this point, the patient or her representative has the opportunity to request withdrawal from the study.

The term "deferred consent" is somewhat misleading because neither the patient's nor the patient's representatives' consent is actually obtained. Rather, the initial decision to place the patient in the experiment is either later ratified or rejected. OPRR recently warned IRBs across the country that deferred consent does not satisfy the federal regulations' informed consent requirements.[158] However, until OPRR's statement of policy, deferred consent had

155. *See* Norman S. Abramson et al., *Clinical Trials and Cerebral Resuscitation Research*, 13 ANNALS EMERGENCY MED. 868, 869 (1984).

156. *See, e.g.*, Abramson et al., *supra* note 10, at 2468.

157. *See* Spivey et al., *supra* note 9, at 1253 (defining the term "deferred consent" as it has developed in the context of emergency medicine).

158. *See OPRR Letter*, *supra* note 18 (reiterating the requirement for obtaining "legally effective informed consent *prospectively* from each research subject or the subject's legally authorized representative").

been used in several studies.[159]

Deferred consent is a superficially clever, but ultimately evasive approach, for addressing the serious ethical and legal problems involved in critical care research. Deferred consent does very little to advance the core objectives of the informed consent doctrine because it provides no special protection for subjects against the unconsented exposure to risks involved in experimentation. As argued previously, focusing on the potential benefit to the patient as the sole reason for relaxing consent requirements does not by itself provide sufficient justification, nor does it protect patients from the greater potential risks involved in experimental medicine than in ordinary clinical settings. In many studies, the risk to the patient from the experimental therapy is immediate, so the mechanism of deferred consent offers an ineffective remedy.[160] Withdrawal of the patient from the study can occur only after the patient has been exposed to the risks inherent in the experiment.[161]

In addition, deferred consent does not sufficiently acknowledge the patient's independent decision-making authority and autonomy until after the experimentation has begun, which is really too little, too late. Deferred consent simply weighs too much in favor of beneficence and too little in favor of patient autonomy. The principle of respect for autonomy imposes difficult yet necessary burdens on the physician-investigator—primarily that the required disclosures about the experiment should not be affected by beneficence concerns that patient-subjects will not make decisions that are in their best interests.[162] Deferred consent overrides these important limitations by giving researchers considerable leeway to make the decisions they

159. *See, e.g.*, Abramson et al., *supra* note 10, at 2466-67 (describing deferred consent procedures in the Brain Resuscitation Clinical Trial, a randomized clinical trial of cardiopulmonary-cerebral resuscitation after cardiac arrest); Prentice et al., *supra* note 12, at 1 (describing randomized trial investigating use of drug for closed head injury as a means of preventing continuing cerebrovascular damage).

160. *See* Spivey et al., *supra* note 9, at 1253.

161. *See, e.g.*, Prentice et al., *supra* note 12, at 3 (describing how any potential risks in study of drug administered to closed head injury victims are immediately incurred by the subject).

162. *See* Katz, *supra* note 14, at 32. As Professor Katz has observed, the Belmont Report is confusing because it does not make clear the distinctions between competing ethical principles that should govern research with competent patients as opposed to incompetent patients. *See id.* at 30 n.71. The Belmont Report is even more confusing in applying the ethical principles to the problem of critical care research where subjects may suffer from only temporary decisional incapacity. The examples discussed in the Belmont Report of populations with diminished autonomy, such as children and the mentally ill, raise different concerns than, for example, a competent adult who may regain decisional capacity in a short timespan. *See Belmont Report*, *supra* note 27.

think should be made for the patient, irrespective of what the patient would actually choose.[163]

It is troubling that an investigator should be given such a degree of discretion in making the decision about research participation. Because of the nature of critical care research, some investigators know very little about the subjects involved. CPR research, for example, often occurs with patients admitted to hospital intensive care units. These facilities are frequently staffed by specialist physicians who likely have had no previous contact with the patients, and the primary care physicians play only a marginal role.[164] Moreover, the risk/benefit calculations involved in deciding whether to become a research subject are highly individualistic. For example, if the expected benefit of a cardiac care study is resuscitation, but the study does not offer other chances for meaningful survival or alleviation of pain, certain patients would not see this as beneficial and would want to decline participation if they were able to communicate their preferences.[165] As the patient's fiduciary, a physician ordinarily would respect these wishes. But the physician's commitment to the welfare of the individual "becomes tainted when, without a patient-subject's full knowledge, we allow the interests of science and society to intrude on the physician-patient relationship."[166]

Nor is it clear that the family members asked to participate in deferred consent are in a better position to articulate the patient's preferences and values. In deferred consent, the surrogate must decide whether to disenroll the subject once the experiment has begun, a very different decision than whether to begin the experiment at all. Family members may justifiably question whether the patient's care and attention will suffer if they request that the subject be removed from the investigation. For example, in a study of post-resuscitation coma which employed the deferred consent process, no family member, once informed about the experiment, removed a patient from trials in progress except when further treatment was regarded as altogether futile. This apparent unanimity in choices of the family member surrogates suggests that they were not making the deferred consent decision in accord with what they believe the patient would

163. Deferred consent is also difficult to justify regarding the class of patients that are conscious but for whom communication may be difficult because it treats them as though they were incompetent when they are not. *See* Grim et al., *supra* note 10, at 254.

164. *See* Luce, *supra* note 64, at 696.

165. *See* Kenneth Iserson, *Informed Consent in Acute Care Research*, 20 ANNALS EMERGENCY MED. 1251, 1255 (1991).

166. Katz, *supra* note 14, at 23.

have wanted. The fact that the experiment was underway, and the treatment implications of removing the patient from the investigation, were important factors that presumably influenced and may have biased the deferred consent process.[167]

E. Advance Directives

In most states, individuals may develop advance directives regarding decisions about health care treatment in the event that they become incapacitated. However, advance directives are of limited use in resolving the problems of informed consent in critical care research. First, they are relatively inflexible mechanisms for effectuating a patient's wishes in the various situations which may involve application of experimental therapies. Formal advance care documents use imprecise terms and obscure hypotheticals; the situation encountered by the patient likely will not correspond accurately to the text of the directive. Because the terms of advanced directives are often vague, they are not capable of articulating in sufficient detail the myriad of situations in which persons may face the choice of experimental treatments. Advance directives are inadequate "because no matter how detailed, [they] cannot possibly anticipate the full range of difficult treatment decisions to be made."[168] In addition, a patient's views may change after execution of the directive.

Perhaps even more important, only a small percentage of the public executes advance directives, despite opinion polls showing most Americans want to exercise control of their health care at critical junctures and despite the enactment of the Patient Self-Determination Act.[169] Estimates indicate that only five to ten percent of the population have executed advance directives.[170]

Advance directives generally take two different forms. First is the "living will," a document used to provide directions regarding preferred medical therapies and the types of treatment the patient

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167. *See* Iserson, *supra* note 165, at 1256.

168. *See* Judith Areen, *The Legal Status of Consent Obtained From Families of Adult Patients to Withhold or Withdraw Treatment*, 258 JAMA 229, 230 (1987).

169. *See* 42 U.S.C. § 1395cc(f) (1994). The Patient Self-Determination Act requires hospitals, nursing homes, and other health care providers receiving federal funding to make information about advance directives available to patients upon admission. *See* Ardath A. Hamman, *Family Surrogate Laws: A Necessary Supplement to Living Wills and Durable Powers of Attorney*, 38 VILL. L. REV. 103, 132-33 (1993); *see also* Jerry A. Menikoff et al., *Beyond Advance Directives—Health Care Surrogate Laws*, 327 NEW ENG. J. MED. 1165, 1165 (1992) (identifying reasons why patients may be reluctant to execute advance directives).

170. *See* Hamman, *supra* note 169, at 105; Portman, *supra* note 85, at 312.

wishes to refuse. However, state statutes enacted to allow the use of living wills generally do not contemplate critical care research situations. Most living will laws are applicable only to persons who are terminally ill and they limit the types of treatment decisions to the refusal or acceptance of "life-sustaining" treatments or artificial life support.[171] Living wills are necessarily limited in scope because they require a person to predict not only the situation and nature of a life-threatening illness, but also what medical interventions might be available.[172] This presents a significant obstacle to using living wills for critical care research because the patient may not even be aware of what experimental therapies will be available in the future and their associated risks and benefits. Accordingly, living wills usually do not help settle the question of a patient's preference for participating in medical investigations.

The second type of advanced directive is the assignment of a durable power of attorney to a designated health care proxy.[173] Statutes authorizing durable powers of attorney, often drafted with the intent of permitting the appointed agent to make financial decisions for the principal, are now being used to appoint surrogates to make health care decisions. In addition, states have begun to enact additional proxy laws specific to health care decision-making, which specify additional information that must be included in the proxy forms and the standards upon which treatment decisions should be based. Under these laws, the surrogate is supposed to make decisions consistent with the wishes of the patient if known; otherwise, the surrogate is obligated to act in the patient's "best interests."[174]

Health care proxies could be helpful for addressing the problems of critical care research to the extent that they allow a patient expressly to designate a surrogate to make decisions regarding participation in experimentation. However, the forms rarely make clear to the patient that the medical decisions made by his or her sur-

171. For example, Maryland allows persons to make advance directives that become effective when the attending physician certifies that the patient is unconscious or incapable of making an informed decision. *See* MD. CODE ANN., HEALTH-GEN. II § 5-602(e) (1995). Although the suggested model form presents a range of critical health care circumstances, such as whether to withdraw artificial hydration and nutrition in the event of a persistent vegetative state or terminal condition, the form does not contemplate the administration of experimental therapy during a period of decisional or communicative incapacity. *See id.* § 5-603.

172. *See* George J. Annas, *The Health Care Proxy and the Living Will*, 324 NEW ENG. J. MED. 1210, 1210-11 (1991).

173. *See id.* at 1211.

174. *See id.*

rogate may involve experimental therapies.[175] While the patient may feel comfortable regarding his or her choice of surrogate for standard therapy, he or she may have different views regarding participation as an experimental subject. In addition, a document granting durable power of attorney for health care decisions may be of limited use in certain critical care research situations, because the designated surrogate may not always be capable of being located in the short time available to begin the experimental treatment.

III. THE NEW FDA PROPOSAL

The FDA has attempted to overcome the limitations of the preceding approaches by developing an elaborate new regulatory proposal for relaxing informed consent. This section discusses the proposed FDA regulations in detail, identifying problems with their intended scope, ambiguity on several issues, and overall rationale.

Under the proposed FDA rules, the primary responsibility is placed upon IRBs to determine whether informed consent should be waived for particular critical care research studies. An IRB may approve a study involving waiver of informed consent if it finds and documents each of the following:

> (1) The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence . . . is necessary to determine what particular intervention is most beneficial;
>
> (2) Obtaining informed consent is not feasible because:
>
> > (i) The subjects will not be able to give consent as a result of their medical condition; and
> >
> > (ii) The intervention under study must be administered before consent from legally authorized representatives is feasible; and
> >
> > (iii) There is no reasonable way to identify prospectively the individuals likely to become eligible for the research because the emergence of the condition to be studied cannot be predicted reliably in particular individuals.
>
> (3) The opportunity for the subjects to participate in the research is in their interest because

175. For example, a Massachusetts model health care proxy appointment form, developed by the state medical society, bar association and other interest groups, is even shorter and states simply that, subject to certain limitations, the proxy has authority "to make all health care decisions for [the patient]." *See id.* at 1213.

(i) A life-threatening situation necessitates intervention, and

(ii) The risk of the investigation is reasonable in light of what is known about the medical condition and the risks and benefits of current therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

(4) The research could not practicably be carried out without the waiver.[176]

The proposed regulations also require that before waiving informed consent, IRBs take additional action to safeguard subjects' rights, including (i) consulting with representatives of the community from which the subjects will be drawn; (ii) disclosing to the public the risks and benefits of the study before its commencement and providing public information regarding the results after the study is completed; and (iii) establishing an independent safety and data monitoring board.[177]

Under the proposed rules, subjects who regain decisional capacity must be informed that they are currently participating in an investigation, or if the subject remains incapacitated, the subject's family member or the subject's legally authorized representative must be informed about the inclusion in the research. The subject (or, if incapacitated, the family member or surrogate) may discontinue participation at any time without penalty or loss of benefits.[178]

A. Limited to Imminent, Life-Threatening Situations

Although the regulations promise to remove significant barriers to critical care research, several features of the proposed rules are troubling. First, their scope is too narrow. IRBs are supposed to approve waiver only if subjects are in a "life-threatening situation."[179] In the preamble to the proposed rule, the FDA indicates that "an IRB can determine that the subjects are in a life-threatening situation if it determines that the medical condition being treated by the proposed intervention poses an imminent risk of loss of life."[180] Although the regulation does not further define "imminent," the overall context of the FDA's preamble notice suggests that this

176. Protection of Human Subjects; Informed Consent, 60 Fed. Reg. 49,086, 49,100 (1995) (to be codified at 21 C.F.R. pt. 50) (proposed Sept. 21, 1995).

177. *See id.* at 49,100-01.

178. *See id.* at 49,101.

179. *See id.* at 49,100.

180. *Id.* at 49,095.

means an immediate threat of loss of life within a period no greater than twenty-four hours.[181]

Defining imminent risk of loss of life in terms of such a narrow time-window poses certain problems for diseases or conditions that are life-threatening, but on progressively longer terms. For example, most stroke victims do not face risk of loss of life within the twenty-four hour period from onset of the condition.[182] The thirty day mortality rate of stroke victims is approximately ten to fifteen percent.[183] Nevertheless, many experimental stroke therapies, to be effective, need to be applied rapidly, while the patient often is unable to provide consent. For example, preliminary clinical trials suggest that the new drug Tissue Plasminogen Activator (TPA) must be applied within three hours of a stroke to be effective, which leaves little time because most stroke victims do not reach the hospital and undergo neurological evaluations until nearly two hours after the stroke.[184] Excluding this population from the proposed rules does not seem fair given the seriousness of complications arising from stroke and the life-threatening nature of the disease over the long term.

In addition, the FDA proposed rules seem too narrow in excluding patients who are not in a "life-threatening" situation, but who could benefit from application of experimental therapy. For example, consider a patient who suffers a serious accident with multiple body injuries. The patient experiences brain trauma while at the same time running a risk of serious non-brain injury, such as the loss of a limb. The patient may be a candidate for certain experimental tissue regrafting procedures in an attempt to save the arm or leg but is unable to consent due to the brain trauma, which is being stabilized by conventional therapy. It is not clear that the FDA rules would allow waiver of informed consent in these circumstances because application of the experimental therapy is not necessitated by the life-threatening situation; rather, the experimental treatment of the arm or leg is secondary to the conventional treatment of the brain trauma.

The distinction between life-threatening situations and others is

181. For example, the preamble notice indicates concerns that nearly all patients dying within the first 24 hours of a critical care injury do so from processes set in motion at the time of injury which require intervention in the field. *See id.* at 49,090.

182. *See* Per Thorvaldsen et al., *Stroke Incidence, Case Fatality, and Mortality in the WHO MONICA Project*, 26 STROKE 361, 367 (1995).

183. *See id.*

184. *See* National Institute of Neurological Disorders and Stroke, *supra* note 10, at 1586; Christine Gorman, *Damage Control*, TIME, (Special Issue), Fall 1996, at 30, 32; Gina Kolata, *New Study Finds Treatment Helps Stroke Patients*, N.Y. TIMES, Dec. 14, 1995, at A1.

simply too crude to make in modern medicine. A life of disfigurement or severe and intractable pain also imposes terrible burdens on the patient and similarly may justify some encroachment upon autonomy concerns. Many treatments keep patients "alive" but impose their own terrible costs. Accordingly, quality of life factors,[185] and other inputs, such as sensitivity analysis, pain thresholds, and mortality rates, are normally taken into account when deciding whether to initiate treatments.[186] Similarly, these factors should come into play when deciding whether the critical care patient is a candidate for experimental therapy.

B. *Insufficient Attention to Autonomy Concerns and Disenrollment Issues*

An additional problem with the FDA approach is that the Agency's justifications for waiver diminish the importance of autonomy as a central concern of informed consent and threaten to undermine application of the doctrine in the standard therapeutic setting. Under the FDA's proposed rule, consent could be waived if a state of "clinical equipoise" exists, where the relative risks of the proposed intervention are unknown or thought to be equivalent or better than the standard therapy and available treatments are unproven or unsatisfactory.[187] This overcompensates for the current legal rigidity regarding the need for prospective consent by, in effect, saying that so long as the patient is already in a grave situation and because the standard therapy is not particularly effective and risk of death is imminent, the goal of patient consent is not as important as the potential benefit investigation of new therapies might bring to the patient and to the population at large. This is not a fair or sensible balance of the competing interests of patient autonomy and the potential benefits of research.

Patient preferences and value choices should be acknowledged and accommodated to the extent possible, regardless of the severity

185. *See, e.g.*, BEAUCHAMP & CHILDRESS, *supra* note 110, at 156-58 (describing some patients' inability to adequately assess the impact of medical treatment on their "quality of life"); Anthony F. Lehman, *Measuring Quality of Life in a Reformed Health System*, 14 HEALTH AFF. 90, 94-96 (1995).

186. *See, e.g.*, Bruce E. Hillner & Thomas J. Smith, *Efficacy and Cost Effectiveness of Adjuvant Chemotherapy in Women With Node-Negative Breast Cancer*, 324 NEW ENG. J. MED. 160, 164-66 (1991); Maxwell J. Mehlman, *Health Care Cost Containment and Medical Technology: A Critique of Waste Theory*, 36 CASE W. RES. L. REV. 778, 791-92, 831-32 (1986).

187. *See* Protection of Human Subjects; Informed Consent, 60 Fed. Reg. 49,086, 49,093 (1995) (to be codified at 21 C.F.R. pt. 50) (proposed Sept. 21, 1995).

of the medical condition or the experimental treatment's likely causation of actual physical injury. Indeed, heightened respect should be shown for patient self-determination when the patient is in a life-threatening situation *because this is, as a practical matter, the time when the patient's preferences and value systems are likely to matter most.* The choices a patient must make (or that must be made when the patient is unable to do so) when facing serious illness and the risk of death implicate profoundly personal, moral, and religious issues such as the value and quality of life, an individual's tolerance for dependence on medical technology, and beliefs about the dying process. Accordingly, the critical care situation is not the time to minimize the importance of respecting patient autonomy and the individual's right to control medical decision-making.

That the FDA has lost sight of this central concept is evident in the agency's discussion of enrollment of minorities and low-income patients in critical care trials. In the preamble notice to its proposed rulemaking, the FDA justifies its new approach in part because it will likely increase the enrollment of minority and low-income patients in critical care studies.[188] The FDA notes that surrogate consent is more easily obtained from white and/or middle and upper income family members than from minority and/or lower income families and speculates that waiver of informed consent will overcome these barriers and increase the enrollment of all patients.[189] The FDA sees this as consistent with the justice principle, ensuring more equitable access to the benefits of research participation. What the FDA does not discuss and rightly acknowledge, however, is that the problems in obtaining surrogate consent from minority and/or low-income family members suggest that certain patients have clear preferences about avoiding research participation. Empirical studies indicate that there can be significant differences by race or ethnicity in attitudes towards medical decision-making.[190] Many African-Americans, for example, are suspicious of enrolling in clinical trials because of the historic and disproportionate abuse of black patients in the name of medical research, often without their consent.[191] To be sure, more needs to be

188. *See id.*

189. *See id.*

190. *See, e.g.*, Annette Dula, *Yes, There are African-American Perspectives on Bioethics, in* AFRICAN-AMERICAN PERSPECTIVES ON BIOMEDICAL ETHICS 193, 199 (Harley Flack & Edmund Pellegrino eds., 1992); Celia J. Orona et al., *Cultural Aspects of Nondisclosure*, 3 CAMBRIDGE Q. HEALTHCARE ETHICS 338, 338-39 (1994).

191. *See generally* Barbara Bernier, *Class, Race, and Poverty: Medical Technologies and Socio-political Choices*, 11 HARV. BLACKLETTER J. 115 (1994) (tracing the historical treatment of African-Americans by the medical community in the name of experimental

done to increase the research participation of minority and low-income patients. However, respecting patient autonomy means that this should not be accomplished simply by waiving consent and making the choice for them. Rather, more difficult steps need to be taken to educate the applicable communities about the research, as well as requiring investigators to follow informed consent procedures with patients or their surrogates that are more refined and racially and/or culturally sensitive.

In addition, the FDA rules do not provide clear and helpful guidance about when and if to disenroll a critical care patient. The proposed regulations require that researchers inform a legal representative and/or family member about the critical care subject's enrollment as soon as possible. The legally authorized representative or a family member, if a legal representative is not reasonably available, may then disenroll the subject at any time.[192] Curiously, the proposed rules allow family members, who are not necessarily legally authorized persons, to disenroll the patient, even after the IRB has, in accord with other FDA requirements, reviewed the protocol to ensure that it poses likely benefits and acceptable risks and has consulted with community representatives about the trial in advance.[193]

On the one hand, the FDA seems to say that the subject's participation is justifiable because of the pre-investigation monitoring procedures followed by the IRB. On the other hand, the Agency allows family members to override this presumption and deny subjects the likely benefits of research participation, even when the family members may not be authorized under state law to act as medical decision-makers. No doubt this is a practical recognition of the fact that continuing the research while family members object would expose the researchers and medical institutions to possible liability, and would just plain look bad. However, if family members are allowed to disenroll the patient, there should be some requirement that this is done because it approximates what the patient would have wanted. Disenrolling a patient can have significant medical implications and the decision should be regarded as important and momentous as the initial decision to enroll the patient. Unfortunately, the FDA rules are silent regarding what standards should guide family members in these instances. The regulations should make clear that family mem-

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medicine from slavery to the present).

192. *See* Protection of Human Subjects; Informed Consent, 60 Fed. Reg. at 49,101. The proposed rules also allow the patient, if he regains decisional capacity, to choose to disenroll. *See id.*

193. *See id.*

bers and any other possible surrogates should use substituted judgment. In addition, the FDA rules need to establish a clear prioritized hierarchy of decision-makers, so that disagreement among family members does not lead to protracted and costly disputes.

C. *Lax Standards for Determining Acceptable Risks and Clinical Equipoise*

The state of clinical equipoise envisioned by the FDA's proposed regulations is not a sufficient justification in and of itself for conducting research without the patient's consent. The FDA rule defines a state of clinical equipoise as existing when:

> the relative benefits and risks of the proposed intervention are unknown, or thought to be equivalent or better than standard therapy. Clinical equipoise has been described as existing when at least a reasonable minority of medical professionals believe the test article is as good as or better than the standard treatment or that the standard treatment to be tested is no better than [a] placebo.[194]

This is a vague and elusive criterion. The FDA proposed rules do not acknowledge directly the inherent uncertainties of biomedical research. As previously discussed, most researchers in good faith will believe that a state of clinical equipoise exists. This has been the justification for not doing controlled clinical studies in many cases.[195] Physicians invariably have an educated hunch going into an experiment that one treatment is superior. However, not obtaining the patient's informed consent is a real harm, no matter how well-intended the researcher's motivations, because it supplants the patient's choice and value preferences, which can vary widely from the researcher's.[196] Moreover, too great a reliance on the principle of beneficence can lead to abuse. For example, researchers contemplating enrolling subjects in an experiment for which it is difficult to talk frankly and openly about the risks may simply wait for patients to suffer a period of decisional incapacity, at which point consent can be deferred or implied.[197]

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194. *Id.* at 49,095.

195. *See* Shultz, *supra* note 60, at 274.

196. *See* Delgado & Leskovac, *supra* note 62, at 98. For example, the subject may have different views about the research in terms of (1) pain thresholds; (2) embarrassment; (3) making money if the research pays for subjects; and (4) helping the scientific enterprise. *See id.*

197. *See* Luce, *supra* note 64, at 697. In *Estate of Leach v. Shapiro*, 469 N.E.2d 1047 (Ohio Ct. App. 1984), plaintiff's estate brought an action alleging the patient was placed on life support without her consent or consent of the family. *See id.* at 1053. The com-

The FDA apparently is attempting to borrow from the equipoise concept first introduced by Charles Fried. According to Fried, only when a doctor can view all arms of a clinical trial as equally promising should he or she proceed with the research.[198] However, insisting upon a state of pure theoretical equipoise would make most experiments unethical because, invariably, physicians have an educated hunch going into a trial that one treatment is superior. To avoid these difficulties, Benjamin Freedman introduced the concept of "clinical equipoise."[199] According to this view, for the investigation to be ethical, a sufficient state of medical uncertainty should exist within the clinical community and the research itself should be designed *so that the experiment will make a difference in resolving the medical issues.*[200]

The FDA would be better off sticking more closely to Freedman's clinical equipoise concept. It is not enough that uncertainty exists and a "reasonable minority" of medical professionals believe that a better treatment is available.[201] The trial must be demonstrated as capable of providing generalizable, acceptable answers. This is an essential criterion that should be satisfied before enrolling patients in such trials without prospective consent—that at least a subject's participation will have mattered so that the specific costs of the state of medical uncertainty will likely not have to be imposed again.

Allowing waiver of informed consent for trials that are not rigidly designed leads to the reduction in value of any information generated by the study. One need not be overly statistical or fastidi-

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plaint also alleged that she received experimental drugs while on life support. *See id.* at 1054. The court noted the potential for abuse in assuming that consent to treatment will be implied as a matter of law during a medical emergency and pointed out that physicians could wait until potentially uncooperative patients become critical and then administer the treatment, realizing that consent will be implied in those situations. *See id.* at 1053.

Indeed, some critical care researchers enrolled patients in experimental resuscitation trials under deferred consent protocols and faced the difficult situation of having to tell the family members about the experiment after the fact when it turned out that the patient was not resuscitated successfully. Apparently, several IRBs concluded that approaching the families and explaining the complexities of the critical care research were too difficult and did not require that the researchers follow-up with discussions with family members. *See* Norman S. Abramson, *Informed Consent for Clinical Resuscitation Research*, 20 ANNALS EMERGENCY MED. 1251, 1252 (1991).

198. *See* CHARLES FRIED, MEDICAL EXPERIMENTATION: PERSONAL INTEGRITY AND SOCIAL POLICY 51 (1974).

199. Benjamin Freedman, *Equipoise and the Ethics of Clinical Research*, 31 NEW ENG. J. MED. 141, 141 (1987).

200. *See id.* at 144 (arguing that research is ethical where a state of uncertainty exists among the entire clinical community such "that the results of the successful clinical trial should be convincing enough to resolve the dispute among clinicians").

201. *See id.*

ous to recognize that the risk of bad science creates an equal risk of bad ethics. Unless there is strict insistence that waiver of informed consent will occur only if the Freedman state of clinical equipoise exists, patients could be exposed to unexamined risks or to studies that fail to advance significantly the confidence level in choosing therapies for their particular conditions.

Consider what happened with the testing of the Alzheimer's drug Cognex (tacrine). An FDA expert panel voted against releasing Cognex based on inconclusive results from clinical studies.[202] Then, the same FDA committee was requested to consider releasing the drug for limited use. Part of the problem arose in the design of the initial two hundred patient study, which featured a controversial "crossover" provision. All patients first received the drug and only those who showed benefit were allowed to proceed to the next phase, where randomization took place between Cognex and a placebo.[203] Cognex tested better, but researchers later wondered whether this was due to the control group suffering from the common problem of the "withdrawal effect," where patients coming off a drug experience faster deterioration. At the time, researchers expressed concern that the poor initial study data left them ill-equipped to compare other Alzheimer's drugs coming to market because Cognex's effects were not understood well enough to be used as a control.[204]

The above discussion is not meant to suggest that waiver of informed consent is permissible only if the trial is a rigorously controlled one with randomization and double-blinding. As Fried has rightly observed, the difference between a controlled trial and a observational study is not between scientific truth and falsehood, but between varying degrees of confidence.[205] The question then becomes whether the costs imposed by that extra degree of confidence are worth it. In most critical care research, the costs seem justified. The stronger the basis for the research results, the better the information that can be transmitted. This aids both sides of the researcher-subject relationship. "The quality of evidence obtained in randomized controlled trials allows physicians and patients to make rational

202. *See* Michael Waldholz, *FDA May Release Drug for Alzheimer's*, WALL ST. J., July 15, 1991, at B1.

203. *See id.*

204. *See id.*

205. *See* FRIED, *supra* note 198, at 159 ("It is ironical indeed that those who, in arguing for RCTs [randomized controlled trials], say we must purge ourselves of absolutionist thinking regarding the rights of individual patients; engage in absolutist thinking themselves regarding the superiority of randomization.").

decisions about treatment. Real freedom of choice in therapy derives from evidence that permits an informed choice."[206] When informed consent is waived, it will always remain uncertain that proceeding with the research was in accord with the critical care patient's preferences. Accordingly, among the additional safeguards needed, apart from attempts to predict or presume the patient's choice, is special scrutiny of the soundness of the research proposal. There should be assurances that the design of the trial meets acceptable statistical criteria so that the data generated is capable of resolving the dispute among most medical professionals.

IV. RECOMMENDATIONS AND CONCLUSION

Determining the proper scope of informed consent standards for critical care research requires the resolution of difficult and often conflicting legal and ethical concerns. No easy, quick-fix solution is apparent. Thus, the best approach attempts some sort of practical compromise, one that balances decision-making authority between researchers, patients, and their families, and furthers, as much as possible, the objectives of the traditional informed consent doctrine, while removing unnecessary legal barriers to important research. The law of informed consent in the non-experimental context has evolved case by case to harmonize autonomy concerns with competing societal interests, such as with the recognition of the emergency exception. But the applicable law has largely been silent regarding the special circumstances of critical care research. A flexible legal framework for consent in the critical care context needs to be developed. This final section recommends three possible approaches for improving the applicable legal standards.

A. Broaden the Time-Window and Reasons for Allowing Waiver

The proposed FDA rules represent a significant start in the right direction by allowing waiver of informed consent requirements under limited circumstances.[207] However, the rules should allow waiver of informed consent where the patient is not in immediate danger of loss of life. The proposed rules are underinclusive in that they exclude a potential class of subjects who are unable to provide consent but who face serious risk of death, disability, and/or pain. The in-

206. John A. Oates & Alastair J. Wood, *The Regulation of Discovery and Drug Development*, 320 NEW ENG. J. MED. 311, 312 (1989).

207. *See* Protection of Human Subjects; Informed Consent, 60 Fed. Reg. 49,086, 49,093 (1995) (to be codified at 21 C.F.R. pt. 50) (proposed Sept. 21, 1995).

formed consent standards need to recognize the realities of medical practice, where it is difficult to make meaningful distinctions between imminent life-threatening situations and other critical care episodes. All such situations impose terrible consequences on patients and their families and warrant a more flexible approach in establishing consent.

The FDA standards enabling IRBs to approve waiver of informed consent should be expressly revised to allow waiver where intervention is necessitated because of a situation that is life-threatening, severely disabling, or reasonably certain to cause enduring or intractable pain. In addition, the regulations should make clear that a critical care condition is not subject to any particular time-window for the onset of death. Rather the standard should be that waiver of informed consent be allowed when: (1) death due to the condition is reasonably medically certain, and (2) there is credible medical evidence to suggest that the probability of death or severe or painful deficit resulting from the experimental therapy is not greater than that arising from the standard treatment.

B. Increased Use of Surrogate Consent Mechanisms

Complementary to the reforms proposed by the FDA, regulatory and legislative change is needed to increase use of surrogate consent procedures. Rather than immediately bypassing the consent process altogether, as proposed in the FDA rules, researchers in critical care situations should first be required, if feasible, to consult a standardized hierarchy of representatives who will act for a patient lacking decisional capacity or the ability to communicate. The surrogates should be directed to make the research participation decisions using a substituted judgment standard, approximating what they think the patient would want.[208] Only if such clearly authorized surrogates are not readily available should the research be allowed to proceed by waiving informed consent, assuming that other applicable criteria have been met.

1. Respect for Autonomy

Increased use of surrogate consent procedures represents an attempt to accommodate more seriously the concerns of personal autonomy in the critical care research context. To the extent that the

208. Of course, if the patient has executed an advance directive that applies to the critical care research situation, the advance directive should be followed and there would be no need to consult a surrogate.

objective of the informed consent doctrine is to promote self-determination, this goal can be furthered short of requiring in all instances that the patient prospectively provide consent. As discussed above, giving effect to patient preferences through surrogate consent, where otherwise the patient would be unable to do so, is a means of respecting patient autonomy and personal dignity. Surrogate consent ensures that there is at least some consideration of the research activity in light of the patient's preferences, to the extent they are known. In this respect, because truly informed prospective consent cannot be obtained, surrogate consent comes as close as possible to ascertaining patient preferences and represents the best way of maximizing autonomy in the situation, while avoiding halting the research altogether.[209]

IRBs will need to be vigilant to ensure that readily accessible procedures for invoking surrogate consent to critical care research do not have the unintended effect of reducing efforts by investigators to educate patients about research protocols and determine the patients' preferences. Physicians may make less of an effort to discuss these topics with, for example, patients in early stages of Alzheimer's, if they know that a surrogate who may be "easier" to talk to will be appointed during the later stages of the disease.

2. Easily Identifiable and Available Surrogates

The need for legislation or regulations that clearly identify the list of available surrogates cannot be overemphasized. The current confusion under many state laws as to who can provide consent has led to a deplorable situation of ignorance and deliberate evasion of the law by certain institutions.[210] If the surrogate list is well-publicized, patients will know what to expect should they become incapacitated and may even be encouraged to discuss their preferences with their applicable surrogates. The more the surrogate consent process becomes understood and standardized, the more likely it is that unwilling subjects will express concerns about experimentation prospectively and that researchers will be able to contact potential surrogates during limited time windows. Legislation and/or regulations making clear the class of potential surrogates would counter the tendency to make critical care research participation decisions clan-

209. *See* Morton Cohen, *The Emergency Exception to Informed Consent: Does it Extend to Human Experimentation?*, 20 ANNALS EMERGENCY MED. 1260, 1264-65 (1991).

210. *See, e.g.*, Prentice et al., *supra* note 12, at 5-6 (describing IRB approval of a study at the University of Nebraska Medical Center that directly violated Nebraska law limiting the ability of surrogates to provide consent).

destinely.

The FDA rules are deficient in this respect because they fail to answer clearly who is a legally authorized representative and do not indicate how to resolve disputes among family members regarding disenrollment. To avoid these problems, authorizing statutes and regulations should make plain the relative decision-making priority of available surrogates, both with respect to enrollment and disenrollment decisions.

The class of available surrogates could include spouses, parents, children, siblings, guardians, other relatives, and close personal friends. The exact group of authorized surrogates and their relative decision-making priority are, of course, subject to reasonable debate. However, it is important, given that many critical care patients are older patients, that the class of available surrogates include the adult children of patients.[211]

3. Preference for Family Member Surrogates

Family members in particular should be authorized and encouraged to act as surrogates. In the standard clinical setting, many physicians follow the common practice of sharing medical information with close family members caring for the patient when the patient is incompetent. This seems appropriate because the family members must live with the consequences of any medical treatment decisions and may have the best understanding of the patient's preferences.[212] Indeed, some courts have stated that the physician's fiduciary obligation to provide informed consent extends to providing this information to family members when the patient is incompetent.[213] Arguably, a logical corollary to this obligation is that the

211. *See, e.g.*, 755 ILL. COMP. STAT. 40/1 to 40/55 (West 1991). The Illinois Health Care Surrogate Act provides a useful model. The law establishes a hierarchy of potential surrogates who may decide to terminate life-sustaining treatment on behalf of patients who lack decisional capacity and who suffer from a terminal condition, permanent unconsciousness, or an incurable or irreversible condition. The class of authorized surrogates and their order of decision-making priority are as follows: (1) the patient's guardian of the person; (2) the patient's spouse; (3) any adult child of the patient; (4) either parent of the patient; (5) any adult brother or sister of the patient, (6) any adult grandchild of the patient, (7) a close friend of the patient; and (8) the patient's guardian of the estate. *See id.* at 40/25.

212. *Cf.* BEAUCHAMP & CHILDRESS, *supra* note 110, at 179-80 (recognizing the historical role of parents as surrogate decision-makers for their children).

213. *See, e.g.*, Estate of Leach v. Shapiro, 469 N.E.2d 1047 (Ohio Ct. App. 1984). In *Leach*, the court reinstated the cause of action of an estate alleging that a woman was placed on life support without her family's consent. *See id* at 1054. The court concluded that "when a patient becomes incompetent, the physician's fiduciary obligations of full

family members provided such information should be able to act accordingly and give surrogate consent on the patient's behalf.

The family's role has been recognized by various courts as important to the medical decision-making process because: (1) the family has a general concern for the patient; (2) the family is most likely to be cognizant of patient preferences; and (3) the family relationship depends on privacy and autonomy and there should be as little interference from the state as possible in medical decision-making when such issues are not easily answered by society as a whole.[214] Also, affording family members a high priority in the decision-making process is consistent with the fact that the family often will have the continuing legal duty for the patient's maintenance and support.[215] In general, the family has to live with and feel the immediate effects of the experimentation decision, such as whether the investigational therapy will increase the chance that the patient lapses into an irreversible coma.[216] Moreover, the family is less likely to treat the subject as an object or a symbol for a cause. Finally, family members are more likely to be available than other persons during critical care situations.

There are acknowledged dangers in affording family members a high priority in surrogate decision-making. An adult patient's wishes may differ from her family members.[217] Moreover, family members may have conflicts of interest when deciding on investigational treatment for critical care patients. An experimental trial that offers uncertain benefits and may prolong the patient's disabling condition can impose terrible emotional and financial burdens on family members.[218] In addition, even if family members are capable of being located during the limited time window for providing consent, they may be suffering from emotional distress and incapable of making a

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disclosure flow to the person acting in the patient's behalf." *Id.*

214. *See* Krasik, *supra* note 81, at 555. Indeed, some jurisdictions have recognized next of kin as having a constitutionally protected property interest in the patient's remains. *See, e.g.*, Brotherton v. Cleveland, 923 F.2d 477, 482 (6th Cir. 1991) (stating that wife's interest in husband's remains included the right to consent to removal of the corneas).

215. *See* Krasik, *supra* note 81, at 556.

216. *See* Hamman, *supra* note 169, at 162.

217. *See, e.g.*, *In re* Guardianship of Kowalski, 382 N.W.2d 861, 867 (Minn. Ct. App. 1986). In *Kowalski*, the father of a physically and mentally impaired woman was appointed, over the objections of the woman's female lover, as guardian for purposes of deciding medical treatment. *See id.* at 863. The court granted the father sole discretion in determining visitation rights, regardless of the daughter's previously expressed preferences. *See id.* at 867-68.

218. *See* Moore, *supra* note 7, at 566.

fully informed decision on the patient's behalf.[219]

Certain of these dangers can be guarded against by requiring that surrogate consent forms and researcher-initiated surrogate consent requests expressly remind surrogates of their obligations to use substituted judgment. Also, the authority of surrogates appointed through default mechanisms could be more limited than the authority of surrogates appointed formally through the making of a health care proxy. For example, the former could consent only to research involving certain risk thresholds but the latter could consent to a broader range of experimental treatments. Similarly, surrogates appointed through default mechanisms should not be allowed to consent for a subject's participation in nontherapeutic research.[220] In addition, it is hoped that to the extent surrogate consent procedures are more readily available and understood, patients will be encouraged to make their preferences known by either informing their potential surrogates or executing advanced directives. Ultimately, the preference for family members derives most support from patient autonomy concerns. Independent research advocates and/or IRB committee members are simply not as likely to know the treatment preferences of individual patients, especially critical care patients with whom they may have had no prior contact. Once decision-making authority is given to someone other than the patient, it makes most sense to transfer this authority to persons most likely to be able to decide as the patient would have wanted.[221]

4. Additional Level of Review

Requiring investigators to seek the consent of a surrogate when

219. *See* Abramson et al., *supra* note 96, at 2829. Clearly, competent patients in similar situations also face considerable stress and their capacity to provide informed consent can also be questioned. The vulnerability and desperation of critically ill people presents difficulty in acknowledging the legitimacy of their choices. However, to discount decisions made under such conditions is to suggest that these decisions can only be made in a vacuum, which undervalues and diminishes the immediate experiences and perceptions of the patient. *See* Moore, *supra* note 7, at 566.

220. Of course, distinguishing in advance between nontherapeutic and therapeutic research may make sense in theory but is not always possible in practice. *See* MUNSON, *supra* note 16, at 339-41. Some research involves the withholding of accepted medical treatment perceived as beneficial but which, after further research, is proven harmful. For example, research into the occurrence of premature blindness in infants, which involved the withholding of standard oxygen tent treatment, revealed that infants kept in the pure oxygen environment were more likely to be blinded. *See id.* at 342.

221. *But see* Ezekiel Emanuel & Linda Emanuel, *Proxy Decision Making For Incompetent Patients,* 267 JAMA 2067, 2070 (1992) (suggesting that family members' independent decisions regarding termination of care must be "restricted and supervised" (citations omitted)).

feasible also encourages additional scrutiny of the research plan by the investigator, forcing physicians to examine again the relative benefits and costs of the activity by having to explain the experiment to outside parties. This process can encourage more rational decision-making and weed out research of uncertain design that poses impermissible risks.[222] In addition, surrogate consent helps to avoid appearances of fraud or duress. Designating an additional party from whom the researcher must attempt to obtain consent serves as a check on institutional bias and addresses concerns that IRB members will be too passive in challenging research of questionable design when the protocols are developed by influential members of the institution's faculty. Thus, requiring that researchers seek surrogate consent if possible offers the limited procedural protection of inserting an additional party and level of review, apart from the monitoring performed by the IRB, into the subject recruitment process.

5. Consistent with Current Legal Trends Regarding Right to Die

Legislation and rulemaking authorizing increased use of surrogates to consent for critical care research would not represent a dramatic departure from the current legal framework in light of the increasing trend acknowledging the right of incompetent patients to exercise decision-making through surrogates in the non-experimental setting. Ironically, several states already allow surrogates to make health care decisions with even more drastic consequences than participation in critical care research, such as the decision to withdraw life-sustaining treatment. It makes little sense to give a surrogate the right to make life or death determinations, but to deny the surrogate a role in apparently less momentous decisions, especially when the decision to participate in critical care research may amount to choosing between the chance of life and reasonably certain death.

The basic legal justification for surrogate decision-making in the right-to-die context is that the incompetent person must still be able to assert the common-law right to self-determination and/or the constitutional right to privacy even if unable to sense a violation of it.[223]

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222. *See* King & Henderson, *supra* note 62, at 1028 (emphasizing the need for physicians to fully consider and clearly communicate the potential risks to the patient).

223. *See, e.g.*, Barber v. Superior Court, 195 Cal. Rptr. 484, 492 (Cal. App. 1983) (discussing the legitimacy of a surrogate's decision to withdraw life-sustaining treatment when there is little chance of the patient recovering cognitive or motor functions); *In re* Hamlin, 689 P.2d 1372, 1375-76 (Wash. 1984) (noting that Washington law allowing a guardian to choose whether to terminate or continue life support is not absolute, but is

Courts have allowed surrogates to make decisions using a substituted judgment standard, reasoning that incompetent persons have the same rights as competent individuals to refuse medical care "because the value of human dignity extends to both."[224]

Admittedly, special factors and considerations present in the context of withdrawing life-sustaining treatment do not apply with the same force to critical care research. The societal concern for respecting the wishes of persons to die with dignity and the particularly emotionally charged decisions involving refusal of life-sustaining treatment indicate that much more is at stake in right-to-die cases than in the critical care research setting. The decision to participate in a medical experiment does not implicate as directly these same fundamental questions. Thus, use of surrogates may, ironically, be more palatable in deciding to withdraw life-sustaining treatment because of the desire to protect the patient's right to privacy with special vigilance and the inclination to help the dying effectuate their intent when they are unable to do so themselves. Nevertheless, the decision to participate in a medical experiment merits at least comparably proportionate protection through use of surrogate consent mechanisms. Because many prospective critical care subjects are in situations where they will likely die or suffer under conventional treatment, participation in an experiment offers the opportunity to fight for life or at least to strive for a better quality of life. Such a decision represents the expression of core personal values just as does the invocation of one's right to die with dignity.

Indeed, the constitutional cases recognizing a liberty interest in refusing medical treatment have also clearly recognized that the Due Process Clause protects an interest in life.[225] Accordingly, surrogate consent procedures for critical care research are consistent with the right to refuse medical treatment. Such a right means giving the patient the chance to "evaluate the potential benefit of treatment and its possible consequences according to one's own values and to make a personal decision whether to subject oneself to the intrusion."[226] Whether the treatment is investigational or involves withdrawing life

limited to directives from a patient of sound mind).

224. Superintendent of Belchertown State Sch. v. Saikewicz, 370 N.E.2d 417, 427 (Mass. 1977).

225. *See, e.g.*, Cruzan v. Director, Mo. Dep't of Health, 497 U.S. 261, 281 (1990) (noting that the State has an interest in safeguarding the personal life or death decision and must impose a heightened evidentiary standard in order to ensure that any decision is made in full view of the specific circumstances and with complete consideration of the State's interest in preserving life).

226. *Id.* at 309 (Brennan, J., dissenting).

support, surrogate consent attempts to respect the incompetent patient's right to make critical medical decisions by approximating as best as possible the patient's choice under the circumstances.

6. Reconsenting/Inaccuracy of Surrogates

Surrogate consent poses many of the same problems as deferred consent. The "reconsenting" procedures required if the patient regains decisional capacity may be challenged rightly as empty, ritualistic mechanisms. At the time of reconsenting, the patient has already been used as a subject. Because even under surrogate consent the patient's preferences can never be truly known, requiring the participation of the decisionally incapacitated means risking injury to their autonomy for the benefit of others. An after-the-fact reconsenting cannot alter the character of the subject's initial participation.[227]

A more troubling problem of increased use of surrogate consent mechanisms is the danger that surrogates will substitute their own interests for the patient's. As already noted, family members may have conflicts of interest when acting as surrogates. Equally problematic is that even when acting with the best of intentions, surrogates may simply not be accurate predictors of what the patient wanted because of the inherent subjectivity of the factors and judgments involved. Relying upon intuitive, subjective decision-making by surrogate family members makes judicial reviewability of such decisions nearly impossible and thus offers little protection to patients who do not have idealized "selfless, loving families" to rely upon.[228] Studies indicate that surrogates, even close family members, often do not adequately understand the preferences of the patients for whom they are acting.[229]

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227. *See* Delgado & Leskovac, *supra* note 62, at 94-95 (regarding reconsent as being extracted rather than freely given).

228. *See Developments in the Law—Medical Technology and the Law*, 103 HARV. L. REV. 1519, 1650 (1991).

229. One such study revealed that surrogate decision-makers who were family members were poor predictors of resuscitation preferences of elderly clinic outpatients, even though the patients themselves thought that their family members would accurately represent their wishes. *See* Allison Seckler et al., *Substituted Judgment: How Accurate Are Proxy Predictions?*, 115 ANNALS OF INTERNAL MED. 92, 94-95 (1991). The family decision-makers achieved statistically significant concordance with patients' preferences but did not achieve moderate strength of agreement; meanwhile, physicians acting as surrogate decision-makers did no better than chance alone in predicting the preferences of patients. *See id.* at 95-96; *see also* Emanuel & Emanuel, *supra* note 221, at 2069 (reviewing studies showing highly significant discrepancies between patients and proxies in quality of life assessments).

Many subjects in critical care research situations are older patients who tend to be more cautious about research participation. Yet it is often younger family members that are called upon to make the decision.[230] These inherent tendencies for inaccurate decisions may be compounded in the critical care research context. The surrogate is being asked to evaluate what the patient would have wanted. However, it is not clear whether this decision should be made from the perspective of the patient before the critical care episode or at the time of the illness. A patient's world view can change dramatically with the onset of sudden illness so that previously discussed treatment preferences with proxy surrogates or otherwise publicly known preferences are not necessarily an indication of how the patient views the situation when undergoing the trauma. Strokes, heart attacks, and other severe and sudden medical episodes can produce enormous anxiety and the unexpected nature of the condition produces emotional harm separate from the underlying medical injury.[231]

It is admitted that surrogate decisions are not and will not be as accurate in practice as promised in theory. Nonetheless, most patients would probably be more comfortable knowing that decisions whether to participate in experimental treatment at a critical time in their lives will, when feasible, be made by family or friends in consultation with physicians, rather than face categorical exclusion from such opportunities or letting the decision be made by an IRB committee or through a protracted guardianship proceeding that promises no better prediction of the patient's preferences.[232] Because the patient will experience most directly the burdens and benefits of the research activity, the patient's interests and preferences, even an imperfect approximation through surrogate consent procedures, should be controlling.[233]

Consistent with the new pragmatic trend in bioethics and health law to reject principle-driven, deductive analysis in favor of evaluat-

230. *See* Sachs & Cassel, *supra* note 147, at 236.

231. *See* Theodore A. Stern, *Psychiatric Management of Acute Myocardial Infarction in the Coronary Care Unit*, 60 AM. J. CARDIOLOGY 59J, 61J-66J (Dec. 28, 1987) (discussing the importance of recognizing and treating psychiatric complications of patients with heart disease).

232. *Cf. In re* Jobes, 529 A.2d 434, 451 (N.J. 1987) (noting that for decisions involving withdrawal of life-sustaining medical treatment, "[c]ourts are not the proper place to resolve the agonizing personal problems that underlie these cases [and o]ur legal system cannot replace the more intimate struggle that must be borne by the patient, those caring for the patient, and those who care about the patient").

233. *See* Shultz, *supra* note 60, at 220.

ing legal rules by how well they function in medical practice,[234] a more flexible and pragmatic approach is needed to apply informed consent requirements to the critical care research setting. The admitted problems with accuracy and conflicts of interest surrounding surrogate consent suggest that lowered expectations are required about what proxy consent can accomplish. Surrogate consent procedures should not be viewed as entirely satisfactory mechanisms for accommodating the ethical and legal problems associated with critical care research. A surrogate consent approach represents a default procedure that attempts to discern patient preferences as best as possible under difficult circumstances. Certainly, more empirical analysis is needed to test the validity of surrogate consent procedures in the research setting. The conventional rationale that the surrogate can properly act on behalf of the incompetent patient may need to be reevaluated. At the very least, the law may need to further contextualize surrogate consent procedures, recognizing those instances where the surrogate is likely to replicate the patient's preferred choice and limiting surrogate consent when this is not feasible.

C. Establishing Endpoints and Use of Expert Surrogates

Even if legislative and regulatory reforms make surrogate consent procedures more readily available, some critical care research studies will still involve extremely limited time windows under which obtaining consent from any surrogate remains impossible. On such occasions, where researchers intend to forego any form of consent, additional safeguards are needed to ensure that patients are not exposed to unnecessary risks or encouraged to pursue likely futile treatments. The FDA rules are deficient in this respect in that they establish too lax a standard of "clinical equipoise" for guiding IRBs in determining whether the risks of the experiment and the state of medical uncertainty warrant waiver of consent.

IRBs should be charged with documenting and providing more clear assurances that the research risks are acceptable. If informed consent cannot function in critical care research as in other settings, IRBs must fill in the gap and take additional steps to protect the safety and dignity of experimental subjects. IRBs must bear strict responsibility for ensuring that the research design is sufficiently

234. *See generally* Wolf, *supra* note 109 (suggesting that a paradigm shift is occurring in bioethics and health law towards a pragmatic philosophy embedded in empiricist investigation and concern for the particular context).

promising and presents an acceptable risk of harm to be even considered for employing surrogate consent mechanisms and/or waiving consent. Offering patients, or their surrogates, desperate choices in times of crisis that present unreasonable risks does not advance patient autonomy and harms the research endeavor generally.[235]

Some commentators have recommended the creation of special advocates, independent of the academic institutions in which the research is to be conducted, to function as monitors of the acceptability of proposed research risks in light of the critical care patient's preferences.[236] However, despite the label, having a special person designated "patient advocate" is no better a guarantee that the patient's interests and preferences will be represented than allowing researchers to consult a readily known hierarchy of surrogates composed of family members and friends. Patient advocates will have no previous knowledge of cardiac arrest victims and accident victims admitted to the hospital in a diminished state. And in the limited time window permitted for application of experimental treatment, it is not clear that patient advocates will be available with any greater frequency than a patient's family and friends. Finally, establishing procedures for the appointment of special advocates represents a far too cumbersome and administratively complicated approach for the limited benefits gained.

A better alternative for addressing these concerns is to establish a mechanism that scrutinizes the proposed critical care research protocol rigorously to ensure that the combination of expected risks and benefits of applying the experimental therapy, in light of current medical knowledge, are equal or better than the standard treatment. Where there is not sufficient time to consult a surrogate or other legal representative, experimentation should be permitted to proceed by waiving consent only if the research protocol has been approved by an IRB committee that has specifically considered the merits of the research risks in light of the inclusion of subjects with diminished autonomy.

IRBs should be required to consider not only how subjects are selected and the degree of risks to which they will likely be exposed, but also what are the endpoints for the experiment. The research protocol should establish mandatory and timely stages for review of the study results by parties not directly involved in the day-to-day

235. *See* King & Henderson, *supra* note 62, at 1048-49.

236. *See, e.g.*, Philip M. Bein, *Surrogate Consent and the Incompetent Experimental Subject*, 46 FOOD DRUG COSM. L.J. 739, 761-62 (1991).

investigation.[237] This would permit rapid termination of the study in the event of unforeseen risks. In addition, establishing timely review of the research progress would ensure that the study is conducted no longer than necessary to obtain generally acceptable results.

In addition, it is recommended that waiver of informed consent occur only if the IRB monitoring and approving the research has sought the judgment of experts in the particular medical field applicable to the experiment.[238] Under this "expert surrogate" approach, IRBs send out surveys asking experts in the field whether they would be prepared to enter a proposed trial as a patient-subject, and whether they would enter the trial if it involved randomization of treatment, use of a placebo, etc. The acceptability of a study to expert surrogates would be useful to IRBs (as well as potential subjects and their surrogates) when faced with difficult research and waiver of consent requests. When the expert surrogate mechanism has been employed, individual physicians and patients who saw no problems with entering a proposed trial indicated they wanted to change their minds once given the results of surveys showing a majority of expert surrogates would not consent.[239]

Expert surrogate surveys thus impart important information to IRBs about the acceptability of the proposed research risks. These surveys are able to combine the theoretical expertise of investigators (who may not be impartial) and the theoretical impartiality of IRBs (which, despite their physician members, may not have sufficient expertise in the area under investigation). Of course, there is the danger that use of expert surrogate mechanisms will inevitably result in truly insightful researchers being slowed down in their research endeavors until their peers recognize their advances. But when IRBs are faced with especially difficult issues, such as waiving informed consent, expert surrogate surveys would prove useful. They would relieve IRBs of some of the difficulties in directly challenging individual investigators on questions of research design. Expert surrogate surveys would also complement and supplement the proposed FDA requirement that IRBs consult with representatives of

237. *See Problems in Securing Informed Consent*, *supra* note 11, at 124 (testimony of Arthur L. Caplan, Director, Center for Bioethics, University of Pennsylvania).

238. *See* William J. MacKillop et al., *The Expert Surrogate System: A Role for the Golden Rule in Clinical Practice*, 4 HUMANE MED. 89, 90 (1988) (proposing an expert surrogate system for monitoring clinical trials).

239. *See id.* (involving participation in clinical trials studying treatments for non-small-cell lung cancer).

the communities from which critical care subjects will be drawn.[240] Evidence of how the research community views the proposed experiment will no doubt affect how the local community will view the experiment. Also important, expert surrogate surveys can counter the possibilities of institutional and/or experimental bias, which may arise when IRBs depend on risk assessments of investigators who are too closely associated and involved with the research protocol.

Demonstrating the acceptability of the research design to expert surrogates also ensures that an individual trial will be capable of generating meaningful clinical answers. Expert surrogates should be asked not only whether the research poses acceptable risks to warrant their participation, but also whether it will be capable of providing experimental data that will resolve pressing therapeutic disputes in the field. The study should not be approved unless a reasonable number of the expert surrogates agree that it can provide meaningful evidence on whether a significant difference exists between the experimental and standard therapies.

These are the additional minimum criteria, apart from the standards established in the proposed FDA rules, that should be insisted upon by each IRB before approving research employing waiver of informed consent. The state of medical uncertainty imposes its own terrible costs upon the critical care patient. These burdens should not have to be experienced in the future by the subject and other critical care patients. Patients and their families should at least know that the patient's participation will have made a meaningful difference.

240. *See* Protection of Human Subjects; Informed Consent, 60 Fed. Reg. 49,100-01 (1995) (to be codified at 21 C.F.R. pt. 50) (proposed Sept. 21, 1995).