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### A "Common" Proposal

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# ARTICLE

## A “COMMON” PROPOSAL

*Stacey A. Tovino\**

### ABSTRACT

The Federal Policy for the Protection of Human Subjects (the “Common Rule”) is codified in separate regulations by seventeen federal departments and agencies, including the Department of Health and Human Services (HHS). HHS’s version of the Common Rule currently contains a basic policy for the protection of all human subjects, codified at Subpart A of the Common Rule, as well as special provisions governing human subjects research involving three sets of vulnerable populations, including pregnant women, fetuses, and neonates (Subpart B); prisoners (Subpart C); and children (Subpart D). This Article proposes that HHS amend the Common Rule to add a new Subpart E governing human subjects research involving adults with impaired decision-making capacity.

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I. INTRODUCTION

This Article responds to the recent request by the federal Department of Health and Human Services (HHS) for guidance regarding how “regulations for protecting human subjects who participate in research might be modernized and revised to be more effective.”<sup>1</sup> As background, current federal regulations governing human subjects research were developed decades ago when research studies were generally conducted at one research site, such as a single university or a single medical center.<sup>2</sup> Although HHS has amended its regulations over the years, the regulations “have not kept pace with the evolving human research enterprise,” including the marked increase in the volume of biomedical and behavioral research; “the proliferation of multi-site clinical trials and observational studies”; the expansion of research in particular areas, including neurology and psychiatry; and the use of new research technologies,

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1. See Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators, 76 Fed. Reg. 44,512, 44,512 (proposed July 26, 2011) (to be codified at 45 C.F.R. pts. 46, 160, 164; 21 C.F.R. pts. 50, 56).

2. See *id.*

including functional magnetic resonance imaging.<sup>3</sup> Stakeholders have criticized the decades-old regulations on many grounds, including the extent and quality of the protections afforded by the regulations’ consent provisions, the lack of calibration between the risks posed by a particular research protocol and the required level of institutional review, and “the multiple [and] differing regulatory requirements that can apply to a single research study.”<sup>4</sup>

This Article focuses on one particular area of regulatory criticism; that is, the lack of federal regulation and the patchwork of state regulation in the context of human subjects research involving adults<sup>5</sup> with impaired decision-making capacity, including adults with neurological, psychiatric, and developmental conditions.<sup>6</sup> Elsewhere, others<sup>7</sup> and I<sup>8</sup> have reviewed the American history of human subjects research, including research studies in which scientists enrolled captive populations of vulnerable individuals in dangerous experiments, the goals of which were unrelated to the individuals’ health conditions.<sup>9</sup> Many individuals with neurological, psychiatric, and

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3. See *id.* at 44,512–13.

4. See *id.* at 44,513–14.

5. HHS-conducted or -supported human subjects research involving children is already regulated at 45 C.F.R. §§ 46.401–409 (2011).

6. Individuals with impaired decision-making capacity include, but are not limited to (1) individuals with disorders of consciousness, such as coma, vegetative state, and minimally conscious state, that eliminate or severely impair cognitive abilities; (2) individuals with neurological conditions, such as dementia, that may impair some or all cognitive abilities; (3) individuals with psychiatric conditions, such as schizophrenia, that may impair some or all cognitive abilities; and (4) individuals with developmental and intellectual disabilities, such as mental retardation, that may impair some cognitive abilities. See *infra* notes 24, 27, 118–122, 162 and accompanying text.

7. For a history of human subjects research in the United States, see, for example, GEORGE J. ANNAS & MICHAEL A. GRODIN, *THE NAZI DOCTORS AND THE NUREMBERG CODE: HUMAN RIGHTS IN HUMAN EXPERIMENTATION* 1–275 (1992); CARL H. COLEMAN ET AL., *THE ETHICS AND REGULATION OF RESEARCH WITH HUMAN SUBJECTS* 3–239 (2005); CYNTHIA MCGUIRE DUNN & GARY L. CHADWICK, *PROTECTING STUDY VOLUNTEERS IN RESEARCH* 1–16 (4th ed. 2012); MARGARET L. EATON & DONALD KENNEDY, *INNOVATION IN MEDICAL TECHNOLOGY: ETHICAL ISSUES AND CHALLENGES* 37–46 (2007); RUTH R. FADEN & TOM L. BEAUCHAMP, *A HISTORY AND THEORY OF INFORMED CONSENT* 151–232 (1986); JONATHAN D. MORENO, *IS THERE AN ETHICIST IN THE HOUSE?: ON THE CUTTING EDGE OF BIOETHICS* 109–52 (2005); LAINIE FRIEDMAN ROSS, *CHILDREN IN MEDICAL RESEARCH* 12–43 (2006); *THE ETHICS OF RESEARCH INVOLVING HUMAN SUBJECTS* 1–144 (Harold Y. Vanderpool ed., 1996).

8. See Stacey A. Tovino, *Neuroimaging Research into Disorders of Consciousness: Moral Imperative or Legal and Ethics Failure?*, 13 VA. J.L. & TECH. 1, 22–42 (2008), [http://www.vjolt.net/vol13/issue1/v13i1\\_a2-Tovino.pdf](http://www.vjolt.net/vol13/issue1/v13i1_a2-Tovino.pdf) (providing an abbreviated history of human subjects research involving vulnerable populations).

9. In the early 1950s, for example, the U.S. Army Chemical Center investigated the use of hallucinogenic compounds as potential chemical warfare agents on a confined population—the patients at the New York State Psychiatric Institute (the “Institute”).

developmental disabilities died or became ill as a result of their research inclusion.<sup>10</sup> In light of this history, some stakeholders have called for stronger legal protections for human subjects who have impaired decision-making capacity.<sup>11</sup> Other stakeholders, including many clinicians and scientists, support further biomedical and behavioral research involving individuals with impaired decision-making capacity in order to contribute to generalizable knowledge regarding the individuals' underlying physical and mental health conditions.<sup>12</sup> Two particular questions

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*Barrett v. United States*, 660 F. Supp. 1291, 1295 (S.D.N.Y. 1987). Pursuant to the Army's research protocol, Institute patients were injected with chemical derivatives of mescaline, a hallucinogenic alkaloid of the phenethylamine class, and clinical response data was provided by the Institute to the Army. *See id.* at 1294–96. At least one research subject—a former tennis professional and ranked tennis player named Harold Blauer, who was receiving psychiatric care at the Institute for major depression and pseudo-neurotic schizophrenia—died following his fifth mescaline injection. *Id.* at 1298–300, 1317. The purpose of the research was not to develop a treatment or cure for depression or the other conditions with which the Institute patients were diagnosed; instead, the research was designed to “provide a firmer basis for the utilization of psychochemical agents . . . for offensive use as sabotage weapons” and to develop protections against the psychochemical agents in military activity. *Id.* at 1295, 1299 (internal quotation marks omitted). Historians, ethicists and law professors who subsequently reviewed the Army's chemical warfare research have concluded that it posed risks to Blauer and his fellow subjects that were unreasonable in relation to the military knowledge that was expected to result, that the research was inappropriately conducted in a captive and vulnerable population of individuals with mental illness whose further treatment was conditioned on participation in the dangerous research protocol, that the researchers failed to inform the research subjects of the military purpose of the experiment and of the known risks associated with mescaline, and that some of the research subjects may not have had the capacity to give consent due to their severe mental illnesses. *See, e.g.*, Cyril H. Wecht, *Research and Experimentation*, in LEGAL MEDICINE 175, 176 (S. Sandy Sanbar, ed., 7th ed. 2007) Moreno, *supra* note 7, at 159–62; Tovino, *supra* note 8, at 27–29; *see also* FADEN & BEAUCHAMP, *supra* note 7, at 159.

10. *See, e.g.*, Tovino, *supra* note 8, at 23, 29–31.

11. *See, e.g.*, Stefan Eriksson, *On the Need for Improved Protections of Incapacitated and Non-Benefiting Research Subjects*, 26 BIOETHICS 15, 15 20–21 (2012) (“[T]he present guidelines allow for the possibility of vulnerable people being exploited, something that is hidden behind a guise of solidarity. Instead we need to address the real issues at stake by rewriting these statutes. . . . However, in order to protect these subjects there is additional need for appointed representatives who monitor research and for legal obligations to compensate for any injuries suffered. Without these or similar measures . . . we won't have an adequate system in place for the protection of non-benefiting persons who are unable to consent to research.”); PRESIDENTIAL COMM'N FOR THE STUDY OF BIOETHICAL ISSUES, MORAL SCIENCE: PROTECTING PARTICIPANTS IN HUMAN SUBJECTS RESEARCH 5 (2011) (“[T]he Commission cannot conclude that all federally funded research provides optimal protections against avoidable harms and unethical treatment. The Commission finds significant room for improvement in several areas where, for example, immediate changes can be made to increase accountability and thereby reduce the likelihood of harm or unethical treatment.”).

12. *See, e.g.*, Scott Y.H. Kim et al., *Proxy and Surrogate Consent in Geriatric Neuropsychiatric Research: Update and Recommendations*, 161 AM. J. PSYCHIATRY 797, 797 (2004) (“There is evidence that conservative risk management strategies by institutional review boards and their institutions may severely restrict research with decisionally impaired subjects.”); Elyn R. Saks et al., *Proxy Consent to Research: The*

over which academic and professional stakeholders (including law professors, ethicists, clinicians, and scientists) frequently disagree include the general question of how human subjects research involving adults with impaired decision-making capacity should be regulated at the federal and state level and the more specific question of who, if anyone, should be permitted to consent to research on behalf of adults who have very impaired or no decision-making capacity.<sup>13</sup>

On July 26, 2011, HHS issued an Advanced Notice of Proposed Rulemaking (ANPR) requesting public comments on proposals to seven areas of current federal regulation as well as answers to seventy-four specific questions relating to human subjects research.<sup>14</sup> Through its proposal of new federal regulations governing human subjects research involving adults with impaired decision-making capacity, this Article responds to one of HHS’s broad proposals relating to improvement of the consent process<sup>15</sup> and three of HHS’s specific questions relating to the adequacy of consent forms, the level of research participant comprehension required, and the desirability of additional consent process requirements.<sup>16</sup>

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*Legal Landscape*, 8 YALE J. HEALTH POL’Y L. & ETHICS 37, 39 (2008) (“It is urgent that research on [Alzheimer’s] disease be strongly encouraged and facilitated.”); Douglas Steinberg, *Consciousness Is Missing—and So Is Research*, 6 EMBO REP. 1009, 1011 (2005) (“[S]ome observers see a moral imperative, not just an ethical trap, in the study of consciousness disorders.”).

13. See, e.g., Evan G. DeRenzo, *Decisionally Impaired Persons in Research: Refining the Proposed Refinements*, 25 J.L. MED. & ETHICS 139, 139 (1997) (“The ethics of involving persons with cognitive impairments and/or mental illness in research continues to gain academic and public attention. . . . [Relevant questions include] not only when and from whom informed consent may be obtained but also under what conditions it is ethically permissible to involve persons in research who are too decisionally impaired to provide their own consent.”); Saks et al., *supra* note 12, at 39 (“When an adult suffers from a disorder that impairs his or her capacity to consent, may another person enroll that individual in research? The answer, it appears, is not a simple ‘yes’ or ‘no,’ but rather ‘it depends.’”).

14. See Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators, 76 Fed. Reg. 44,512, 44,514, 44,517–29 (proposed July 26, 2011) (to be codified at 45 C.F.R. pts. 46, 160, 164; 21 C.F.R. pts. 50, 56) (summarizing the seven sets of potential refinements and listing the seventy-four specific questions).

15. HHS’s third broad proposal relates to “[i]mprovement of consent forms and the consent process.” *Id.* at 44,514.

16. HHS’s 36th question asks,

What additional information, if any, should be required by the regulations to assure that consent forms appropriately describe to subjects, in concise and clear language, alternatives to participating in the research study and why it may or may not be in their best interests to participate? What modifications or deletions to the required elements would be appropriate?

*Id.* at 44,523. HHS’s 38th question asks, “Should the regulations require that, for certain types of studies, investigators assess how well potential research subjects comprehend the

This Article proceeds as follows: Part II of this Article examines federal and state authorities governing human subjects research involving adults with impaired decision-making capacity. Part II finds that current federal law does not provide specific guidance regarding the conduct of human subjects research involving adults with impaired decision-making capacity or consent to research by or on behalf of adults with impaired decision-making capacity and that state law in this area varies widely, when it exists. Part II also finds that the lack of federal regulation and the patchwork of state law has made it difficult for American scientists, academic medical centers, institutional review boards, scientific journals, and funding agencies to agree on an applicable ethical and legal framework, especially when research may be conducted in a laboratory located in one city but will draw research participants who are residents of neighboring states, as well as in the context of multi-site and multi-state research.<sup>17</sup> Part II further finds that the federal Office for Human Research Protections and some members of the clinical and scientific communities support reliance on legislation governing consent to treatment in the absence of state law specifically addressing consent to research.<sup>18</sup>

Given the support by the government and some members of the clinical and scientific communities for reliance on legislation governing consent to treatment to answer research-related questions, Part III of this Article examines and identifies the salient features of federal regulation and state legislation governing consent to treatment. Part IV argues that legislation governing consent to treatment should not be used to answer questions relating to consent to research because (i) treatment and research are intrinsically different activities; (ii) government-supported reliance on legislation governing consent to treatment to answer questions relating to consent to research could provide continued legal and conceptual support for the therapeutic misconception; and (iii) the content of legislation governing consent to treatment may be inappropriate for research-related questions in light of the unique role of the researcher—that is, the role of collecting data and reporting research results, not holding the best physical and mental health

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information provided to them before they are allowed to sign the consent form?" *Id.* HHS's 40th question asks, "Would informed consent be improved if the regulations included additional requirements regarding the consent process, and if so, what should be required? For example, should investigators be required to disclose in consent forms certain information about the financial relationships they have with study sponsors?" *Id.*

17. See *infra* text accompanying note 99.

18. See *infra* text accompanying notes 113–114.

interests of research participants as paramount. To support the argument that legislation governing consent to treatment should not be used to answer questions relating to consent to research, Part IV references and relies on other areas of health law that distinguish treatment and research and establish more stringent requirements for research.

Part V of this Article finds that the current law review and other academic literatures tend to polarize conversations about the regulation of human subjects research involving adults with impaired decision-making capacity into strong protection-based arguments, on the one hand, and clinical- and research-based arguments made in support of further biomedical and behavioral research, on the other.<sup>19</sup> Part V contends that the literature could benefit from a more well-rounded dialogue that includes insights from not only law professors, ethicists, clinicians, and scientists, but also from laypersons, including current and future patients and human subjects.<sup>20</sup> Stated slightly differently, Part V suggests that lawmakers will continue to struggle crafting regulations that protect and promote the autonomy of laypersons until lawmakers better understand (i) the conditions under which laypersons would consent to participate in research, including riskless and risky research; (ii) whether and when laypersons would grant a surrogate the authority to make a substituted research participation decision; and (iii) the amount of leeway laypersons would give to surrogates in making substituted research participation decisions.

To this end, Part V analyzes empirical studies investigating current public attitudes towards human subjects research involving adults with impaired decision-making capacity.<sup>21</sup> These empirical studies report somewhat surprising findings; that is, that (i) surrogate consent to research is "probably" or "definitely" acceptable in the context of minimal risk research; (ii) surrogate consent to research may be appropriate in the context of more risky studies; (iii) lay (or noncourt-appointed) surrogates should be permitted to consent to riskless research on behalf of relatives with impaired decision-making capacity; (iv) enrolling individuals who are unable to consent to research in research studies that offer no potential for medical benefit is consistent with the preferences of at least some individuals and, therefore, should not be absolutely prohibited provided there is sufficient evidence that participation in such research is consistent with

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19. See *infra* note 246 and accompanying text.

20. See *infra* text accompanying notes 247–248.

21. See *infra* text accompanying notes 255–300.

the preferences of such individuals; (v) requiring a completed advance research directive (ARD) prior to research participation by an individual with impaired decision-making capacity may be unduly restrictive in light of studies suggesting that the rate of ARD completion is likely to be low; and (vi) allowing some or complete surrogate leeway, even over prior first-person consent, is consistent with the preferences of at least some individuals and should not be absolutely prohibited provided there is sufficient evidence that surrogate leeway is consistent with the preferences of such individuals.<sup>22</sup>

Rather than relabeling legislation governing consent to treatment in an attempt to make it applicable to both the treatment and research settings, Part VI argues that HHS should add a new subpart (a Subpart "E") to 45 C.F.R. Part 46 specifically governing human subjects research involving adults with impaired decision-making capacity. The regulations proposed in Part VI would reconcile potential conflicts of interest between and among researchers, surrogates, and adult research participants by requiring researchers to recognize themselves and convey to research participants and/or surrogates, as appropriate, (i) the conceptual distinctions between treatment and research; (ii) the specific differences between individualized, adaptable treatment methods and protocol-driven, double-blind, randomized, placebo-controlled research procedures; (iii) the known, suspected, and unknown risks associated with the research protocol; and (iv) the likelihood that research participants may not directly benefit from the research.

## II. CONSENT-TO-RESEARCH REGULATION

Investigators whose research is designed to improve clinical practice in the areas of neurology, psychiatry, geriatrics, emergency medicine, and critical care, among other specialties, frequently design research protocols that involve individuals with impaired decision-making capacity.<sup>23</sup> Some of

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22. See *infra* text accompanying notes 249–254.

23. See, e.g., B. Lynn Beattie, *Consent in Alzheimer's Disease Research: Risk/Benefit Factors*, 34 CAN. J. NEUROLOGICAL SCI. (SUPP.1) S27, S29 (2007) (noting that research in Alzheimer's disease is complicated by the disease itself, which affects the subject's decision-making capacity for participation in research); Scott Y. H. Kim et al., *Assessing the Competence of Persons with Alzheimer's Disease in Providing Informed Consent for Participation in Research*, 158 AM. J. PSYCHIATRY 712, 712 (2001) (noting that even relatively mild Alzheimer's disease can significantly impair consent-giving capacity in the research context and that research in the field of Alzheimer's disease therapeutics increasingly includes participation by subjects with relatively mild Alzheimer's disease);

these protocols involve the neuroimaging of individuals who have disorders of consciousness, including coma, vegetative state, and minimally conscious state.<sup>24</sup> In one recent study, scientists from the United Kingdom and Argentina used functional magnetic resonance imaging to investigate the neural correlates of motor preparation in response to verbal commands in a group of human subjects who met diagnostic criteria for vegetative state, defined as "the absence of awareness of self or the environment and preserved autonomic functions."<sup>25</sup> In a second recent study, scientists from the United Kingdom and Belgium used functional magnetic resonance imaging to assess individuals with disorders of consciousness with respect to their "ability to generate willful,

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Ukamaka M. Oruche, *Research with Cognitively Impaired Participants*, 13 J. NURSING L. 89, 89 (2009) (noting that research involving individuals with cognitive impairments is necessary to improve understanding of illnesses such as Alzheimer's disease, Huntington's chorea, cerebrovascular disease, psychiatric disorders, chronic alcoholism, and AIDS dementia complex).

24. See, e.g., M. R. Coleman et al., *Towards the Routine Use of Brain Imaging to Aid the Clinical Diagnosis of Disorders of Consciousness*, 132 BRAIN 2541, 2541–51 (2009) (describing the functional brain imaging findings from a group of forty-one individuals with disorders of consciousness who undertook a hierarchical speech processing task, concluding that functional neuroimaging has the potential to inform the diagnostic decision-making process for persons with disorders of consciousness); Davinia Fernández-Espejo et al., *Combination of Diffusion Tensor and Functional Magnetic Resonance Imaging During Recovery from the Vegetative State*, BMC NEUROLOGY, Sept. 3, 2010, at 1, <http://www.biomedcentral.com/content/pdf/1471-2377-10-77.pdf> (using functional magnetic resonance imaging "to investigate cortical responses to passive language stimulation as well as task-induced deactivations related to the default-mode network" in one patient in the vegetative state "at one month post-ictus and . . . twelve months later when he had recovered consciousness"); Joseph J. Fins, *Neuroethics, Neuroimaging, and Disorders of Consciousness: Promise or Peril?*, 122 TRANSACTIONS AM. CLINICAL & CLIMATOLOGICAL ASS'N 336, 336–37, 339–43 (2010) (reviewing research using functional magnetic resonance imaging and positron emission tomography to elucidate brain states); Olivia Gosseries et al., *Disorders of Consciousness: What's in a Name?* 28 NEUROREHABILITATION 3, 4–9 (2011) (summarizing research studies designed to investigate the residual neural capacity of individuals with disorders of consciousness); Luaba Tshibanda et al., *Neuroimaging After Coma*, 52 NEURORADIOLOGY 15, 15–21 (2010) (summarizing research studies using magnetic resonance spectroscopy, diffusion tensor imaging, and functional magnetic resonance imaging to assess patients with disorders of consciousness); Audrey Vanhaudenhuyse et al., *Default Network Connectivity Reflects the Level of Consciousness in Non-Communicative Brain-Damaged Patients*, 133 BRAIN 161, 161–69 (2010) (using functional magnetic resonance imaging to investigate default network connectivity in individuals with disorders of consciousness, including coma, vegetative state, minimally conscious state, and locked-in syndrome).

25. See Tristan Andres Bekinschtein et al., *Functional Imaging Reveals Movement Preparatory Activity in the Vegetative State*, FRONTIERS HUM. NEUROSCIENCE, Jan. 27, 2011, at 1, 1–3, 6–7 (citation omitted) (reporting results that may reflect residual voluntary processing in some patients in the vegetative state and suggesting that the identification of such activity using functional magnetic resonance imaging may complement more traditional clinical assessments of patients in the vegetative state).

neuroanatomically specific, blood-oxygenation-level-dependent responses during two . . . mental-imagery tasks.”<sup>26</sup>

Other protocols are designed to investigate the safety and efficacy of experimental drugs and other interventions for individuals who have mild, moderate, or severe dementia or mental illness and may have restricted or limited decision-making capacity.<sup>27</sup> In one recent study, scientists at the University of California at San Diego, the University of California at Irvine, and Rush University Medical Center in Chicago conducted a phase 1 clinical trial of nerve growth factor (NGF) gene delivery in eight individuals with early-stage probable Alzheimer’s disease.<sup>28</sup> The study involved the implantation of autologous fibroblasts genetically modified to express human NGF into the subjects’ forebrains.<sup>29</sup>

Still other protocols, especially those designed to improve clinical practice in the emergency room, may involve experimental interventions for individuals with mild, moderate, and severe traumatic brain injuries. In one illustrative study, scientists at Korea’s Seo-Ulsan Boram Hospital investigated the accuracy of diffusion-weighted magnetic resonance imaging in assessing unconscious trauma patients when their computed

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26. See Martin M. Monti et al., *Willful Modulation of Brain Activity in Disorders of Consciousness*, 362 NEW ENG. J. MED. 579, 579, 588 (2010) (concluding that some individuals in vegetative or minimally conscious states may have brain activations that reflect some awareness and cognition).

27. See, e.g., Linda Beuscher & Victoria T. Grando, *Challenges in Conducting Qualitative Research with Persons with Dementia*, 2 RES. GERONTOLOGICAL NURSING 6, 6–7 (2009) (discussing consent to research and other challenging issues raised by the conduct of qualitative research involving individuals with dementia); Sabina Gainotti et al., *How Are the Interests of Incapacitated Research Participants Protected Through Legislation? An Italian Study on Legal Agency for Dementia Patients*, PLOS, June 2010, at 1, 1, <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0011150> (noting that “[r]esearch involving individuals with compromised mental ability can be ethically challenging” due to “their [impaired] ability to give free and informed consent”); S.Y.H. Kim et al., *Surrogate Consent for Dementia Research: A National Survey of Older Americans*, 72 NEUROLOGY 149, 149 (2009) (“Research in novel therapies for Alzheimer’s Disease (AD) relies on persons with AD as research subjects.”); Robin Pierce, *A Changing Landscape for Advance Directives in Dementia Research*, 70 SOC. SCI. & MED. 623, 623, 629 (2010) (noting that “one of the primary challenges to conducting research on dementia . . . is the gradual loss of the capacity to consent” to research participation by individuals with dementia).

28. Mark H. Tuszynski et al., *A Phase 1 Clinical Trial of Nerve Growth Factor Gene Therapy for Alzheimer Disease*, 11 NATURE MED. 551, 551–52 (2005).

29. See *id.* The study detected “no adverse effects attributable to the delivery of NGF itself or to the gene-delivery vector after 18–24 months of monitoring, including weight loss or pain”; found that post-experiment functional neuroimaging showed significant increases in cortical 18-fluorodeoxyglucose uptake, “a reversal of usual decline in Alzheimer disease”; and concluded that “[a]dditional clinical trials of NGF for Alzheimer disease are warranted.” *Id.*

tomography (CT) brain scans were unremarkable.<sup>30</sup> In a second study, scientists at China’s Hangzhou Normal University and Zhejiang University investigated the efficacy of unilateral decompressive craniectomy and unilateral routine temporoparietal craniectomy in reducing intracranial pressure in patients with unilateral acute post-traumatic brain injury.<sup>31</sup>

Federal and state laws that govern the conduct of research studies such as these may best be described as an incomplete patchwork.<sup>32</sup> As discussed in more detail in Part II.A–B, below, the federal and state governments have for more than three decades swung back and forth between the competing goals of protecting vulnerable human subjects and fostering biomedical and behavioral health research.<sup>33</sup> One result is that federal law still does not contain specific regulations governing human subjects research involving adults with impaired decision-making capacity,<sup>34</sup> some states support such research with few restrictions,<sup>35</sup> and other states prohibit all such research without the prospect of either direct medical benefit to the potential human subject or obtaining generalizable knowledge about the human subject’s disorder or condition.<sup>36</sup> Issues on which stakeholders disagree include (i) whether researchers should be required to demonstrate that a research study classified as minimal risk<sup>37</sup> relates to an individual’s psychiatric, neurological,

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30. Je Sung You et al., *Use of Diffusion-Weighted MRI in the Emergency Department for Unconscious Trauma Patients with Negative Brain CT*, 27 EMERGENCY MED. J. 131, 131–32 (2010).

31. See Wusi Qiu et al., *Effects of Unilateral Decompressive Craniectomy on Patients with Unilateral Acute Post-Traumatic Brain Swelling After Severe Traumatic Brain Injury*, CRITICAL CARE, R185, Nov. 23, 2009, at 1, 1–2, 4–5, <http://ccforum.com/content/pdf/cc8178.pdf> (finding that unilateral decompressive craniectomy (DC) lowers intracranial pressure, “reducing the mortality rate and improving neurological outcomes over unilateral routine temporoparietal craniectomy[;]” also finding that “[DC] increases the incidence of delayed intracranial hematomas and subdural effusion, some of which need secondary surgical intervention”).

32. See *infra* Part II.A–B; see also Oruche, *supra* note 23, at 92 (summarizing gaps in federal and state regulation of human subjects research involving individuals with cognitive impairments).

33. See, e.g., Kim et al., *supra* note 27, at 149–50 (explaining that “policy uncertainties have continued for three decades” and that “policy discussions regarding surrogate-based research (SBR) have continued for three decades without a clear resolution”).

34. See *infra* Part II.A.

35. See *infra* Part II.B (describing California’s law on such research); see also Carl H. Coleman, *Research with Decisionally Incapacitated Human Subjects: An Argument for a Systematic Approach to Risk-Benefit Analysis*, 83 IND. L.J. 743, 760–61 (2008).

36. See *infra* Part II.B (discussing New Jersey’s law on such research).

37. HHS defines “minimal risk” to mean that “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 tests.” 45 C.F.R. § 46.102(i) (2011).

or other condition before an individual with the condition is permitted to be enrolled in the research; (ii) whether it is ever permissible to enroll individuals with impaired decision-making capacity in research classified as greater than minimal risk and, if so (A) whether the greater than minimal risk research intervention must hold out the prospect of direct benefit to the individual; (B) whether the individual is required to have executed an advance research directive through which the individual gave prior consent to research participation; (C) whether a surrogate may consent to the individual's research participation in the absence of an advance research directive; and (D) whether a special standing panel or other similar body that has expertise in research involving individuals with impaired decision-making capacity also should be required to review and approve the individual's research participation.<sup>38</sup>

#### A. Federal Law

Over the past three decades, various federal commissions and regulatory agencies have provided different responses to these questions. On February 2, 1978, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (Commission) issued a report and recommendations relating to human subjects research involving institutionalized individuals with "mental infirmity."<sup>39</sup> Among other things, the Commission recommended that individuals who lack decision-making capacity be allowed to participate in minimal risk research, but only if the research related to the individual's condition or the individual assents or does not object to the research.<sup>40</sup> For example, an individual with severe dementia but without osteoporosis would be permitted to be

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38. See, e.g., Kim et al., *supra* note 27, at 149 (noting that policies for surrogate consent for research remain unsettled after decades of debate). In 2002, for example, the Executive Vice Chancellor of UCLA issued a university-wide moratorium on approval of research involving individuals with impaired decision-making capacity unless a court-appointed conservator consented to the individual's research participation. See Saks et al., *supra* note 12, at 41–42 & n.10 (citing Memorandum from Daniel M. Neuman, Executive Vice Chancellor, Univ. of Cal., L.A., to the Deans, Department Chairs, Division Chiefs, Investigators, and Research Personnel of Univ. of Cal., L.A., RE: Moratorium on IRB Approval of Surrogate or Proxy Informed Consent for Human Subjects Research (Sept. 30, 2002)). Although California law has since been changed to allow surrogates to consent to research participation on behalf of individuals with impaired decision-making capacity, not all state legislatures agree with the approach taken by California. See *infra* Part II.B.

39. See generally THE NAT'L COMM'N FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, RESEARCH INVOLVING THOSE INSTITUTIONALIZED AS MENTALLY INFIRM (1978).

40. *Id.* at 7–8.

enrolled in minimal risk dementia research, but not minimal risk osteoporosis research. For research that posed greater than minimal risk, the Commission recommended that the research intervention hold out the prospect of direct benefit to the individual.<sup>41</sup> For example, the Commission would allow an individual with severe depression to be enrolled in greater than minimal risk research, but only if the research held out the prospect of alleviating the individual’s depression.

Although the former Department of Health, Education, and Welfare (HEW) proposed regulations on November 17, 1978, based on the Commission’s report (Proposed Regulations),<sup>42</sup> HEW never adopted final regulations addressing research involving individuals with impaired decision-making capacity.<sup>43</sup> The Proposed Regulations would have allowed minimal risk research involving individuals lacking decision-making capacity to proceed if the research was relevant to the individual’s condition, the individual assented or did not object to research participation, and the individual’s legally authorized representative (LAR) consented to the individual’s participation.<sup>44</sup>

The Proposed Regulations also would have allowed the conduct of greater than minimal risk research involving individuals who lack decision-making capacity if the research involved an intervention that held out the prospect of direct benefit for the individual, the risks were justified by the prospect of benefit to the individual, “[t]he relation of the risk to anticipated benefit . . . [was] at least as favorable as that presented by available alternative approaches,” the individual assented to research participation, and the individual’s LAR consented to the individual’s participation.<sup>45</sup>

In addition, the Proposed Regulations would have allowed the conduct of greater than minimal risk research involving individuals who lack decision-making capacity even if the research did not hold out the prospect of direct benefit if the risk involved represented a minor increase over minimal risk, the anticipated knowledge was of vital importance for understanding

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41. *Id.* at 11.

42. Protection of Human Subjects: Proposed Regulations on Research Involving Those Institutionalized as Mentally Disabled, 43 Fed. Reg. 53,950, 53,950–56 (proposed Nov. 17, 1978).

43. *See* 45 C.F.R. §§ 46.101–505 (2011) (lacking incorporation of the proposed regulations).

44. Protection of Human Subjects: Proposed Regulations on Research Involving Those Institutionalized as Mentally Disabled, 43 Fed. Reg. at 53,955 (proposing 45 C.F.R. § 46.505(b)(2)).

45. *Id.* at 53,956 (proposing 45 C.F.R. § 46.506(a)(1)–(4)(ii)).

or ameliorating the individual's disorder or condition, and the individual gave informed consent to research participation.<sup>46</sup> If the individual lacked capacity to give informed consent, the Commission would require the individual to assent to research participation and the individual's LAR to consent to the individual's participation.<sup>47</sup> If the individual lacked the capacity to assent but did not object to research participation, both the individual's LAR and a court of competent jurisdiction must consent to the individual's participation.<sup>48</sup>

Finally, the Proposed Regulations would have allowed the conduct of research not otherwise approvable if the research presented an "opportunity to further the understanding, prevention, or alleviation of a serious problem affecting" the individuals' health or welfare and the Secretary of HEW, "after consultation with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following opportunity for public review and comment," determined that (i) the research would "be in accord with basic ethical principles of beneficence, justice, and respect for persons," (ii) that the "research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of individuals institutionalized as mentally disabled," and (iii) that "[a]dequate provisions [were] made for obtaining consent of those [individuals] capable of giving fully informed consent, the assent of other [individuals], and the consent of their [LARs], and, where appropriate, the authorization of a court of competent jurisdiction."<sup>49</sup>

On April 18, 1979, the Commission published in the *Federal Register* its "Ethical Principles and Guidelines for the Protection of Human Subjects of Research" (Belmont Report), which identified and examined three basic ethical principles (respect for persons, beneficence, and justice) that are relevant to the conduct of human subjects research.<sup>50</sup> The Belmont Report also recognized, however, that (i) special provisions may need to be made for research participants with impaired decision-making capacity, (ii) the principle of respect for persons may require consent to research participation to come from a third party who

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46. *Id.* (proposing 45 C.F.R. § 46.507(a)(1)–(4)(i)).

47. *Id.* (proposing 45 C.F.R. § 46.507(a)(4)(ii)).

48. *Id.* (proposing 45 C.F.R. § 46.507(a)(4)(iii)).

49. *Id.* (proposing 45 C.F.R. § 46.508(a)–(b)).

50. Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, 44 Fed. Reg. 23,192, 23,192–94 (Apr. 18, 1979).

is most likely to understand the individual’s situation and to act in the individual’s best interest, and (iii) the third party should have the opportunity to observe the research as it proceeds and withdraw the individual from the research if withdrawal is in the individual’s best interest.<sup>51</sup> By 1991, a total of seventeen federal agencies, including HEW and its successor, HHS, published proposed and final regulations governing human subjects research (the “Common Rule”) that were based in large part on the three ethical principles identified in the Belmont Report.<sup>52</sup> Today, the Common Rule contains a “Basic HHS Policy for the Protection of Human Subjects” (Basic Policy), which is codified at Subpart A of the Common Rule,<sup>53</sup> as well as special provisions governing human subjects research involving three sets of vulnerable populations, including pregnant women, fetuses, and neonates (Subpart B),<sup>54</sup> prisoners (Subpart C),<sup>55</sup> and children (Subpart D).<sup>56</sup>

The Common Rule does not, however, contain a special subpart governing research involving adults with impaired decision-making capacity.<sup>57</sup> As a result, proposed research that would involve adults with impaired decision-making capacity must satisfy only four general provisions set forth in the Basic Policy. First, institutional review boards (IRBs) must ensure that a researcher’s selection of subjects for the research protocol is equitable.<sup>58</sup> In assessing selection equity, the Basic Policy instructs reviewing IRBs to be “particularly cognizant of the special problems of research involving vulnerable populations, such as . . . mentally disabled persons.”<sup>59</sup> The Basic Policy does not expand on the special problems associated with individuals who have mental disabilities.<sup>60</sup> Second, IRBs must ensure that, “[w]hen some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as . . . mentally disabled

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51. *Id.* at 23,195.

52. Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators, 76 Fed. Reg. 44,512, 44,512, 44,529 (proposed July 26, 2011) (to be codified at 45 C.F.R. pts. 46, 160, 164; 21 C.F.R. pts. 50, 56).

53. 45 C.F.R. §§ 46.101–124 (2011).

54. 45 C.F.R. §§ 46.201–207.

55. 45 C.F.R. §§ 46.301–306.

56. 45 C.F.R. §§ 46.401–409.

57. *See* 45 C.F.R. §§ 46.101–505 (lacking a Subpart for research involving adults with impaired decision-making capacity).

58. 45 C.F.R. § 46.111(a)(3).

59. *Id.*

60. 45 C.F.R. §§ 46.101–505 (failing to provide details on the special problems associated with individuals who have mental disabilities).

persons, . . . additional safeguards have been included in the study to protect the rights and welfare of these subjects.”<sup>61</sup> The Basic Policy does not identify the content of such additional safeguards.<sup>62</sup> Third, “[i]f an IRB regularly reviews research that involves a vulnerable category of subjects, such as . . . mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.”<sup>63</sup> The Basic Policy does not expand on the requirement for the inclusion of individuals who are knowledgeable about and experienced in working with individuals with mental disabilities.<sup>64</sup> Finally, IRBs must ensure that informed consent to research participation has been obtained from each prospective subject or the subject’s LAR,<sup>65</sup> defined elsewhere in the Basic Policy as “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.”<sup>66</sup> The phrase

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61. 45 C.F.R. § 46.111(b).

62. 45 C.F.R. §§ 46.101–505 (neglecting to specify what the additional safeguards entail).

63. 45 C.F.R. § 46.107(a). Although the Basic Policy does not expand on this requirement, the National Institutes of Health recently explained that an IRB that regularly reviews research involving individuals with impaired decision-making capacity should consider including as members (i) “professionals with the appropriate background, knowledge and experience in working with individuals with impaired [decision-making] capacity;” (ii) “representatives of [relevant] patient advocacy groups;” (iii) “experts in the assessment of consent capacity; and/or” (iv) “experts on the scientific and ethical issues relevant to studies involving vulnerable populations.” Office of Extramural Research, *Research Involving Individuals with Questionable Capacity to Consent: Points to Consider*, NAT’L INSTS. HEALTH (Nov. 2009), <http://grants.nih.gov/grants/policy/questionablecapacity.htm>. The Subcommittee for the Inclusion of Individuals with Impaired Decision Making in Research (SIIIDR) of the Secretary’s Advisory Committee on Human Research Protections (SACHRP) within the Office for Human Research Protections (OHRP) similarly recommends that IRBs consider including as members (i) “[p]atients, former patients, patient advocates or family members or others who can represent the views and perspectives of the research participants;” (ii) “[i]ndividuals with specific professional expertise related to the nature and consequences of impaired consent capacity in the study population;” (iii) “[o]ther individuals who can provide information relevant to the circumstances and context in which the participant and LAR will be recruited (e.g., the long term care facility, critical care unit, or mental health center);” and (iv) “[i]ndividuals with expertise regarding applicable legal and regulatory requirements for consent to research by an LAR.” SEC’Y’S ADVISORY COMM. ON HUMAN RESEARCH PROTECTIONS, RECOMMENDATIONS FROM THE SUBCOMMITTEE FOR THE INCLUSION OF INDIVIDUALS WITH IMPAIRED DECISION MAKING IN RESEARCH (SIIIDR) 6–7 (2009), available at <http://www.hhs.gov/ohrp/sachrp/20090715letterattach.pdf>.

64. 45 C.F.R. §§ 46.101–505 (declining to elaborate on the inclusion of such individuals).

65. 45 C.F.R. §§ 46.111(a)(4), 46.116.

66. 45 C.F.R. § 46.102(c) (emphasis added).

*applicable law* is generally thought to refer to state law<sup>67</sup> although, as discussed in more detail at Part II.B below, state law on this topic varies widely if it exists.

In light of the Common Rule’s lack of specific guidance regarding research involving individuals with impaired decision-making capacity, a national commission and federal agencies have issued nonbinding recommendations for the conduct of research involving individuals with impaired decision-making capacity.<sup>68</sup> In December 1998, the Clinton Administration’s National Bioethics Advisory Commission (NBAC) issued a special report entitled “Research Involving Persons with Mental Disorders That May Affect Decisionmaking Capacity” (Report).<sup>69</sup> In the Report, the NBAC recommended allowing minimal risk research that would involve individuals with disorders that may affect decision-making capacity if one of the following three requirements has been satisfied: (i) the individual has the capacity to consent and does consent to research participation; or, if the individual does not have the capacity to consent, (ii) the individual executed an advance research directive stating the individual’s desire to participate in the research and the individual’s LAR consents to the individual’s research participation; or (iii) the individual’s LAR consents to the individual’s research participation.<sup>70</sup> The NBAC further recommended allowing greater than minimal risk research, but only if the research offered the prospect of direct medical benefit to the individual and, as in the case of minimal risk research, one of the three requirements listed in the preceding sentence has been satisfied.<sup>71</sup> If the research protocol involved greater than minimal risk but did not offer the prospect of direct medical benefit to the individual, the NBAC would require either one of the first two requirements to be satisfied or would require a special standing panel with expertise on research involving individuals with mental disorders that may affect decision-making capacity to approve the individual’s research participation.<sup>72</sup> Working groups in 2001<sup>73</sup> and

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67. See, e.g., Request for Information and Comments on Research that Involves Adult Individuals with Impaired Decision-Making Capacity, 72 Fed. Reg. 50,966, 50,969 (Sept. 5, 2007).

68. See *infra* text accompanying notes 69–87.

69. See generally NAT’L BIOETHICS ADVISORY COMM’N, RESEARCH INVOLVING PERSONS WITH MENTAL DISORDERS THAT MAY AFFECT DECISIONMAKING CAPACITY (1998).

70. *Id.* at 60 (Chapter 5, Recommendation 10).

71. *Id.* (Chapter 5, Recommendation 11).

72. *Id.* at 61 (Chapter 5, Recommendation 12).

73. HHS Working Grp. on the NBAC Report, *Analysis and Proposed Actions Regarding the NBAC Report: Research Involving Persons with Mental Disorders that May Affect Decisionmaking Capacity*, U.S. DEPT HEALTH & HUM. SERVICES (Jan. 16, 2001), <http://aspe.hhs.gov/sp/nbac/a.shtml>.

2002<sup>74</sup> responded to the NBAC's Report with additional recommendations, including a proposal to adopt an additional category of research ("minor increase over minimal risk"), although neither the NBAC nor the working group recommendations were adopted by a federal agency in formal regulations.<sup>75</sup>

On September 5, 2007, HHS published in the *Federal Register* a formal request for public comments addressing whether additional guidance or a new subpart of the Common Rule is needed to address research involving adults with impaired decision-making capacity.<sup>76</sup> Although the closing date for the receipt of comments was January 14, 2008,<sup>77</sup> HHS did not issue any proposed or final regulations subsequent to its request for comments.

Due to the lack of formal federal regulation, several federal agencies and committees have released informal guidance regarding the conduct of human subjects research involving individuals with impaired decision-making capacity.<sup>78</sup> In November 2008, the Office for Human Research Protections (OHRP) posted on its website answers to certain frequently asked questions.<sup>79</sup> The OHRP's answers do not provide clear guidance, especially for researchers involved in multi-site, multi-state investigations. In response to one frequently asked question ("Who can be a [LAR] for the purpose of providing consent on behalf of a prospective subject?"), the OHRP explains that some state laws identify those persons who are eligible to serve as a LAR, while other state laws do not.<sup>80</sup> According to the OHRP, "IRBs may wish to consult with legal counsel when deciding who can serve as [a] LAR for subjects of proposed research."<sup>81</sup> In response to a second frequently asked question ("When may a [LAR] provide consent on behalf of an adult with diminished decision-making capacity?"), the OHRP explains that the

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74. NAT'L HUMAN RESEARCH PROTECTIONS ADVISORY COMM. (NHRPAC), REPORT FROM NHRPAC ON INFORMED CONSENT AND THE DECISIONALLY IMPAIRED 1-4 (2002), available at <http://www.hhs.gov/ohrp/archive/nhrpac/documents/nhrpac10.pdf>.

75. Tovino, *supra* note 8, at 40.

76. See Request for Information and Comments on Research that Involves Adult Individuals with Impaired Decision-Making Capacity, 72 Fed. Reg. 50,966, 50,966, 50,968 (Sept. 5, 2007).

77. *Id.* at 50,966.

78. See *infra* text accompanying notes 79-87.

79. Office for Human Research Protections, *Informed Consent—FAQs*, U.S. DEP'T HEALTH & HUM. SERVICES, <http://answers.hhs.gov/ohrp/categories/1566> (last visited Jan. 1, 2013).

80. *Id.*

81. *Id.*

Common Rule “should be consulted in addition to the laws of the jurisdiction in which the research is conducted.”<sup>82</sup>

In addition to the OHRP’s answers to frequently asked questions, the Subcommittee for the Inclusion of Individuals with Impaired Decision-Making in Research (SIIDR) of the Secretary’s Advisory Committee on Human Research Protections (SACHRP) of the OHRP approved at meetings held on March 27, 2008, and March 4, 2009, recommendations regarding the inclusion of individuals with impaired decision-making capacity.<sup>83</sup> When state or local law does not identify the individuals who are eligible to serve as a surrogate, the SIIDR recommended obtaining consent from a priority-ordered list of individuals, including

- (a) a person designated by the individual, while retaining the decisional capacity to do so, to make decisions for him/her regarding participation in research;
- (b) a person designated by the individual, while retaining the decisional capacity to do so, to make decisions for him/her regarding non-research health care decisions;
- (c) the individual’s legal guardian with authority to make health care decisions for him or her;
- (d) the spouse, or if recognized by applicable law, the civil union partner or domestic partner;
- (e) an adult son or daughter;
- (f) a parent;
- (g) an adult brother or sister; [and]
- (h) an adult who has exhibited special care and concern for the prospective research participant.<sup>84</sup>

In addition to the SIIDR’s recommendations, the National Institutes of Health (NIH) released in November 2009 certain “Points to Consider” with respect to research involving individuals with impaired decision-making capacity.<sup>85</sup> In its Points to Consider, the NIH recognized that many states do not have laws specifically governing the consent-to-research process and noted that stakeholders frequently rely on laws governing consent to treatment.<sup>86</sup> On this issue, the NIH concludes that “IRBs may wish to consult with legal counsel

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82. *Id.*

83. SEC’Y’S ADVISORY COMM. ON HUMAN RESEARCH PROTECTIONS, *supra* note 63, at 1.

84. *Id.* at 14.

85. Office of Extramural Research, *supra* note 63.

86. *Id.*

when determining who can serve as [a] LAR for subjects of proposed research.”<sup>87</sup>

Most recently, HHS, on July 26, 2011, issued its ANPR “request[ing] comment on how . . . regulations for protecting human subjects who participate in research might be modernized and revised to be more effective.”<sup>88</sup> Although the ANPR does not specifically focus on the issues raised by research involving individuals with impaired decision-making capacity, the ANPR does recognize that the landscape of research activities has changed dramatically since HHS adopted the Common Rule,<sup>89</sup> that there has been a proliferation of research in the areas of neurology, psychiatry, and the social and behavioral sciences,<sup>90</sup> and that new technologies, including functional magnetic resonance imaging, have been employed to assist in answering research questions.<sup>91</sup> Given the rapid growth and expansion of human subjects research, the ANPR proposes changes to seven broad aspects of HHS’s current regulatory framework<sup>92</sup> and requests comment on seventy-four specific questions relating to the regulation of human subjects research.<sup>93</sup> One set of proposed changes relates to “[i]mprovement of consent forms and the consent process.”<sup>94</sup> More specifically, Question #36 asks,

What additional information, if any, should be required by the regulations to assure that consent forms appropriately describe to subjects, in concise and clear language, alternatives to participating in the research study and why it may or may not be in their best interests to participate? What modifications or deletions to the required elements would be appropriate?<sup>95</sup>

Question #38 further asks, “Should the regulations require that, for certain types of studies, investigators assess how well potential research subjects comprehend the information provided to them before they are allowed to sign the consent form?”<sup>96</sup>

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87. *Id.*

88. Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators, 76 Fed. Reg. 44,512, 44,512 (proposed July 26, 2011) (to be codified at 45 C.F.R. pts. 46, 160, 164; 21 C.F.R. pts. 50, 56).

89. *See id.* at 44,513.

90. *See id.* at 44,512–13.

91. *See id.* at 44,513.

92. *See id.* at 44,514 (listing seven broad sets of proposed changes).

93. *See id.* at 44,517–29.

94. *Id.* at 44,514.

95. *Id.* at 44,523.

96. *Id.*

Finally, Question #40 asks, “Would informed consent be improved if the regulations included additional requirements regarding the consent process, and if so, what should be required?”<sup>97</sup>

As of this writing, HHS has yet to issue proposed or final regulations in response to the comments received by HHS on the ANPR.<sup>98</sup> As a result, the conduct of human subjects research involving adults with impaired decision-making capacity remains legally and ethically murky, especially in the context of multi-site, multi-state clinical trials.<sup>99</sup>

### B. State Law

Although the federal government has yet to issue regulations governing research involving individuals with impaired decision-making capacity, some states do have relevant laws, although these laws vary widely in their application, scope, and regulation.<sup>100</sup> Below, the laws of California, Missouri, and New Jersey are used to illustrate the variety of state approaches to the regulation of human subjects involving individuals with impaired decision-making capacity.

California law is favorable for researchers who wish to conduct research involving individuals with impaired decision-making capacity. California law allows a surrogate to consent to research on behalf of an individual who is “unable to consent and does not express dissent or resistance to participation,” even if the research does not pose the prospect of direct medical benefit, so long as the research “relate[s] to the cognitive impairment, lack of capacity, or serious or life-threatening disease[ ] and

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97. *Id.*

98. See Kristen Rosati, American Health Lawyers Association, *The Tissue Issue: Recent Developments in Biospecimen Research, Legal Issues Affecting Academic Medical Centers and Other Teaching Institutions* 5 (Jan. 26, 2012) (transcript available at [http://www.healthlawyers.org/Events/Programs/Materials/Documents/AMC12/papers/G\\_rosati.pdf](http://www.healthlawyers.org/Events/Programs/Materials/Documents/AMC12/papers/G_rosati.pdf)); see also Office for Human Research Protection, *ANPRM Frequently Asked Questions (FAQs) July 2011*, U.S. DEPARTMENT HEALTH & HUM. SERVICES, <http://www.hhs.gov/ohrp/humansubjects/anprmqanda.html> (last visited Jan. 1, 2013) (asserting that the public will have an additional opportunity to comment before the Common Rule is changed).

99. See, e.g., Kim et al., *supra* note 12, at 797 (“Despite a wave of initiatives in the late 1990s to clarify policy, surrogate consent for research continues to be a murky legal area and incapable subjects in the United States still lack clear regulatory protection.”); SEC’Y’S ADVISORY COMM. ON HUMAN RESEARCH PROTECTIONS, *supra* note 63, at 2.

100. See, e.g., Kim et al., *supra* note 12, at 798 (“Previous reviews of state laws and regulations on proxy or surrogate consent for research have revealed tremendous heterogeneity . . . .”); Saks et al., *supra* note 12, at 37–79 (surveying state laws governing consent to research by legally authorized representatives on behalf of individuals with impaired decision-making capacity).

condition[ ]” of the individual.<sup>101</sup> Under California law, the surrogate shall have reasonable knowledge of the subject and shall be selected from the following priority-ordered list of persons:

- (1) The [individual’s] agent pursuant to an advance health care directive.
- (2) The conservator or guardian of the person having the authority to make health care decisions for the individual.
- (3) The spouse of the [individual].
- (4) [A domestic partner].
- (5) An adult son or daughter of the person.
- (6) A custodial parent of the person.
- (7) Any adult brother or sister of the person.
- (8) Any adult grandchild of the person.
- (9) An available adult relative with the closest degree of kinship to the person.<sup>102</sup>

California research surrogates are required to base research participation decisions on “the [individual’s] . . . health care instructions, if any, and other wishes, to the extent known” by the surrogate.<sup>103</sup> “Otherwise, the surrogate . . . shall make the decision in accordance with the [individual’s] best interests.<sup>104</sup> “In determining the [individual’s] best interests, the [surrogate] shall consider the [individual’s] personal values and his or her best estimation of what the [individual] would have chosen if he or she were capable of making a decision” regarding research participation.<sup>105</sup> California law prohibits surrogates from receiving compensation in exchange for consenting to an individual’s research participation.<sup>106</sup>

Missouri law is much less descriptive (and permissive) than California law. Missouri law prohibits certain public and private mental health facilities and programs from conducting research involving certain individuals with “intellectual disabilities, developmental disabilities, mental illness, mental disorders or alcohol or drug abuse unless such research is intended to alleviate or prevent the disabling conditions or is reasonably

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101. CAL. HEALTH & SAFETY CODE § 24178(b)–(c) (West 2006).

102. CAL. HEALTH & SAFETY CODE § 24178(c)(1)–(9) (West 2006).

103. CAL. HEALTH & SAFETY CODE § 24178(g) (West 2006).

104. *Id.*

105. *Id.*

106. CAL. HEALTH & SAFETY CODE § 24178(i) (West 2006).

expected to be of direct therapeutic benefit to the participants.”<sup>107</sup> Missouri law does not address whether a surrogate may consent to research on behalf of an individual with impaired decision-making capacity.<sup>108</sup>

New Jersey law requires research involving individuals with “cognitive impairments, lack of capacity, or serious physical or behavioral conditions and life-threatening diseases” to either (i) offer the prospect of direct benefit to the person and maintain an appropriate balance of research benefits and risks; or (ii) be “likely to yield generalizable knowledge about the [person’s] disorder or condition;” not be, by its nature, able to be conducted without the participation of persons with impaired decision-making capacity; and “involve[] no more than a minor increase over minimal risk.”<sup>109</sup> A New Jersey research protocol that meets one of these two sets of requirements may proceed if consent is obtained from the individual or a surrogate,<sup>110</sup> defined as

an authorized representative with reasonable knowledge of the subject, who shall include any of the following persons, in the following descending order of priority:

- (1) the guardian of the subject who has the authority to make health care decisions for the subject;
- (2) the health care representative of the subject pursuant to an advance directive for health care;
- (3) the spouse or civil union partner, as applicable, of the subject;
- (4) the domestic partner . . . of the subject;
- (5) an adult son or daughter of the subject;
- (6) a custodial parent of the subject;
- (7) an adult brother or sister of the subject;
- (8) an adult grandchild of the subject;
- (9) an available adult relative with the closest degree of kinship to the subject.<sup>111</sup>

Many states do not have laws governing the conduct of human subjects research involving adults with impaired decision-making capacity.<sup>112</sup> In states that lack research-specific

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107. MO. ANN. STAT. § 630.192 (West Supp. 2012).

108. See Susan E. Hickman et al., *The POLST (Physician Orders for Life-Sustaining Treatment) Paradigm to Improve End-of-Life Care: Potential State Legal Barriers to Implementation*, 36 J.L. MED. & ETHICS 119, 126, 128, 133 (2008).

109. N.J. STAT. ANN. § 26:14–3(a)–(b) (West Supp. 2012).

110. See N.J. STAT. ANN. § 26:14–4(a) (West Supp. 2012).

111. N.J. STAT. ANN. § 26:14–5(a)(1)–(9) (West Supp. 2012).

112. See, e.g., SEC’Y’S ADVISORY COMM. ON HUMAN RESEARCH PROTECTIONS, *supra*

laws, some researchers and research institutions rely on state laws that govern consent to treatment, including laws like the Texas, New York, and Washington laws discussed at Part III.B, below.<sup>113</sup> Moreover, it is the current policy of the OHRP to permit a surrogate to consent to research if the surrogate is authorized under state law to consent to the “procedures involved in the research” under state laws governing consent to treatment.<sup>114</sup> In addition, the SIIIDR currently recommends, in the absence of a specific law governing consent to research, that a surrogate who is designated to make nonresearch health care decisions be ranked second in the priority-ordered list of persons who are eligible to make research participation decisions.<sup>115</sup> In summary, some researchers, some research institutions, the OHRP, the SIIIDR, and other stakeholders believe that a surrogate who is authorized to consent to treatment also should be permitted to consent to an individual’s research participation.<sup>116</sup> Part III, next, examines federal and state legislation governing consent to treatment. Then, Part IV argues that legislation governing consent to treatment should not be used to answer research-related questions.

### III. CONSENT-TO-TREATMENT LEGISLATION

In the clinical context, *decision-making capacity* refers to a patient’s cognitive and emotional capacity to consider information relating to the risks and benefits of a proposed diagnostic examination, medical treatment, or surgical procedure; the ability to make a decision to consent or refuse to consent to such examination, treatment, or procedure; and the

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note 63, at 2 (“Very few states specifically define legally authorized representatives (LARs) for research, and most state’s laws are silent on the topic. Virtually no state laws address the many ethical issues that arise when LARs are involved in research decision-making, leaving it to IRBs and institutions to invent solutions.”).

113. See, e.g., Office of Extramural Research, *supra* note 63 (“In most jurisdictions, LAR appointment processes are not specific to the research setting and institutions rely on the laws governing the use of LARs for clinical care.”).

114. See, e.g., SEC’Y’S ADVISORY COMM. ON HUMAN RESEARCH PROTECTIONS, *supra* note 63, at 13 (explaining, at Recommendation 8(b), that “[i]n states with laws or regulations that address consent to treatment but do not specifically consider consent to research, current OHRP interpretation permits consent to research by individuals authorized under laws that allow consent to the ‘procedures involved in the research’”).

115. *Id.* (recommending, at Recommendation 9(a)(ii)(b), in the absence of applicable state law, that a person who is designated to make nonresearch health care decisions be ranked second in the priority-ordered list of persons who are eligible to make research participation decisions).

116. See *id.* at 13–14.

ability to communicate that decision.<sup>117</sup> Neurologists, psychiatrists, geriatricians, and emergency medicine physicians, among other clinicians, frequently treat patients with impaired decision-making capacity.<sup>118</sup> Some of these patients may be in a coma or vegetative state and have no present decision-making capacity.<sup>119</sup> Other patients may have mild, moderate, or severe neurological disorders, including Parkinson’s disease, Alzheimer’s disease, and related dementias, which may restrict their decision-making capacity.<sup>120</sup> Still other patients may have

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117. See, e.g., Gregory L. Larkin, Catherine A. Marco & Jean T. Abbott, *Emergency Determination of Decision-Making Capacity: Balancing Autonomy and Beneficence in the Emergency Department*, 8 ACADEMIC EMERGENCY MED. 282, 282 (2001) (“Decision-making capacity includes the ability to receive, process, and understand information, the ability to deliberate, the ability to make choices, and the ability to communicate those preferences.”); Roy C. Martin et al., *Medical Decision-Making Capacity in Cognitively Impaired Parkinson’s Disease Patients Without Dementia*, 23 MOVEMENT DISORDERS 1867, 1867 (2008) (defining medical decision-making capacity as the “cognitive and emotional capacity to accept a proposed treatment, to refuse treatment, or to select among treatment alternatives”).

118. See, e.g., Grant V. Chow et al., *CURVES: A Mnemonic for Determining Medical Decision-Making Capacity and Providing Emergency Treatment in the Acute Setting*, 137 CHEST 421, 421–27 (2010) (addressing the evaluation of decision-making capacity in the emergency context); Paul J. Eslinger, *Neurological and Neuropsychological Bases of Empathy*, 39 EUR. NEURO. 193, 198 (1998) (remarking that neurologists and neuropsychologists address a variety of issues, including cognitive impairment); Edmund Howe, *Ethical Aspects of Evaluating a Patient’s Mental Capacity*, PSYCHIATRY, Jul. 2009, at 15, 15 (noting that nonpsychiatrist physicians frequently consult with psychiatrists to help make determinations regarding patients’ decision-making capacity); James M. Lai & Jason Karlawish, *Assessing the Capacity to Make Everyday Decisions: A Guide for Clinicians and an Agenda for Future Research*, 15 AM. J. GERIATRIC PSYCHIATRY 101, 101 (2007) (noting that “[c]ompetency assessments are a common and necessary part of caring for older patients with cognitive impairment[s]” and that geriatricians “face considerable challenges in accurately and reliably identifying impaired competency”); *id.* at 103 (“[D]ischarge planners, case managers, and clinicians in hospitals, skilled nursing facilities, and emergency departments [frequently] must decide whether a patient with functional impairments is capable of making decisions.”).

119. See, e.g., Rowan H. Harwood, Robert Stewart & Peter Bartlett, *Safeguarding the Rights of Patients Who Lack Capacity in General Hospitals. Do the Bournwood Proposals for England and Wales Help or Hinder?*, 36 AGE & AGEING 120, 120 (2007) (“Many people . . . in coma[s] are admitted to hospital[s], but lack the capacity to consent to admission.”); Sheila A. M. McLean, *Permanent Vegetative State and the Law*, 71 J. NEUROLOGY, NEUROSURGERY & PSYCHIATRY (NEUROLOGY IN PRACTICE SUPPLEMENT 1) i26, i26 (2001) (noting that patients in a vegetative state lack capacity to consent to treatment).

120. See, e.g., Jason Karlawish, *Measuring Decision-Making Capacity in Cognitively Impaired Individuals*, 16 NEURO SIGNALS 91, 91–98 (2008) (reviewing studies of the capacity to consent to treatment and research in the context of Alzheimer’s disease and related dementias; and noting that individuals with Alzheimer’s disease and related dementias frequently experience losses in decision-making capacity); Martin et al., *supra* note 117, at 1867–74 (assessing decision-making capacity in patients with Parkinson’s disease (PD) compared to healthy older adults; and suggesting that impairment in decision-making capacity is already present in cognitively impaired PD patients without dementia and that such impairment increases as these patients develop dementia);

severe mental illnesses (such as schizophrenia with disturbance of thought and perception) that limit their decision-making capacity.<sup>121</sup> Other patients may be experiencing a temporary loss of decision-making capacity due to alcohol or drug intoxication or mild traumatic brain injury, although they may be expected to fully regain their decision-making capacity in the very near future.<sup>122</sup> As these examples show, an individual's decision-making capacity is not always conclusively present or absent but occurs along a continuum that depends on the nature and severity of the patient's physical and mental health conditions and the timing of the patient's symptom occurrence.<sup>123</sup> Neurological, psychiatric, and other health conditions do not invariably impair an individual's decision-making capacity, and patient-specific assessments always are necessary.<sup>124</sup>

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Jennifer Moye et al., *Neuropsychological Predictors of Decision-Making Capacity Over 9 Months in Mild-to-Moderate Dementia*, 21 J. GEN. INTERNAL MED. 78, 78–83 (2006) (examining rates and neuropsychological predictors of decision-making capacity among older adults with dementia; and finding that “[s]ome patients with mild-to-moderate dementia develop clinically relevant impairment[s] of [decision-making] capacity within a year”).

121. See, e.g., Delphine Capdevielle et al., *Competence to Consent and Insight in Schizophrenia: Is There an Association? A Pilot Study*, 108 SCHIZOPHRENIA RES. 272, 272–73 (2009) (“Data from studies of treatment decision processes by schizophrenic patients have suggested that, as a group, these patients perform significantly worse on many measures in comparison to those suffering from depression, other medical illnesses (such as heart disease, HIV infection) or healthy control subjects.”); John H. Coverdale, Laurence B. McCullough & Frank A. Chervenak, *Assisted and Surrogate Decision Making for Pregnant Patients Who Have Schizophrenia*, 30 SCHIZOPHRENIA BULL. 659, 659 (2004) (explaining that “[s]chizophrenia can chronically and variably impair a woman's decisions concerning the management of [her] pregnancy,” including decisions regarding pregnancy continuation).

122. See, e.g., Larkin, Marco & Abbott, *supra* note 117, at 283–84 (noting that patients who are intoxicated present challenges in the context of determining decision-making capacity); Office of Extramural Research, *supra* note 63 (“For individuals with conditions that bring about fluctuating levels of consent capacity, it is important to consider the timing of the assessment and consent; it may make sense to time the initial consent carefully to avoid periods when prospective subjects may be experiencing heightened impairments, e.g., an individual with . . . acute drug intoxication.”); K.L. Triebel et al., *Treatment Consent Capacity in Patients with Traumatic Brain Injury Across a Range of Injury Severity*, 78 NEUROLOGY 1472, 1475 (2012).

123. Office of Extramural Research, *supra* note 63, at 2 (noting that decision-making capacity for individuals with disabilities occurs along a continuum); Larkin, Marco & Abbott, *supra* note 117, at 282 (“[Decision-making capacity] is a dynamic . . . and changing talent; in practice it may be assessed on a non-dichotomous spectrum of capacity, pertaining to the particular health care decisions at hand. Often, impairment is situational; the same patient may be competent for one decision and not another, depending on the gravity and consequences of the decision and the potential for harm.”).

124. See, e.g., Capdevielle et al., *supra* note 121, at 273 (explaining that “a subgroup of patients with schizophrenia, even when acutely ill, performs no worse than the general population” on measures of treatment decision processes (citations omitted)); *The MacArthur Treatment Competence Study: Executive Summary*, MACARTHUR RES. NETWORK ON MENTAL HEALTH & L. (May 2004), <http://www.macarthur.virginia.edu/>

*A. Federal Law*

Other than general references to the doctrine of informed consent to treatment and state law provisions regarding legal representatives, federal law does not specifically address impaired clinical decision-making capacity, first-person consent to treatment, or surrogate consent to treatment.<sup>125</sup> For example, federal regulations that establish requirements applicable to Medicare-participating hospitals simply provide,

The patient or his or her representative (as allowed under State law) has the right to make informed decisions regarding his or her care. The patient’s rights include being informed of his or her health status, being involved in care planning and treatment, and being able to request or refuse treatment.<sup>126</sup>

Federal regulations governing Medicare-participating hospices, which provide palliative care to patients with terminal conditions, similarly give hospice patients a general right to be involved in developing their own hospice plans of care as well as the right to refuse unwanted care.<sup>127</sup> If a hospice patient has been adjudged incompetent under state law by a court of proper jurisdiction, federal regulations generally provide that “the rights of the [hospice] patient are to be exercised by the person appointed pursuant to state law to act on the patient’s behalf.”<sup>128</sup> “If a state court has not adjudged a [hospice] patient incompetent, [federal law provides that] any legal representative designated by the patient in accordance with state law may exercise the patient’s rights to the extent allowed by state law.”<sup>129</sup> Federal regulations governing Medicare-participating nursing homes also are general in nature: “Unless adjudged incompetent or otherwise found to be incapacitated under the laws of the State, [patients have the right to] participate in planning care and treatment or changes in care and treatment.”<sup>130</sup>

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treatment.html (“Most patients hospitalized with serious mental illness have abilities similar to persons without mental illness for making treatment decisions. Taken by itself, mental illness does not invariably impair decision-making capacities. On the other hand, a substantial percentage of hospitalized patients—up to half in the group with schizophrenia when all four types of abilities are considered—show high levels of impairment.” (emphasis omitted)).

125. See Saks et al., *supra* note 12, at 40, 52, 59–60.

126. 42 C.F.R. § 482.13(b)(2) (2010).

127. 42 C.F.R. § 418.52(c)(2)–(3).

128. 42 C.F.R. § 418.52(b)(2).

129. 42 C.F.R. § 418.52(b)(3).

130. 42 C.F.R. § 483.10(d)(3).

*B. State Law*

Unlike federal law, almost every state has enacted a law that specifically defines *decision-making capacity* and *incapacity*, establishes the process for obtaining the informed consent of patients with capacity, establishes the process for obtaining surrogate consent in the event a patient lacks capacity, identifies the persons in priority order who are eligible to serve as a surrogate for health care decisions, and identifies the standard that a surrogate should use in deciding whether to consent to medical treatment on behalf of a patient.<sup>131</sup> Illustrative laws from Texas, New York, and Washington are examined below. Although these state laws vary in some important respects, they establish relatively uniform consent-to-treatment policies and procedures and may be used to illustrate the general approach that most state legislatures have taken with respect to health care decisions that involve individuals with impaired decision-making capacity.

The Texas Consent to Medical Treatment Act (Texas Act)<sup>132</sup> defines *decision-making capacity* as “the ability to understand and appreciate the nature and consequences of a decision regarding medical treatment and the ability to reach an informed decision in the matter”<sup>133</sup> and *incapacity* as “lacking the ability, based on reasonable medical judgment, to understand and appreciate the nature and consequences of a treatment decision, including the significant benefits and harms of and reasonable alternatives to any proposed treatment decision.”<sup>134</sup> A patient with decision-making capacity has the right to consent or refuse to consent to recommended medical treatments and surgical procedures.<sup>135</sup> If a patient is “comatose, incapacitated, or otherwise mentally or physically incapable of communication” and does not have an advance directive, then a competent adult surrogate from a priority-ordered list “who has decision-making capacity, [who] is available after a reasonably diligent inquiry, and [who] is willing to consent to medical treatment on behalf of the patient may consent to medical treatment on behalf of the

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131. See *infra* text accompanying notes 132–172.

132. TEX. HEALTH & SAFETY CODE ANN. § 313.001 (West 2010).

133. TEX. HEALTH & SAFETY CODE ANN. § 313.002(3) (West 2010).

134. TEX. HEALTH & SAFETY CODE ANN. § 313.002(5) (West 2010).

135. 25 TEX. ADMIN. CODE § 601.4(a)(1) (2012) (Tex. Med. Disclosure Panel, Informed Consent) (codifying Texas’s standard disclosure and consent form, which contains the following header: “You have the right, as a patient, to be informed about your condition and the recommended surgical, medical, or diagnostic procedure to be used so that you may make the decision whether or not to undergo the procedure after knowing the risks and hazards involved” (emphasis omitted)).

patient.”<sup>136</sup> The following individuals may serve as a surrogate, but only if an individual in a previous class is not available after a reasonably diligent inquiry:

- (1) the patient’s spouse;
- (2) an adult child of the patient who has the waiver and consent of all other qualified adult children of the patient to act as the sole decision-maker;
- (3) a majority of the patient’s reasonably available adult children;
- (4) the patient’s parents; or
- (5) the individual clearly identified to act for the patient by the patient before the patient became incapacitated, the patient’s nearest living relative, or a member of the clergy.<sup>137</sup>

“Any dispute as to the right of a party to act as a surrogate decision-maker must be resolved only by a court of record having jurisdiction.”<sup>138</sup> “Any medical treatment consented to [by a surrogate] must be based on knowledge of what the patient would desire, if known.”<sup>139</sup> The Texas Act concludes by prohibiting surrogates from consenting to certain health care services and treatments, including voluntary inpatient mental health services and electroconvulsive treatment.<sup>140</sup>

The New York Family Health Care Decision Act (New York Act) defines *decision-making capacity* as “the ability to understand and appreciate the nature and consequences of proposed health care, including the benefits and risks of and alternatives to proposed health care, and to reach an informed decision.”<sup>141</sup> A patient with decision-making capacity has the right to consent or refuse to consent to recommended medical treatments and surgical procedures.<sup>142</sup> If a patient is determined

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136. TEX. HEALTH & SAFETY CODE ANN. §§ 313.003(a), 313.004(a) (West Supp. 2012).

137. TEX. HEALTH & SAFETY CODE ANN. § 313.004(a)(1)–(5) (West 2010).

138. TEX. HEALTH & SAFETY CODE ANN. § 313.004(b) (West 2010).

139. TEX. HEALTH & SAFETY CODE ANN. § 313.004(c) (West 2010).

140. TEX. HEALTH & SAFETY CODE ANN. § 313.004(d)(1)–(2) (West 2010).

141. N.Y. PUB. HEALTH LAW § 2994–a(5) (McKinney 2012).

142. N.Y. PUB. HEALTH LAW § 2504(1) (McKinney 2012) (“Any person who is eighteen years of age or older . . . may give effective consent for medical, dental, health and hospital services for himself or herself, and the consent of no other person shall be necessary.”); *see also* Schloendorff v. Soc’y of N.Y. Hosp., 105 N.E. 92, 93 (N.Y. 1914) (“Every human being of adult years and sound mind has a right to determine what shall be done with his own body.”), *abrogated on other grounds by* Bing v. Thunig, 143 N.E.2d 3 (N.Y. 1957); *In re Storar*, 420 N.E.2d 64, 71 (N.Y. 1981) (“In this State . . . there is no statute which prohibits a patient from declining necessary medical treatment or a doctor from honoring the patient’s decision. To the extent that existing statutory and decisional

to lack decision-making capacity, a surrogate has the right to consent or refuse to consent to recommended medical treatments and surgical procedures on behalf of the patient.<sup>143</sup> The following individuals in the following priority order are eligible to serve as a surrogate if an individual in a higher class is not reasonably available, willing, and competent to act:

- (a) A guardian authorized to [make health care decisions];
- (b) The spouse, if not legally separated from the patient, or the domestic partner;
- (c) A son or daughter eighteen years of age or older;
- (d) A parent;
- (e) A brother or sister eighteen years of age or older;
- (f) A close friend.<sup>144</sup>

The standard for surrogate decision-making in New York is “patient’s wishes” if known followed by “the patient’s best interests.”<sup>145</sup> More specifically, a “surrogate shall make health care decisions: (i) in accordance with the patient’s wishes, including the patient’s religious and moral beliefs; or (ii) if the patient’s wishes are not reasonably known and cannot with reasonable diligence be ascertained, in accordance with the patient’s best interests.”<sup>146</sup> Factors to be considered by the surrogate in assessing the patient’s best interests, if the patient’s wishes are not known, include

the dignity and uniqueness of every person; the possibility and extent of preserving the patient’s life; the preservation, improvement or restoration of the patient’s health or functioning; the relief of the patient’s suffering; and any medical condition and such other concerns and values as a reasonable person in the patient’s circumstances would wish to consider.<sup>147</sup>

Unlike the Texas Act, the New York Act establishes a procedure that is designed to secure a treatment decision in cases

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law manifests the State’s interest on this subject, they consistently support the right of the competent adult to make his own decision by imposing civil liability on those who perform medical treatment without consent, although the treatment may be beneficial or even necessary to preserve the patient’s life.”), *superseded by statute*, Surrogate’s Court Procedure Act, N.Y. SURR. CT. PROC. ACT LAWS § 1750-b (McKinney 2011), *as recognized in In re M.B.*, 846 N.E.2d 794, 795–97 (N.Y. 2006) (granting a guardian full medical decision-making power); *Fosmire v. Nicoleau*, 551 N.E.2d 77, 80–82 (N.Y. 1990) (“The common law of this State established the right of a competent adult to determine the course of his or her own medical treatment.”).

143. N.Y. PUB. HEALTH LAW § 2994–d(3)(a)(i) (McKinney 2012).

144. N.Y. PUB. HEALTH LAW § 2994–d(1)(a) to (f) (McKinney 2012).

145. N.Y. PUB. HEALTH LAW § 2994–d(4)(a) (McKinney 2012).

146. *Id.*

147. *Id.*

involving patients who lack capacity and have no family members or friends who are eligible to serve as a surrogate.<sup>148</sup> “The specific procedures to be followed depend on whether the decision involves routine medical treatment [or] major medical treatment” and the type of facility in which the treatment is to be provided.<sup>149</sup> If a hospital is unable to identify an individual who is eligible to serve as a surrogate for a patient who lacks decision-making capacity, “the hospital [itself] shall identify, to the extent reasonably possible, the patient’s wishes and preferences, including the patient’s religious and moral beliefs, about pending health care decisions.”<sup>150</sup> In so doing, the hospital shall not be influenced by its own financial interests or the financial interests of any affiliated physician or other health care provider.<sup>151</sup> With respect to routine medical treatments, including the administration of medications, the extraction of bodily fluids for analysis, and dental care performed with a local anesthetic, the New York Act authorizes the patient’s attending physician to consent to such treatments if the physician believes the treatments are in accordance with the patient’s wishes or, if the patient’s wishes are unknown, the treatments are in the patient’s best interests.<sup>152</sup> With respect to major medical treatments (including any procedures involving general anesthesia, significant invasions of bodily integrity requiring an incision or other significant invasions of bodily integrity, the use of physical restraints, or the use of psychoactive medications), the New York Act permits the attending physician to make a recommendation for such treatments after consulting with hospital staff directly responsible for the patient’s care.<sup>153</sup> If one other physician designated by the hospital or the patient’s residential care facility independently determines that a major medical treatment is appropriate, the treatment may be carried out at the hospital.<sup>154</sup>

Unlike the Texas Act, the New York Act also requires notice of the patient’s lack of capacity and of the surrogate’s appointment to be given to certain parties, including

- (a) the patient, where there is any indication of the patient’s ability to comprehend the information; (b) to at

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148. N.Y. PUB. HEALTH LAW § 2994–g (McKinney 2012).

149. N.Y. PUB. HEALTH LAW § 2994–g(2)(b) (McKinney 2012).

150. N.Y. PUB. HEALTH LAW § 2994–g(1) (McKinney 2012).

151. N.Y. PUB. HEALTH LAW § 2994–g(2)(b) (McKinney 2012).

152. N.Y. PUB. HEALTH LAW §§ 2994–d(4), 2994–g(2)(b), (3)(a)–(b) (McKinney 2012).

153. N.Y. PUB. HEALTH LAW § 2994–g(4)(a) to (b)(i) (McKinney 2012).

154. See N.Y. PUB. HEALTH LAW § 2994–g(4)(b)(ii) to (iii) (McKinney 2012).

least one person on the surrogate list highest in order of priority when persons in prior classes are not reasonably available; [and] (c) if the patient was transferred [to the hospital] from a mental hygiene facility, to the director of the mental hygiene facility and to [its legal services provider].<sup>155</sup>

The New York Act also clarifies that, regardless of the patient's lack of decision-making capacity, the patient's present expressed wishes almost always govern.<sup>156</sup> If a patient objects to the determination of incapacity, the choice of surrogate, or to a particular health care decision, for example, the patient's objection or decision prevails unless

- (a) a court of competent jurisdiction has determined that the patient lacks decision-making capacity or the patient is or has been adjudged incompetent for all purposes and, in the case of a patient's objection to treatment, makes any other finding required by law to authorize the treatment, or
- (b) another legal basis exists for overriding the patient's decision.<sup>157</sup>

The New York Act strictly regulates the process pursuant to which a patient is determined to lack decision-making capacity.<sup>158</sup> In general, an attending physician is required to "make an initial determination that [the] . . . patient lacks decision-making capacity to a reasonable degree of medical certainty."<sup>159</sup> The attending physician's initial determination "shall include an assessment of the cause and extent of the patient's incapacity and the likelihood that the patient will regain decision-making capacity."<sup>160</sup> If the attending physician has determined that a patient lacks decision-making capacity due to mental illness, then either (i) the attending physician must be licensed to practice medicine in New York and must be board-certified (or eligible for board certification) by the American Board of Psychiatry and Neurology or the American Osteopathic Board of Neurology and Psychiatry; or (ii) a second physician who meets the requirements in the previous clause must also independently determine that the patient lacks decision-making capacity.<sup>161</sup> If the attending physician has determined that a patient lacks decision-making capacity due to an intellectual or developmental

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155. N.Y. PUB. HEALTH LAW § 2994–c(4)(a) to (c) (McKinney 2012).

156. See N.Y. PUB. HEALTH LAW § 2994–c(6) (McKinney 2012).

157. *Id.*

158. See N.Y. PUB. HEALTH LAW § 2994–c(2) to (3) (McKinney 2012).

159. N.Y. PUB. HEALTH LAW § 2994–c(2) (McKinney 2012).

160. *Id.*

161. N.Y. PUB. HEALTH LAW § 2994–c(3)(c)(i) (McKinney 2012).

disability, then either (i) the attending physician must be employed by one of a number of state schools for individuals with developmental disabilities, or the physician must have “been employed for a minimum of two years to render care and service in a facility operated or licensed by the [New York State Office for People With Developmental Disabilities],” or the physician must have “been approved by the commissioner of mental retardation and developmental disabilities in accordance with [certain] regulations [that require] . . . specialized training or three years experience in treating developmental disabilities”; or (ii) another physician or clinical psychologist who meets the requirements in the previous clause also must independently determine that the patient lacks decision-making capacity.<sup>162</sup>

In two situations, the attending physician’s initial determination must be subject to an independently made concurring determination.<sup>163</sup> The first situation involves a patient who is receiving care in a residential health care facility, in which case “a health or social services practitioner employed by or otherwise formally affiliated with the facility must independently determine whether [the] patient lacks decision-making capacity.”<sup>164</sup> The second situation involves a patient who is receiving care in a general hospital and with respect to whom a surrogate is requesting the withholding or withdrawal of life-sustaining treatment, in which case “a health or social services practitioner employed by or otherwise formally affiliated with the facility must also independently determine whether [the] patient lacks decision-making capacity.”<sup>165</sup> If the health or social services practitioner consulted “disagrees with the attending physician’s determination, the matter shall be referred to [an] ethics review committee if it cannot otherwise be resolved.”<sup>166</sup>

Washington State’s surrogate consent-to-treatment procedures are considerably less detailed than those established in New York. Washington’s informed consent law (Washington Act) classifies an individual as *incompetent* for purposes of giving informed consent for health care if the individual is “incompetent by reason of mental illness, developmental disability, senility, habitual drunkenness, excessive use of drugs, or other mental incapacity, of either managing his or her property or caring for

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162. N.Y. PUB. HEALTH LAW § 2994–c(3)(c)(ii) (McKinney 2012).

163. N.Y. PUB. HEALTH LAW § 2994–c(3)(a) to (b) (McKinney 2012).

164. N.Y. PUB. HEALTH LAW § 2994–c(3)(b)(i) (McKinney 2012).

165. N.Y. PUB. HEALTH LAW § 2994–c(3)(b)(ii) (McKinney 2012).

166. N.Y. PUB. HEALTH LAW § 2994–c(3)(d) (McKinney 2012).

himself or herself, or both.”<sup>167</sup> A competent adult patient has the right to consent or refuse to consent to recommended medical treatments and surgical procedures.<sup>168</sup> In situations involving an incompetent adult patient, consent may be obtained from an individual who is eligible to serve as a surrogate, according to the following priority-ordered list:

- (i) The appointed guardian of the patient, if any;
- (ii) The individual, if any, to whom the patient has given a durable power of attorney that encompasses the authority to make health care decisions;
- (iii) The patient’s spouse;
- (iv) Children of the patient who are at least eighteen years of age;
- (v) Parents of the patient; and
- (vi) Adult brothers and sisters of the patient.<sup>169</sup>

If the health care provider seeking informed consent from a surrogate “makes reasonable efforts to locate and secure authorization from a [surrogate] in the first or succeeding class and finds no such person available, authorization may be given by any [surrogate] in the next class in the order of descending priority.”<sup>170</sup> Before consenting to proposed health care on behalf of a patient, the Washington Act requires the surrogate to determine in good faith that the patient, if competent, would have consented to the proposed health care.<sup>171</sup> “If such a determination cannot be made, the decision to consent to the proposed health care may be made only after determining that the proposed health care is in the patient’s best interests.”<sup>172</sup>

#### IV. CONSENT-TO-TREATMENT LEGISLATION SHOULD NOT BE USED TO ANSWER CONSENT-TO-RESEARCH QUESTIONS

The Texas, New York, and Washington Acts vary in some important respects. The Acts use slightly different terminology (i.e., “decision-making capacity” and “incapacity” in Texas, “decision-making capacity” in New York, and “incompetency” in Washington), for example. The Acts also define these terms differently (i.e., “the ability to understand and appreciate the

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167. WASH. REV. CODE ANN. § 11.88.010(1)(e) (West 2006 & Supp. 2012); WASH. REV. CODE ANN. § 7.70.065(1) (West 2007 & Supp. 2012).

168. See WASH. REV. CODE ANN. § 7.70.050(1) (West 2007 & Supp. 2012).

169. WASH. REV. CODE ANN. § 7.70.065(1)(a)(i)–(vi) (West Supp. 2012).

170. WASH. REV. CODE ANN. § 7.70.065(1)(b) (West Supp. 2012).

171. WASH. REV. CODE ANN. § 7.70.065(1)(c) (West Supp. 2012).

172. *Id.*

nature and consequences” of a health care decision in Texas and New York and “mental illness, developmental disability, senility, habitual drunkenness, excessive use of drugs, or other mental incapacity” in Washington), and prioritize differently the individuals who are eligible to serve as a surrogate (i.e., Texas prioritizes traditional opposite-sex spouses whereas New York and Washington place domestic partners on an equal footing with spouses). The Texas Act provides only one standard for surrogate decision-making, that is, what the patient would have desired, if known. In New York and Washington, the patient’s best interests may be used as a standard if the patient’s wishes are unknown. The New York Act stringently regulates all aspects of the surrogate consent-to-treatment process, including the credentials and experience of the attending physician who makes the initial determination that the patient lacks decision-making capacity, the procedure by which a second health care provider makes an independent concurring determination, the factors to be considered in assessing whether a particular treatment is in a patient’s best interests (if the patient’s wishes are unknown), and the situations in which a physician is authorized to make a minor or major medical treatment decision on behalf of a patient when the patient lacks decision-making capacity and a legally authorized surrogate does not exist. Texas and Washington, on the other hand, very generally and without much detail regulate the surrogate consent-to-treatment process.

From a bird’s eye view, however, all three state laws take the same general approach to informed consent to treatment and surrogate health care decision-making. That is, all three state laws provide that (i) competent adult patients have the right to consent or refuse to consent to recommended medical treatments and surgical procedures; (ii) a surrogate may consent to treatment on behalf of an incapacitated or incompetent adult patient; (iii) the surrogate shall be selected from a priority list of reasonably available competent adults; and (iv) the surrogate shall consent to health care that the patient would have desired, if that desire is known.

As discussed above, many states do not have laws governing the conduct of human subjects research involving adults with impaired decision-making capacity.<sup>173</sup> In the absence of research-

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173. See, e.g., SEC’Y’S ADVISORY COMM. ON HUMAN RESEARCH PROTECTIONS, *supra* note 63 (“Very few states specifically define legally authorized representatives (LARs) for research, and most state’s laws are silent on the topic. Virtually no state laws address the many ethical issues that arise when LARs are involved in research decision-making, leaving it to IRBs and institutions to invent solutions.”).

specific state laws, some researchers and research institutions rely on state laws that were designed for the treatment setting, and such reliance is supported by the OHRP.<sup>174</sup> Contrary to this position, I argue that (i) legislation governing consent to treatment should not be used to answer research-related questions; and (ii) HHS should adopt regulations specifically governing human subjects research involving individuals with impaired decision-making capacity that should be used to answer all research-related questions. The reasons supporting these arguments are set forth below.

First, treatment and research are intrinsically different activities. *Treatment* may be defined as “the provision, coordination, or management of health care and related services by one or more health care providers” to a particular individual.<sup>175</sup> The definition of *treatment* is based on the concept of *health care*, which has been defined as care, services, or procedures related to the health of a particular individual.<sup>176</sup> *Health care* is frequently defined to include “[p]reventive, diagnostic, therapeutic, rehabilitative, maintenance, or palliative care” that is provided to a particular individual, as well as counseling, assessments, and procedures that relate to the physical or mental condition or functional status of a particular individual.<sup>177</sup> Activities thus are classified as treatment when they involve a health care service provided by a health care provider that is tailored to the specific preventive, diagnostic, therapeutic, or other health care needs of a particular individual.<sup>178</sup>

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174. See, e.g., Office of Extramural Research, *supra* note 63 (“In most jurisdictions, LAR appointment processes are not specific to the research setting and institutions rely on the laws governing the use of LARs for clinical care.”); SEC’Y’S ADVISORY COMM. ON HUMAN RESEARCH PROTECTIONS, *supra* note 63 (explaining, at Recommendation 8(b), that “[i]n states with laws or regulations that address consent to treatment but do not specifically consider consent to research, current OHRP interpretation permits consent to research by individuals authorized under laws that allow consent to the ‘procedures involved in the research’”; and recommending, at Recommendation 9(a)(ii)(b), in the absence of applicable state law, that a person who is designated to make nonresearch health care decisions be ranked second in the priority-ordered list of persons who are eligible to make research participation decisions).

175. See, e.g., 45 C.F.R. § 164.501 (2011) (definition of *treatment* set forth in the HIPAA Privacy Rule).

176. See, e.g., 45 C.F.R. § 160.103 (definition of *health care* set forth in the HIPAA Privacy Rule).

177. See, e.g., *id.*; TEX. CIV. PRAC. & REM. CODE ANN. § 74.001(10) (West Supp. 2012).

178. See, e.g., Standards for Privacy of Individually Identifiable Health Information, 65 Fed. Reg. 82,462, 82,626 (Dec. 28, 2000) (codified at 45 C.F.R. pts. 160, 164) (“The activities described by ‘treatment,’ therefore, all involve health care providers supplying health care to a particular patient. While many activities beneficial to patients are offered to entire populations or involve examining health information about entire populations,

*Research*, on the other hand, is defined as “a systematic investigation, including research development, testing and evaluation, [that is] designed to develop or contribute to generalizable knowledge.”<sup>179</sup> Knowledge is considered *generalizable* “when it can be applied to either a population inside or outside of the population served by the [institution conducting the research].”<sup>180</sup> The purpose of research, then, is to collect data that will lead to the creation of generalizable knowledge that may result in the production of new therapies or the improvement of existing therapies.<sup>181</sup>

Compared side by side, the differences between treatment and research become clear. First, the primary purpose of treatment is to maintain or improve a particular patient’s health, whereas the primary purpose of research is to gain knowledge that will result in the creation of new treatments for future patients.<sup>182</sup> Second, physicians providing treatment frequently adjust, substitute, and change therapies to meet the specific health needs of particular patients.<sup>183</sup> Investigators conducting research, however, must follow approved research protocols and are not permitted to adjust, substitute, or change the experimental intervention (other than to allow the research

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treatment involves health services provided by a health care provider and tailored to the specific needs of an individual patient.”).

179. See, e.g., 45 C.F.R. § 46.102(d) (2011) (definition of *research* set forth in the federal Common Rule); *id.* § 164.501 (definition of *research* set forth in the federal HIPAA Privacy Rule).

180. See, e.g., Standards for Privacy of Individually Identifiable Health Information, 65 Fed. Reg. at 82,625; Protection of Human Subjects, 45 C.F.R. §§ 46.005, 46.006 (2011).

181. See, e.g., Rebecca Dresser, *The Ubiquity and Utility of the Therapeutic Misconception*, 19 SOC. PHIL. & POL’Y, no. 2, at 271, 272 (2002) (“Although some research participants may receive a health benefit, research is designed to generate data that could lead to improved care for future patients.”); *id.* at 285 (“[I]nvestigators in the research setting focus primarily on the need to obtain valid scientific data.”); Gail E. Henderson et al., *Clinical Trials and Medical Care: Defining the Therapeutic Misconception*, 4 PLOS MED. 1735, 1737 (2007) (“[T]here is consensus that the defining characteristic of research is to create generalizable knowledge through answering a scientific question.”); *id.* at 1737 box 2 (“Clinical research is designed to produce generalizable knowledge and to answer questions about the safety and efficacy of intervention(s) under study in order to determine whether or not they may be useful for the care of future patients.”).

182. See, e.g., Dresser, *supra* note 181, at 285 (“[P]hysicians in the medical setting seek solely to benefit the patient. In contrast, investigators in the research setting focus primarily on the need to obtain valid scientific data.”); Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, 44 Fed. Reg. 23,192, 23,193 (Apr. 18, 1979) (distinguishing clinical practice from biomedical and behavioral research).

183. See, e.g., Dresser, *supra* note 181, at 272 (“After treatment begins, medication dosages may be increased if the patient fails to respond to the standard dosage, or decreased if the patient experiences unwanted side effects. Patients who fail to improve when taking one medication may be switched to another one.”).

participant to discontinue participation) in response to the wants or needs of a particular participant.<sup>184</sup> Third, a treating physician has a primary duty of loyalty to his or her patients and is charged with recommending treatments that the physician believes are in each patient's best interests.<sup>185</sup> On the other hand, researchers who do not also have a treatment relationship with their research participants generally are not considered to have a fiduciary or primary duty of loyalty to their research participants.<sup>186</sup> In theory, investigators design (and research

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184. See, e.g., Paul S. Appelbaum, Charles W. Lidz, & Thomas Grisso, *Therapeutic Misconception in Clinical Research: Frequency and Risk Factors*, IRB: ETHICS & HUM. RES., Mar.–Apr. 2004, at 1, 1 (explaining that researchers are obligated “to protect the validity of the data they generate [by] using . . . techniques [such] as randomized assignment, placebo control groups, double-blind procedures, and fixed treatment protocols, which often preclude personalized decisions from being made”); Paul S. Appelbaum, *Clarifying the Ethics of Clinical Research: A Path Toward Avoiding the Therapeutic Misconception*, AM. J. BIOETHICS, Spring 2002, at 22, 22 (explaining that “the use of randomization, double-blind procedures, adherence to strict protocols, and administration of placebos” in research studies “may be undertaken because they advance the scientific validity of the research study, rather than because they serve the subject”); Dresser *supra* note 181, at 272 (“Research methods that minimize ambiguity and bias in data collection rule out the individualized approach that is the hallmark of clinical care. In research, the intervention an individual receives is usually determined by random assignment instead of a physician’s clinical judgment.”). Although research participants have a legal right to withdraw from a research study at any time, they do not have the right to adjust, substitute, or change an experimental intervention. See 45 C.F.R. § 46.116(a)(8) (2011).

185. See, e.g., TOM L. BEAUCHAMP & JAMES F. CHILDRESS, PRINCIPLES OF BIOMEDICAL ETHICS 173 (5th ed. 2001) (explaining that the goal of medicine is to promote the welfare of individual patients); COUNCIL ON ETHICAL & JUDICIAL AFFAIRS, AM. MEDICAL ASS’N, CODE OF MEDICAL ETHICS OF THE AMERICAN MEDICAL ASSOCIATION 374 (2010) (Opinion 10.015) (“The relationship between patient and physician is based on trust and gives rise to physicians’ ethical obligations to place patients’ welfare above their own self-interest and above obligations to other groups, and to advocate for their patients’ welfare. Within the patient-physician relationship, a physician is ethically required to use sound medical judgment, holding the best interests of the patient as paramount.”); Nat’l Library of Med., *Greek Medicine: “I swear by Apollo Physician . . .”: Greek Medicine from the Gods to Galen*, NAT’L INSTITUTES HEALTH, [http://www.nlm.nih.gov/hmd/greek/greek\\_oath.html](http://www.nlm.nih.gov/hmd/greek/greek_oath.html) (last visited Jan. 1, 2013) (containing the Hippocratic Oath, in which the physician pledges to “benefit [the physician’s] patients according to [the physician’s] greatest ability and judgment”).

186. See, e.g., *Suthers v. Amgen, Inc.*, 372 F. Supp.2d 416, 429 (S.D.N.Y. 2005) (refusing to find a fiduciary duty running from the sponsor of an independent research study to the individuals who participated in the research); *Greenberg v. Miami Children’s Hosp. Research Inst., Inc.*, 264 F. Supp.2d 1064, 1072 (S.D. Fla. 2003) (refusing to find a fiduciary duty running from Canavan disease researchers to their research participants); *Moore v. Regents of the Univ. of Cal.*, 793 P.2d 479, 486 (Cal. 1990) (explaining that the regents of the defendant university and its affiliated researchers were not physicians and therefore did not owe the plaintiff patient a fiduciary duty); Dresser, *supra* note 181, at 292 (recommending that researchers explain to participants as part of the consent-to-research process that the researchers’ primary loyalty is to future patients, not current research participants). Notwithstanding these cases, some attorneys who represent research participants continue to assert that the researcher–participant relationship constitutes a fiduciary relationship. See, e.g., Alan C. Milstein, *Research Malpractice and*

participants consent to participate in) research protocols with the understanding of the differences between treatment and research<sup>187</sup> and with the knowledge that research participation may not directly benefit the participant and may pose personal health risks to the participant.<sup>188</sup>

Because *treatment* and *research* are intrinsically different activities, I worry that allowing research institutions to rely on legislation specifically designed and labeled for the treatment setting to answer research-related questions could provide continued legal and conceptual support for the therapeutic misconception. First coined in 1982, “therapeutic misconception” refers to the conflation of the goals of research with the goals of clinical care.<sup>189</sup> With respect to research participants, a

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*the Issue of Incidental Findings*, 36 J.L. MED. & ETHICS 356, 358 (2008) (“Once the research subject or the guardian for a minor subject signs the informed consent document, a fiduciary relationship is formed between the PI [(Principal Investigator)] and the research subject. The very nature of scientific research on human subjects creates special relationships out of which fiduciary duties arise, similar to the physician/patient relationship. The fiduciary relationship is formed not only by the informed consent agreement between the parties, but also by the trust the subject necessarily places in the researcher. In the context of human subjects research, a special relationship is created between the human subject and those responsible for the design, approval, and implementation of the experiment because the latter have a duty to protect human subjects both under the Common Rule and common law.” (footnote omitted)). In addition, some courts have found that researchers have “special relationships” with their research participants that can give rise to unspecified tort-like duties. *See, e.g.*, *Grimes v. Kennedy Krieger Inst., Inc.*, 782 A.2d 807, 846 (Md. 2001) (“[S]pecial relationships, out of which duties arise, the breach of which can constitute negligence, can result from the relationships between researcher and research subjects.”). *See generally* Stacey A. Tovino, *Incidental Findings: A Common Law Approach*, 15 ACCOUNTABILITY IN RESEARCH 242, 250–54 (2008) (discussing the concepts of fiduciary duty and fiduciary relationships in the context of neuroimaging research).

187. *See, e.g.*, 45 C.F.R. § 46.116(a)(1) (2011) (requiring research participants to be informed that they are participating in research); 45 C.F.R. § 46.102(d) (defining *research* as “a systematic investigation, including research development, testing and evaluation, [that is] designed to develop or contribute to generalizable knowledge”). As discussed in more detail below, some research participants and researchers may be operating under a therapeutic misconception. *See infra* text accompanying notes 189–198.

188. *See, e.g.*, 45 C.F.R. § 46.116(a)(2) (2011) (requiring research participants to be informed of reasonably foreseeable risks and discomforts before they may consent to participate in the research).

189. *See* Appelbaum, Lidz & Grisso, *supra* note 184, at 1–6 (defining therapeutic misconception with reference to research participants’ inappropriate assumption that decisions about their care are being made solely with their benefit in mind; and reporting data confirming that many research participants carry strong expectations that the research, like the therapy they may have received previously, is designed and will be executed in a manner of direct benefit to them); Appelbaum, *supra* note 184, at 22 (explaining that Appelbaum and colleagues first described the therapeutic misconception phenomenon in 1982); Laura B. Dunn et al., *Assessment of Therapeutic Misconception in Older Schizophrenia Patients with a Brief Instrument*, 163 AM. J. PSYCHIATRY 500, 500 (2006) (defining the therapeutic misconception as the “conflation of the goals and procedures of clinical research with those of usual clinical care”).

therapeutic misconception is said to occur when a participant transfers to the research setting the presumption that applies in the clinical setting, that is, the presumption that the physician is acting only with the patient's best interests in mind.<sup>190</sup> Studies of the nature and frequency of the therapeutic misconception (and of two related concepts, therapeutic misestimation and the therapeutic optimism) among research participants show that many research participants underappreciate research risks, unrealistically hope for direct therapeutic benefit, fail to recognize altruism and contribution to science as motives for participating in research, and, more generally, conflate research with clinical care.<sup>191</sup> One of the most important concepts requiring communication during the consent-to-research process is the

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190. See Appelbaum, *supra* note 184, at 22; Henderson et al., *supra* note 181, at 1736 box 1 (“Therapeutic misconception exists when individuals do not understand that the defining purpose of clinical research is to produce generalizable knowledge, regardless of whether the subjects enrolled in the trial may potentially benefit from the intervention under study or from other aspects of the clinical trial.”).

191. See, e.g., Appelbaum, Lidz & Grisso, *supra* note 184, at 1, 2–7 (reporting “the first systematic attempt to assess the frequency of [therapeutic misconception] across a range of clinical research projects”; finding that “31.1% . . . of participants expressed inaccurate beliefs regarding the degree of individualization of their treatment . . . , while 51.1% . . . manifested an unreasonable belief in the nature or likelihood of benefit”; and concluding that subjects frequently overestimate the likely benefits of entry into research studies, underestimate risks, and conflate research with ordinary treatment); Christopher Daugherty et al., *Perceptions of Cancer Patients and Their Physicians Involved in Phase I Trials*, 13 J. CLINICAL ONCOLOGY 1062, 1064–67 (1995) (reporting data showing that 85% of thirty Phase I clinical trial research participants decided to participate in a Phase I trial for reasons of possible therapeutic benefit while only 33% completely understood the purpose of the trial in which they were participating; and concluding that patients who participate in Phase I trials are strongly motivated by the hope of therapeutic benefit and that altruistic feelings appear to have a limited and inconsequential role in motivating patients to participate); Dunn et al., *supra* note 189, at 501–04 (examining the frequency of a key aspect of therapeutic misconception in eighty-seven middle-age and older patients with schizophrenia or schizoaffective disorder; and concluding that patients with schizophrenia show a substantial incidence of beliefs associated with therapeutic misconception); Charles W. Lidz et al., *Therapeutic Misconception and the Appreciation of Risks in Clinical Trials*, 58 SOC. SCI. & MED. 1689, 1689–97 (2004) (reporting results from a study involving the interview of 155 research participants from forty different clinical trials at two different U.S. medical centers; and concluding that research participants often agree to participate in research “with only the most modest appreciation of the risks and disadvantages of participation”); Robin E. Matutina, *The Concept Analysis of Therapeutic Misconception*, 17 NURSE RESEARCHER, no. 4, 2010, at 83, 86–87 (identifying elements present in therapeutic misconception, including patients confusing research with treatment, believing they will receive physical benefit from study participation, and failing to list altruism and contribution to science as motives for participating in the study). Some authors classify a research participant's underappreciation of research risks and unrealistic hope for direct therapeutic benefit not as therapeutic misconception but, instead, as therapeutic misestimation or therapeutic optimism. See, e.g., Daniel S. Goldberg, *Eschewing Definitions of the Therapeutic Misconception: A Family Resemblance Analysis*, 36 J. MED. & PHIL. 296, 299 (2011) (discussing therapeutic misconception, therapeutic misestimation, and therapeutic optimism).

difference between treatment and research and how a research study is different than what the patient would ordinarily encounter in the clinical setting.<sup>192</sup> Failure to distinguish research from ordinary treatment and failure to understand the consequences of research participation (including the likelihood and nature of any risks and the potential lack of any direct medical benefit) can undermine true informed consent.<sup>193</sup>

Part of the problem is that researchers themselves may be operating under a therapeutic misconception.<sup>194</sup> Several studies, case reports, and histories suggest that some researchers (i) view the purpose of clinical trials as benefiting individual research participants rather than creating generalizable knowledge for the purpose of advancing future therapy;<sup>195</sup> (ii) have an unreasonable expectation of their participants' direct therapeutic benefit;<sup>196</sup> and

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192. See Appelbaum, *supra* note 184, at 23; Henderson et al., *supra* note 181, at 1735 ("Ethicists have argued that informed consent to participate in research should include clarification of the differences between [the] two activities [of treatment and research].").

193. See, e.g., Appelbaum, Lidz & Grisso, *supra* note 184, at 2 ("[Therapeutic misconception] may constitute a major obstacle to meaningful decision-making."); Dresser, *supra* note 181, at 285 ("The therapeutic misconception conflicts with the long-standing and widely accepted research-ethics principle of respect for persons. This principle holds that morally permissible research takes place only when the studied individuals have made an informed and voluntary choice to participate. Patients who enroll in research without understanding how such participation will change the management of their condition are insufficiently informed. Such individuals have not given researchers valid permission to elevate scientific considerations above the individuals' own best interests."); Dunn et al., *supra* note 189, at 500 (explaining that the therapeutic misconception may impede informed consent); Lidz et al., *supra* note 191, at 1689 ("[F]ailure to distinguish the consequences of research participation from receiving ordinary treatment may seriously undermine the informed consent of research subjects.").

194. See, e.g., Appelbaum, *supra* note 184, at 23 ("If we are to disabuse research subjects of unrealistic beliefs regarding the therapeutic benefits of participating in studies, surely we must first take the same step with the researchers themselves. . . . Confused investigators generate confused subjects; the latter then enroll in studies, seeking therapeutic benefits that are almost certain not to accrue."); Goldberg, *supra* note 191, at 308–13 (examining why researchers also may be operating under a therapeutic misconception).

195. See, e.g., Steven Joffe & Jane C. Weeks, *Views of American Oncologists About the Purposes of Clinical Trials*, 94 J. NAT'L CANCER INST. 1847, 1851 (2002) (reporting the results of a survey studying American cancer specialists about their beliefs regarding clinical trials; concluding that many respondents viewed the main societal purpose of clinical trials as benefiting the participants rather than as creating generalizable knowledge to advance future therapy; and opining that this view conflicts with established principles of research ethics).

196. See, e.g., Dresser, *supra* note 181, at 277 ("[S]tudies find that physicians are at times unrealistically optimistic about an experimental intervention's prospects."); Goldberg, *supra* note 191, at 308 (maintaining that some perpetrators of human subjects research abuses "unreasonably believed the persons they experimented on would receive direct benefit"); Gail E. Henderson et al., *Uncertain Benefit: Investigators' Views and Communications in Early Phase Gene Transfer Trials*, 10 MOLECULAR THERAPY 225, 226–27 (2004) (finding that 46% (eighteen of the thirty-nine) investigators studied in early phase gene transfer research expected subjects in the trials to receive direct benefit).

(iii) use a patient's or surrogate's hope of cure or desire to receive treatment as leverage to obtain their consent to research participation.<sup>197</sup> As one way of ensuring that research participants do not consent to research while under the guise of a therapeutic misconception, bioethicists and attorneys routinely recommend that researchers and their coordinators not personally harbor unrealistic beliefs about the benefits and risks associated with particular research protocols and be capable of appropriately distinguishing between evidence-based medicine and experimental research in oral and written communications with their potential research participants.<sup>198</sup>

Notwithstanding the bioethics and legal communities' widespread recognition of and concern regarding the therapeutic misconception, researchers, participants, and others continue to operate under its shroud.<sup>199</sup> If, by federal agency recommendation,<sup>200</sup>

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197. See, e.g., Paul A. Lombardo, *Dwarves: Uninformed Consent and Eugenic Research*, 25 ETHICS & MED. 149, 149–50, 155–57, 159 (2009) (examining the plan of American biologist and eugenics leader Charles B. Davenport to conduct an experimental castration on a boy whom Davenport referred to as a “Mongoloid dwarf”; noting Davenport's reliance on a speculative therapeutic justification (that of easing the boy's “marked eroticism”) to justify the experiment and elicit consent from the boy's mother; explaining, “[Davenport's] desire to use the excuse of therapeutic prerogative as the mask behind which to hide his true goals—suggesting that surgery was for the patient's benefit rather than primarily to aid scientific discovery—indicates his sensitivity to the potential that others would find such research both legally and ethically problematic”; and concluding: “The researchers used the patient's (or their surrogate decisionmaker's) hope of cure, or at least acquiescence to treatment, as leverage for advancing an agenda more concerned with research than therapy”).

198. See, e.g., Jessica Wilen Berg, *Legal and Ethical Complexities of Consent with Cognitively Impaired Research Subjects: Proposed Guidelines*, 24 J.L. MED. & ETHICS 18, 18 (1996) (remarking that judges and lawyers seek to ensure that research subjects' rights are protected); Dresser, *supra* note 181, at 277 (reporting empirical evidence showing that “patients . . . form impressions about research studies based on discussions with their personal physicians” and may decide to participate in research very quickly if the physician urges participation); *id.* at 279 (referencing studies finding that research coordinators conflated research with treatment); Mildred K. Cho & David Magnus, *Therapeutic Misconception and Stem Cell Research*, NATURE REP. (Sept. 27, 2007), <http://www.nature.com/stemcells/2007/0709/070927/full/stemcells.2007.88.html> (referencing studies suggesting that “researchers can and should guard against encouraging the therapeutic misconception, both in informed-consent forms and in publications”; and concluding, in the context of stem cell research, that, “although all researchers working with human subjects must guard against the therapeutic misconception, stem cell scientists have a particularly heavy burden to make sure that research donors and research subjects alike understand that, so far, experiments are exactly that”).

199. See, e.g., Berg, *supra* note 198, at 19 (discussing concerns in the legal community); Dresser, *supra* note 181, at 276 (“Despite widespread recognition of and expressed concern about the therapeutic misconception, investigators and physicians continue to promote it.”); *id.* at 290 (“Despite periodic expressions of concern, the research system and the larger society continue to tolerate—and to promote—the conflation of research and therapy.”); *id.* at 294 (“Until now, beneficiaries of the therapeutic misconception have preferred to maintain the status quo.”); Lombardo, *supra* note 197, at

we allow researchers to rely on legislation that by title and content applies to only the treatment setting, we may be continuing to blur important distinctions between treatment and research,<sup>201</sup> at least at the legal level. Of course, state legislatures could quickly fix part of the problem by renaming<sup>202</sup> and amending<sup>203</sup> their consent-to-treatment statutes to clarify that they also apply in the research setting. The more important substantive question is whether the content of state legislation governing consent to treatment is appropriate for the research setting. I argue that it is not for at least two different reasons.

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159 ("Both informed consent and the therapeutic misconception remain major issues in research ethics today.").

200. See *supra* text accompanying notes 114–116.

201. See Appelbaum, *supra* note 184, at 23 (expressing similar concerns).

202. For example, the Texas Act could be renamed the Texas Consent to Medical Treatment and Research Participation Act, the New York Act could be renamed the New York Family Health Care and Research Participation Act, and the Washington Act could be renamed the Washington Informed Consent to Treatment and Research Participation Act.

203. By further example, the Texas Act could be amended with italicized additions and stricken deletions, as follows:

Tex. Health & Safety Code Ann. § 313.004.

Consent for Medical Treatment *and Research Participation*.

(a) If an adult ~~individual patient . . . in a hospital or nursing home . . .~~ is comatose, incapacitated, or otherwise mentally or physically incapable of communication, an adult surrogate from the following list, in order of priority, who has decision-making capacity, is available after a reasonably diligent inquiry, and is willing to consent to medical treatment *or research participation* on behalf of the individual ~~patient~~ may consent to medical treatment *or research participation* on behalf of the *individual patient*:

- (1) the *individual's patient's* spouse;
- (2) an adult child of the *individual patient* who has the waiver and consent of all other qualified adult children of the *individual patient* to act as the sole *treatment or research participation* decision-maker;
- (3) a majority of the *individual's patient's* reasonably available adult children;
- (4) the *individual's patient's* parents; or
- (5) the *person individual* clearly identified to act for the *individual patient* by the *individual patient* before the *individual patient* became incapacitated, the *individual's patient's* nearest living relative, or a member of the clergy.

(b) Any dispute as to the right of a party to act as a surrogate decision-maker may be resolved only by a court of record having jurisdiction under Chapter V, Texas Probate Code.

(c) Any medical treatment *or research protocol* consented to under Subsection (a) must be based on knowledge of what the *individual patient* would desire, if known.

(d) Notwithstanding any other provision of this chapter, a surrogate decision-maker may not consent to:

- (1) voluntary inpatient mental health services;
- (2) *standard or experimental* electro-convulsive treatment; or
- (3) the appointment of another surrogate decision-maker.

First, many state consent-to-treatment laws contain a “patient’s wishes if known” followed by “the patient’s best interests” standard for surrogate decision-making.<sup>204</sup> Under the New York Act, for example, surrogates are required to make health care decisions “(i) in accordance with the patient’s wishes, including the patient’s religious and moral beliefs; or (ii) if the patient’s wishes are not reasonably known and cannot with reasonable diligence be ascertained, in accordance with the patient’s best interests.”<sup>205</sup> Many commentators believe that the first standard, the “patient’s wishes if known” standard, works very well in the treatment setting and may also be used in the research setting without violating ethical and legal principles. That is, if an adult individual with decision-making capacity is informed of the nature of a particular research study and comprehends the known (and appreciates the existence of unknown) risks and benefits of the study, and expresses by clear and convincing evidence the individual’s wish to be enrolled in the study in the event the individual loses decision-making capacity, many ethicists and attorneys would be comfortable with allowing the individual to be enrolled in the study if the study minimizes research risks and satisfies other federal requirements relating to human subjects research.<sup>206</sup> The ethical principle of “respect for autonomy” and the legal principle of “self-determination” suggest that we should respect the competent individual’s informed decision to participate in the study.<sup>207</sup>

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204. See, e.g., N.Y. PUB. HEALTH LAW § 2994-d(4)(a) (McKinney 2012).

205. *Id.*

206. See, e.g., Palaniappan Muthappan, Heidi Forster & David Wendler, *Research Advance Directives: Protection or Obstacle?* 162 AM. J. PSYCHIATRY 2389, 2390 (2005) (“Adults who are unable to provide informed consent should be enrolled in clinical research only with sufficient evidence that such enrollment is consistent with their competent preferences.”); Saks et al., *supra* note 12, at 66 (“[O]ne can imagine many cases of research with decisionally impaired people that would not be controversial to most people. Take the case, for example, of a person giving an advance directive consenting to a particular research study, prior to becoming decisionally impaired. Assume that the study involves known procedures and risks that have not changed over time and that the subject clearly understood when giving the advance consent.”).

207. See, e.g., Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, 44 Fed. Reg. 23,192, 23,193 (Apr. 18, 1979) (“An autonomous person is an individual capable of deliberation about personal goals and of acting under the direction of such deliberation. To respect autonomy is to give weight to autonomous persons’ considered opinions and choices while refraining from obstructing their actions unless they are clearly detrimental to others. To show lack of respect for an autonomous agent is to repudiate that person’s considered judgments [or] to deny an individual the freedom to act on those considered judgments . . . .”); BEAUCHAMP & CHILDRESS, *supra* note 185, at 58 (“The autonomous individual acts freely in accordance with a self-chosen plan . . . .”).

The contingent standard, the “patient’s best interests” standard, also is believed to work well in the treatment setting because physicians have both an ethical and legal obligation to place their patients’ welfare above their own financial, economic, and other self-interests and to hold the best interests of their patients as paramount.<sup>208</sup> Even in situations in which a patient lacks decision-making capacity, a surrogate who consents to a treatment on behalf of the patient should be consenting to a treatment that a physician is recommending because the physician believes the treatment is in the patient’s best interests.<sup>209</sup> Of course, the “patient’s best interests” standard does not always work perfectly in the treatment setting. A careless physician may negligently recommend, order, or perform a particular medical treatment, for example, and the surrogate may have relied on the physician’s treatment recommendation in making a decision to consent to the treatment on behalf of the patient. Or, a surrogate who stands to inherit a patient’s estate or otherwise has a conflict of interest may refuse to consent to a physician-recommended treatment that likely would have been in the patient’s best physical and mental health interests. In general, however, the “patient’s best interest” standard is believed to work well in the treatment setting because physicians have an ethical and legal duty to serve their patients’ best interests and most surrogates do in fact make health care decisions that they believe are in their patients’ best interests.<sup>210</sup>

The problem is that the “best interests” standard may not work as routinely well in the research setting. Many biomedical and behavioral investigations are designed to study the safety and efficacy of experimental interventions.<sup>211</sup> If an experimental intervention, such as an experimental new drug for Alzheimer’s

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208. See *supra* note 185 and accompanying text.

209. See *supra* note 185 and accompanying text.

210. David I. Shalowitz, Elizabeth Garrett-Mayer & David Wendler, *The Accuracy of Surrogate Decision Makers: A Systematic Review*, 166 ARCHIVES INTERNAL MED. 493, 495 (2006) (detailing the results of studies that show surrogates correctly predicted patients’ preferred treatment with 68% accuracy).

211. See, e.g., 21 C.F.R. § 312.21(a) (2010) (describing Phase I research studies, which are designed “to determine the metabolism and pharmacologic actions of [an experimental] drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness”); 21 C.F.R. § 312.21(b) (describing Phase II research studies, which are designed “to evaluate the effectiveness of [a] drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug”); and 21 C.F.R. § 312.21(c) (describing Phase III research studies, which are designed “to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of [a] drug and to provide an adequate basis for physician labeling”).

disease or schizophrenia, has not yet been proven safe (and its efficacy has yet to be studied), an individual who is enrolled in a protocol studying the intervention's safety may be subject to significant physical and emotional health risks and may not enjoy any direct therapeutic benefit.<sup>212</sup> In the typical Phase I drug trial, for example, researchers assess a drug's safety, tolerability, pharmacokinetics, and pharmacodynamics.<sup>213</sup> Because only a very small percentage of individuals respond positively to experimental drugs tested in Phase I trials and because the chance of death and the likelihood of other side effects may be comparable to the chance of direct benefit, Phase I trials may not confer any aggregate survival advantage for research participants.<sup>214</sup> Stated another way, it is very likely that research participation in a Phase I trial will not be in an individual research participant's best physical and mental health interests.<sup>215</sup> Of course, not all research studies are Phase I trials and some research studies do happen to benefit individuals who have the health condition under investigation. Generally speaking, however, many research studies are not in the best physical or mental health interests of their participants (even if it is in the *researcher's* best interests to enroll the participants in the study).<sup>216</sup> Stated slightly differently, the physician's,

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212. See, e.g., Complaint—Civil Action, *Gelsinger v. Trustees of the Univ. of Penn.*, (Pa. C. 2000), available at [http://www.sskrplaw.com/files/gelsinger\\_complaint.pdf](http://www.sskrplaw.com/files/gelsinger_complaint.pdf) (lawsuit filed by parents on behalf of their eighteen-year-old son, Jesse Gelsinger, who died following his participation in Phase I gene research conducted at the University of Pennsylvania that was not expected to have any direct therapeutic benefit and that had killed monkeys during animal testing).

213. See, e.g., CTR. FOR DRUG EVALUATION & RESEARCH, U.S. DEP'T OF HEALTH & HUMAN SERVS., GUIDANCE FOR INDUSTRY: ESTIMATING THE MAXIMUM SAFE STARTING DOSE IN INITIAL CLINICAL TRIALS FOR THERAPEUTICS IN ADULT HEALTHY VOLUNTEERS 2 (2005) (describing the objectives of Phase I drug trials as assessment of the experimental therapeutic's tolerability, pharmacodynamics, and pharmacokinetics).

214. See, e.g., Goldberg, *supra* note 191, at 305 (discussing the therapeutic misconception in the context of Phase I oncology trials); Matthew Miller, *Phase I Cancer Trials: A Collusion of Misunderstanding*, HASTINGS CENTER REP., July–Aug. 2000, at 34, 35; Dresser, *supra* note 181, at 275 (“Phase I chemotherapy trials have very little chance of helping trial participants to live longer or feel better.”); Robert Steinbrook, *The Gelsinger Case*, in *THE OXFORD TEXTBOOK OF CLINICAL RESEARCH ETHICS* 110, 111–12, 114–15 (Ezekial J. Emanuel et al. eds., 2008) (discussing the Gelsinger lawsuit, which was settled by the University of Pennsylvania and involved a Phase I gene study that not only did not confer a survival advantage to the plaintiffs' decedent son but also was dangerous to research participants).

215. Cf. Kim et al., *supra* note 12, at 801 (“The . . . standard of ‘best interests’ of the potential subject is problematic for research consent, since the point of research participation may not be for direct health benefits to the subject, although it is possible that a promising treatment may be available only within a research protocol and therefore the best-interest standard could at times be relevant.”).

216. See Miller, *supra* note 214, at 36–37 (describing the difficulty in reconciling the research trials' methods with the patients' expectations during patient enrollment).

surrogate’s, and patient’s interests usually are aligned in the treatment setting. In the research setting, the researcher has a duty to generate data that will contribute to generalizable knowledge, while the surrogate has a duty to carry out the prospective participant’s wishes or do what is in the participant’s best interests. Many times, a researcher’s need to enroll participants in a study will conflict with the surrogate’s obligation to do what is in the individual’s best physical and mental health interests.<sup>217</sup>

This problem is compounded by the fact that legislation governing consent to treatment is drafted in a manner that suggests that physician-recommended treatments usually are in a patient’s best physical and mental health interests, which fails to take into account the conflicts of interest that exist in the research context. Under the New York Act, for example, factors to be considered by the surrogate in assessing the patient’s best interests include “the possibility and extent of preserving the patient’s life; the preservation, improvement or restoration of the patient’s health or functioning; [and] the relief of the patient’s suffering.”<sup>218</sup> These factors focus overwhelmingly on the prospect of therapeutic benefit. In order to be appropriate for the research setting, consent-to-treatment legislation would have to require consideration of the known, suspected, and unknown physical and emotional health risks associated with the experimental intervention and the individual’s or surrogate’s comprehension of the likelihood that the intervention will yield no therapeutic benefit.

So far, this Part has argued that *treatment* and *research* are intrinsically different activities, that government-supported reliance on legislation governing consent to treatment to answer research-related questions could provide continued legal and conceptual support for the therapeutic misconception, and that the content of legislation governing consent to treatment may be inappropriate for research-related questions because researchers have a duty to collect data and report research results, not to hold the best physical and mental health interests of their participants as paramount. Rather than relabeling legislation governing consent to treatment in an attempt to make it applicable to both the treatment and research settings,<sup>219</sup> HHS should enact stand-alone consent-to-research regulations that specifically address the issues posed by research involving adults

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217. *See id.*

218. N.Y. PUB. HEALTH LAW § 2994–d(4)(a) (McKinney 2012).

219. *See supra* notes 202–203.

with impaired decision-making capacity and that take into account the potential conflicts of interest between and among researchers, surrogates, and participants. That is, HHS should adopt regulations that require researchers to recognize and convey to surrogates of prospective research participants who have impaired decision-making capacity (i) the conceptual distinctions between treatment and research; (ii) the specific differences between individualized, adaptable treatment methods and protocol-driven double-blind, randomized, placebo-controlled research procedures; (iii) the known, suspected, and unknown risks associated with the research study;<sup>220</sup> and (iv) the likelihood that the research participant may not directly benefit from the research.<sup>221</sup> Why? Because federal and state regulations and statutes are part and parcel of the public discourse about human subjects research ethics, and they must convey a more balanced and nuanced understanding of the possible risks and benefits of research participation.<sup>222</sup>

My proposal for research-specific regulations is supported by other substantive areas of health law that distinguish between treatment and research and establish more stringent requirements for research. In the context of health information confidentiality, for example, the federal Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule establishes the level of individual permission that is required before a covered entity may use or disclose the individual's protected health information (PHI) for a variety of activities, including treatment<sup>223</sup> and research.<sup>224</sup> Although the HIPAA Privacy Rule allows a covered entity to freely use and disclose an

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220. See, e.g., Henderson et al., *supra* note 181, at 1737 box 2 ("For intervention(s) under study in clinical research, there often is less knowledge and more uncertainty about the risks and benefits to a population of trial participants than there is when a doctor offers a patient standard interventions."); Lidz, *supra* note 191, at 1691.

221. See, e.g., Dresser, *supra* note 181, at 285 ("[H]ardly anyone acknowledges the relative scarcity of cases in which clinical-trial participants have their lives significantly extended or improved."); *id.* at 291 (recommending that researchers prepare one-page forms that highlight the differences between research and treatment and that emphasize participants' low chance of directly benefiting from research participation); *id.* at 292 (recommending that researchers provide participants with information regarding randomization, placebo groups, and other research methods; explain how study participants are treated differently than patients; and emphasize the nature and extent of the differences between treatment and research); *id.* at 293 ("[R]esearchers must give patients stark, bold, and dramatic signs that research is different than clinical care.").

222. See *id.* at 293 ("[P]ublic discourse about research must convey a more sober and qualified picture of what patients can gain and lose from enrolling in research studies.").

223. 45 C.F.R. § 164.506(a), (c)(1)–(2) (2011).

224. 45 C.F.R. § 164.512(i) (establishing the level of individual permission that is required before a covered entity may use or disclose the individual's PHI for purposes of research).

individual's PHI for the covered entity's own treatment activities<sup>225</sup> and to freely disclose an individual's PHI to another health care provider for the recipient provider's treatment activities<sup>226</sup> without obtaining the individual's prior authorization for the treatment use or disclosure, the HIPAA Privacy Rule regulates research activities much more stringently. When an individual's PHI will be used or disclosed for a research activity, the HIPAA Privacy Rule requires the individual to execute a prior written authorization form<sup>227</sup> containing certain core elements<sup>228</sup> and required statements,<sup>229</sup> unless an institutional review board or a privacy board has approved a waiver of the otherwise required authorization form,<sup>230</sup> or the individual is deceased,<sup>231</sup> or the information will be used as part of a records review that is preparatory to research,<sup>232</sup> or the information requested is a limited data set and the researcher has agreed to sign a data use agreement pursuant to which the researcher agrees to protect the confidentiality of the PHI.<sup>233</sup> According to HHS, the reason for the more stringent regulation of research in the context of health information confidentiality is that individuals expect, when they request treatment from a health care provider, that their information will be used and disclosed for reasons relating to that treatment,<sup>234</sup> but not for research purposes.<sup>235</sup> The requirement for prior written authorization in

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225. 45 C.F.R. § 164.506(c)(1).

226. 45 C.F.R. § 164.506(c)(2).

227. Standards for Privacy of Individually Identifiable Health Information, 65 Fed. Reg. 82,462, 82,520 (Dec. 28, 2000) (codified in 45 C.F.R. pts. 160, 164) ("In the final rule, we . . . require covered entities to obtain an authorization for the use or disclosure of protected health information the covered entity creates for the purpose of research that includes treatment of individuals, except as otherwise permitted by § 164.512(i).").

228. 45 C.F.R. § 164.508(c)(1) (listing the core elements).

229. 45 C.F.R. § 164.508(c)(2) (listing the required statements).

230. 45 C.F.R. § 164.512(i)(1)(i).

231. 45 C.F.R. § 164.512(i)(1)(iii).

232. 45 C.F.R. § 164.512(i)(1)(ii).

233. See 45 C.F.R. § 164.514(e)(1), (e)(3)–(4).

234. See OFFICE FOR CIVIL RIGHTS, U.S. DEPT OF HEALTH & HUMAN SERVS., USES AND DISCLOSURES FOR TREATMENT, PAYMENT, AND HEALTH CARE OPERATIONS 1 (2003), available at <http://www.hhs.gov/ocr/privacy/hipaa/understanding/coveredentities/sharingfortpo.pdf> ("Many individuals expect that their health information will be used and disclosed as necessary to treat them . . . . To avoid interfering with an individual's access to quality health care or the efficient payment for such health care, the Privacy Rule permits a covered entity to use and disclose protected health information, with certain limits and protections, for treatment . . . .").

235. See, e.g., Standards for Privacy of Individually Identifiable Health Information, 64 Fed. Reg. 59,918, 59,952 (proposed Nov. 3, 1999) (codified at 45 C.F.R. § 164.508 (2011)) ("Authorization would be required for these [nonhealth-care-related] uses and disclosures because individuals probably do not envision that the information they provide when getting health care would be disclosed for such unrelated purposes.").

the context of research is designed to alert the individual that a covered entity is seeking to use or disclose the individual's PHI for a research activity and to allow the individual to control the research-related information use or disclosure, including by allowing the individual to refuse to authorize the information use or disclosure.<sup>236</sup>

Further, in the context of health insurance, both public health care programs and private health plans distinguish evidence-based medical treatments, on the one hand, and biomedical and behavioral experiments on the other. Through federal statutes and regulations governing the Medicare and Medicaid programs, HHS clarifies that such programs will cover health care items and services that are medically necessary, but not items and services that are not reasonable and necessary for the diagnosis or treatment of illness or injury,<sup>237</sup> including some experimental and investigative treatments.<sup>238</sup> In their plan documents, private health plans also distinguish evidence-based medical treatments and medical experiments.<sup>239</sup> For example,

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236. See, e.g., *id.* ("Further, once a patient's protected health information is disclosed outside of the treatment and payment arena, it could be very difficult for the individual to determine what additional entities have seen, used and further disclosed the information. Requiring an authorization from the patient for such uses and disclosures would enhance individuals' control over their protected health information.").

237. See, e.g., 42 U.S.C. § 1395n(a)(2) (2006 & Supp. III 2010) (requiring a physician to certify the medical necessity of home health services, medical and other health services, outpatient physical therapy services, outpatient occupational therapy services, outpatient speech pathology services, comprehensive outpatient rehabilitation facility services, and partial hospitalization services before Medicare will pay for such services); 42 U.S.C. § 1395y(a)(1)(A) (2006 & Supp. III 2010) (allowing Medicare Part A and B payments to be made only for reasonable and necessary health care items and services and excluding those items that are not reasonable and necessary for the diagnosis or treatment of illness or injury).

238. See, e.g., BLUECROSS BLUESHIELD OF NORTH CAROLINA, MEDICARE C/D MEDICAL COVERAGE POLICY: INVESTIGATIONAL (EXPERIMENTAL) SERVICES (2012), [http://www.bcbsnc.com/assets/services/public/pdfs/bluemedicare/medicalpolicy/investigational\\_services.pdf](http://www.bcbsnc.com/assets/services/public/pdfs/bluemedicare/medicalpolicy/investigational_services.pdf) (generally excluding from coverage (with some exceptions) "investigational" and/or "experimental" services, defined as "medical, surgical, psychiatric, and other health care services, supplies, treatments, procedures, drug therapies, or devices that are determined by the Plan to be either: (a) not generally accepted or endorsed by health care professionals in the general medical community as safe and effective in treating the condition, illness, or diagnosis for which their use is proposed, or (b) not proven by scientific evidence to be safe and effective in treating the condition, illness or diagnosis for which their use is proposed").

239. See, e.g., STUDENT HEALTH INSURANCE PLAN OF THE UNIVERSITY OF NEVADA, LAS VEGAS 32 (2010–2011), <https://wfs.wellsfargo.com/ProductServices/A%20to%20Z/StudentInsurance/UNLV/graduatestudents/Documents/UNLV%2011%2012%20FINAL%20Aetna%20brochure.pdf>; UPMC HEALTH PLAN POLICY & PROCEDURE MANUAL: EXPERIMENTAL AND INVESTIGATIVE SERVICES, POLICY MP.079 (2012), <http://www.upmchealthplan.com/pdf/pandp/pay.008.pdf> (defining the "technologies, devices, procedures, injectable drugs and biologics, vaccines and medical treatments that are generally not covered" due to their experimental or investigative nature).

private health plans routinely except from coverage experimental and investigative services (and classify services as experimental or investigative if (i) “[t]here [is] insufficient outcomes data available from controlled clinical trials published in the peer reviewed literature . . . to substantiate [the intervention’s] safety and effectiveness for the disease or injury involved”; (ii) “[i]f required by the FDA, approval has not been granted for marketing”; (iii) “[a] recognized national medical or dental society or regulatory agency has determined, in writing, that [the intervention] is experimental, investigational, or for research purposes”; or (iv) “the written protocol or protocols used by the treating facility . . . states that [the intervention] is experimental, investigational, or for research.”<sup>240</sup>)

Finally, in the context of human subjects research, even the Common Rule does not allow state-required consent-to-treatment forms<sup>241</sup> to be used by an individual or a surrogate who is consenting to research if that state form does not comply with the Common Rule requirements. Instead, the Common Rule requires a research-specific consent form that includes certain basic<sup>242</sup> and additional<sup>243</sup> required elements, that has been approved by an IRB, and that has been signed by the subject or the subject’s LAR.<sup>244</sup> Importantly, the Common Rule’s first required element is that the consent-to-research form must state that the study involves research, not treatment.<sup>245</sup>

## V. EMPIRICAL DATA ASSESSING LAY ATTITUDES TOWARDS HUMAN SUBJECTS RESEARCH

The previous Part argued that *treatment* and *research* are intrinsically different activities, that government-supported reliance on legislation governing consent to treatment to answer research-related questions could provide continued legal and conceptual support for the therapeutic misconception, and that the content of consent-to-treatment legislation may be inappropriate for research-related questions

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240. Robert Taylor-Manning, *Undefined Experimental Treatment Exclusions in Health Insurance Contracts: A Proposal For Judicial Response*, 66 WASH. L. REV. 809, 809 (1991); STUDENT HEALTH INSURANCE PLAN OF THE UNIVERSITY OF NEVADA, LAS VEGAS, *supra* note 239, at 32 (emphasis omitted).

241. See, e.g., 25 TEX. ADMIN. CODE § 601.4(a)(1) (2012) (Tex. Med. Disclosure Panel, Informed Consent) (requiring Texas physicians to obtain a patient’s consent to treatment on a standard form).

242. See 45 C.F.R. § 46.116(a)(1)–(8) (2011) (listing eight basic elements).

243. See 45 C.F.R. § 46.116(b)(1)–(6) (listing six additional elements).

244. See 45 C.F.R. § 46.117(a).

245. See 45 C.F.R. § 46.116(a)(1).

because researchers have a duty to collect data and report research results, not to hold the best physical and mental health interests of their participants as paramount. The previous Part further argued that HHS should adopt stand-alone consent-to-research regulations that specifically address the issues posed by research involving adults with impaired decision-making capacity and that take into account the potential conflicts of interest between and among researchers, surrogates, and participants. To inform the content of such regulations, Part V argues that HHS should at least familiarize itself with the empirical literature that assesses lay attitudes towards human subjects research involving individuals with impaired decision-making capacity.

As background, the current law review and other academic literatures tend to polarize conversations about the appropriateness of human subjects research involving individuals with impaired decision-making capacity into protectionist and autonomy-based arguments, on the one hand, and clinical- and research-based arguments made in support of further biomedical and behavioral research on the other.<sup>246</sup> The current lack of federal regulation is, perhaps, a result of HHS's uncertainty regarding which of two binary positions—a protection-oriented position or a research-favorable position—HHS should adopt. This Part suggests that insights from the lay public, including current and potential patients and human subjects, may assist HHS in understanding the values of the laypersons its regulations are designed to protect.<sup>247</sup> Until lawmakers better understand laypersons' attitudes towards human subjects research involving individuals with impaired decision-making capacity, the willingness of laypersons to allow surrogates to make research participation decisions on their behalf, and the amount of leeway that laypersons would

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246. See, e.g., AGS Ethics Committee, *Informed Consent for Research on Human Subjects with Dementia*, 46 J. AM. GERIATRICS SOC'Y 1308, 1308 (1998) (noting the debate over when research can be conducted on those with impaired decision-making capacity “address[es] the tension between providing adequate protection for subjects who are vulnerable as a result of diminished capacity and allowing promising research to go forward”); Berg, *supra* note 198, at 18, (“When science takes man as its subject, tensions arise between two values basic to Western society: freedom of scientific inquiry and protection of individual inviolability.” (citing JAY KATZ, *EXPERIMENTATION WITH HUMAN BEINGS* 1 (1972)); DeRenzo, *supra* note 13, at 139 (“While taking care that research not move forward so ruthlessly that we erode the fabric of our moral community, we must be equally careful not to impede unnecessarily needed ethically and socially acceptable research.” (endnote omitted)).

247. See Kim et al., *supra* note 33, at 150 (“[T]here have been very few attempts to understand the attitudes of the lay public or of stakeholder groups regarding [surrogate-based research].”).

grant their surrogates, lawmakers will struggle to craft regulations that reflect the values of such laypersons.<sup>248</sup>

This Part thus analyzes empirical studies assessing current public attitudes regarding human subjects research involving adults with impaired decision-making capacity. As discussed in more detail below, these empirical studies somewhat surprisingly report that (i) surrogate consent to research is “probably” or “definitely” acceptable in the context of minimal risk research;<sup>249</sup> (ii) surrogate consent to research may be appropriate in the context of more risky studies;<sup>250</sup> (iii) lay (or noncourt-appointed) surrogates should be permitted to consent to riskless research on behalf of relatives with impaired decision-making capacity;<sup>251</sup> (iv) enrolling individuals who are unable to consent to research in research studies that offer no potential for medical benefit is consistent with the preferences of at least some individuals and, therefore, should not be absolutely prohibited provided there is sufficient evidence that participation in such research is consistent with the preferences of such individuals;<sup>252</sup> (v) requiring a completed advance research directive (ARD) prior to research participation by an individual with impaired decision-making capacity may be unduly restrictive in light of studies suggesting that the rate of ARD completion is likely to be low;<sup>253</sup> and (vi) allowing some or complete surrogate leeway, even over prior first-person consent, is consistent with the preferences of at least some individuals and should not be absolutely prohibited provided there is sufficient evidence that surrogate leeway is consistent with the preferences of such individuals.<sup>254</sup> Representative studies are examined below.

In 2002, researchers from the NIH, the National Institutes of Mental Health, and the Center for Research Methodology and Biometrics in Denver published the results of a study designed to systematically assess, for the first time, the attitudes of healthy

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248. See, e.g., Jason Karlawish et al., *Older Adults' Attitudes Toward Enrollment of Non-Competent Subjects Participating in Alzheimer's Research*, 166 AM. J. PSYCHIATRY 182, 183 (2009) (“Until we better understand whether people are willing to participate in nonbeneficial research that enrolls persons with Alzheimer's disease and why they are willing, policymakers cannot develop research ethics policies that respect the values of the people they are designed to protect and that will resolve the controversy that has caused some states and institutional review boards to limit substantially the practice of proxy consent for research.”).

249. See *infra* text accompanying note 279.

250. See *infra* text accompanying notes 280–283 and 293.

251. See *infra* text accompanying notes 267–268 and note 274.

252. See *infra* text accompanying note 261.

253. See *infra* text accompanying note 262.

254. See *infra* text accompanying notes 289, 294, 298, and 300.

individuals who were familiar with clinical research (due to having a family history of Alzheimer's Disease (AD) and prior research participation) towards five of the most prominent proposed safeguards for research participants with impaired decision-making capacity, that is, "1) restrictions on research with no potential for medical benefit, 2) formal research advance directives, 3) proxy decision makers, 4) restrictions on research not associated with the individuals' impairments, and 5) respect for subjects' dissent."<sup>255</sup>

The study authors found that "[t]he vast majority of respondents were willing to participate in clinical research" if their ability to consent became impaired.<sup>256</sup>

[Ninety-two percent] were willing to participate in a study that involved taking experimental medication that might help them; 80% were willing to take experimental medication that had no chance of helping them; 99% were willing to participate in a study that involved a computer task that would not help them; and 98% were willing to participate in a study involving two X-rays that would not help them.<sup>257</sup>

With respect to their attitudes toward ARDs,

[89% of respondents] said they were willing to fill out [an ARD] if asked to do so by their family, and . . . [86%] said they would be willing if asked by their doctor. Eighty-one percent said they preferred giving advance instructions rather than allowing their family to make research [participation] decisions for them [in the event of a loss of capacity to give first-person consent] . . . Eighty-eight percent stated that their family could enroll them in research in the absence of [an ARD], and 80% stated that their families could enroll them in a potential benefit research even when their [ARD] opposed [research participation].<sup>258</sup>

Finally, with respect to the completion of ARDs, few (only 16% of the 246) ARD forms were actually completed by the subjects and returned to the subject's home research institution within one year.<sup>259</sup> However,

[95%] of the returned [ARDs] indicated a willingness to participate in research that offered a potential for medical

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255. See Dave Wendler et al., *Views of Potential Subjects Toward Proposed Regulations for Clinical Research with Adults Unable to Consent*, 159 AM. J. PSYCHIATRY 585, 585, 589 (2002).

256. *Id.* at 586.

257. *Id.*

258. *Id.* at 589.

259. *Id.*

benefit; 95% indicated a willingness to participate in minimal risk research with no potential for medical benefit; [and] 51% indicated a willingness to participate in greater than minimal risk research with no potential for medical benefit.<sup>260</sup>

The study authors ultimately concluded that enrolling individuals who are unable to consent to research in a research study that offers no potential for medical benefit is consistent with the preferences of at least some individuals and, therefore, should not be absolutely prohibited provided there is sufficient evidence that research participation is consistent with the preferences of such individuals.<sup>261</sup> The study authors also concluded that requiring such evidence to be provided in a formal ARD may be unduly restrictive, especially because so few of the respondents actually returned completed ARDs.<sup>262</sup>

The following year, researchers from the University of Sherbrooke and the Sherbrooke University Geriatric Institute published the results of a questionnaire-based study designed to elicit the opinions of four different groups of concerned individuals (“older adults, informal caregivers of cognitively impaired individuals, researchers in ageing [sic], and members of institutional review boards”) regarding who should decide whether an older adult with impaired decision-making capacity will participate in research.<sup>263</sup> The study questionnaire included (i) five questions describing hypothetical studies that progressively increased the risk to the subject’s health, including spending a few hours per week with a pet (Question 1), a quality-of-sleep study (Question 2), a new cream for treating bedsores (Question 3), an experimental drug designed to slow the progress of AD that carries the risk of constipation and dizziness (Question 4), and painful brain injections that could reverse the course of AD but that also involve serious risks of infection (Question 5); (ii) two more general questions exploring the conditions under which “the respondent feels it is acceptable to solicit a cognitively impaired individual for research” (Questions 6 and 7); and (iii) a final, more personal question “ask[ing] the respondents to specify in what cases they would agree that a concerned relative who lacks legal authority decide on their

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260. *Id.*

261. *Id.*

262. *Id.* at 589–90.

263. See Gina Bravo, Mariane Pâquet & Marie-France Dubois, *Opinions Regarding Who Should Consent to Research on Behalf of an Older Adult Suffering from Dementia*, 2 *DEMENTIA* 49, 49, 51–52 (2003).

behalf whether they will participate in a study, in the event that they themselves become mentally incapacitated” (Question 8).<sup>264</sup> (As background, the then-current law in Quebec allowed family members to make healthcare decisions on behalf of patients with impaired decision-making capacity but allowed only court-appointed legal guardians to consent to research on behalf of human subjects with impaired decision-making capacity.<sup>265</sup>)

The study authors found that a significant proportion of those surveyed did not agree with the current law in Quebec.<sup>266</sup> In fact, most respondents supported the participation of individuals with impaired decision-making capacity in research and would require the consent of a legal guardian only when risks were involved.<sup>267</sup> Indeed,

[i]n the absence of risk to the subject’s health [(Questions 1 to 3)], less than one-third of the respondents chose the legal guardian alone as the person best suited to make a substituted decision. As the hypothetical study became more risky [(Questions 4 and 5)], [the study authors found] an increase in the proportion of respondents who preferred that the surrogate decision-maker be legally appointed.<sup>268</sup>

(However, the proportion of respondents who believed that individuals with impaired decision-making capacity should “be excluded from the study also increased, [making] the choice of the best surrogate decision maker irrelevant.”<sup>269</sup>)

The study authors also found that “[70%] of the respondents considered it acceptable to invite [older adults with impaired decision-making capacity] to participate in a hypothetical study that involved serious risks to their health [(Question 5)], mostly with the legal guardian’s consent.”<sup>270</sup> “Opinions differed slightly when respondents were asked the two general questions” (Questions 6 and 7) that lacked any context.<sup>271</sup> “More respondents, especially among older adults and informal caregivers, opted simply to exclude [individuals with cognitive impairments] from research.”<sup>272</sup> The study authors interpreted this finding as “prudence [that] could be due to the vagueness

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264. *Id.* at 52, 54–57.

265. *Id.* at 50 (citation omitted).

266. *See id.* at 61–62.

267. *Id.* at 63.

268. *Id.* at 61–62.

269. *Id.* at 62.

270. *Id.*

271. *Id.*

272. *Id.*

inherent in the notion of risks and benefits.”<sup>273</sup> In the end, the study authors concluded that their findings suggested support for amending Quebec legislation to allow lay (or nonguardian) surrogates to consent to riskless research on behalf of relatives with impaired decision-making capacity.<sup>274</sup>

In 2005, researchers from the University of Michigan and the University of Rochester Medical Center published the results of a study designed “to elicit the views of those at heightened risk of [AD] regarding how they would balance the need for research in [AD] with the need to protect vulnerable [subjects with impaired decision-making capacity].”<sup>275</sup> Using a mailed questionnaire, “the [study] authors surveyed the participants at one of the sites of the AD Anti-Inflammatory Prevention Trial”<sup>276</sup> and measured responses regarding the “acceptability of surrogate consent for [ten] research scenarios of varying degrees of risks and benefits, given from the perspectives of social policy, personal preferences for self, and preferences when deciding on behalf of a loved one.”<sup>277</sup> The ten research scenarios involved an observation, an interview, a blood draw, a magnetic resonance imaging (MRI) procedure, a lumbar puncture, a drug challenge, a biopsy, a drug randomized controlled trial (RCT), a vaccine, and a gene transfer.<sup>278</sup>

Of the 229 participants who responded, a large majority (more than 90%) responded that surrogate consent to research was “probably” or “definitely” acceptable in the context of minimal risk research studies (including observation, interview, and blood draws) as well as RCTs of new medications.<sup>279</sup> A smaller majority responded that surrogate consent to research was appropriate in the context of more invasive studies.<sup>280</sup> For example, 56% of the participants responded that a brain biopsy study was “probably” or “definitely” acceptable and 54% responded that a gene transfer study was “probably” or “definitely” acceptable by society.<sup>281</sup> The study authors further found that

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273. *Id.*

274. *Id.* at 63.

275. See Scott Y.H. Kim et al., *What Do People at Risk for Alzheimer Disease Think About Surrogate Consent for Research*, 65 *NEUROLOGY* 1395, 1395 (2005).

276. *Id.* at 1395. “[A]ll participants [were] 70 years old or older with at least one first-degree relative with dementia.” *Id.*

277. *Id.*

278. *Id.* at 1398 tbl.3.

279. *Id.* at 1395–97, 1398 tbl.3.

280. *Id.* at 1396.

281. *Id.* at 1396, 1398 tbl.3.

[t]he acceptability of [surrogate consent to research] was generally highest from the first-person perspective, then from the societal perspective, and lowest from a surrogate's perspective of considering what to do for a loved one. For the lumbar puncture [research scenario], for example, 69%, 65%, and 61% felt the study was ["probably" or "definitely"] acceptable from the point of view of self, society, and surrogate[, respectively].<sup>282</sup>

The study authors ultimately concluded that laypersons at heightened risk of AD do discriminate among research scenarios of varying risks and burdens and that laypersons also are supportive of surrogate consent to research even when the risks and burdens are significant to the subjects.<sup>283</sup>

In 2009, researchers from the University of Michigan, the University of Pennsylvania, the Mayo Clinic, and Columbia University published the results of a survey designed "to assess the views of a nationally representative, policy-relevant sample of the general public (namely, older Americans) regarding surrogate consent for four research scenarios of varying degrees of risk and potential benefit" as well as the extent of latitude or leeway that people would be willing to confer on their surrogates.<sup>284</sup> "[Following] a brief introductory background on AD and the rationale for the survey," a random subsample (n = 1,515) of the 2006 wave of the Health and Retirement Study (HRS), a biennial survey of a nationally representative sample of Americans aged fifty-one and older, were given one of four surrogate-consent based research (SBR) scenarios that approximated real studies in AD, including "a lumbar puncture . . . , a randomized controlled trial . . . of a new drug, a vaccine study, and a first-in-human gene transfer neurosurgical study. . . . Then, the subjects were asked three questions,"<sup>285</sup> including (i) "If patients cannot make their own decisions about being in studies like this one, should our society allow their families to make the decision in their place?"; (ii) "Suppose you wanted to give a close family member instructions for the future, in case you ever became unable to make decisions for yourself. Would you say you would want to participate in the study?"; and (iii) "How much freedom or leeway would you give the close family member to go against your preference and instead . . . enroll/not enroll . . . you in the study?"<sup>286</sup>

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282. *Id.* at 1396–97.

283. *Id.* at 1399–400.

284. *See* Kim et al., *supra* note 27, at 150.

285. *Id.* at 149–50.

286. *Id.* at 150, 152 tbl.2.

Most of the respondents stated that . . . society should allow family [SBR] (67.5% to 82.5%, depending on the scenario)<sup>[287]</sup> and [that they personally] would . . . want to participate in SBR (57.4% to 79.7%).<sup>[288]</sup> Most respondents would also grant some or complete leeway to their surrogates (54.8% to 66.8%), but this was true mainly of those willing to participate.<sup>[289]</sup>

“[A] significant minority (up to 45% for the gene transfer scenario) would not allow leeway.”<sup>290</sup> The study authors also found a trend toward lower willingness to participate in SBR among individuals who identified as racial or ethnic minorities.<sup>291</sup>

The study authors formally concluded that “[f]amily surrogate consent-based dementia research is broadly supported by older Americans” and that “[w]illingness to allow leeway to . . . surrogates needs to be studied further for its ethical significance for surrogate-based research policy.”<sup>292</sup> The study authors further concluded that “even for invasive studies[,] the prior probability of an older American’s willingness to participate in SBR is high.”<sup>293</sup> The study authors also concluded that, “even among those who are not willing to participate, there is a sizable minority who are willing to confer some leeway on their surrogates.”<sup>294</sup> The study authors recognized several limitations in their work, including the complicated scientific and policy issues surrounding surrogate consent for research, and the study’s focus on dementia, which may not generalize to other areas of SBR.<sup>295</sup>

Also in 2009, researchers from the University of Pennsylvania and the Philadelphia VA Medical Center published the results of a research study designed to assess willingness to have a surrogate make research participation decisions and, for each of two AD biomarker studies (including a minimal risk

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287. The percentage of respondents providing positive responses for each of the four surrogate-based research scenarios for the first question (whether society should allow family surrogate consent) was 67.5% (gene transfer), 70.5% (vaccine), 72.0% (lumbar puncture), and 82.5% (drug randomized controlled study). *Id.* at 152 tbl.2.

288. The percentage of respondents providing positive responses for each of the four surrogate-based research scenarios for the second question (whether one would want to participate in the study) was 57.4% (vaccine), 68.7% (gene transfer), 70.8% (lumbar puncture), and 79.7% (drug randomized controlled study). *Id.*

289. *Id.* at 149, 151–52 & tbl. 2.

290. *Id.* at 153.

291. *Id.*

292. *Id.* at 149, 153–54.

293. *Id.* at 154.

294. *Id.*

295. *Id.*

blood draw and a greater than minimal risk blood draw and lumbar puncture), willingness to grant advance consent, and willingness to grant a surrogate leeway over advance consent.<sup>296</sup> Of the 538 persons age sixty-five and older who resided in the southeastern Pennsylvania region and participated in the study, the majority (83%) granted advance consent to a blood draw study and nearly half (48%) to a blood draw plus lumbar puncture.<sup>297</sup> A large majority of the respondents (96%) were willing to identify a surrogate who would make research participation decisions “and most were willing to grant their proxy leeway over their advance consent.”<sup>298</sup> “Combining [their] preferences for advance consent and leeway, the proportion [of respondents] who would permit being enrolled in the blood draw and [spinal fluid samples studied], respectively, were 92% and 75%.”<sup>299</sup> The study authors formally concluded that their data suggest that “[o]lder adults generally support enrolling [individuals with impaired decision-making capacity associated with AD] into research that does not present a benefit to [such individuals]” and that “[w]illingness to grant [surrogate] leeway over advance consent and a favorable attitude [towards] biomedical research substantially explain[s such] willingness.”<sup>300</sup> The proposals set forth in Part VI of this Article are designed to reflect, to some extent, the empirical data presented in this Part V.

#### VI. A PROPOSAL FOR A NEW SUBPART “E” TO THE COMMON RULE

At least three options for the future regulation of research involving adults with impaired decision-making capacity emerge. The first option is to continue our current system of no specific federal regulation and varying, if any, state regulation. This option would continue to give research protocol creation and approval discretion to researchers and IRBs, which have at their disposal nonbinding federal guidance and recommendations, including the OHRP’s answers to the public’s frequently asked questions, the SIIIDR’s recommendations, and the NIH’s “Points to Consider.” This option provides significant flexibility to researchers and IRBs, although research subjects may be under- or over-protected due to the lack of binding regulatory authority and significant researcher and IRB discretion.

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296. See Karlawish et al., *supra* note 248, at 183.

297. *Id.* at 183–85.

298. *Id.* at 182, 185.

299. *Id.*

300. *Id.* at 182, 186.

Second, an organization such as the Uniform Law Commission (ULC) could adopt a “Uniform Research Involving Adults with Impaired Decision-Making Capacity Act” that could serve as model legislation for states that do not have any research-specific provisions and for states that already have such legislation when that legislation is different than neighboring states. The ULC already has adopted other uniform health and safety-related laws, including the Uniform Anatomical Gift Act (currently adopted by forty-five states and the District of Columbia)<sup>301</sup> and the Uniform Health-Care Decisions Act (currently adopted by six states).<sup>302</sup> If adopted by all fifty states, this option would result in standard surrogate consent to research provisions, which would be especially helpful for researchers involved in multi-site, multi-state studies who currently must adhere to a number of varying state laws. Given that only six states have adopted the relatively noncontroversial Uniform Health-Care Decisions Act, it is unlikely that a majority of states would immediately adopt a “Uniform Research Involving Adults with Impaired Decision-Making Capacity Act,” thus resulting in a continuing patchwork of state law.

Third, HHS could add new provisions to the Common Rule that would specifically govern, for the first time at the federal level, human subjects research involving adults with impaired decision-making capacity. The new provisions could be codified at 45 C.F.R. Part 46 (Subpart E) and would follow the current Basic Policy for the Protection of Human Research Subjects (Subpart A) and the special regulatory provisions that already apply to pregnant women, fetuses, and neonates (Subpart B); prisoners (Subpart C); and children (Subpart D). This option would result in national research standards applicable to adults with impaired decision-making capacity. Depending on the particular standards that are adopted, however, research subjects could continue to be under- or over-protected.

This Article supports the third option; that is, the addition by HHS of a new Subpart E to the Common Rule specifically governing human subjects research involving adults with impaired decision-making capacity. The first option is unacceptable because it promotes reliance on legislation

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301. See *Legislative Fact Sheet - Anatomical Gift Act (2006)*, UNIFORM L. COMMISSION, [http://www.uniformlaws.org/LegislativeFactSheet.aspx?title=Anatomical Gift Act \(2006\)](http://www.uniformlaws.org/LegislativeFactSheet.aspx?title=Anatomical%20Gift%20Act%20(2006)) (last visited Jan. 3, 2013).

302. See *Legislative Fact Sheet - Health-Care Decisions Act*, UNIFORM L. COMMISSION, [http://uniformlaws.org/LegislativeFactSheet.aspx?title=Health-Care Decisions Act](http://uniformlaws.org/LegislativeFactSheet.aspx?title=Health-Care%20Decisions%20Act) (last visited Jan. 3, 2013).

governing consent to treatment to answer research-related questions, which I found in Part IV to be problematic because (i) treatment and research are intrinsically different activities; (ii) government-supported reliance on legislation governing consent to treatment to answer questions relating to consent to research could provide continued legal and conceptual support for the therapeutic misconception; and (iii) the content of legislation governing consent to treatment is inappropriate for research-related questions in light of the unique role of the researcher, that is, the role of collecting data and reporting research results, not holding the best physical and mental health interests of research participants as paramount. Although the substance of the second option could be virtually identical to the substance of the third option, I believe it unlikely that fifty states will adopt a “Uniform Research Involving Adults with Impaired Decision-Making Capacity Act” when only six states have, to date, adopted the relatively noncontroversial Uniform Health-Care Decisions Act.

This Article thus proposes the following structure for a new Subpart E to the Common Rule:

45 C.F.R. PART 46

*Subpart E: Additional Protections Pertaining to Biomedical and Behavioral Research Involving Adults with Impaired Decision-Making Capacity*

§ 46.501: Applicability.

§ 46.502: Purpose.

§ 46.503: Definitions.

§ 46.504: Additional Duties of Institutional Review Boards.

§ 46.505: Minimal Risk Research.

§ 46.506: Greater than Minimal Risk Research Involving the Prospect of Direct Benefit.

§ 46.507: Greater than Minimal Risk Research Likely to Yield Generalizable Knowledge About Conditions Causing or Resulting in Impaired Decision-Making Capacity.

§ 46.508: Additional Consent Form and Process Requirements.

The first section, proposed § 46.501, would address the applicability of Subpart E. Specifically, § 46.501 would state that the regulatory provisions in Subpart E apply to all biomedical and behavioral research conducted or supported by the Department of Health and Human Services involving adults with impaired decision-making capacity. (If HHS’s July 26, 2011 proposal to expand the Common Rule “to all [human subjects]

research, regardless of funding source, conducted at institutions in the [United States] that receive some Federal funding from a Common Rule agency” is adopted,<sup>303</sup> then proposed § 46.501 would simply state that the regulatory provisions in Subpart E apply to all biomedical and behavioral research involving adults with impaired decision-making capacity conducted at an institution in the United States that receives some federal funding from a Common Rule agency.) Proposed § 46.501 also would specify that the requirements of Subpart E are in addition to, not instead of, those imposed under the other Subparts of Part 46, including Subpart A’s Basic Policy for the Protection of Human Research Subjects.

The second section, proposed § 46.502, would address the purpose of Subpart E. Specifically, proposed § 46.502 would explain that some individuals, due to neurological, psychiatric, developmental, and other conditions, are unable to comprehend sufficient information and may be incompetent to give informed consent to their own research participation. Proposed § 46.502 also would explain, however, that additional research on the physical and mental health conditions that cause or result in impaired decision-making capacity remains necessary due to the lack of available treatments. Proposed § 46.502 should clearly state that it is the purpose of Subpart E to permit the conduct of responsible biomedical and behavioral investigations while providing additional safeguards for adults with impaired decision-making capacity.

The third section, proposed § 46.503, would define specific terms used in Subpart E. Terms requiring definition would include, at a minimum, “Adults with Impaired Decision-Making Capacity,” “Assent,” “Consent,” “Greater than Minimal Risk,” “Legally Authorized Representative,” “Minimal Risk,” and “Surrogate.” Although many of these definitions can be taken from regulatory provisions codified elsewhere in the Common Rule, the definition of “Adults with Impaired Decision-Making Capacity” will be specific to Subpart E as will “Surrogate.” With respect to “Adults with Impaired Decision-Making Capacity,” HHS (through proposed regulations) should seek public comment on the range of physical and mental health conditions that cause

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303. See Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators, 76 Fed. Reg. 44,512, 44,514 (proposed July 26, 2011) (to be codified at 45 C.F.R. pts. 46, 160, 164; 21 C.F.R. pts. 50, 56) (discussing HHS’s proposal to extend federal regulatory protection “to all research, regardless of funding source, conducted at institutions in the [United States] that receive some Federal funding from a Common Rule agency for research with human subjects”).

or result in impaired decision-making capacity that could be used to illustrate the types of persons who would be included in this definition. With respect to “Surrogate,” HHS (through proposed regulations) should seek public comment on the classes of individuals (and their relative order) who may make a research participation decision on behalf of an adult with impaired decision-making capacity. Given that some empirical studies support the use of lay surrogates (versus legal guardians, legal conservators, and other court-appointed surrogates) for decisions regarding research participation when the research involves only minimal risk,<sup>304</sup> the identification and relative ordering of lay and legal surrogates should be carefully evaluated and should include, at a minimum, consideration of the following individuals: (i) the individual’s agent pursuant to an advance research directive; (ii) the conservator or guardian of the individual; (iii) the spouse or domestic partner of the individual; (iv) an adult son or daughter of the individual; (v) a custodial parent of the individual; (vi) any adult brother or sister of the individual; (vii) any adult grandchild of the individual; and (viii) an available adult relative with the closest degree of kinship to the individual. Again, HHS (through proposed regulations) should solicit comments on the relative priority of these individuals.

The fourth section, proposed § 46.504, would specify an additional duty of IRBs in research that involves adults with impaired decision-making capacity. Specifically, proposed § 46.504 would require IRBs to find that there are good reasons to involve adults with impaired decision-making capacity as research subjects. Stated another way, IRBs would be required to find that a proposed research protocol can be conducted only if adults with certain neurological, psychiatric, developmental, and other physical and mental conditions are involved. If the research can be conducted with alternative (healthy) populations, then individuals with impaired decision-making capacity should not be enrolled in the research. The substance of proposed § 46.504 is supported by the current empirical literature, which reports wide agreement that individuals with impaired decision-making capacity should not be involved in research that can adequately be performed with healthy individuals with intact decision-making capacity.<sup>305</sup> Because there remains to be conducted important research on conditions that cause impaired decision-making capacity that will require the inclusion of individuals

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304. See *supra* text accompanying note 267.

305. Kim et al., *supra* note 12, at 797–98.

with such conditions,<sup>306</sup> the remainder of Subpart E (including proposed §§ 46.505–507) are necessary.

The fifth section, proposed § 46.505, would govern minimal risk research involving adults with impaired decision-making capacity. Specifically, proposed § 46.505 would state that minimal risk biomedical or behavioral research involving adults with impaired decision-making capacity may be carried out if (i) the research is relevant to the individual’s condition; (ii) the individual has given prior consent to participate in such research through an ARD, or gives current assent to such research participation, or does not object to such research participation; and (iii) the individual’s surrogate consents to the individual’s research participation. This provision is supported by the current empirical literature that reports that laypersons support the use of lay surrogates for research participation decisions made in the context of minimal risk research.<sup>307</sup> Given that the empirical literature finds some, but not unanimous, support for surrogate leeway, additional empirical research should be conducted to assess laypersons’ desires with respect to the procession of minimal risk research when the individual objects but the experimental intervention holds out the prospect of direct benefit to the individual.

The sixth section, proposed § 46.506, would govern research involving adults with impaired decision-making capacity in the context of greater than minimal risk research that involves the prospect of direct benefit to the individual. Specifically, if a greater than minimal risk research study holds out the prospect of direct benefit for an individual, proposed § 46.506 would clarify that such research may proceed, but only if (i) the intervention that holds out the prospect of direct benefit is only available in the context of research; (ii) the risk is justified by the prospect of benefit to the subjects; (iii) the relation of the risk to the anticipated benefit is at least as favorable as that presented by available alternative approaches; (iv) the individual has given prior consent to participate in such research through an ARD, or gives current assent to such research participation, or does not object to such research participation; and (v) the individual’s LAR consents to the individual’s research participation. This proposal is supported by the current empirical literature that reports support for the conduct of greater than minimal risk research that holds out the prospect of direct benefit.<sup>308</sup>

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306. *Id.* at 798.

307. *See supra* text accompanying notes 267 & 274.

308. Beattie, *supra* note 23, at S27–28; Kim et al., *supra* note 12, at 801 (“For [adults

The seventh section, proposed § 46.507, would govern research involving adults with impaired decision-making capacity in the context of greater than minimal risk research that does not involve the prospect of direct benefit. Perhaps the most controversial, this provision would answer the question whether it is permissible to enroll incapacitated individuals in risky research that likely will not benefit them. As discussed in more detail in Part V, the current empirical literature does not support an outright prohibition on this type of research. That is, such research is consistent with the preferences of at least some individuals<sup>309</sup> who perhaps recognize that gene transfer studies, vaccine studies, immunotherapy, and drug studies—although posing significant health and other risks—can form the basis of future safe and efficacious treatments.<sup>310</sup> Proposed § 46.507 would allow such research, but only if (i) the anticipated knowledge is of vital importance for the understanding or amelioration of the type of disorder or condition of the individual; and (ii) the individual has given prior consent to research participation of this type involving greater than minimal risk and no prospect of direct benefit through an advance research directive; or (iii) the individual gives current assent to research participation and the individual's LAR consents to the individual's research participation, *but only after a finding of clear and convincing evidence that research participation is consistent with the prior expressed preferences of the individual*. The requirement for clear and convincing evidence that research participation is consistent with the individual's prior expressed preferences will prevent the involvement and exploitation of vulnerable research participants who would not have wanted to participate in such research, but will respect the autonomy of individuals who, for altruistic or other reasons, would have wanted to participate in the research. The requirement for clear and convincing evidence mirrors the type of evidence that is required by many states with respect to the withholding or withdrawal of life-sustaining treatment from individuals who, due to their conditions, are not able to express their consent to such withholding or withdrawal.<sup>311</sup>

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who lack decision-making capacity], there is little controversy that research involving . . . anticipated direct benefit to the subject that is reasonable in relation to the risk [is permissible].”).

309. See *supra* text accompanying notes 261 & 293.

310. See, e.g., Beattie, *supra* note 23, at S29–30; Kim et al., *supra* note 12, at 798.

311. See, e.g., ALA. CODE § 22-8A-11(c) (Lexis Nexis 2006); OKLA. STAT. ANN. tit. 63, §§ 3080.3, 3080.4(A)(2) (West 2004 & Supp. 2012).

A final section, proposed § 46.508, is necessary to deal with the likelihood of subject, surrogate, and researcher therapeutic misconception. That is, proposed § 46.508 would require researchers to convey to subjects and surrogates during the informed consent conversation, as well as to include in the consent-to-research form, language addressing (i) the conceptual distinctions between treatment and research; (ii) the specific differences between individualized, adaptable treatment methods and protocol-driven, double-blind, randomized, placebo-controlled research procedures; (iii) the known, suspected, and unknown risks associated with the research protocol; and (iv) the likelihood that research participants may not directly benefit from the research. Language addressing these topics would be in addition to the other consent form and process requirements set forth in Subpart A of the Common Rule.<sup>312</sup>

## VII. CONCLUSION

This Article has proposed that HHS amend the Common Rule to add a new Subpart E governing human subjects research involving adults with impaired decision-making capacity. Although HHS has amended the Common Rule several times over the last few decades, “[the regulations] have not kept pace with the evolving human research enterprise,” including the marked increase in the volume of biomedical and behavioral research, “the proliferation of multi-site clinical trials and observational studies,” the expansion of research in particular areas, including neurology and psychiatry, and the use of new research technologies, including functional magnetic resonance imaging.<sup>313</sup> Stakeholders have criticized the decades-old regulations on many grounds, including the extent and quality of the protections afforded by the regulations’ consent provisions, the lack of calibration between the risks posed by a particular research protocol and the required level of institutional review, and “the multiple . . . [and] differing regulatory requirements that can apply to a single research study.”<sup>314</sup> The proposals in this Article not only respond to these criticisms in the context of

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312. See 45 C.F.R. § 46.116 (2011) (establishing the general requirements for informed consent to research participation); 45 C.F.R. § 46.117 (2011) (establishing requirements relating to the documentation of informed consent to research participation).

313. Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators, 76 Fed. Reg. 44,512, 44,512–13 (proposed July 26, 2011) (to be codified at 45 C.F.R. pts. 46, 160, 164; 21 C.F.R. pts. 50, 56).

314. See *id.* at 44,513–14.

research involving adults with impaired decision-making capacity, but they also create an appropriate balance among competing interests, that is, the protection of vulnerable human research subjects, the respect for (and promotion of) research subject autonomy, and the need for additional research into the neurological, psychiatric, developmental, and other conditions that result in impaired decision-making capacity.