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REGULATING RESEARCH WITH DECISIONALLY IMPAIRED INDIVIDUALS: ARE WE MAKING PROGRESS?

Diane E. Hoffmann^{*}
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INTRODUCTION^{****}

The National Bioethics Advisory Commission (NBAC or Commission), as well as advisory panels in two states (New York and Maryland) have recently issued recommendations urging new regulation of research with decisionally impaired individuals.¹ These

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¹See NATIONAL BIOETHICS ADVISORY COMMISSION, RESEARCH INVOLVING PERSONS WITH MENTAL DISORDERS THAT MAY AFFECT DECISIONMAKING CAPACITY 2 (1998) [hereinafter NBAC REPORT]; NEW YORK STATE DEPARTMENT OF HEALTH ADVISORY WORK GROUP ON HUMAN SUBJECT RESEARCH INVOLVING THE PROTECTED CLASSES, RECOMMENDATIONS ON THE OVERSIGHT OF HUMAN SUBJECT RESEARCH INVOLVING THE PROTECTED CLASSES 28-33 (1998) [hereinafter NEW YORK REPORT]; and JACK SCHWARTZ, OFFICE OF THE MARYLAND ATTORNEY GENERAL, FINAL REPORT OF THE ATTORNEY GENERAL'S WORKING GROUP ON RESEARCH

recent governmental initiatives have resurrected a quarter-century old policy debate over whether this kind of research should be governed by regulations beyond those applicable to all human subjects. Considerations underlying the central question include how the population needing special regulatory protection should be defined, what limitations should be placed on the risk to which subjects are exposed, and how much discretion about these matters should be left to research investigators and local review boards.

Fueling this debate is a core ethical issue: how can research with subjects who are unable to consent be justified? The Nuremberg Code, a post-war foundational document regarding research ethics, states that the “voluntary consent of the human subject is absolutely essential.”² “This means that the person involved should have legal capacity to give consent....”³ This language effectively rules out research involving decisionally incapacitated subjects and is cited as the central authority by those objecting to such research.⁴

Yet, the prohibition suggested by the Nuremberg Code is itself ethically troublesome to many who point out that, “[b]ecause new treatments must eventually be tested in persons suffering from the relevant condition, a policy totally excluding incapable subjects from research would preclude the development of improved treatment for persons with serious psychiatric disorders, dementia, and other mentally debilitating conditions.”⁵ A source of authority for those who

Involving Decisionally Incapacitated Subjects 1 (1998) (on file with the DePaul Journal of Health Care Law) [hereinafter Maryland Report].

²The Nuremberg Code (1947), *reprinted in* JAY KATZ, *EXPERIMENTATION WITH HUMAN BEINGS* 305-06 (1971).

³*Id.*

⁴Some commentators have suggested that the Nuremberg Code’s wording, which “seems to rule out research with children, with emergency patients, and with the decisionally impaired,” is more expansive than the Code’s intended scope. Jonathan D. Moreno, *Regulation of Research on the Decisionally Impaired: History and Gaps in the Current Regulatory System*, 1 J. HEALTH CARE L. & POL’Y 1, 12 (1998). The judges who issued the decision embodying the Code may only have intended “to rule out non-beneficial and highly risky experiments with easily coerced subjects such as prisoners.” *Id.*

⁵REBECCA DRESSER, NATIONAL BIOETHICS ADVISORY COMMISSION, *Research Involving Persons with Mental Disabilities: A Review of Policy Issues and Proposals*, in RESEARCH

argue that it is ethical to conduct research with the decisionally impaired is the Declaration of Helsinki (Declaration).⁶ The Declaration includes in its principles the following: "Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation."⁷ This statement appears to assume the passage of national legislation permitting family members to consent to participation in research for an incapacitated individual. The implication of the statement is that sometimes the pursuit of scientific knowledge justifies research that the Nuremberg Code would prohibit, although the Declaration does not fully account for the circumstances under which proxy consent would be ethically permissible.⁸

These two documents provide the historical context for the examination of subsequent efforts to regulate research with this population. Phrases from the documents have become battle flags for advocates. Those who believe that research with decisionally impaired subjects is ethically suspect, a danger to be avoided, often use the Nuremberg Code as the starting point for arguments that this research should be severely restricted.⁹ Those whose premise is that research with decisionally impaired subjects is ethically permissible, a necessity in the fight against serious illness, often use the Declaration of Helsinki as the starting point for arguments that this research must not be hobbled with restrictions.¹⁰ This article will examine how these

INVOLVING PERSONS WITH MENTAL DISORDERS THAT MAY AFFECT DECISIONMAKING CAPACITY
COMMISSIONED PAPERS 5, 7 (1998)

⁶See World Medical Association, Declaration of Helsinki (1948), adopted by the World Medical Assembly in 1964 and revised in 1975 and 1983, in *THE ETHICS OF RESEARCH INVOLVING HUMAN SUBJECTS - FACING THE 21ST CENTURY* 433 (Harold Y. Vanderpool, ed., 1996).

⁷*Id.*

⁸The Declaration suggests that when research is solely for the advancement of scientific knowledge—that is, contains no element of possible direct therapeutic benefit for the subjects—"[t]he subjects should be volunteers...." *Id.*

⁹See KATZ, *supra* note 2, at 305-06.

¹⁰See *id.*

seemingly irreconcilable moral views play out in the policymaking process.

Over twenty-five years ago, the U.S. Department of Health, Education and Welfare (DHEW) published an early working document as a prelude to proposed rules on research with “individuals institutionalized as mentally infirm.”¹¹ The proposals in the working document and proposed rules published a few years later¹² would have significantly restricted—perhaps even effectively ended—this research. The proposals ultimately were abandoned, primarily because of comments from researchers that they would be too restrictive and burdensome on the research community.¹³

Since DHEW abandoned its regulatory effort, little has changed, at least in terms of governmental policy directives. Federal regulations merely call on Institutional Review Boards (IRBs) to be attentive to the need for “additional safeguards...to protect the rights and welfare” of research subjects who “are likely to be vulnerable to coercion or undue influence, such as...mentally disabled persons....”¹⁴ No state comprehensively regulates research with decisionally impaired individuals.¹⁵

¹¹See Protection of Human Subjects, 38 Fed. Reg. 31,738, 31,738 (1973) (proposed Nov. 16, 1973).

¹²See Protection of Human Subjects, Research Involving Those Institutionalized as Mentally Infirm, Reports and Recommendations for Public Comment, 43 Fed. Reg. 11327 (Mar. 17, 1978).

¹³See Moreno, *supra* note 4, at 13.

¹⁴45 C.F.R. § 46.111(b) (1999).

¹⁵See Diane E. Hoffmann & Jack Schwartz, *Proxy Consent to Participation of the Decisionally Impaired in Medical Research – Maryland's Policy Initiative*, 1 J. HEALTH CARE L. & POL'Y 123, 125-26 (1998).

This article reviews the history of attempts to regulate research with the decisionally impaired and examines the question whether the recent proposals will merely reprise failed efforts of the past or instead mark progress toward consensus on the appropriate level of regulatory protection. In so doing, this article addresses some of the significant changes in the relevant research, social, and legal arenas during the past quarter-century as well as the more complex regulatory research environment that exists today, and their likely impact on the policymaking outcome.

EARLY REGULATORY EFFORTS: THE 1970s

Initial Proposals by the Department of Health, Education, and Welfare

The federal government first gave serious attention to the issue of research with those lacking decisional capacity in October 1973. At that time, the Secretary of DHEW issued a notice of "proposed rulemaking" and commented that "DHEW through the National Institutes of Health, had appointed a special study group to review and recommend policies and special procedures for the protection of children, prisoners, and the institutionalized mentally infirm in research...."¹⁶ A draft of the study group's report was published in the Federal Register in November, 1973.¹⁷ The report was not considered proposed rulemaking but rather "a draft working document" for public review and comment.¹⁸

The draft defined "mentally infirm" as the "mentally ill, the mentally retarded, the emotionally disturbed, the psychotic, the senile,

¹⁶Protection of Human Subjects, 38 Fed. Reg. 31,738, 31,738 (1973) (proposed Nov. 16, 1973).

¹⁷*See id.*

¹⁸*See id.* The Federal Register Notice, in fact, stated "[i]t must be clearly understood by the reader that the material that follows is *not* proposed rulemaking in the technical sense, and is not presented *as* Departmental, Public Health Service, or NIH policy. Rather it is a draft working document on which early public comment and participation is invited." *Id.* The drafters also recognized the controversial nature of the proposal. In the introduction to the draft, Robert S. Stone, Director of the National Institutes of Health, commented that "[t]here may be elements in the recommendations which will provoke debate and controversy." *Id.*

and others with impairments of a similar nature, residing as patients in an institution, regardless of whether or not the individual has been determined to be legally incompetent.”¹⁹ Individuals institutionalized as mentally infirm were considered especially in need of protections for two reasons. First, they “might lack the...capacity to comprehend relevant information, and to make informed judgments concerning their participation” in research.²⁰ Second, “they experience a diminished sense of personal integrity as a result of confinement in an institution.”²¹

Of particular focus was the question of informed consent and how it might be obtained in order to conduct research with individuals in this category.²² In the section on “general policy considerations,” the draft stated:

Whereas it is clear by law that consent of a parent or legal representative is valid for established and generally accepted therapeutic procedures performed on a child or an incompetent adult, it is far from clear that it is adequate for research procedures. In practice, parental or guardian consent generally has been accepted as adequate for therapeutic research, although the issue has not been definitively resolved in the courts. When research might expose a subject to risk without defined therapeutic benefit or other positive effect on that subject’s well-being, parental or guardian consent appears to be insufficient.²³

¹⁹*Id.* at 31,740.

²⁰*Id.*

²¹*See* Protection of Human Subjects, 38 Fed. Reg. at 31,745.

²²*See id.* at 31,740.

²³*Id.* The draft also raised the possibility that legal guardians might not always have the best interest of the institutionalized individual foremost in their decisionmaking. Because long-term management of patients with mental disabilities is very expensive and time-consuming, the draft speculated that a research proposal that might “reduce either the expense or the supervision required in caring for such persons might be appealing, whether or not there is correlative benefit to the patient.” *Id.* at 31,745.

The draft concluded that, in general, research on the mentally infirm was not acceptable.²⁴ The draft did leave the door open, however, for some types of research.²⁵ These included “projects in which: the proposed research concerns diagnosis, treatment, prevention, or etiology of the disability from which [the subjects] suffer; the necessary information can be obtained only from those subjects; or the studies concern institutional life *per se*.”²⁶ The draft further required that the subject’s legal guardian give consent to the individual’s participation in any research protocol, and that where the individual had “sufficient mental competency to understand what [was] proposed and to express an opinion as to his or her participation” that the individual give his or her consent.²⁷

In cases where a protocol included mentally infirm subjects, the research was to be overseen by a “Protection Committee.”²⁸ The Protection Committee was to be overseen by an “Organizational Review Committee of the institution in which the research” was to be conducted or by which the research was sponsored.²⁹ The Protection Committee³⁰ was to provide guidance in the selection of subjects, monitor the progress of the research with special attention to “adverse effects on subjects,” “evaluat[e] the process and reasonableness of consent of the legal guardian and (where applicable) of the subject,” and advise the legal guardian and subject of the appropriateness of the subject’s continued participation in the research.³¹ Members of the committee could not have “any association with the research under review and the majority of members could not have any association

²⁴*See id.*

²⁵*See id.*

²⁶*See* Protection of Human Subjects, 38 Fed. Reg. at 31,745.

²⁷*Id.* at 31,748.

²⁸*Id.* at 31,745.

²⁹*Id.*

³⁰*See id.* at 31,746 (stating that the Protection Committee was to be composed of at least five members who would be competent to “deal with the medical, legal, social and ethical issues involved in the [proposed research]”).

³¹*See* Protection of Human Subjects, 38 Fed. Reg. at 31,748.

with any organization or individual conducting or supporting the [research].”³²

The Organizational Review Committee, in addition to its obligations for all research on human subjects within an institution, was to ensure that all aspects of the research would be “ethically appropriate for performance on healthy individuals,” “conduct at least one on-site visit” to the institution where the research was being performed, “prepare a report of the visit,”³³ and “review and approve or modify the procedures proposed by the applicant to be followed by the Protection Committee in subject selection and recruitment.”³⁴

Based on critical commentary received on the draft report, in August 1974, DHEW published its proposed rules for research on vulnerable subjects.³⁵ When these proposed rules were issued, however, the agency’s Federal Register notice pointed out that “[c]oincidentally with the development of the notice of proposed rulemaking set forth [herein],” the National Research Act was passed by both Houses of Congress and signed by the President.³⁶ The Act established an eleven-member National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research.³⁷ The Commission was charged with identifying the basic ethical principles that should underlie the conduct of human subject research and

³²*Id.* at 31,746. Furthermore, “no more than one-third of the members [could] be individuals engaged in research, development, or demonstration activities involving human subjects.” *Id.*

³³*Id.* at 31,748. The report was to include “discussion of such matters as living conditions, availability of medical care, and quality of food.” *Id.*

³⁴*Id.*

³⁵*See* Protection of Human Subjects, 39 Fed. Reg. 30,648, 30,652 (1974) (to be codified at 45 C.F.R. pt. 46) (proposed Aug. 23, 1974). On May 30, 1974, HEW published basic regulations governing research with all human subjects, *See* Protection of Human subjects, 30 Fed. Reg. 18,914 (1974) (to be codified at 45 C.F.R. pt. 46)(proposed May 30, 1974). DHEW stated in the preamble to those regulations that it would “propose further rules to provide additional protection for research subjects with diminished capacity to provide informed consent, including institutionalized individuals with mental disability.” Protection of Human Subjects, 43 Fed. Reg. 53,950, 53,950 (1978) (to be codified at 45 C.F.R. pt. 46) (proposed Nov. 17, 1978).

³⁶*See* Protection of Human Subjects, 39 Fed. Reg. at 30,648.

³⁷*See* National Research Act, Pub. L. No. 93-348, § 201(b)(1), 88 Stat. 342 (1974).

developing guidelines for research to assure that it be conducted in accordance with these ethical principles.³⁸ More specifically, the Commission was required to address research with children, prisoners, and those institutionalized as mentally infirm.³⁹

In light of the four hundred and fifty comments regarding the November 1973 proposed guidelines for research on vulnerable populations, DHEW made several modifications to its earlier draft.⁴⁰ DHEW received over forty comments specifically directed at the provisions covering research on the institutionalized mentally infirm.⁴¹ One common criticism was the use of the term "infirm."⁴² Commenters noted that it reflected an "antiquated notion of mental illness."⁴³ DHEW agreed with the concern and changed the term to disabled.⁴⁴

In contrast, DHEW rejected suggestions that, in its view, weakened what it considered essential protections for those institutionalized as mentally infirm.⁴⁵ For example, some argued that the restriction limiting research with this population to protocols that related to the particular subject's impairment was too narrow.⁴⁶ Instead, they suggested, the provision should include "any illness from which the person suffers so that, for example, an institutionalized mentally disabled person with cancer could not be denied the benefits of research in cancer therapy."⁴⁷ Despite these arguments, the Department concluded that research unrelated to the cause of this vulnerable population's mental disability was not appropriate because of the potential risks to the group.⁴⁸ As in the earlier draft, research could

³⁸See *id.* at § 202(a)(1)(A)(i).

³⁹See *id.* at § 202(a)(2).

⁴⁰See Protection of Human Subjects, 39 Fed. Reg. 30,648 (1974) (to be codified at 45 C.F.R. pt. 46) (proposed Aug. 23, 1974).

⁴¹See *id.* at 30,652.

⁴²See *id.*

⁴³See *id.*

⁴⁴See *id.*

⁴⁵See Protection of Human Subjects, 39 Fed. Reg. at 30,652.

⁴⁶See *id.*

⁴⁷*Id.*

⁴⁸See *id.*

only be performed on those institutionalized as mentally disabled if it was "related to the etiology, pathogenesis, prevention, diagnosis, or treatment of mental disability or the management, training or rehabilitation of the mentally disabled and [sought] information which [could] not be obtained from subjects who [were] not institutionalized mentally disabled."⁴⁹

Furthermore, DHEW retained the original scope of the proposal, largely rejecting suggestions that regulations should be established for research involving "students, laboratory employees, seriously ill or terminal patients, the noninstitutionalized mentally disabled, and other special groups."⁵⁰ DHEW's response to this suggestion was that "abuses relat[ed] to these groups [were] less evident and that they [were] afforded the protection of the existing regulations" governing all human subjects.⁵¹ DHEW did state, however, that it would consider dealing with those who were legally incompetent but not institutionalized in a subsequent notice of proposed rulemaking.⁵²

The National Commission's Process and Recommendations

DHEW did not move forward in this area while the National Commission was performing its own analyses regarding research with those institutionalized as mentally infirm. The task of the Commission on this topic specifically was to:

- (1) Identify the requirements for informed consent to participation in biomedical and behavioral research by the institutionalized mentally infirm, and
- (2) investigate and study biomedical and behavioral research conducted or supported under programs administered by the Secretary of HEW and involving the

⁴⁹*Id.* at 30,655.

⁵⁰*See* Protection of Human Subjects, 39 Fed. Reg. at 30,648.

⁵¹*Id.*

⁵²*See id.* at 30,652.

institutionalized mentally infirm to determine the nature of the consent obtained.⁵³

The Commission was to use this information as a basis for making recommendations to the Secretary of Health, Education, and Welfare "to assure that biomedical and behavioral research conducted or supported under programs administered by him met the requirements respecting informed consent identified by the Commission."⁵⁴

On April 10, 1976, the Commission conducted a public hearing on the issue of research involving the mentally infirm.⁵⁵ Commentators included both researchers and advocates for this population. The comments reflected the environment in which research on this population was conducted and the attitudes of those engaged in this research at the time.⁵⁶ Virtually all of those commenting supported the research enterprise, believing it necessary to make progress in the care and treatment of the mentally infirm.⁵⁷ The differences among the comments focused on the extent to which research on this population should be regulated beyond existing DHEW requirements for human subject research generally.⁵⁸

The view of researchers that additional regulation may be counterproductive was perhaps best expressed by Dr. Roger Meyer, of Harvard Medical School, who commented that "the current environment is hostile toward needed research in biology and behavioral sciences."⁵⁹ He and others also expressed the view that it was inappropriate to categorize all individuals with mental disabilities as unable to give consent; doing so, in fact, ran "counter to modern concepts of mental illness and to court decisions which have restored their civil rights and limited judgments of incompetency."⁶⁰

⁵³Protection of Human Subjects, 43 Fed. Reg. at 11,328 (Mar. 17, 1978).

⁵⁴*Id.*

⁵⁵*See id.* (summarizing the testimony of fourteen individuals).

⁵⁶*See id.*

⁵⁷*See id.*

⁵⁸*See* Protection of Human Subjects, 43 Fed. Reg. at 11,352-55.

⁵⁹*Id.* at 11,352.

⁶⁰*Id.*

Among advocates for the mentally infirm, the statement by the American Bar Association's (ABA) Commission on the Mentally Disabled was the most detailed.⁶¹ While the ABA's Commission generally supported the practice of research with this population, it asserted that "experimentation" on this group should only be permitted when, among other criteria, "the research poses no more than minimal risk."⁶² The ABA Commission further argued that nontherapeutic research should not be performed over the objection of any subject, no matter how the objection is expressed.⁶³ Therapeutic research should only be carried out on those institutionalized as mentally infirm under these criteria, with two exceptions.⁶⁴ More than minimal risk research could be performed if "absolutely necessary to preserve the life, health or physical safety of the research subject" and if there was evidence of a "high level of therapeutic justification, the objections of [the subject] could be overridden with proper third-party consent and review

⁶¹*See id.*

⁶²*Id.* The ABA Commission advocated the following prerequisites:

- (1) The protocol has scientific merit, verified by an independent multidisciplinary committee;
- (2) medical care, direct care and other institutional services are sufficient;
- (3) the experimentation will not reduce the amount or quality of therapy available to research subjects or to other residents;
- (4) the research poses no more than minimal risk;
- (5) the research is related to mental disability and seeks information that cannot be obtained from other subject groups; and
- (6) the information sought is of significance for the advancement of acknowledged scientific or medical goals.

Id. at 11,353.

⁶³*See* Protection of Human Subjects, 43 Fed. Reg. at 11,353.

⁶⁴*See id.*

procedures.”⁶⁵ Furthermore, the term “therapeutic” was to be strictly defined “in terms of individual necessity and benefits.”⁶⁵

Of all the advocacy groups, Stewart Brown, representing the Pennsylvania Association for Retarded Citizens, took a position that was perhaps most protective of potential subjects.⁶⁷ He argued that those conducting research on this population should be “qualified and licensed” and that a “regulatory-type agency should enforce regulations and impose sanctions where violations [were] discovered.”⁶⁸

On March 17, 1978, DHEW published Notice of the National Commission’s Report and Recommendations on *Research Involving Those Institutionalized As Mentally Infirm*⁶⁹ and asked for public comments before May 16, 1978.⁷⁰ In the Report, the Commission recommended that research involving those institutionalized as mentally infirm be conducted or supported only when “an Institutional Review Board”⁷¹ reviewed the research design, the qualifications of the research investigator, and the adequacy of pre-clinical studies.⁷² With respect to the rights and welfare of human subjects, the IRB was to determine that:

⁶⁵*Id.*

⁶⁶*Id.*

⁶⁷*Id.* at 11,355.

⁶⁸*See* Protection of Human Subjects, 43 Fed. Reg. at 11,355.

⁶⁹The Commission retained the term “mentally infirm” because this term was used in the 1974 National Research Act. The Commission acknowledged, however, the comments received on DHEW’s November 16, 1973, proposed policy stating that the term should not be used. *See id.* at 11,329.

⁷⁰*See id.*

⁷¹*See* National Research Act, Pub. L. No. 93-348, § 474(a), 88 Stat. 342 (1974) (stating that “[t]he Secretary [of HEW] shall by regulation require that each entity which applies for a grant or contract under this Act for any project or program which involves the conduct of biomedical or behavioral research involving human subjects submit in or with its application for such grant or contract assurances satisfactory to the Secretary that it has established (in accordance with regulations which the Secretary shall prescribe) a board (to be known as an ‘Institutional Review Board’) to review biomedical and behavioral research involving human subjects conducted at or sponsored by such entity in order to protect the rights of the human subjects of such research.”)

⁷²*See* Protection of Human Subjects, 43 Fed. Reg. at 11,328, 11,330.

⁷³*Id.*

- there are good reasons to involve institutionalized persons in the conduct of the research;
- risk of harm or discomfort is minimized by using the safest procedures consistent with sound research design and by using procedures performed by diagnostic or treatment purposes whenever possible;
- adequate provisions [have been] made to protect the privacy of the subjects and to maintain confidentiality of data;
- selection of subjects among those institutionalized as mentally infirm will be equitable; [and]
- adequate provisions [have been] made to assure that no prospective subject will be approached to participate in the research unless a person who is responsible for the health care of the subject has determined that the invitation to participate in the research and such participation itself will not interfere with the health care of the subject.⁷³

Of particular concern to the Commission was that individuals institutionalized as mentally infirm not be included in research studies where it was possible to obtain the same information from noninstitutionalized individuals.⁷⁴ The IRB, then, was to consider whether the research being proposed would be “exploitive” of the institutionalized population by assessing whether the research would be

⁷³*Id.*

⁷⁴*See id.* at 11,331. Under contract with the Commission, the Survey Research Center at the University of Michigan (SRC) examined research being conducted around the country with individuals institutionalized as mentally infirm. The SRC report was based on a sample of studies reviewed by IRBs at 61 institutions. Research on this population constituted 9 percent of the research reviewed by these IRBs. In terms of subject selection, the SRC found that in “13% of projects involving the mentally infirm, the investigator did not mention the mental condition of the subjects as a factor in subject selection.” The Commission speculated that it was possible that these studies could have been conducted on other populations and may have been conducted on this population as a means of convenience. *Id.* at 11,341.

“relevant to the subjects’ emotional or cognitive disability, whether individuals with the same disability [would be] reasonably accessible to the investigator outside the institutional setting, and whether the research [was] designed to study the nature of the institutional process or the effect of some aspect of institutionalization on persons with a particular disability.”⁷⁵ Concerning selection of subjects within the institution, the Commission recommended that subjects be selected so that “any burdens of research do not fall disproportionately on those who are least able to make decisions regarding participation in research.”⁷⁶ The Commission also addressed the situation in which a potential subject’s physician or therapist was involved in the proposed research.⁷⁷ In those situations, in order to avoid conflicts of interest, the Commission recommended that “independent clinical judgment” be obtained to determine the appropriateness of including a patient in the proposed research.⁷⁸

The Commission’s report included an influential analysis of the relationship among the risk-benefit profile of the research, subject assent, and third-party consent.⁷⁹ If the research in question involved *no more than minimal risk*⁸⁰ and the subject was incapable of

⁷⁵*Id.* at 11,331.

⁷⁶*Id.*

⁷⁷Protection of Human Subjects, 43 Fed. Reg. at 11,331–32.

⁷⁸*Id.* The SRC report, done for the Commission, found that in approximately 25 percent of the research with the mentally infirm, investigators enrolled their own patients. *See id.* at 11,341.

⁷⁹The SRC study investigators found that written consent was sought in more than 80 percent of the research they reviewed involving the mentally infirm. Third-party consent was obtained in approximately one third of these cases. Third-party consent was most frequently obtained in research involving the mentally retarded and was obtained from the subject’s parents, other relatives, or legal guardians. *See id.* at 11,342. When interviewed, “most investigators reported that third party consent served to protect subjects “very well” or “fairly well,” but almost one-fifth of the investigators indicated otherwise. Reasons given included the third party’s not being able to understand the research or not caring about protecting the subject’s rights. *Id.*

⁸⁰Minimal risk was defined by the Commission to mean the “risk (probability and magnitude of physical or psychological harm or discomfort) that is normally encountered in the daily lives, or in the routine medical or psychological examination, of normal persons.” *Id.* at 11,332. For subjects institutionalized as mentally infirm, the Commission elaborated that “routine examination procedures present no more than minimal risk if the likely impact of such

consenting, the Commission stated that the research must be “relevant to the subject’s condition.”⁸¹ In addition, the Commission recommended that the subject “assent”⁸² or, at least not object to participation.⁸³ If the subject did object, the subject could not participate in the research unless authorized to do so by a court of competent jurisdiction.⁸⁴ In such cases, the Commission recommended that this authorization not be sought unless the research included an intervention or monitoring procedure that would be of direct benefit to the subject.⁸⁵ In addition, “where appropriate,” the Commission recommended that the IRB appoint “a consent auditor” to “observe the consent process and determine...whether each prospective subject consents, or being incapable of consenting, assents or objects to participation in the research.”⁸⁶

procedures on them is similar to what would be experienced by normal persons undergoing the procedures.” *Id.* On the other hand, the Commission Report stated that an:

IRB may determine that prospective subjects who are institutionalized as mentally infirm are likely to react more severely than normal persons to certain routine procedures; in such instances, the procedures present more than minimal risk to the subjects.... For each research protocol, the IRB must determine the degree of risk that would be presented to normal persons and then consider whether such risk is heightened by the illness or institutionalization of the prospective subjects or class of subjects.

Id.

⁸¹*Id.*

⁸²The Commission used the term assent to “describe authorization by a person whose capacity to understand and judge is somewhat impaired by illness or institutionalization, but who remains functional.” Protection of Human Subjects, 43 Fed. Reg. at 11,332. It further explained the standard as requiring “that the subject know what procedures will be performed in the research, choose freely to undergo those procedures, communicate this choice unambiguously, and be aware that subjects may withdraw from participation.” *Id.* The standard was “intended to require a lesser degree of comprehension by the subject than would generally support informed consent.” *Id.*

⁸³*See id.*

⁸⁴*See id.*

⁸⁵*See id.*

⁸⁶*Id.*

If the research under consideration involved *greater than minimal risk*, the Commission recommended that the research not be performed on this population unless it included an intervention that held out the prospect of direct benefit⁸⁷ to the subject or included a monitoring procedure “necessary to maintain the well-being of those subjects.”⁸⁸ This risk would be acceptable if “all available treatments for a serious condition [had] been tried without success, and the remaining option [was] a new intervention under investigation.”⁸⁹ If the subject was incapable of consenting, the Commission recommended that the subject assent to participation.⁹⁰ If the subject was incapable of assenting but did not object to participation, the Commission stated that the permission of a guardian or court should be obtained.⁹¹ If, however, the subject objected to participation in the research, his or her participation could only be authorized by a court of competent jurisdiction and only if the prospective benefit could not be obtained other than by participating in the research.⁹² For this type of research, the Commission recommended that an IRB determine the need to appoint an auditor “to observe and assure the adequacy of the consent process...”⁹³ and if there was a “substantial question about the ability of the subjects to assent or there [was] a significant degree of risk involved in the research, the appointment of a consent auditor by the IRB would be appropriate.”⁹⁴

⁸⁷See Protection of Human Subjects, 43 Fed. Reg. at 11,332. The Commission described a direct benefit as one that held out the possibility of fairly immediate benefit. *Id.* at 11,333.

⁸⁸See *id.* at 11,333.

⁸⁹*Id.*

⁹⁰See *id.* at 11,332.

⁹¹See *id.*

⁹²Protection of Human Subjects, 43 Fed. Reg. at 11,332. An example of this type of situation, according to the Commission, would be where a new drug is being tested by the FDA for effectiveness and its use is not permitted outside of the drug trial. See *id.* at 11,333.

⁹³*Id.* The auditor was not to be involved “(except in the capacity of consent auditor) with the research for which subjects [were] being sought.” In addition, the auditor was to be a person “familiar with the physical, psychological and social needs of the class of prospective subjects, as well as their legal status.” *Id.*

⁹⁴*Id.*

The Commission also addressed research that posed *greater than a minimal risk with no possibility of direct benefit* to the subject population.⁹⁵ Under these circumstances, the research could be conducted only if the anticipated risk of participation in the research was a “minor increase over minimal risk,”⁹⁶ the knowledge expected from the research was “of vital importance for the understanding or amelioration of the type of disorder or condition of the subjects” or could “reasonably be expected to benefit the subjects in the future.”⁹⁷ Regarding participation of subjects incapable of giving consent, participation would be permissible if the subject assented to participation.⁹⁸ If the subject was incapable of assenting but did not object to participation, the subject could participate only with the consent of a legally appointed guardian.⁹⁹ If the subject objected to participation, he or she could not participate in the research.¹⁰⁰ For this level of risk, the Commission recommended the mandatory appointment of a consent auditor by the IRB to observe the consent process and “determine whether each subject consents, or is incapable of consenting and assents, or objects to participation.”¹⁰¹

⁹⁵*See id.* at 11,334.

⁹⁶*Id.* at 11,333.

⁹⁷Protection of Human Subjects, 43 Fed. Reg. at 11,333. Such benefit could be remote to the subjects, “such as the eventual development of better treatment for their condition.” *Id.* at 11,334. As the Commission wrote in its later *Belmont Report*:

Some populations, especially institutionalized ones, are already burdened in many ways by their infirmities and environments. When research is proposed that involves risks and does not include a therapeutic component, other less burdened classes of persons should be called upon first to accept these risks of research, *except where the research is directly related to the specific conditions of the class involved.*

THE NATIONAL COMMISSION FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, THE BELMONT REPORT: ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH 19 (1978) (emphasis added).

⁹⁸*See* Protection of Human Subjects, 43 Fed. Reg. at 11,334.

⁹⁹*See id.*

¹⁰⁰*See id.*

This recommendation was particularly controversial even among Commission members.¹⁰² One commissioner, in fact, submitted a dissenting statement focusing on this recommendation, in which he argued as follows:

Since it is accepted that normal persons should not be enrolled in nontherapeutic research with more than minimal risk unless they can give informed and meaningful consent, it is doubly unreasonable that the institutionalized mentally infirm should be so enrolled when society has had so much recent concern for their greater protection, and when they live in environments which seriously discourage any kind of decision making and the nature of their illnesses weakens their abilities to choose responsibly in most of life's usual situations.¹⁰³

Lastly, the Commission addressed research that involved *greater than a minor increase above minimal risk and did not hold out the prospect of direct benefit to the subject.*¹⁰⁴ Under these circumstances, the research could only be performed if:

(II) The research present[ed] an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of persons institutionalized as mentally infirm; and

(B) A national ethical advisory board and, following opportunity for public review and comment, the head of the responsible Federal department or agency have determined that:

(I) The conduct of the research will be in accord with the

¹⁰¹*Id.* In all cases, the consent auditor was to be independent of the research team. *See id.* at 11,357.

¹⁰²*Id.*

¹⁰³Protection of Human Subjects, 43 Fed. Reg. at 11,358 (Robert E. Cooke, Commissioner, dissenting).

¹⁰⁴*See id.* at 11,334.

basic ethical principles that should underlie the conduct of research involving human subjects; and

(II) adequate provisions are made for obtaining consent or assent of each subject or permission from a guardian of the person.¹⁰⁵

The Commission stated explicitly that “because of the importance of the ethical issues at stake, debate [on this type of research] should be in a public forum, and conduct of the research should be delayed pending Congressional notification and a reasonable opportunity for Congress to take action regarding the proposed research.”¹⁰⁶

Revisions by the Department of Health, Education, and Welfare

On November 17, 1978, eight months after the Commission’s Report was printed in the Federal Register, DHEW issued its proposed rules on *Research Involving Those Institutionalized as Mentally Disabled*.¹⁰⁷ The proposed rules took into consideration the more than one hundred comments received on the Commission’s report.¹⁰⁸ While the proposed rules “in essence” accepted the Commission’s recommendations, they did depart from the Commission in some significant ways.¹⁰⁹ For example, the proposed rules included a statement that DHEW was considering a requirement that consent auditors be appointed for *all* research with this population (even minimal risk research) and that an independent advocate be appointed for each research subject.¹¹⁰

¹⁰⁵*Id.*

¹⁰⁶*Id.*

¹⁰⁷Protection of Human Subjects, 43 Fed. Reg. 53,950, 53,950 (1978) (to be codified at 45 C.F.R. pt. 46) (proposed Nov. 17, 1978). DHEW formally rejected the term “mentally infirm” and adopted the term “mentally disabled” in large part as a result of comments received on their November 16, 1974 proposed policy.” *Id.*

¹⁰⁸*See id.*

¹⁰⁹*See id.*

¹¹⁰*See id.* at 53,952. An advocate was defined to mean an individual appointed by the IRB to act “in the best interests of the subject” and who would be “construed to carry the fiduciary responsibilities of a guardian ad litem” toward the subject. This individual could not

For subjects determined capable of assenting but not consenting, DHEW also stated that it was considering whether to: 1) follow the Commission's recommendation to allow the subjects' participation if their guardians or legally authorized representatives (LAR), as DHEW termed them,¹¹¹ consented, or 2) require additional protections including the "consent of...the Secretary, based upon the advice of an expert panel, or...an advocate."¹¹² Also, with regard to subjects incapable of assenting, the Department stated that it was considering whether to:

- (1) [b]ar their involvement in such research (on the assumption that needed research could be done using other subjects);
- (2) adopt the Commission's recommendation, which would permit their participation if they do not object and the legally authorized representative and a court of competent jurisdiction give their approval;
- (3) require, in addition to the approval of the legally authorized representative and the court, approval by the Secretary; or
- (4) require, in addition to that of the representative and the court, approval by an advocate.¹¹³

These rules were clearly more protective of research subjects institutionalized as mentally disabled than those proposed by the

have any financial interest in the institution conducting or sponsoring the research. Moreover, an advocate was to be familiar with "the physical, psychological, and social needs and the legal status of the class of individuals institutionalized as mentally disabled in the institution in which the research is conducted." *Id.* at 53,955.

¹¹¹The term "legally authorized representative" was substituted by DHEW for the term "guardian" by the Commission "since the latter [it said] is normally associated with persons having responsibility for minors, while these regulations apply both to adults and minors institutionalized as mentally disabled." *Id.* at 53,952.

¹¹²Protection of Human Subjects, 43 Fed. Reg. at 53,952.

¹¹³*Id.*

Commission. They were also the subject of considerable controversy. In fact, the proposed rules were ultimately rejected primarily because of comments from researchers that they would prevent needed research.¹¹⁴

According to Al Jonsen, a former member of the National Commission and prominent bioethicist, "officials at the National Institute of Mental Health (NIMH) and the Agency for Drug Addiction and Mental Health Association, objected that the recommendations would stifle important research with their populations."¹¹⁵ Groups like the Association of American Medical Colleges also found the proposed regulations overly burdensome, commenting that the requirements of consent auditor, patient advocate, and appointment of a guardian were "ponderous mechanisms of no demonstrated value."¹¹⁶

Twice in the next several years, the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research urged the Department to take up this issue again.¹¹⁷ However, according to at least one source, the Department "declined to do so, reportedly due to a lack of consensus on the need for them as well as the alleged adequacy of existing regulations."¹¹⁸

¹¹⁴Although these proposed rules were never adopted, DHEW did adopt rules for research on other vulnerable populations including prisoners, pregnant women and fetuses and children. See 45 C.F.R. § 46.205 (2000) (providing for "additional protections pertaining to research, development, and related activities involving fetuses, pregnant women, and human in vitro fertilization").

¹¹⁵See Jonathan Moreno, *supra* note 4, at 13.

¹¹⁶Letter from John A. D. Cooper, M.D., *President of AAMC*, to Honorable Joseph A. Califano, Jr., *Secretary of Health, Education, and Welfare* (Jan. 16, 1979) (on file with the authors).

¹¹⁷See Clarence J. Sundram, *In Harm's Way: Research Subjects Who Are Decisionally Impaired*, 1 J. HEALTH CARE L. & POL'Y 36, 45 (1998).

¹¹⁸*Id.* (citing Robert J. Levine, *Proposed Regulations for Research Involving Those Institutionalized as Mentally Infirm: A Consideration Of Their Relevance in 1996*, IRB, Sept.-Oct. 1996, at 1).

**SOCIETAL TRENDS INFLUENCING THE NATURE OF
POTENTIAL REGULATION:
FROM THE 1970s TO THE 1990s**

Between the late 1970s and late 1990s, there were no new significant efforts to regulate research with the decisionally impaired population. Yet, during that time a number of significant societal, legal and medical changes took place that profoundly influenced attitudes toward the care and treatment of the decisionally impaired and may have affected the more recent proposals to regulate research with the decisionally impaired as well as how different groups now view the need for regulation of research with this group. These developments, described below, provide the backdrop for analyzing the recent proposals for regulation and the political reaction to them.

Deinstitutionalization

In the first half of the 20th century, aggressive efforts at finding treatments and cures for mental illness were undertaken in institutional settings.¹¹⁹ Although psychoanalysis or talk therapy, based on the work of Sigmund Freud in the late 1800s, had become the cornerstone of psychiatric practice, other, more interventionist, techniques were also developed with mixed results.¹²⁰ Electroconvulsive therapy, a way of producing seizures through the administration of electrical shocks, became widespread in the treatment of psychosis.¹²¹ While effective in some patients, electroconvulsive therapy often resulted in disconcerting side effects, such as memory loss.¹²² During the 1930s, a surgical procedure known as a lobotomy, in which the frontal lobes of the brain

¹¹⁹See MICHAEL H. STONE, *HEALING THE MIND: A HISTORY OF PSYCHIATRY FROM ANTIQUITY TO THE PRESENT* 139-174 (1997).

¹²⁰See *id.*

¹²¹See RALPH REISNER & CHRISTOPHER SLOBOGIN, *LAW & THE MENTAL HEALTH SYSTEM: CIVIL AND CRIMINAL ASPECTS* 870 (2nd ed. 1990).

¹²²See Note, *Regulation of Electroconvulsive Therapy*, 75 MICH. L. REV. 363, 368 (1976).

were removed, was shown to reduce aggressiveness in animals.¹²³ A modified form of the procedure was performed on humans.¹²⁴

While helping some of the mentally ill, these treatments were generally ineffective in the treatment of schizophrenia and the number of individuals in the country with the illness grew considerably.¹²⁵ In 1954, however, a breakthrough in treatment of schizophrenia came with the availability of a drug called chlorpromazine,¹²⁶ a tranquilizer. The new drug was able to sedate individuals without the systemic effects of other tranquilizers available at the time.¹²⁷ Those who administered the drug to schizophrenic patients in mental institutions reported dramatic results.¹²⁸ In the late 1950s and early 1960s, a number of other antipsychotic drugs came on the market.¹²⁹ None were any more effective but they differed in terms of side effects and dosing requirements.¹³⁰ These “antipsychotics” became widely available and allowed many who had spent years in institutions to live in the community.¹³¹

¹²³See VICTORIA SHERROW, *MENTAL ILLNESS* 45 (1996).

¹²⁴See *id.* at 46 (stating that “[b]y 1960, about fifty thousand lobotomies had been performed in America, most on patients labeled incurable. Lobotomies reduced violent behavior in some patients but did not restore normal functioning. Many were left in a vegetative state, with severe brain damage; others developed seizure disorders. About 5 percent died.”)

¹²⁵See *id.* (“In 1904, about two out of every one thousand Americans were diagnosed as schizophrenic. By 1955, that number had doubled”).

¹²⁶Chlorpromazine is also known by the trade name Thorazine. It was the first of the antipsychotics, which are sometimes referred to as neuroleptics or drugs that act on the nervous system. See MERRIAM WEBSTER’S COLLEGIATE DICTIONARY 781 (10th ed. 1993) (a neuroleptic is “any of the powerful tranquilizers (as the phenothiazines) used especially to treat psychosis and believed to act by blocking dopamine nervous receptors...”).

¹²⁷See RENÉ SPIEGEL, *PSYCHOPHARMACOLOGY: AN INTRODUCTION* 36-40 (3rd ed. 1996). See also Richard Mindham, *Pharmacological Aspects of Mental Illness*, in *MENTAL ILLNESS: CHANGES AND TRENDS* 206 -207 (Phillip Bean, ed., 1983).

¹²⁸See SPIEGEL, *supra* note 127, at 39- 40; see also Mindham, *supra* note 127, at 206.

¹²⁹See STONE, *supra* note 119, at 188. Examples of these early antipsychotics include haloperidol (Haldol) and thioridazine (Mellaril). See *id.*

¹³⁰See Mindham, *supra* note 127, at 207.

¹³¹These drugs were specifically aimed at schizophrenia. While the drugs were effective, they all had significant side effects. Some of these side effects included “acute dysonia (muscle spasms) and akathisia (restlessness). *Id.* at 208. In addition, these agents

In 1955, the number of residents in mental hospitals was at its all time peak of 559,000.¹³² As the “introduction of neuroleptic drugs became widespread”¹³³ and individuals could be treated as outpatients, a long-term decline in the number of residents in these institutions began.¹³⁴ By 1970, the number of inpatients in these facilities was 339,000.¹³⁵ By 1978, the trend toward deinstitutionalization was well on its way.¹³⁶ In 1989 the number of institutionalized individuals was approximately 100,000.¹³⁷

While the process of deinstitutionalization began in the 1950s, fostered by exposés of sometimes abysmal conditions¹³⁸ and by the availability of major tranquilizers,¹³⁹ certain events accelerated the deinstitutionalization effort.¹⁴⁰ The push for deinstitutionalization was part of the larger “community mental health movement” advocated by President John F. Kennedy.¹⁴¹ As part of this movement, “[p]oliticians, mental health professionals, and others spoke out on behalf of the mentally ill, challenging the long-standing stigma against them. The government took a more active role in promoting mental health and

were thought to have a greater likelihood of producing a long-term, irreversible neurological side effect known as tardive dyskinesia (uncontrollable muscle spasms). *See id.*

¹³²*See* Richard W. White, Jr., *Mental Patients' Rights Should Be Limited*, in *MENTAL ILLNESS: OPPOSING VIEWPOINTS* 195, 199 (William Barbour ed., 1995).

¹³³*Id.*

¹³⁴*See id.*

¹³⁵*See id.*

¹³⁶*See id.* at 199-200.

¹³⁷*See* DAVID A. ROCHEFORT, *FROM POORHOUSES TO HOMELESSNESS: POLICY ANALYSIS AND MENTAL HEALTH CARE* 219 (1993).

¹³⁸*See id.* In an illustrated exposé of the problems of mental health institutions in *Life* magazine in 1946 entitled “Bedlam 1946,” journalist Albert Maisel called these institutions “a shame and a disgrace.” *Id.* at 672. Some reports revealed that patients were being used as guinea pigs to test improbable hypotheses about the causes of mental illness. One physician, Dr. Henry Cotton, removed the tonsils and teeth of many patients, to prevent the infections that he believed could cause mental illness. Other physicians, believing that extreme fevers might reduce mental illness, exposed patients intentionally to infectious diseases such as malaria and typhoid to bring on a high fever. SHERROW, *supra* note 123, at 60.

¹³⁹*See* STONE, *supra* note 119, at 203.

¹⁴⁰*See* Albert R. Roberts & Linda Farris Kurtz, *Historical Perspectives on the Care and Treatment of the Mentally Ill* 14 J. SOCIOLOGICAL & SOCIAL WELFARE 75, 85 (1987). *id.*

¹⁴¹*See id.* at 82-85.

making services available to more people throughout the country.”¹⁴² These activities included increased funding for the study of mental illness¹⁴³ and a promise of increased federal support for the care of the mentally ill.¹⁴⁴

A combination of aggressive litigation and federal financial support for individuals outside of institutions further accelerated the deinstitutionalization of mentally ill individuals.¹⁴⁵ A 1972 law suit, *Wyatt v. Stickney*,¹⁴⁶ advanced the claim that involuntarily committed patients had a right to treatment.¹⁴⁷ This treatment entailed, as one commentator opined, “staffing ratios and physical amenities so expensive that hospitals could not afford to meet them.”¹⁴⁸ As a result, while a few institutions did improve their conditions, many state mental hospitals began to discharge patients more rapidly in order to achieve improved staff-to-patient ratios.¹⁴⁹ According to one author, in addition to other lawsuits, the availability of federal Supplemental Security

¹⁴²See SHERROW, *supra* note 123, at 55. This governmental interest in mental health was in large part a result of the military’s experience during World War II. About 18 percent of draftees were rejected because of some type of mental illness. *See id.* at 56. Individuals who served in the war were also vulnerable to mental health problems due to the prolonged stress of military service. *See id.*

¹⁴³*See id.* at 57 (stating that, in 1946, Congress established the National Institute of Mental Health, which was to improve services for the treatment of mental health and conduct research on the causes of mental health problems).

¹⁴⁴See SHERROW, *supra* note 123, at 64. In 1955, Congress established the Joint Commission on Mental Illness and Health, which conducted the first “nationwide survey of mental illness in the United States.” *Id.* at 64. In its 1960 report, the Commission made note of the disparity that had long existed in funding for mental health programs as compared to other medical problems and blamed the inequity “in part on unfair public perceptions of mental illness—for example, that it is often not recognized as illness and that the behavior of the mentally ill frightened and upset people.” *Id.* In 1963, Congress passed the Mental Health Centers Act, which was to provide funds to communities to construct and staff community based mental health centers. *See id.* at 65.

¹⁴⁵See RALPH REISNER, *LAW AND THE MENTAL HEALTH SYSTEM: CIVIL AND CRIMINAL ASPECTS* 1041 (3d ed. 1999).

¹⁴⁶*See Wyatt v. Stickney*, 344 F. Supp. 373 (M.D. Ala. 1972).

¹⁴⁷*See id.* at 373.

¹⁴⁸*See White, supra* note 132, at 198.

¹⁴⁹*See id.* at 199.

Insurance (SSI) in 1974 furthered the deinstitutionalization movement.¹⁵⁰

While many mentally ill patients were able to make the transition from institution to community successfully, residing in halfway houses or other supervised settings, others were not.¹⁵¹ Many, including the elderly with dementia, as well as those under sixty years of age with chronic mental illness, went to nursing homes.¹⁵² Also, because most states did not provide adequate outpatient services for this group, many became homeless and received no care or treatment.¹⁵³ One might even describe them as having been socially abandoned.¹⁵⁴

This trend toward deinstitutionalization shifted the focus of regulation of research from the institutionalized mentally disabled to the broader population of individuals with decisional impairments.

Autonomy and the Decisionally Impaired

Other changes in the law and public policy reflect a movement from paternalism to autonomy, a recognition of the rights of the decisionally impaired to make their own decisions about a multitude of issues affecting their lives.¹⁵⁵ This paradigm shift has led, for example, to some individuals who suffer from mental illness themselves becoming

¹⁵⁰See *id.* See also ANN BRADEN JOHNSON, *OUT OF BEDLAM: THE TRUTH ABOUT DEINSTITUTIONALIZATION* 98 (1990) (stating that in "the first year SSI was available, state hospitals saw a nationwide decrease in population of 13.3 percent, the largest decrease ever").

¹⁵¹See JOHNSON, *supra* note 150, at 119.

¹⁵²See *id.* (quoting a 1977 U.S. General Accounting Office (GAO) Report stating that nursing homes had become the "largest single place of care for the mentally ill of all ages").

¹⁵³See *id.* at 181 (stating that after the institutions were closed, the mentally ill were to be given care in halfway houses or community centers, but officials and taxpayers never came up with enough money).

¹⁵⁴See Michael Winerip, *Bedlam in the Streets*, N.Y. TIMES, May 23, 1999, Section 6 (Magazine), at 42. See also Richard Jed Wyatt & Evan G. DeRenzo, *Scienceless to Homeless*, 234 SCL 1309, 1309 (1986) (identifying a societal failure to conduct the research necessary to determine whether deinstitutionalization would, in fact, benefit the institutionalized).

¹⁵⁵See Arlene Mayerson, *1970's and Onward—The Civil Rights Perspective*, in THE LEGAL RIGHTS OF CITIZENS WITH MENTAL RETARDATION 105 (Lawrence A. Kane, Jr., et al., eds., 1988).

more active participants in the debate about the regulation of research with this population.¹⁵⁶

The Disability Rights Movement

The disability rights movement, in particular, has had a profound effect on the care and treatment of those with cognitive and decisional impairments.¹⁵⁷ In *The Legal Rights of Citizens with Mental Retardation*, Arlene Mayerson states that

[A] profound shift in disability policy occurred in the decade of the 1970's. Rising visibility and activism in the disability rights movement, as well as passage of the first broad cross-disability piece of legislation, challenged traditional ideas about disability. The anthem of the disability rights movement became self-determination—disabled people demanded control over their own affairs on every level, from governmental decision-making to personal care. They attacked the medical model as oppressive. Doctors, social workers and other professionals were no longer accepted as the primary spokespersons; instead, disabled people began to speak for themselves.¹⁵⁸

As a result of the movement, disabled individuals established advocacy groups “to promote self-advocacy and independence.”¹⁵⁹ Groups such as “People First”¹⁶⁰ emerged to enable individuals “with mental disabilities to gain a sense of power over their own lives, by developing means of self-help and support and establishing mental health and mental retardation services responsive to their needs.”¹⁶¹ These groups

¹⁵⁶See Rick Weiss, *Bioethics Group Divided over Research on Mentally Ill*, WASH. POST, Nov. 16, 1998, at A6.

¹⁵⁷See Mayerson, *supra* note 155.

¹⁵⁸*Id.*

¹⁵⁹*Id.*

¹⁶⁰See *What Is People First* (visited Jan. 11, 2000) <<http://www.open.org/~people1/whatis.htm>> (describing People First as “developmentally disabled people joining together to learn how to speak for ourselves”).

¹⁶¹ROBERT M. LEVY AND LEONARD S. RUBENSTEIN, *THE RIGHTS OF PEOPLE WITH MENTAL*

have undertaken noticeable efforts to influence legislative and regulatory policies regarding their care and treatment.¹⁶²

The Law on Treatment Refusal

Concurrently, courts began to change their views, questioning the “paternalistic” approach of institutions and recognizing the autonomy interests of patients.¹⁶³ Prior to the 1970s, courts, for the most part, deferred to institutional authorities in the care, treatment, and custody of institutionalized mental patients.¹⁶⁴ In 1972, with the federal court case of *Wyatt v. Stickney*,¹⁶⁵ courts started to recognize some rights of institutionalized patients. While the court ruled that institutionalized mentally ill patients had “a right to be free from unnecessary or excessive medication,” the court did not recognize their right to refuse medication.¹⁶⁶ Yet, regarding research, the court stated, “[p]atients shall have a right not to be subjected to experimental research without the express and informed consent of the patient if the patient is able to give such consent, and of his guardian or next of kin, after opportunities

DISABILITIES 5 (1996). According to one source, membership in statewide self-advocacy groups for the mentally retarded has grown rapidly with over 1,000 such groups in existence today – a threefold increase from 1990. See THE STATE OF THE STATES IN DEVELOPMENTAL DISABILITIES 13-14 (David Braddock et al. eds., 5th ed.1998). The National Alliance for the Mentally Ill, a grassroots, self-help and family organization dedicated to improving the lives of people with severe mental illnesses, was founded in 1979. See *National Alliance for the Mentally Ill* (visited Jan. 2, 2000) <<http://www.nami.org/about/twentyrs.html>>.

¹⁶²In the early 1990s over 800 self advocacy groups joined together to establish a national organization called Self Advocates Becoming Empowered (SABE). The group has developed “an advocacy agenda calling for the phase-down and closure of all state operated” institutions for the developmentally disabled in the U.S. THE STATE OF THE STATES IN DEVELOPMENTAL DISABILITIES *supra* note 161, at 14. See also SABE USA’s *Online Directory* (visited Jan. 22, 2000) <<http://www.sabeusa.org>> (describing organization).

¹⁶³See Dennis E. Cichon, *The Right to “Just Say No:” A History and Analysis of the Right to Refuse Antipsychotic Drugs*, 53 LA. L. REV. 283, 286 (1992).

¹⁶⁴See *id.* This approach contrasted markedly with court decisions affirming the right of non-institutionalized individuals to make decisions about their care and treatment. While the requirement for informed consent, for example, was already adopted by the courts for most individuals, it was not required for individuals in mental hospitals. See also PAUL S. APPELBAUM, *ALMOST A REVOLUTION: MENTAL HEALTH LAW AND THE LIMITS OF CHANGE* 118 (1994) (discussing informed consent).

¹⁶⁵See *Wyatt v. Stickney*, 344 F. Supp. 387 (M.D. Ala. 1972).

¹⁶⁶*Id.* at 400.

for consultation with independent specialists and with legal counsel....”¹⁶⁷

In 1978 and 1979, federal district courts in New Jersey¹⁶⁸ and Massachusetts¹⁶⁹ issued opinions concluding that involuntarily committed mental patients had a legal right to refuse antipsychotic drugs.¹⁷⁰ While courts have differed in their approaches to these cases and the rationale supporting their determination, most courts have now recognized a right to refuse medication and other therapies by institutionalized mental patients.¹⁷¹

The Law on Civil Commitment

The move away from paternalism and toward autonomy is further reflected in changes in civil commitment laws. Specifically, the basis for civil commitment shifted from the need to treat to the need to confine those deemed a danger to themselves or others.¹⁷² This policy shift was in large part the result of the holding in *Lessard v. Schmidt*,¹⁷³ a 1972 federal court decision. In *Lessard*, a federal district court held that “the state must bear the burden of proving that there is an extreme

¹⁶⁷*Id.*

¹⁶⁸*See Rennie v. Klein*, 476 F. Supp. 1294 (D. N.J. 1979), *stay granted* by 481 F. Supp. 552 (D. N.J. 1979), *vacated en banc*, 653 F.2d 836 (3d Cir. 1981), *vacated and remanded*, 458 U.S. 1119 (1982), *opinion on remand*, 720 F.2d 266 (3d Cir. 1983) (*en banc*).

¹⁶⁹*See Rogers v. Okin*, 478 F. Supp. 1342 (D. Mass. 1979), *aff'd in part, rev'd in part*, 634 F.2d 650 (1st Cir. 1980), *vacated sub nom.*

¹⁷⁰*See Cichon*, *supra* note 163, at 286.

¹⁷¹*See id.* (stating that courts have differed on the right's legal source and, in particular, on the procedural safeguards necessary to protect the right). Historically, state courts were quicker to recognize the right of a mentally ill patient to refuse medication than the federal courts. From 1980 to 1990, federal courts that addressed the issue, adopted a professional judgment standard under which “patients could not refuse medication unless the decision to administer drugs constituted a substantial departure from accepted judgment, practices or standards.” William M. Brooks, *Reevaluating Substantive Due Process As a Source of Protection for Psychiatric Patients to Refuse Drugs*, 31 IND. L. REV. 937, 939 (1998). Since 1990, however, the Supreme Court has heard two cases involving a psychiatric patient's right to refuse medication while in prison or while pending trial. In these cases, the Court appears to have embraced a “broader reading of the right to refuse” treatment under the federal Constitution. *Id.* at 940.

¹⁷²*See Lessard v. Schmidt*, 349 F. Supp. 1078 (E.D. Wis. 1972).

¹⁷³*See id.* at 1078.

likelihood that if the person is not confined he will do immediate harm to himself or others.”¹⁷⁴ In addition to defining dangerousness narrowly, the *Lessard* court called for greater due process safeguards in the commitment process.¹⁷⁵ These requirements included representation by counsel, adequate notice of charges justifying detention, attendance at the hearing, exclusion of hearsay evidence, the privilege against self-incrimination, and a standard of proof beyond a reasonable doubt.¹⁷⁶

By the end of the 1970s, all states had commitment laws that resembled the substance of the *Lessard* decision.¹⁷⁷ These statutes either restricted commitment to persons who were dangerous to themselves or others (defining dangerousness to include “grave disability” as well), or were interpreted as already providing these requirements so as to remain constitutionally valid.¹⁷⁸ These changes were not without controversy. According to some critics, these laws made it nearly impossible to commit patients involuntarily.¹⁷⁹ One author stated that “a patient must literally be slashing his wrists or brandishing a weapon before he can be held in a hospital.”¹⁸⁰ Opposition to this view stems in large part from a concern for civil liberties.¹⁸¹ Advocates for the mentally ill are sharply divided on the issue: “[w]hile parent advocacy groups want to change the rules on involuntary commitment, patient groups want to keep the policy strict,” that is, continue to make it difficult to institutionalize the mentally ill against their will.¹⁸²

¹⁷⁴*See id.* at 1093.

¹⁷⁵*See id.*

¹⁷⁶*See id.*

¹⁷⁷*See* APPELBAUM, *supra* note 164, at 28.

¹⁷⁸*See id.*

¹⁷⁹*See* Erica E. Goode, *When Mental Illness Hits Home*, U.S. NEWS & WORLD REP., Apr. 24, 1989, at 54.

¹⁸⁰*Id.*

¹⁸¹*See* White, *supra* note 132, at 201.

¹⁸²*Id.* In response, it appears, to concerns of parent advocacy groups, the restrictive standards of some states have been relaxed. Since the late 1970's, some states have expanded their restrictions for commitment beyond the justification of an immediate likelihood of harm to self or others. *See* APPELBAUM, *supra* note 164, at 49. In 1979, a Washington State statute

The Law on Guardianship and Advance Care Planning

Another example of the law's movement to afford those with decisional incapacities more autonomy involves the effort to limit the scope of state court guardianship orders.¹⁸³ A 1976 Washington statute mandated that courts impose only such "specific limitations and disabilities on a disabled person to be placed under a limited guardianship as the court finds necessary for such person's protection and assistance."¹⁸⁴ Under this standard, persons "institutionalized as mentally infirm...retain the right to consent or refuse to consent to research absent specific evidence concerning inability to exercise that right."¹⁸⁵

The limited guardianship movement was largely supported by developments in thinking about decisional incapacity and its ties to functional ability.¹⁸⁶ Capacity, it was recognized, was not an all or nothing issue, rather capacity is nuanced, with different levels of capacity required for different tasks.¹⁸⁷ While courts do not consistently write limited guardianship orders, a significant majority of "state legislatures have taken major strides in recognizing the need for and appropriateness of limited orders."¹⁸⁸

redefined grave disability to include "severe deterioration in routine functioning" of a person's physical and mental condition. WASH. REV. CODE ANN. § 71.05.020(1) (1995). Also, a North Carolina statute broadened the definition of danger to self to include behavior that is grossly irrational, inappropriate, or a sign of severely impaired judgment, creating a presumption that patients cannot care for themselves. N.C. GEN. STAT. § 122-58.2 (1995). In addition, several states have expanded their commitment criteria, facilitating hospitalization of certain classes of mentally ill persons. See APPELBAUM, *supra* note 164, at 49. These states are Alaska, Arizona, Colorado, Hawaii, Kansas, Rhode Island, and Texas. *See id.*

¹⁸³See Sally Balch Hurme, *Current Trends in Guardianship Reform*, 7 MD. J. CONTEMP. L. ISSUES 143, 145 (1995-1996).

¹⁸⁴Protection of Human Subjects, Research Involving Those Institutionalized As Mentally Infirm, Reports and Recommendations for Public Comment, 43 Fed. Reg. 11,327, 11,348 (Mar. 17, 1978) (quoting WASH. REV. CODE ANN. § 11.88.010 (2) (Supp. 1976)).

¹⁸⁵*Id.*

¹⁸⁶See Hurme, *supra* note 183, at 157-161.

¹⁸⁷See Peter V. Rabins, *Issues Raised by Research Using Persons Suffering from Dementia Who Have Impaired Decisional Capacity*, 1 J. HEALTH CARE L. & POL'Y 22, 23-25 (1998).

¹⁸⁸See Sally Balch Hurme, *Limited Guardianship: Its Implementation Is Long Overdue*, 28 CLEARINGHOUSE REVIEW 660, 663 (1994).

Paralleling the adoption of "limited guardianship" provisions has been the establishment of guidelines for the execution of advance directives. Today, all states have statutory regulations regarding some type of advance directive (living wills¹⁸⁹ and durable powers of attorney (DPA) for health care.)¹⁹⁰ These documents allow individuals, while competent, to express their wishes for medical treatment should they become decisionally incapacitated, especially concerning life-prolonging medical treatment.¹⁹¹ While virtually all states had enacted living will laws by the early 1980s, practitioners (both physicians and health law attorneys) soon realized that there were significant limitations to the static nature of living wills,¹⁹² and advocated, instead, that individuals execute a DPA in which they could name a trusted family member or friend to make medical treatment decisions on their behalf should they become incapacitated.¹⁹³ In these documents, patients might also express their wishes for medical treatment according to a number of hypothetical medical scenarios.¹⁹⁴

¹⁸⁹Living wills are written expressions of an individual's wishes regarding receipt of medical treatment if they should become terminally ill and medically incapacitated. See WILLIAM J. CURRAN ET AL., *HEALTH CARE LAW AND ETHICS* 637 (5th ed. 1998).

¹⁹⁰A recent survey of advance directive legislation of all fifty states and the District of Columbia found that, as of July 1999, 48 states have living will statutes. See ABA Commission on Legal Problems of the Elderly, *Health Care Surrogate Decision-Making Legislation* (visited Apr. 18, 2000) <<http://www.abanet.org/elderly/health.html>>. The exceptions are Massachusetts and Michigan. Of these states, 16 have a combined advance directive statute merging DPA's for health care and living wills. See *id.* These states are Alabama, Arizona, Connecticut, Delaware, Florida, Hawaii, Kentucky, Maine, Maryland, Minnesota, Mississippi, New Jersey, New Mexico, Oklahoma, Oregon, and Virginia. All 50 states and the District have some type of health care DPA statute, whether it be contained in a combined statute or only within a living will statute. See *id.* Eleven states currently have special mental health advance directive statutes. These states are Alaska, Hawaii, Idaho, Illinois, Minnesota, North Carolina, Oklahoma, Oregon, Texas, Utah, and Wyoming. See *id.*

¹⁹¹See NORMAN L. CANTOR, *ADVANCE DIRECTIVES AND THE PURSUIT OF DEATH WITH DIGNITY* 23-24 (1993).

¹⁹²See *id.* at 35 (describing the statutory constraints contained in living-will type laws).

¹⁹³See BARRY R. FURROW ET AL., *HEALTH LAW* 715 (1995) (stating that "[i]n the early 1990s, the durable power of attorney quickly became the preferred form of advance directive").

¹⁹⁴See Diane E. Hoffmann, Sheryl Itkin Zimmerman & Catherine J. Tompkins, *The Dangers of Directives or False Security of Forms*, 24 *J. OF LAW, MED. & ETHICS* 5, 6 (1996).

Advance directives have also been developed as a tool for choice in psychiatric treatment and research participation. The Bazelon Center for Mental Health Law, for example, offers a "Psychiatric Advance Directive" that allows for both the designation of a proxy and "instructions about hospitalization and alternatives to hospitalization, medications, electroconvulsive therapy (ECT), emergency interventions (including seclusion, restraint and medication) and experimental studies or drug trials."¹⁹⁵ Commentators have also analyzed the circumstances under which advance directives of this kind might be used.¹⁹⁶ Moreover, advance directives (specifically, DPA) have been used by subjects in dementia research at the Clinical Center of the National Institutes of Health¹⁹⁷ and are included in the more recent proposals to regulate research with the decisionally impaired.¹⁹⁸

Proxy Decision Making

At the same time that legislatures were passing laws authorizing the implementation of advance directives, in furtherance of the autonomy interest of people who wished to anticipate future periods of incapacity, it became clear that many individuals were disinclined to execute these documents.¹⁹⁹ Other mechanisms were needed to allow for

¹⁹⁵See Judge David L. Bazelon Center for Mental Health Law, Inc., *Psychiatric Advance Directive* (visited January 10, 2000) <<http://www.bazelon.org/advdir.html>>.

¹⁹⁶See Patricia Backlar, *Anticipatory Planning for Research Participants with Psychiatric Disorders Like Schizophrenia*, 4 PSYCH., PUB. POL'Y & L. 829 (1998).

¹⁹⁷See Alison Wichman, *Protecting Vulnerable Research Subjects: Practical Reality of Institutional Review Board Review and Approval*, 1 J. HEALTH CARE L. & POL'Y 88, 95-97 (1998). Advance directives for research purposes, however, have the same weaknesses as advance directives for clinical purposes. Instructional advance directives, in particular, often fail to provide useful guidance for clinical care. See, e.g., Joan M. Teno et al., *Do Advance Directives Provide Instructions That Direct Care?*, 45 J. AM. GERIATRICS SOC. 508 (1997); Joanne Lynn, *Why I Don't Have a Living Will*, 19 L., MED. & HEALTH CARE 101 (1991). With regard to proxy advance directives, the proxy's decisions may not correspond to what the individual would want done. See, e.g., Daniel P. Sulmasy et al., *The Accuracy of Substituted Judgments in Patients with Terminal Diagnoses*, 128 ANNALS OF INTERNAL MED. 621 (1998); J. Suhl et al., *The Myth of Substituted Judgment: Surrogate Decision Making Regarding Life Support Is Unreliable*, 154 ARCHIVES OF INTERNAL MED. 90 (1994).

¹⁹⁸See *infra* note 242 and accompanying text.

¹⁹⁹See FURROW, *supra* note 193 at 715.

decisionmaking regarding end-of-life care for individuals lacking decisional capacity. As a result, many states passed new laws or expanded existing surrogate consent laws²⁰⁰ allowing family members, and, in some cases, close friends of a patient, to make medical treatment decisions for an individual lacking decisional capacity.²⁰¹

By 1999, thirty-seven states had passed surrogate health care consent statutes.²⁰² In many states devoid of such statutes, courts articulated approval of surrogate consent.²⁰³ In both court decisions and statutes, the surrogate was expected to decide consistent with the patient's preferences and values (if known), or if not known, then consistent with what would be in the patient's best interest.²⁰⁴ This movement was facilitated by a presumption that family members are trustworthy and are better able to make these types of decisions for patients than are the courts.²⁰⁵ This was particularly true in the area of end of life decisionmaking. While state legislatures and state courts recognized the authority of surrogates (agents and family members) to consent to an incapacitated person's receipt of medical treatment, for the most part they did not address consent to participation in research.²⁰⁶ Yet, the legal recognition of family decisionmakers in the realm of clinical decisionmaking paved the way for families to have a voice in the research context.

²⁰⁰These existing laws typically allowed a family member to consent to medical treatment for another but not to refuse life sustaining treatment. *See, e.g.,* MD. CODE ANN., HEALTH GEN. I § 20-107 (1993), *repealed by* Acts 1993, ch. 372, § 1 (effective Oct. 1, 1993).

²⁰¹Typically, these surrogate consent statutes listed, in order of priority, who could make these various decisions, *see, e.g.,* Virginia's Health Care Decisions Act, A1) guardian or committee; 2) patient's spouse; 3) adult child of patient; 4) parent of patient; 5) adult brother or sister of patient; or 6) any other relative of patient in descending order of blood relationship. VA. STAT. § 54.1-2986 (A) (Michie 1998).

²⁰²*See Health Care Surrogate Decision-Making Legislation* (visited Jan. 11, 2000) <<http://www.abanet.org/elderly/health.html>>.

²⁰³*See* FURROW, *supra* note 193, at 718. *See also* New York State Task Force on Life and the Law, WHEN OTHERS MUST CHOOSE: DECIDING FOR PATIENTS WITHOUT CAPACITY (1992) 33-35 [hereinafter New York State Task Force].

²⁰⁴*See* New York State Task Force, *supra*, note 204 at 35.

²⁰⁵*See id.* at 51.

²⁰⁶*See* Hoffmann & Schwartz, *supra* note 15, at 125.

Advances in the Treatment and Diagnosis of Mental Illness and Diseases of the Brain

Another historical factor shaping the current debate regarding the regulation of research with the decisionally impaired is the progress that has been made in the treatment and diagnosis of mental illness and diseases of the brain. Twenty-five years ago, when the Commission's recommendations were first published, there had not been long-term experience with antipsychotics and other drugs for the treatment of mental illness, and the psychiatric research and treatment community was somewhat divided between those advocating psychotherapy and those advocating pharmacotherapeutic agents.²⁰⁷ Today, drug therapy is the primary approach to treatment of individuals with serious psychiatric illness.²⁰⁸ There appears to be a consensus now that "[p]sychoanalysis and its derivatives...have not proved to be effective as primary treatment for serious psychiatric illness (e.g., schizophrenia and manic-depressive illness)."²⁰⁹ That view, along with the development of effective medications for the treatment of these disorders, "led to a quiet revolution within American psychiatry and a return to its medical roots."²¹⁰

While the development of psychotropic medications revolutionized psychiatry and led to deinstitutionalization in the 1970's, many of the most promising breakthroughs in drug treatment have been relatively recent.²¹¹ In the last decade a number of new drugs for the treatment of schizophrenia—including, risperidone, olanzapine and

²⁰⁷See Sheldon H. Preskorn, *Mental Disorders Are Medical Diseases*, in MENTAL ILLNESS: OPPOSING VIEWPOINTS 29 (William Barbour, ed. 1995).

²⁰⁸See *id.*

²⁰⁹*Id.*

²¹⁰*Id.* This revised understanding about the methods of psychiatric care evolved "over a period from the late 1960s to the 1980s. During those years, psychiatry changed more fundamentally than did any other area of medicine." *Id.* at 34.

²¹¹See E. Fuller Torrey, *Mental Disorders are Medical Diseases*, in MENTAL ILLNESS: OPPOSING VIEWPOINTS 264, 269 (William Barbour, ed. 1995). In the late 1970s and eighties there was a hiatus in new drug developments for treatment of mental illness. See *id.* The lack of developments in this area may have been due in part to the lack of research money given to NIMH. See *id.* According to one author, "by 1985 the federal government was spending the same amount of research money on schizophrenia as it was on tooth decay." *Id.*

quetiapine—all with many fewer side effects than the prior generation of drugs, were approved by the FDA.²¹² Newer drugs have also been recently developed for the treatment of depression.²¹³ These medications, known as selective serotonin reuptake inhibitors (SSRIs), are used more extensively than the older “tricyclics.”²¹⁴ The more common use of the SSRIs has been attributed to “a less problematic side effect profile in these drugs, their lack of toxicity when taken in overdoses, and their ease of administration (once-a-day dosing).”²¹⁵ In addition to these developments, the first two drugs for the treatment of Alzheimer’s disease were approved by the FDA within the last few years.²¹⁶

While drug developments have received attention, probably the most significant progress in psychiatric research during the past twenty years has been our heightened neuroscientific understanding of the brain.²¹⁷ The development of magnetic resonance imaging (MRI) and positron emission tomography (PET) scans have enabled scientists to actually observe the brain and have offered psychiatric researchers the

²¹²See Grayson Norquist & Steven E. Hyman, *Advances in Understanding and Treating Mental Illness: Implications for Policy*, HEALTH AFF., Sept. 1, 1999, at 38. These new drugs, referred to as “atypical antipsychotics” do not require weekly blood monitoring and are better able to treat “the negative symptoms of schizophrenia such as withdrawal from social contacts.” *Id.* at 38-39. They are also significantly more expensive than the older drugs they have begun to replace. *See id.* at 40.

²¹³*See id.*

²¹⁴*See id.*

²¹⁵*See id.* at 39.

²¹⁶*See Donepezil (Aricept) Drug for Alzheimer’s: Use, Side Effects, Interactions* (visited Jan. 11, 2000) <<http://www.virtualdrugstore.com/alzheimer/donepezil.html>>. The first, Tacrine HCL (Cognex) was approved by the FDA and came on the market in 1993. The second, donepezil HCL (Aricept), was approved in 1996. These drugs are not a cure or complete treatment for Alzheimer’s disease, but do delay the progression of the disease. *Donepezil (Aricept) Drug for Alzheimer’s: Use, Side Effects, Interactions* (visited Jan. 11, 2000) <<http://www.virtualdrugstore.com/alzheimer/donepezil.html>>. *See also* Susan Cruzan, *FDA Announces Approval of TACRINE HYDROCHLORIDE* (visited Jan. 11, 2000) <<http://www.fda.gov/bbs/topics/NEWS/NEW00434.html>> (announcing the Food and Drug Administration’s approval of tacrine hydrochloride, the first drug approved specifically to treat symptoms of Alzheimer’s disease).

²¹⁷*See Decade of the Brain Home Page (Library of Congress)* (visited Jan. 2, 2000) <<http://www.lcweb.loc.gov/loc/brain>> (“In 1990, President Bush proclaimed the nineties the decade of the brain”).

opportunity to test hypotheses that they were previously unable to test.²¹⁸

These gains in psychiatric research and treatment have occurred in large part because of the involvement of mentally ill individuals in that research. In the debate over current efforts to regulate this research, researchers believe such efforts may lead to sacrificing future gains in understanding and treating mental illnesses and brain disorders.

REGULATORY POSSIBILITIES AND POLICY CAUTION: THE LATE 1990s AND BEYOND

Recent Governmental Initiatives

Against this background of prior regulatory failure and an increasingly complex legal and medical environment, the recent state and federal governmental initiatives to more stringently regulate research with the decisionally impaired, reflect a noteworthy insistence that the protection of these vulnerable subjects requires a renewed effort to find a policy solution.²¹⁹ Within a six-month span in 1998, a Maryland working group, convened by the Maryland Attorney General, recommended state legislation on research involving “decisionally incapacitated subjects;”²²⁰ a New York advisory work group, convened by the New York Commissioner of Health, recommended regulations on research involving “protected classes,” including adults who either lack or are likely to lose decisional capacity,²²¹ and the NBAC, created by President Clinton in 1995, issued a lengthy report and policy

²¹⁸See Norquist & Hyman, *supra* note 212, at 36.

²¹⁹In addition to the three initiatives discussed in the text, the National Institutes of Health has developed what it terms “points to consider,” which it has posted on its web site “to assist IRBs and clinical investigators in their effort to protect participants who are, or may be, or may become decisionally impaired.” National Institutes of Health, *Interim - Research Involving Individuals with Questionable Capacity to Consent: Points to Consider* (visited Dec. 23, 1999) <<http://grants.nih.gov/grants/policy/questionablecapacity.htm>>.

²²⁰MARYLAND REPORT, *supra* note 1, at 1.

²²¹NEW YORK REPORT, *supra* note 1, at 28-33.

recommendations on research involving “persons with mental disorders that may affect decisionmaking capacity.”²²²

Of these three initiatives, only New York’s effort was the result of litigation. In *T.D. v. New York State Office of Mental Health*,²²³ plaintiffs—consisting of patients involuntarily hospitalized at various New York State psychiatric facilities who had been adjudicated incapable of consenting to medical treatment—challenged regulations promulgated by the Office of Mental Health.²²⁴ The plaintiffs alleged that, under the regulations, they could be forced to participate in research without their consent.²²⁵ The regulations were struck down at the trial court level because they were not consistent with a state statute requiring the Commissioner of Health to consent to all research involving children and incompetent adults.²²⁶

On appeal, the appellate court upheld the trial court decision, and further deemed the regulations invalid based on additional statutory, common law, and constitutional grounds.²²⁷ The appellate court decision raised concern among researchers nationwide who feared they might be prevented from conducting scientifically valuable research on the psychiatric population.²²⁸ However, New York’s highest court, while upholding the lower court decisions, ruled that, in declaring the

²²²NBAC REPORT, *supra* note 1, at 2.

²²³*See T.D. v. New York State Office of Mental Health*, 626 N.Y.S.2d 1015 (Sup. Ct. 1995) *aff’d*, 650 N.Y.S.2d 173 (App. Div. 1996), *appeal dismissed*, 680 N.E.2d 617 (N.Y. 1997), *leave to appeal granted*, 684 N.E.2d 281 (N.Y. 1997), *appeal dismissed* 668 N.Y.S.2d 153 (N.Y. 1997).

²²⁴*See T.D. v. New York State Office of Mental Health*, 626 N.Y.S.2d at 1017.

²²⁵*See id.*

²²⁶*See id.* at 1021.

²²⁷*See T.D. v. New York State Office of Mental Health*, 650 N.Y.S.2d at 183. *See also Hoffmann & Schwartz, supra* note 15, at 129 (noting that based on the appellate court decision, residents in a New York state facility operated or licensed by the Office of Mental Health who lack decision-making capacity [could] not be subjects in any (non federally funded) research determined to be “non therapeutic” and to pose a greater than minimal risk unless the individual (prior to incapacity) gave “specific consent or designated a suitable surrogate from whom such consent” could be obtained).

²²⁸*See Hoffmann & Schwartz, supra* note 15, at 129.

regulations invalid on additional grounds, the appellate court had issued “an inappropriate advisory opinion.”²²⁹

As a result of the trial court’s original ruling, however, a regulatory vacuum existed, and the Commissioner of Health could hardly fill it without first obtaining expert advice about the relevant ethical and policy issues.²³⁰ The other two efforts, however, were entirely discretionary. The Maryland Attorney General perceived a problem—a gap in both federal and state law concerning proxy consent for research participation—and sought to develop a consensus on how to address it.²³¹ NBAC chose the issue of research involving decisionally impaired subjects as a topic for its first report on non-genetic human subjects research.²³² Thus, the Maryland and NBAC initiatives, in particular, suggest that at least some in the policy arena believe that the conduct of research with impaired-capacity subjects is a problem, not simply a condition. The distinction is important for the development of public policy—“[f]or a condition to be a problem, people must become convinced that something should be done to change it.”²³³

A belief that something should be done, however, is but the first step and does not necessarily imply agreement about the nature of the remedial action. Among the three governmental initiatives, one finds broadly similar recommendations in a number of areas as well as areas of disagreement.²³⁴ All three initiatives adopted similar frameworks in

²²⁹See *T.D. v. New York State Office of Mental Health*, 668 N.Y.S.2d. 153, 154 (N.Y. 1997).

²³⁰See *id.* at 185 (noting that the Commissioner of Health would likely issue new regulations governing human subjects research in response to the court’s invalidation of the regulations).

²³¹See Hoffmann & Schwartz, *supra* note 15, at 134. In light of uncertainty about the authority of agents and surrogates to consent to participation in research on behalf of decisionally impaired individuals, as well as the strong and differing views expressed by some researchers and advocates, the Maryland Attorney General’s Offices established what was called a “Working Group” to begin a dialogue on the issue. *Id.*

²³²See Exec. Order No. 12,975, 60 Fed. Reg. 52,063, 52065 (1995) (“[As a] first priority” the NBAC was to assess the “protection of the rights and welfare of human research subjects”).

²³³J. W. KINGDON, *AGENDAS, ALTERNATIVES, AND PUBLIC POLICIES* 114 (1995).

²³⁴Because it is a federal entity, NBAC addressed some matters—for example,

their regulatory approach. Research on this population was first divided into two categories: research affording the prospect of direct medical benefits to participants and research without this prospect.²³⁵ Research was also categorized according to level of risk.²³⁶ Although proxy decisionmakers are given authority to enroll those lacking capacity in research, more protections are required, and greater restrictions on proxy decisionmakers are imposed, if research has no prospect of direct medical benefit or poses more than minimal risk.²³⁷ Many points emphasized are substantively similar to points emphasized in the earlier regulatory efforts by DHEW. These include:

- *Need for research with this population.* Researchers should not recruit subjects with impaired capacity if the research could be done with other subjects.²³⁸
- *Justification of research design.* Researchers should be expected to pay especially careful attention to the risk-benefit profile of research involving these subjects.²³⁹
- *Informed consent.* Individuals with psychiatric or other disorders potentially affecting their decision-making capacity are not, for that reason alone, disqualified from giving informed consent for research

membership on an IRB by individuals who can represent the subject population—that were thought by Maryland and New York to be beyond the scope of a state effort. The omission of these matters from the Maryland and New York reports does not necessarily imply disagreement with NBAC.

²³⁵See Hoffmann & Schwartz, *supra* note 15, at 137-38.

²³⁶See *id.* at 139.

²³⁷See *id.* at 139-49 (discussing Working Group's consideration of five factual scenarios concerning research protocols with different levels of risk and potential benefits).

²³⁸See NBAC REPORT, *supra* note 1, at 10; NEW YORK REPORT, *supra* note 1, at 30; MARYLAND REPORT, *supra* note 1, at 3, A8-A9.

²³⁹See NBAC REPORT, *supra* note 1, at 10; NEW YORK REPORT, *supra* note 1, at 30-31; MARYLAND REPORT, *supra* note 1, at 3, A13-A16.

participation. Researchers should pay careful attention to capacity assessment.²⁴⁰

- *Assent and objection.* Potential research subjects who are incapable of giving informed consent but who are capable of giving assent—that is, explicit, albeit not informed, permission—for research participation should be asked for assent. Individuals should not be compelled to participate in research over their objection.²⁴¹

Newer provisions, not included in earlier regulatory drafts, but common to all three recent proposals include:

- *Advance planning for research.* Individuals with present capacity who can anticipate future incapacity (for example, people with early Alzheimer's disease) should be able to express their wishes about future research participation. They should also be allowed to pick their own "legally authorized representatives." The exact effect of planning documents, however, was one area of disagreement among the three governmental efforts.²⁴²
- *Research involving the prospect of direct medical benefit or involving no greater than minimal risk.* Family members or others who may authorize clinical care for an incapacitated patient should be permitted to authorize participation in these categories of research.²⁴³

²⁴⁰See NBAC REPORT, *supra* note 1, at 57-58; NEW YORK REPORT, *supra* note 1, at 32; MARYLAND REPORT, *supra* note 1, at 3, A9-A11.

²⁴¹See NBAC REPORT, *supra* note 1, at 57-58; NEW YORK REPORT, *supra* note 1, at 32; MARYLAND REPORT, *supra* note 1, at 3, A21-A23.

²⁴²See NBAC REPORT, *supra* note 212, at 61; MARYLAND REPORT, *supra* note 210, at 3.

²⁴³See NBAC REPORT, *supra* note 1, at 53-54. Earlier proposals for research with institutionalized individuals, including the National Commission Report, did not include

Areas of disagreement among the three proposals include:

- *Characterization of the subject population.* To the dismay of many commentators, NBAC focused its analysis on “persons with mental disorders that may affect decisionmaking capacity.”²⁴⁴ Maryland and New York considered that decisional incapacity itself, regardless of its clinical origin, was the key factor in identifying a class of vulnerable subjects.²⁴⁵
- *Independent capacity assessment.* According to NBAC, when research involves greater than minimal risk, a professional who is independent of the research team should assess the potential subjects’ capacity to consent, unless “there are good reasons” for using a less formal procedure.²⁴⁶ Neither Maryland nor New York would mandate this kind of independent capacity assessment.²⁴⁷
- *Levels of risk and proxy authority.* NBAC recognized

consent by a family member even at this level of risk. Patient assent or lack of objection was required. If a patient objected to participation, additional protections were required. *See supra* note 229 and accompanying text; MARYLAND REPORT, *supra* note 1, at 4; NEW YORK REPORT, *supra* note 1, at 26-27.

²⁴⁴*See* NBAC REPORT, *supra* note 1, at 2. NBAC acknowledged that “[p]ersons with mental disorders are not...unique in being at risk for loss of decisionmaking capacity.” NBAC REPORT, *supra* note 1, at 5. NBAC explained rather cryptically that it “principally focused its attention on those who may be primarily considered for research protocols because it is their particular mental disorder that is being studied.” *Id.* Taking NBAC to task for retaining its “mental disorders” focus despite vehement objections during the public comment period, one prominent psychiatrist accused NBAC of perpetuating “outmoded stereotypes.” Robert Michels, *Are Research Ethics Bad for Our Mental Health?*, 340 NEW ENG. J. MED. 232, 1427-30 (1999).

²⁴⁵*See* MARYLAND REPORT, *supra* note 1, at 3; NEW YORK REPORT, *supra* note 1, at 2.

²⁴⁶*See* NBAC REPORT, *supra* note 1, at 58; This recommendation is similar to the “consent auditor” recommendation of the National Commission. *See supra* text accompanying notes 86 and 94.

²⁴⁷*See* MARYLAND REPORT, *supra* note 1, at 3; NEW YORK REPORT, *supra* note 1, at 30.

only two levels of risk, minimal and greater than minimal. In NBAC's view, when research presents greater than minimal risk and no prospect of direct medical benefit, a legally authorized representative should have authority to agree to research participation in an IRB-approved protocol only if the protocol were also approved by a special federal review panel.²⁴⁸ This approach, in the view of many commentators, would present a formidable barrier to various types of research involving, most significantly, brain imaging procedures like MRI.²⁴⁹ These and similar procedures have been viewed as falling into an intermediate risk category, "minor increase over minimal risk."²⁵⁰ Both Maryland and New York retained this intermediate risk category. Maryland would allow only a relatively small subset of legally authorized representatives (proxies named in durable powers of attorney for health care) to agree to an incapacitated subject's participation in this kind of research. New York would allow a broader group of legally authorized representatives (family members acting as surrogates) to do so.

Aftermath of the Initiatives—Policymakers' Caution

Each of the three initiatives recommended policy action. NBAC recommended amendments to the federal regulations governing research on human subjects, the New York task force recommended new Health Department regulations, and the Maryland working group

²⁴⁸See NBAC REPORT, *supra* note 1, at 54. The NBAC envisioned that, after acquiring sufficient experience with protocol-by-protocol review, the federal panel would adopt guidelines enabling IRB approval of certain types of greater-than-minimal-risk research. See *id.*

²⁴⁹See, e.g., Michels, *supra* note 244, at 1428 ("The NBAC considers the present system for evaluating a patient's capacity to consent to dangerous treatment inadequate even to assess the capacity to consent to MRI for research purposes").

²⁵⁰This characterization of an intermediate level of risk is found in the Department of Health and Human Services regulations governing research with children. See 45 C.F.R. § 46.406(a) (2000).

recommended enactment of a statute.²⁵¹ However, none of the recommendations has been implemented thus far.

Although the Secretary of Health and Human Services has taken NBAC's report under advisement, no regulatory action seems likely in the near future. Moreover, NBAC requested states "to confirm, by statute or court decision" that proxies for clinical purposes have authority to act as "legally authorized representatives" and that friends as well as relatives be able to serve in this capacity.²⁵² NBAC also requested state legislatures to ensure that "persons who choose to plan for future research participation are entitled to choose" their research proxies.²⁵³ No state legislature has yet acted on these recommendations.

Action pursuant to the New York recommendations has been delayed in part by the resignation of the former Commissioner of Health and appointment of a successor, who would naturally require time to familiarize herself with the issues. Action has also been delayed because the recommendations produced sharp criticism from both advocates and researchers.²⁵⁴ A series of articles that appeared in the *New York Post* on the task force recommendations in early 1999 provide some insights into the politics of the situation.²⁵⁵ According to one article, John Cardinal O'Connor, "evoking Nazi Germany, warned...that the recommendations were dangerous" and "[a]dvocates for the mentally ill vowed to go to court if necessary to block them."²⁵⁶ A subsequent article stated that "hundreds of advocates for the mentally ill protested at the Capitol" against what they viewed as recommendations supporting "state-sponsored drug experiments using

²⁵¹See NBAC REPORT, *supra* note 1, at 53; MARYLAND REPORT, *supra* note 1, at 2; NEW YORK REPORT, *supra* note 1, at 29.

²⁵²See NBAC REPORT, *supra* note 1, at 52.

²⁵³See *id.* at 52-53.

²⁵⁴See Gregg Birnbaum, *Gov Says He's All Ears in Drug-Testing Furor*, N.Y. POST, Jan. 20, 1999, at 12.

²⁵⁵See *infra* notes 256-260.

²⁵⁶See Gregg Birnbaum, *O'Connor Boosts Drug-Test Protesters*, N.Y. POST, Mar. 10, 1999, at 12.

vulnerable people as ‘human guinea pigs.’”²⁵⁷ The article further recounted that Cardinal O’Connor, prior to a meeting on this issue with Governor Pataki, said that “to allow experiments with some risk—and no benefit to the subject—on adults who are too ill to consent on their own...could be a potentially horrifying thing.”²⁵⁸

A short time later, an article appeared expressing the views of the research and medical community.²⁵⁹ The article described how many of the city’s leading hospitals and medical schools were lobbying the state to relax the proposed regulations and that they had “warned the state Health Department that the regulations will stifle research and cause drug companies to divert their funding to states that have less red tape.”²⁶⁰

The Maryland Attorney General’s effort to win passage of detailed regulatory legislation collapsed after a divisive legislative hearing.²⁶¹ On the one hand, a representative of the pharmaceutical manufacturers complained of the burdens that the proposal would place on researchers, and academic medical centers lamented the additional burden on IRBs.²⁶² On the other hand, the Maryland Catholic Conference and various patient advocacy and disability rights groups attacked the proposal as opening the door to exploitation of vulnerable people.²⁶³ The legislators, appalled by the length and complexity of the

²⁵⁷*Id.*

²⁵⁸*Id.*

²⁵⁹Gregg Birnbaum, *Hospitals Fight for Freedom to Experiment*, N.Y. POST, Mar. 24, 1999, at 20.

²⁶⁰*Id.*

²⁶¹*See* GENERAL ASSEMBLY OF MARYLAND FINAL STATUS REPORT OF PROPOSED LEGISLATION (1999 Session) (reporting that SB 307 was reported out unfavorably by the Judicial Proceedings Committee) [hereinafter GENERAL ASSEMBLY OF MARYLAND].

²⁶²*See* testimony of the Pharmaceutical Research and Manufacturers of America in Opposition to Maryland Senate Bill 307 (March 8, 1999) (on file with the authors). *See also* testimony of David B. Mallot, M.D., Associate Professor of Psychiatry and Associate Dean for Medical Education, University of Maryland, Baltimore (March 11, 1999) (on file with the authors).

²⁶³*See* testimony of The Maryland Catholic Conference on Senate Bill 307 Presented Thursday, March 11, 1999 by Richard J. Dowling; testimony of The Arc of Maryland in opposition to SB 307 (March 11, 1999); testimony of Jamey George (for MCIL Resources for

proposal and discomfited by the controversy, promptly voted to halt the bill.²⁶⁴

A More Complicated Context for Regulation

Today, as compared to twenty years ago, the context in which the debate over regulation of research with the decisionally impaired takes place is a much more complex one, with strong and cogent voices on each side. Arguments for and against the need for this type of regulation push and pull policymakers in opposite directions and make significant regulatory change a slim possibility at present.

The Pull for the Status Quo

Today, arguments of the potential for great breakthroughs in research on psychiatric illnesses and diseases of the brain pull policy makers in the direction of opposing more stringent regulation of research in this area. With the relatively recent development of brain imaging techniques, researchers are hoping to find “biological indicators” for specific mental illnesses.²⁶⁵ In fact, “intensive efforts are under way to find such markers based on abnormalities found in brain structure or functioning for many mental disorders and on abnormalities in cognitive testing.”²⁶⁶

These recent developments bolster researchers’ contentions that greater progress is imminent and regulations now will impede breakthroughs that may result not only in treatment of many forms of mental impairment but also in cures for these devastating illnesses.²⁶⁷

Independent Living, Inc. in opposition to SB 307 (March 11, 1999); and Testimony Regarding SB 307 by the Maryland Legislative Lobby for Life, Inc. (March 11, 1999) (on file with the authors).

²⁶⁴See GENERAL ASSEMBLY OF MARYLAND, *supra* note 261.

²⁶⁵See Norquist & Hyman, *supra* note 212, at 36.

²⁶⁶*Id.*

²⁶⁷See Robert Pear, *Inspector Warns of Hazards in Experimental Drug Tests*, THE PLAIN DEALER, May 30, 1998, at A8 (stating that “[s]cientists are reporting explosive growth in promising new biomedical research, with hundreds of products being tested on tens of thousands of patients, including children and people with severe mental illnesses”). See also Weiss, *supra* note 156, at A6 (quoting David Shore of the National Institute of Mental

Some members of NBAC, in fact, argued that the NBAC proposals went too far and would, in all likelihood, stifle important and needed research.²⁶⁸

Another argument of those opposed to more regulation in research is that researchers and IRBs are already adopting many of the suggestions called for by the recent regulatory proposals. These critics argue that, although there has been no change in this area since 1973 on the federal level either legislatively or through regulation, some subtle but recognizable changes are being made.

These changes are likely to be a response to the availability and visibility of the proposals by the prestigious NBAC and the states of Maryland and New York, but other factors may also be at play. For example, researchers may fear additional litigation such as the *T.D. v. New York State Office of Mental Health* case in New York, as well as the revitalized enforcement efforts of NIH's Office of Protection from Research Risks (OPRR) and the accompanying potential loss of research dollars.²⁶⁹ As one prominent psychiatric researcher, Dr.

Health as saying, "[t]his is probably not the best time to put the brakes on...since the science is now progressing very fast and Congress has recently become generous with funds").

²⁶⁸See NBAC REPORT, *supra* note 1, at 85-86 (Bernard, Lo, dissenting)

[T]he Commission's recommendations...raise barriers to research that involves only small increases over minimal risks and is likely to result in important knowledge about the participant's disease. Hence, the recommendations will thwart a better understanding of the pathophysiology of the diseases that impair decisionmaking capacity, while providing little additional protection to vulnerable subjects. This is not the correct balance between protecting vulnerable persons and developing better treatments for patients with brain disorders.

Id. See also Patricia Maldonado, *Presidential Commission Makes Recommendations to Protect Mentally Ill*, BOSTON GLOBE, Nov. 18, 1998, (reporting that, in a letter to the Commission, Dr. Robert W. Buchanan of the Maryland Psychiatric Research Center, said "some of the commission's recommendations "reinforce concerns' among researchers that the commission is "antipsychiatric research").

²⁶⁹See, e.g., Jeffrey Brainard, *U.S. Suspends Human-Subjects Research at Virginia Commonwealth U.*, CHRON. HIGH. ED., Jan. 28, 2000, at A34; Jeffrey Brainard & D.W. Miller, *Federal Regulators Suspend University Medical Studies in Pennsylvania and Alabama*, CHRON. HIGH. ED., Jan. 24, 2000; Jeffrey Brainard, *Watchdog Agency Blocks New Human-Research Projects at U. of Illinois at Chicago*, CHRON. HIGH. ED., Sept. 10, 1999, at A44;

William Carpenter, recently commented, "Although I believe much of the present public attention is ill-informed and unfair, the field has received a wake-up call." He outlined several suggestions for heightened subject protection that he said "have worked well" at his research facility.²⁷⁰ These included soliciting patient comment on proposed research and consent forms, including clinicians other than research investigators in the capacity assessment and informed consent process, conducting the informed consent process as a bona fide "educational procedure" with special efforts to overcome the "therapeutic misconception," and providing "educational and sensitivity-raising sessions in ethics for investigators and staff."²⁷¹ NIMH is also proposing the implementation of guidelines designed to provide additional protections for decisionally impaired research subjects.²⁷²

Another example of incremental change in this area is direct involvement by patient volunteers and advocates in IRBs.²⁷³ The National Alliance for the Mentally Ill (NAMI) has initiated a program to train and place NAMI members on IRBs across the country.²⁷⁴ With the first group of NAMI trainees almost fully placed, and the NAMI Program presented at a recent meeting of IRB members and administrators,²⁷⁵ NAMI is receiving requests for trainees and other advocacy groups are discussing training their members.²⁷⁶

Paulette Walker Campbell, *Government Suspends Most Human Research Projects at Duke U.*, CHRON. HIGH. ED., May 13, 1999, at 20.

²⁷⁰See William T. Carpenter, Jr., *The Challenge to Psychiatry as Society's Agent for Mental Illness Treatment and Research*, 156 AM. J. PSYCH. 1307 (1999).

²⁷¹*Id.* at 1309-10.

²⁷²See David Shore & Steven E. Hyman, *An NIMH Commentary on the NBAC Report*, 46 BIOLOGICAL PSYCHIATRY 868, 1013-16 (1999).

²⁷³See *NAMI Invests in Mental Health Research Subject Education*, THE BLUE SHEET, Nov. 11, 1998.

²⁷⁴See *id.*

²⁷⁵See *id.*

²⁷⁶See *id.*

The Push for More Stringent Regulation

On the other hand, the push for more stringent regulations gains momentum with every new account of research abuses of vulnerable persons depicted in the popular press.²⁷⁷ These have not been limited to research on the decisionally impaired but have included research with racial minorities, the terminally ill, and other patients. For example, only recently has the federal government unequivocally apologized for the Tuskegee Syphilis study.²⁷⁸ In addition, a 1995 federal report revealed ethical lapses in a number of studies involving radiation, including some in which decisionally impaired subjects were involved.²⁷⁹

Recent press coverage has described questionable research practices across a wide spectrum including research with individuals who are mentally ill or have other decisional impairments.²⁸⁰ Some articles have focused on conflicts of interest, in which physicians pressure patients into enrolling in clinical trials so that the physicians may receive the enrollment fee paid by the drug company testing their product.²⁸¹ Other articles have exposed physician researchers engaging in fraudulent reporting of data in order to satisfy drug sponsors.²⁸² These articles erode public trust in the research enterprise.

Generally, articles discussing research on the mentally impaired have focused on a few controversial types of research. These include washout and challenge studies.²⁸³ Washout studies require that

²⁷⁷See *infra* notes 278-82 and 293.

²⁷⁸See Alison Mitchell, *Clinton Regrets 'Clearly Racist' U.S. Study*, N.Y. TIMES, May 17, 1997, at A1, available in 1997 WL 17838570.

²⁷⁹See *Human Radiation Experiments: Roadmap to the Project: ACHRE Report* (visited Jan. 17, 2000) <<http://www.tis.eh.doe.gov/ohre/roadmap/achre/report.html>>.

²⁸⁰See *infra* notes 291-294.

²⁸¹See Kurt Eichenwald & Gina Kolata, *Drug Trials Hide Conflicts for Doctors*, N.Y. TIMES, May 16, 1999, at A1 (stating that SmithKline Beecham P.L.C., was paying \$1,610 for each patient that doctors signed up and that doctors can earn as much as \$500,000 to \$1 million a year for recruiting patients into clinical drug trials).

²⁸²See Kurt Eichenwald & Gina Kolata, *A Doctor's Drug Studies Turn into Fraud*, N.Y. TIMES, May 17, 1997, at A1 (reporting on practices of Dr. Robert Fiddes who allegedly became rich by "conducting research fraud of audacious proportions, cutting corners and inventing data to keep the money flowing from the drug industry.")

individuals be taken off their medication for a period of time.²⁸⁴ In studies seeking an understanding of the physiology of mental illness, scans are then taken of the brain to observe the natural course of the disease and its impact on the brain.²⁸⁵ Washout may also be necessary to make sure an individual is cleansed of one drug before a new drug is offered as part of a clinical trial.²⁸⁶ Challenge studies also require that individuals be taken off their medications.²⁸⁷ Research subjects are given drugs that exacerbate symptoms or induce psychosis.²⁸⁸ These “challenge agents” enable scientists to use the subjects as models for studying psychotic illnesses.²⁸⁹

Articles in the lay press have focused on the risks inherent in these studies. In a number of cases, individuals were allegedly harmed and were not given informed consent prior to enrollment in the studies.²⁹⁰ Reports that a schizophrenic patient who had participated in a washout study committed suicide in 1991 by jumping off the roof of a building at the University of California at Los Angeles²⁹¹ were taken by critics as damning evidence of the risks associated with this type of research.²⁹² A series in the Boston Globe in November 1998 focused, in large part, on patients who were enrolled in washout and challenge studies without being told that they might experience relapses or be exposed to drugs

²⁸³See *infra* note 293.

²⁸⁴NBAC REPORT, *supra* note 1, at 13-14. Sometimes these medication free periods are referred to as “drug holidays.” *Id.* at 14.

²⁸⁵See *id.*

²⁸⁶See *id.* at 14 (“[S]uch a protocol often seeks to return the individual to a medication free baseline state so that behavior can be assessed or new drugs introduced without the confounding factor of other substances already in the person’s system”).

²⁸⁷See *id.*

²⁸⁸See *id.*

²⁸⁹NBAC REPORT, *supra* note 1, at 13.

²⁹⁰See *infra* notes 291-93.

²⁹¹See Philip J. Hilts, *Agency Faults a UCLA Study for Suffering of Mental Patients*, N.Y. TIMES, Mar. 10, 1994, at A1 (reporting that the OPRR found that the experiment “failed to comply with the requirements of H.H.S. regulations by not telling patients the extent of the risks they would be asked to take and not telling them that ordinary treatment would be safer for most of them”).

²⁹²See Editorial, *When Mental Patients Are at Risk*, N.Y. TIMES, Mar. 31, 1999, at A28.

that would exacerbate their symptoms.²⁹³ An editorial appearing in the *Globe* on the heels of the series characterized the articles as presenting “an ethical wasteland where doctors not only cause anguishing psychotic symptoms in formerly functioning patients, but occasionally drive them to suicide.”²⁹⁴ Individuals who bring forth this list of abuses argue that, while regulation of research with this population is necessary, the regulatory proposals do not go far enough.

Researchers defend this type of research by arguing that the conditions being studied are uniquely human conditions and there are no animal models for developing treatment.²⁹⁵ Researchers further contend that the risks of these studies have been exaggerated and that adequate safeguards for subject welfare are in place.²⁹⁶ The goal of these studies, according to the NBAC, “is to generate disease manifestations in a controlled setting so that they can be more fully understood and so that appropriate interventions can be designed, attempted, and evaluated.”²⁹⁷ Yet, the NBAC Report raised several questions about these studies including whether it is “possible to obtain informed consent to participate in a study designed to provoke symptoms” and “whether the relationship between risks and potential benefits can ever justify enrolling individuals in such studies when the protocols include intentionally inducing what would otherwise be considered harmful.”²⁹⁸ Those arguing for more stringent regulations express skepticism about the ability of IRBs to protect research subjects. Rejecting arguments that self improvement by IRBs is sufficient without additional regulations, critics argue that there are deeper, more fundamental

²⁹³See Robert Whitaker & Dolores Kong, *Doing Harm: Research on The Mentally Ill*, BOSTON GLOBE, Nov. 15-18, 1998, at A1 (four-part series).

²⁹⁴See Editorial, *Unethical Experimentation*, BOSTON GLOBE, Nov. 19, 1998, at A26.

²⁹⁵See Whitaker & Kong, *supra* note 293.

²⁹⁶See William T. Carpenter & Robert R. Conley, *Sense and Nonsense: An Essay on Schizophrenia Research Ethics*, 35 SCHIZOPHRENIA RESEARCH 219, 222-23 (1999).

²⁹⁷*Id.* See also Franklin G. Miller & Donald L. Rosenstein, *Psychiatric Symptom-Provoking Studies: An Ethical Appraisal*, 42 BIOLOGICAL PSYCHIATRY 403 (1997) (“Encouraging open discussion of potentially problematic psychiatric research coupled with refinement of research guidelines may obviate excessive regulatory restrictions that could hamper valuable research and its contribution to improved patient care”).

²⁹⁸See NBAC REPORT, *supra* note 1, at 13-14.

problems with the IRB system that these modifications do not address.²⁹⁹ For example, a June 1998 report of the Department of Health and Human Services Office of the Inspector General identified deficiencies in IRB oversight and concluded that IRBs are under considerable stress—faced with many more protocols for review than they can adequately handle.³⁰⁰ Others have criticized IRBs as being captives of the institutions over which they preside, heavily dominated by researchers and others motivated by the cash flow that comes to academic institutions from research grants,³⁰¹ with only a token member from the community or representative of patient interests.³⁰²

The Politics of Change—Alliances and Divergences Among Advocacy Groups for the Mentally Ill and those with Dementia

The complexity of regulating research in this area is further compounded by unexpected political alliances and rifts between advocacy groups that, in other circumstances, would be regarded as allies. New voices of patients, not heard twenty-five years ago; differences in perspective based upon disease category; and diverging interests between patients and family members have splintered stakeholders that might otherwise be unified in their approach to this issue.³⁰³

²⁹⁹See *Institutional Review Boards: A Time for Reform Before the House Resources Subcomm., House Government Reform and Oversight Comm., 108th Cong. (1998)*.

³⁰⁰See *Institutional Review Boards: A Time for Reform Before the House Resources Subcomm., House Government Reform and Oversight Comm., 108th Cong. 1 (1998)*; NAMI INVESTS IN MENTAL HEALTH RESEARCH SUBJECT EDUCATION, FINAL REPORT: EVALUATION OF NIH IMPLEMENTATION OF SECTION 491 OF THE PUBLIC HEALTH SERVICE ACT, MANDATING A PROGRAM OF PROTECTION FOR RESEARCH SUBJECTS 1 (1998).

³⁰¹See Sundram, *supra* note 117, at 49-50 (referring to the 1996 GAO Report which raised concerns about IRB “lack of independence, and collegial and institutional pressures upon IRB members that cloud their role as a safeguard on research practices”).

³⁰²See Adil E. Shamoo & Joan L. O’Sullivan, *The Ethics of Research on the Mentally Disabled*, in *HEALTH CARE ETHICS—CRITICAL ISSUES FOR THE 21ST CENTURY* 242 (J.F. Monagle & D.C. Thomasma, eds., 1998).

³⁰³See Weiss, *supra* note 156, at A6 (stating that regulating psychiatric research “has even split the vociferous community of patient advocates, including the 185,000-member National Alliance for the Mentally Ill (NAMI). One camp perceives research as the key to

Patient advocacy groups have been the strongest proponents of research with decisionally impaired, even research that requires the involvement of persons unable to provide their own informed consent. Advocacy groups representing Alzheimer's disease patients have long been supporters of research, actively entering into partnership with researchers to assist in study advertisement and recruitment.³⁰⁴ Advocates for psychiatric patients, particularly NAMI, have also been strong supporters of research.³⁰⁵ Yet many factors have contributed to differences of opinion between these two patient groups regarding the regulation of research with those lacking decisionmaking capacity, including differences in disease manifestation and sequelae. Specifically, Alzheimer's disease is a late-onset disorder.³⁰⁶ Although there are subsets of the disorder that present in middle life, the overwhelming majority of cases surface at the end of the life span.³⁰⁷ Because of this fact, persons who suffer from Alzheimer's disease are likely to remain in the care of their extended families from whom they

curing mental illness and wants to assure that new regulations are not unduly restrictive. The other camp sees its former colleagues as having sold out to wealthy pharmaceutical companies and private research enterprises, which in recent years have sought to integrate themselves into the patient advocacy movement").

³⁰⁴In 1982, the Alzheimer's Association initiated its own grants program and since then "has awarded \$60 million in research funding." The Association "has a long commitment to the direct support of research grants as well as a commitment, through public policy efforts, to increase federal funding for Alzheimer's disease research. See Alzheimer's Association (visited Jan. 24, 2000) <<http://www.alz.org>>. See also Local Opportunities for Participation in Research (visited Jan. 24, 2000) <<http://www.alzcmd.org>> (Maryland Chapter of the Alzheimer's Association website listing local clinical trials and other research opportunities for Alzheimer's patients.)

³⁰⁵See Senate Bill 307, Before the Senate Judicial Proceedings Committee, (Mar. 11, 1999) (testimony of Bill O'Brien, Chair of the NAMI Maryland Subcommittee on Research Ethics). See also Laurie M. Flynn & Ronald S. Honberg, *Achieving Proper Balance in Research with Decisionally Impaired Subjects: NAMI's Perspective on the Working Group's Proposal*, 1 J. HEALTH CARE L. & POL'Y 174, fn 50 (1998) (describing NAMI standards established for the protection of research subjects). But see Weiss, *supra* note 303, at A6 (describing the schism between members of NAMI over this issue).

³⁰⁶See Eleanor P. Lavretsky & Lissy F. Jarvik, *Etiology and Pathogenesis of Alzheimer's Disease: Current Concepts*, in ALZHEIMER'S DISEASE: A HANDBOOK FOR CAREGIVERS 80 (Ronald C. Hamdy et al. eds., 2d ed. 1994)

³⁰⁷See *id.* ("The prevalence of dementia from all causes, ranges from 5% to 10% among persons age 65 and older and the rate increases exponentially as age advances").

can draw much support and sympathy.³⁰⁸ In contrast, psychiatric illness tends to strike much earlier in life, leaving many persons with psychiatric illness unable to finish school, start or sustain careers, or establish their own families.³⁰⁹ Unlike Alzheimer's disease patients who have had a chance to contribute to society and raise a family, it is not uncommon for persons with psychiatric disease to have caused much burden and heartache for their families for many years.³¹⁰ Much more so than in the Alzheimer's context, a split exists between persons with mental illness and their family members regarding research on this population and how it should be regulated.³¹¹ As might be expected, relatives of individuals with a psychiatric disease are largely supportive of regulations that allow for family consent to participation in research of a patient lacking decisional capacity.³¹² Some individuals with mental illness, however, fear that they might, all too quickly, be tagged as decisionally impaired and enrolled, by a member of their family, in a clinical trial in which they would not wish to participate.³¹³ The division is analogous to the debate over the laws for civil commitment—family members of the mentally ill would like to see the laws loosened to allow more flexibility in committing mentally ill

³⁰⁸See Curtis B. Clark & Lynda Westerly, *Elder Abuse*, in *ALZHEIMER'S DISEASE: A HANDBOOK FOR CAREGIVERS*, 329 (Ronald C. Hamdy et al. eds., 2d ed. 1999).

³⁰⁹See Laura Lee Hall & Laurie Flynn, *Consumer and family concerns about research involving human subjects research*, in *ETHICS IN PSYCHIATRIC RESEARCH* 219-38 (Harold Alan Pincis et al. eds., 1999).

³¹⁰See *id.*

³¹¹See *id.*

³¹²See *id.*

³¹³*Amici* in the *T.D.* case criticized the New York regulations on research with institutionalized patients as allowing surrogates to consent to such participation without guidelines that require them to consider what the patient would have wanted or what would be in their best interest and argued that "without proper guidelines, surrogates may be influenced, however, subconsciously, by such improper considerations as the perception that the patient's continued care is dependent on participation in research, or desperation for a cure even when the research is non therapeutic." Brief for proposed *Amici Curiae*, *The Bazelon Center for Mental Health Law, et al. T.D. v. New York State Office of Mental Health*, 650 N.Y.S.2d 173 (App. Div. 1996)(No. 5136/91). See also Richard Ketai et al., *Family Influence in the Recruitment of Schizophrenic Research Subjects*, 138 *AM. J. PSYCHIATRY* 351 (1981) (finding "striking manipulation" by family members to have their schizophrenic relatives participate in high risk research).

patients so that they can be treated; mentally ill patients prefer the narrow criteria of “dangerousness” to remain the commitment standard.³¹⁴

Another difference in disease manifestation has contributed to differences in the political force of each of these groups. Alzheimer’s disease is a disease of the modern age. It has only been in the twentieth century that persons have lived long enough to develop the disorder. Psychiatric disease, in contrast, has been observed and recorded throughout all of human history. These differences, in part, contribute to the differentials in social stigma associated with these diseases. Although we now know that the loss of our mental faculties in late life is not normal aging but a manifestation of brain disease, we still tend to feel more kindly to our elderly neighbor when we find him or her wandering, disoriented and confused, than we do towards the young schizophrenic who gets on the subway with us, talking to him or herself and gesticulating in the air. These differential emotional reactions—pity versus fear, sympathy versus aversion—also contribute to differences in funding streams and reimbursement for care of persons with either of these conditions.³¹⁵

Thus, the sectors of support for research that, by the very nature of the questions it asks, involves persons decisionally unable to provide their own informed consent, have been composed mostly of physician-investigators, patient family members, and the friends of science in the halls of the U.S. Congress and state legislatures. Those raising concerns about the vulnerability of these subjects, and thus the need for caution and increased protections, on the other hand, have been disability rights advocates, medical ethicists and former decisionally-

³¹⁴See *supra* note 182 and accompanying text.

³¹⁵See Winerip *supra* note 154, at 45-46. The differences in social support for these two kinds of conditions show themselves in how their care is paid for by our society. *See id.* Much of our tax dollars goes to taking care of persons with Alzheimer’s disease. *See id.* These are the residents of our nation’s nursing homes who are taken care of with Medicaid dollars. *See id.* According, however, to a 1998 study by The Bazelon Center for Mental Health Law, “[f]ewer than half of the Americans with schizophrenia receive adequate care” and “spending by the 50 states on treatment for the seriously mentally ill is a third less today than it was in the 1950s (once numbers are adjusted for inflation and population growth).” *Id.*

impaired subjects, themselves.³¹⁶ The former is a political alliance of the strong and powerful. The latter is a political alliance of what traditionally has been the weak and fragmented. As a result of many of the societal, legal and medical changes that have taken place in the last twenty years—deinstitutionalization, the disability rights movement, increased rights of the disabled to refuse medical treatment and limitations on our ability to institutionalize them or appoint a guardian to make decisions for them, and the development of medications that allow many of those with mental illnesses to function in the community—the voices of those with mental illness and disorders that affect the brain are now being heard. Yet, these voices are not speaking in unison and further complicate the future of regulatory initiatives.

Longer Run Prospects—Working Toward the Opening of the Policy Window

Given the history of controversy in this area and the sharply differing views of many participants in the debate, inaction on the three sets of recommendations to regulate research on the decisionally incapacitated is not surprising. This is especially true given the inability to reach consensus on the core ethical issue, that is, whether research that poses more than a minimal risk may be ethically conducted on persons who are both unable to give consent and unlikely to benefit from participation in the research. Indeed, the most likely short-term outcome is that the irreconcilable views of influential forces (researchers, academic institutions, pharmaceutical manufacturers, patient rights groups, family advocates, religious organizations) will lead policymakers to view inaction as the safest course.³¹⁷

Yet, policy inaction does not necessarily mean that progress on this issue will not continue. The very fact of three governmental initiatives, ratifying simultaneously the need for greater care when

³¹⁶See Wichman, *supra* note 197, at 93 (“Vulnerable research subjects are people who are relatively or absolutely incapable of protecting their interests”).

³¹⁷In that event, advocates might pursue a litigation-oriented strategy, with unpredictable consequences. If other courts were to accept the now-vacated opinion of the intermediate appellate court in *T.D.*, policy change will be constitutionally compelled. See *supra* notes 223-230, and accompanying text.

capacity-impaired subjects are enrolled in research, helps change the *zeitgeist*, the set of expectations that researchers and IRBs bring to the conduct and review of this type of research. The policy proposals, or publicity about them, may also have contributed to the phenomenon of improved self-regulation discussed above. Many psychiatric researchers, for example, will pay more attention than ever to capacity assessment and risk reduction. IRBs will continue to expand their membership to include those who can better represent the perspective of impaired-capacity subjects. Assent procedures will be made more explicit. None of these changes requires regulatory or legislative action. That they are incommensurable does not make them insubstantial.

Moreover, the struggles over the NBAC, Maryland, and New York reports may be viewed as an essential, albeit often frustrating, part of policy development. Policy change occurs, according to the trenchant analysis of a leading political scientist, John W. Kingdon, when three “streams of processes” come together: “(1) problem recognition, (2) the formation and refining of policy proposals, and (3) politics.”³¹⁸ At certain times, “when a policy window opens,” these three streams merge into action: “A problem is recognized, a solution is available, [and] the political climate makes the time right for change....”³¹⁹

In other countries with significant biomedical research activities, the time has been right for change. In Canada, the Tri-Council Working Group completed and submitted its Code of Ethical Conduct for Research Involving Humans to the Medical Research Council of Canada (MRC), the Natural Sciences and Engineering Research Council of Canada (NSERC), and the Social Sciences and Humanities Research Council of Canada (SSHRC).³²⁰ This Code includes several articles specifically limiting the conditions under which persons unable to provide their own informed consent can be entered into research.³²¹

³¹⁸See KINGDON, *supra* note 233, at 87.

³¹⁹*Id.* at 88.

³²⁰See Canadian Tri-Council Report, *Code of Conduct for Research Involving Humans*, (visited Jan. 20, 2000) <<http://www.ethics.ubc.ca/code>>.

³²¹See *id.*

In Europe, the Council of Europe also issued convention articles explicitly limiting the involvement of persons in research unable to give their own voluntary consent.³²²

In the United States, the very existence of the three governmental initiatives, against a backdrop of extensive analysis and commentary in the academic literature,³²³ suggests that research with impaired-capacity subjects is now recognized as a problem. Still missing, as the reaction to the initiatives demonstrates, is anything approaching consensus about a solution. Thus, formal adoption of even modest regulatory proposals may still be far off. In Maryland, for example, the Attorney General recently proposed a drastically revised bill characterized by that office as “incrementally helpful in protecting vulnerable subjects, not unduly burdensome to investigators or IRBs, focused on matters that even people who disagree sharply about other things might accept as common ground, and relatively short and uncomplicated.”³²⁴ Avoiding the most controversial areas in the bill rejected earlier in the year, the Attorney General’s more recent proposal did not try to define “legally authorized representatives” or allocate authority by reference to risk categories. Nor did it address research advance directives. In that respect, the proposal maintained the status quo. In essence, the proposal merely sought to remind investigators and IRBs that they

³²²See Council of Europe Report, *Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine* (visited Jan. 20, 2000) <<http://www.coe.fr/eng/legaltext/164e.htm>>.

³²³See, e.g., Philip M. Bein, *Surrogate Consent and the Incompetent Experimental Subject*, 46 FOOD DRUG COSMETIC L.J. 739 (1991); Jessica Wilen Berg, *Legal and Ethical Complexities of Consent with Cognitively Impaired Research Subjects: Proposed Guidelines*, 24 J. LAW, MED & ETHICS 18 (1996); Richard J. Bonnie, *Research with Cognitively Impaired Subjects*, 54 ARCH. OF GEN. PSYCHIATRY 105 (1997); Evan DeRenzo, *Surrogate Decision Making for Severely Cognitively Impaired Research Subjects: The Continuing Debate* 3 CAMBRIDGE Q. OF HEALTHCARE ETHICS 539 (1994); Evan G. DeRenzo, *The Ethics of Involving Psychiatrically Impaired Persons in Research*, IRB, Nov.-Dec. 1994, at 7; Rebecca Dresser, *Mentally Disabled Research Subjects: The Enduring Policy Issues*, 276 JAMA 67 (1996); Jason H.T. Karlawish & Greg A. Sachs, *Research on the Cognitively Impaired: Lessons and Warnings from the Emergency Research Debate*, 45 J. AM. GERIATRL SOC. 474 (1997).

³²⁴See Letter from Jack Schwartz, Maryland Assistant Attorney General, to Multiple Recipients (Oct. 6, 1999) (on file with the authors).

needed to think carefully about the welfare of these research subjects and that they are accountable to the public for their decisions.³²⁵

Most who commented on the new proposal, including some who had opposed the Attorney General's original proposal, agreed that it represented a step forward, with modest benefits for subjects and no appreciable burden on the research enterprise. The pharmaceutical manufacturers, however, continued to oppose any additional state regulation. Moreover, one influential patient advocacy group also opposed the revised proposal, arguing that it was inadequate because it did not, for example, prohibit controversial procedures like "washout" studies.³²⁶ Under the circumstances, the Attorney General concluded that the proposal still could not generate sufficient legislative support and withdrew it.

This latest episode in the Maryland policymaking process exemplifies the difficulty of trying to achieve consensus even on narrow issues in this public, legislative debate. As Kingdon observes, policy change can be accomplished if a proposal is "available, worked through, and ready to go."³²⁷ This cannot now be said about research with impaired-capacity subjects. Indeed, the core ethical disagreement may never be resolved³²⁸ and future legislative and regulatory initiatives

³²⁵*See id.* The proposal contains a requirement for IRB review of research, whatever its funding source, involving "decisionally incapacitated individuals" and individuals with a "potentially incapacitating condition"; a requirement for investigators to describe their plans for capacity assessment and assent, together with protection for subjects who refuse to assent; a requirement for an IRB to consider the investigator's plans as well as other appropriate measures to protect the research subjects, to document the IRB's decisions in its minutes, and to respond to valid complaints; and provisions for public access to IRB minutes and approved consent documents and for research subject access to research protocols, with protection for proprietary information. *Id.*

³²⁶*See supra* notes 283-294, and accompanying text.

³²⁷KINGDON, *supra* note 233, at 143.

³²⁸In part, this may be a result of a lack of empirical data informing the policy debate. At present, we do not know how many decisionally impaired individuals are harmed as a result of their participation in research, nor do we know how the various proposals put forward would affect actual research *e.g.*, whether they would prevent some beneficial forms of research. *See, e.g.*, Letter from Laura L. Cain, Esq., *Maryland Disability Law Center*, to The Honorable Walter Baker, *Senate Judicial Proceedings Committee*, regarding SB 307, The Decisionally Incapacitated Research Subject Protection Act (Mar. 11, 1999) (on file with the authors) (stating that "[w]e find no credible evidence to support a claim that research or advancements

may simply be history repeated: prolonged, contentious debate followed by inaction. Against this pessimistic view, however, must be set both short-term gains and long-term possibilities. Actual progress has been and likely will continue to be registered in less formal ways, as funding agencies, academic institutions, IRBs, and researchers adopt reforms that they regard as ethically sound and practically feasible. This kind of incremental, ad hoc reform is likely to be responsive to educational initiatives, the development of professional guidelines, and, not least, the possibility (or threat) of formal regulation. Consequently, without the pressure that efforts to achieve policy change exerts, progress on this front may be elusive.

An additional reason for continued pursuit of a policy consensus is that sometimes years of effort unexpectedly pay off. As Kingdon points out, the framing of a solution that fits a problem, is broadly endorsed by policy advocates, and is politically acceptable often takes considerable time. Those working on possible solutions ("policy entrepreneurs," Kingdon calls them) must be willing "to invest their resources—time, energy, reputation, and sometimes money—in the hope of a future return."³²⁹ Policy advocates need time to refine their arguments, engage competing solutions, educate policymakers and the public, float trial balloons, and assess technical feasibility and cost. "Softening up seems to be necessary before a proposal is taken seriously. Many good proposals have fallen on deaf ears because they arrived before the general public, the specialized publics, or the policy communities were ready to listen. Eventually, such a proposal might be resurrected, but only after a period of paving the way."³³⁰ Just as the debate over DHEW's proposed rules and the National Commission's recommendations began the "softening up" process a quarter-century ago, so the three recent governmental initiatives carried it significantly forward. For the sake of the research subjects to whom society owes a special duty of care, and for the sake of the moral values that should be

in the treatment of mental disorders or impairments would halt in the absence of a pool of decisionally-incapacitated subjects").

³²⁹KINGDON, *supra* note 233, at 122.

³³⁰*Id.* at 130.

at the heart of the research enterprise, governmental agencies or bodies should continue to develop regulatory proposals for public review and debate.