

**PROXY CONSENT TO PARTICIPATION OF THE  
DECISIONALLY IMPAIRED IN MEDICAL RESEARCH  
— MARYLAND'S POLICY INITIATIVE**

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I. INTRODUCTION

**DO YOU HAVE A LOVED ONE WITH MEMORY LOSS?**

***RESEARCH TO FIND TREATMENTS FOR  
ALZHEIMER'S DISEASE IS BEING CONDUCTED AT***

**The Innovative Clinical Research Center**

Study participants will receive **FREE** medical care for Alzheimer's disease, **FREE** memory assessment tests, **FREE** study medication, and frequent monitoring. . . .

To qualify for a research program, your loved one must:

- Have a responsible family member or other caregiver who will attend study visits and ensure that study medication is properly taken
- Have symptoms of Alzheimer's disease—such as gradually worsening short term memory, judgment, and ability to perform daily activities
- Be in otherwise good health.

To learn about our studies, please contact . . . .<sup>1</sup>

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1. Advertisement, *Do You Have a Loved One With Memory Loss?*, WASH. POST, Oct. 6, 1996, at A22.

This advertisement appeared in a Washington, D.C. area newspaper in the fall of 1996. It illustrates the demand for research subjects who are “decisionally impaired”—that is, incapable of providing informed consent to participation in medical research. The advertisement suggests that “loved ones” may consent to participation in medical research for those who are unable to consent themselves. Do proxies have that authority? Should they? If the answer is yes, should limits be placed on that authority, and what should those limits be? This article discusses an effort in Maryland to answer these questions and establish guidelines for research with those who lack decision-making capacity.

## II. CURRENT LEGAL UNCERTAINTY

### A. *Research-Specific Provisions*

Federal regulations regarding research on human subjects provide for two fundamental safeguards: approval by an institutional review board (IRB)<sup>2</sup> and informed consent.<sup>3</sup> The latter requirement provides that “no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject’s legally authorized representative.”<sup>4</sup> The term “legally authorized representative” is circuitously defined as “an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the procedure(s) involved in the research.”<sup>5</sup> Apart from these provisions, federal regulations provide little guidance or safeguards for the conduct of research on decisionally impaired patients.<sup>6</sup> In 1978, the former Department of Health, Education and Welfare proposed regulations that would have provided additional safeguards for research on individuals institutionalized as mentally disabled.<sup>7</sup> However, these regulations were abandoned in the face of sharp controversy, in particular

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2. 45 C.F.R. § 46.103(b) (1996) (explaining that federal support for research involving human subjects will be provided only if the institution where the research is to be conducted has certified that the research has been reviewed and approved by an IRB and will be subject to continuing review by the IRB).

3. 45 C.F.R. § 46.116 (1996).

4. *Id.*

5. 45 C.F.R. § 46.102(c) (1996).

6. The federal regulations do establish additional safeguards for research involving fetuses, pregnant women and human *in vitro* fertilization, 45 C.F.R. §§ 46.201-211 (1996), prisoners, 45 C.F.R. §§ 46.301-306 (1996), and children, 45 C.F.R. §§ 46.401-409 (1996), but not for research on cognitively impaired individuals.

7. *See* 43 Fed. Reg. 53,954 (Nov. 17, 1978).

the argument that they unfairly singled out the mentally ill and institutionalized for protections.<sup>8</sup>

Because federal law leaves unanswered the question of who is a "legally authorized representative" for consent to research, researchers who seek to rely on this provision of federal law must turn to relevant state law for guidance. Unfortunately, little, if any, state law directly addresses this issue.

The little law that is available applies primarily to institutionalized individuals and either prohibits incapacitated persons from participating in experimental research or significantly limits the circumstances under which these individuals can participate in research.<sup>9</sup> Most of the statutes that address the issue require judicial approval or approval by a court-appointed guardian or conservator. For example, California law allows for consent by a conservator, but "only for medical experiments related to maintaining or improving the health of the subject or related to obtaining information about a pathological condition of the subject."<sup>10</sup> A number of states require court approval before a guardian or conservator may consent to participation in med-

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8. See Jessica Wilen Berg, *Legal and Ethical Complexities of Consent with Cognitively Impaired Research Subjects: Proposed Guidelines*, 24 J. L. MED. & ETHICS 18, 19 (1996); Richard J. Bonnie, *Research with Cognitively Impaired Subjects: Unfinished Business in the Regulation of Human Research*, 54 ARCH. GEN. PSYCHIATRY 105, 108 (1997).

9. See, e.g., ALASKA STAT. § 47.30.830 (Michie 1996) (prohibiting experimental research on state mental health patients that involve "any significant risk of physical or psychological harm"); DEL. CODE ANN. tit. 16, § 5175(f) (1995) (prohibiting any resident of a state mental hospital from being approached "to participate in pharmaceutical research if [the] patient is incapable of understanding the nature and consequences of [the] patient's consent."); DEL. CODE ANN. tit. 16, § 5174 (1995) (prohibiting certain classes of state mental hospital residents, regardless of competency, from participating in pharmaceutical research); MASS. REGS. CODE tit. 104, §§ 13.01-.05 (1995) (prohibiting research on patients in mental facilities that will not provide direct, therapeutic benefit and prohibiting research on patients with mental disabilities where the risk is more than minimal and exceeds the benefit to the subject); MO. ANN. STAT. § 630.115(8) (West Supp. 1997) (preventing state mental health patients from being "the subject of experimental research," with exceptions, and prohibiting biomedical or pharmacological research from being performed on any individual with mental disabilities if that research will have no direct therapeutic benefit on the individual research subject).

10. See, e.g., CAL. HEALTH & SAFETY CODE § 24175(b)(1) (West 1992) and CAL. PROB. CODE § 2354 (West 1991) (permitting conservator of patient who has not been adjudicated incompetent to consent to medical experimentation where patient does not object to participation or where the conservator acts in good faith during a medical emergency); CAL. HEALTH & SAFETY CODE § 24175(b)(2) (West 1992) and CAL. PROB. CODE § 2355(a) (West 1991) (permitting conservator of patient who has been adjudicated to lack the capacity to give informed consent to consent even if the patient objects). In both provisions of the California code, informed consent given by a person other than the human subject may "only be for medical experiments related to maintaining or improving the health of the human subject or related to obtaining information about a pathological condition of the human subject." CAL. HEALTH & SAFETY CODE § 24175(e) (West 1992).

ical research by an individual lacking decision-making capacity,<sup>11</sup> and the court must determine that the experimental treatment would be in the "best interests" of the ward.<sup>12</sup>

A few state statutes permit the parent of a child with mental retardation to consent to the child's participation in medical research,<sup>13</sup> but generally statutes do not explicitly allow parents or other relatives to consent to participation in medical research on behalf of a decisionally impaired relative. Of the statutes that address the issue, none appears to permit research on cognitively impaired individuals with consent of a non-court-appointed proxy unless there are additional safeguards. In some cases, a statute may appear to allow consent by a non-court appointed representative with little oversight, but regulations provide additional protections. For example, the Virginia mental health statute states that an individual who is a patient or resident of a hospital or other facility operated, funded, or licensed by the Department of Mental Health, Mental Retardation and Substance Abuse Services shall "[n]ot be the subject of experimental or investigational research without his prior written and informed consent or that of his legally authorized representative."<sup>14</sup> This law does not define "legally authorized representative" and appears to provide little in the way of protections for institutionalized individuals lacking decision-making capacity. However, regulations promulgated under the statute provide that "[n]on-therapeutic research using patients or residents within an institution [for the mentally ill or mentally retarded] is forbidden unless it is determined by the research review committee

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11. See, e.g., CONN. GEN. STAT. ANN. § 45a-677(e) (West Supp. 1997) (providing that a guardian may only consent to experimental biomedical or behavioral medical procedure or participation in any behavioral experiment "if it is intended to preserve the life or prevent serious impairment of the physical health of the ward or it is intended to assist the ward to regain his abilities and has been approved for that person by the court").

12. 405 ILL. COMP. STAT. ANN. 5/2-110 (West 1993) (providing that parent or guardian cannot consent to ward's participation in any "unusual, hazardous, or experimental services" without approval by court and a determination that such services are in the "best interests" of the ward); MINN. STAT. ANN. § 525.56(3)(4)(a), (b) (West Supp. 1997) (prohibiting a guardian or conservator from giving consent to experimental treatment of any kind unless the procedure is first approved by the court, which must determine if the procedure is in the "best interests" of the ward); N.H. REV. STAT. ANN. § 464-A:25(I)(c)-(e) (1995) (establishing that court can authorize guardian to consent to experimental treatment only after ensuring that such treatment is in the "best interest" of the ward).

13. See FLA. STAT. ANN. § 393.13(4)(c)(6) (West Supp. 1997) (explaining that mentally retarded patient may provide required consent if competent; otherwise parents or legal guardian may do so); WYO. STAT. ANN. § 25-5-132 (Michie 1997) (a resident of a state institution for the mentally retarded has the right to refuse to be subjected to experimental medical or psychological research unless the research is authorized by a court, his guardian, or his parent or guardian *ad litem* if the resident is a minor).

14. VA. CODE ANN. §§ 37.1-84.1 (Michie 1996).

that such non-therapeutic research will not present greater than minimal risk."<sup>15</sup>

Perhaps the most ambitious effort to set standards for research on decisionally impaired individuals has been that of New York State. New York public health statutes provide that each public or private institution or agency that conducts human research "shall establish a human research review committee."<sup>16</sup> The consent of the committee and the Commissioner of the Department of Health are required for all research "involving minors, incompetent persons, mentally disabled persons, and prisoners."<sup>17</sup> Additionally, regulations adopted by the New York State Office of Mental Health set forth procedures to be followed for the participation of human subjects who lacked the capacity to provide informed consent or who were minors in potentially high-risk research involving mental illness.<sup>18</sup> However, the regulations were struck down at the trial court level as invalid and unenforceable because they were found to be inconsistent with the state statute requiring the Commissioner of the Department of Health to consent to all research involving children and incompetent adults.<sup>19</sup>

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15. 12 VA. ADMIN. CODE 5-20-40 (Michie 1997).

16. N.Y. PUB. HEALTH LAW § 2444 (McKinney 1996).

17. *Id.*

18. N.Y. COMP. CODES R. & REGS. tit. 14, § 527.10 (1995). These regulations required that before an IRB approve research on this group, it ensure that (1) "[r]isks to subjects [be] reasonable in relation to anticipated benefits . . . to patients, and the importance of the knowledge that [would] reasonably be expected to result" § 527.10 (d)(4)(ii); (2) "the study could not be carried out without the involvement of the incapable subjects," and that if the research "involved more than minimal risk and/or invasive procedures" that the project be "likely to produce knowledge which has overriding therapeutic importance for the understanding or treatment of a condition which is presented by the patient in question." § 527.10(d)(6). The regulations further set forth detailed requirements for disclosure of information to the patient or his representative regarding the risks and benefits of the research. § 527.10(e)(1). Of most significance was that the regulations provided that if a patient lacked capacity to consent to participation in a research study, consent could be obtained from "(a) an individual appointed pursuant to a duly executed durable power of attorney specifying the authority to consent or withhold consent to participation in research; or (b) an individual designated by the patient to consent or withhold consent to the patient's participation . . ." § 527.10(e)(2)(iii).

The regulations further specified that the individual designated by the patient may not be "a current employee, servant or agent of the facility and may not be affiliated with the research project." *Id.* If an individual does not designate a person to consent on his or her behalf, the regulations provided that consent could be obtained from "the patient's spouse, parent, adult child, adult sibling, guardian or a committee of the person which is authorized to consent to research" and that in the absence of a person from this list consent could be obtained from "a close friend or a court of competent jurisdiction." § 527.10(e)(2)(iv).

19. *See* T.D. v. New York State Office of Mental Health, 626 N.Y.S.2d 1015 (N.Y. Sup. Ct. 1995); *aff'd* 650 N.Y.S.2d 173 (N.Y. App. Div. 1996), *appeal dismissed by* 680 N.E.2d 617 (N.Y. 1997), *leave to appeal granted by* 684 N.E.2d 281 (N.Y. 1997). *See* N.Y. PUB. HEALTH LAW

In a subsequent decision, an appellate court agreed with this finding, but took a step further by also holding that the regulations adopted by the New York State Office of Mental Health failed to provide for adequate notice to potential subjects, failed to include review procedures regarding a determination that the subject lacked decision-making capacity, and therefore violated the due process clauses of both the New York Constitution<sup>20</sup> and the Fourteenth Amendment of the United States Constitution.<sup>21</sup> The court also held that the regulations violated New York common law and two other state statutes. The court stated that for regulations of this kind to meet constitutional standards, they must "at the very least, contain appropriate and specific provisions for notice to the potential subject that his or her capacity is being evaluated and for appropriate administrative and judicial review of a determination regarding capacity."<sup>22</sup> The court explained that a constitutional analysis of the regulations was justified because the Commissioner of Health would be likely to issue new regulations governing human subjects research in response to the court's invalidation of the regulations issued by the Commissioner of Mental Health.<sup>23</sup>

Without clear statutory guidance on this issue, investigators in most states who wish both to perform research on decisionally impaired individuals and to have secure legal protection would need to seek approval from the courts, probably by means of appointment of a guardian who would be authorized to make such decisions. This procedural requirement derives from the state's historical role of *parens patriae*, protecting incompetent individuals and ensuring that decisions for their care are made consistently with their best interests. At least one court has come to this conclusion. In *Kaimowitz v. Michigan*

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§ 2444, subdiv. 2 (McKinney 1985) (where subject is an incompetent person, mentally disabled person, minor, or prisoner, consent of subject, institution's human research review committee and the Commissioner of Health must be obtained). Plaintiffs in the case were "patients involuntarily hospitalized at various psychiatric facilities in New York State subject to supervision by the [Office of Mental Health]" who had been adjudicated incapable of giving consent to medical treatment and subsequently were given "beneficial medication over their objection." 626 N.Y.S.2d at 1017. These patients brought suit on their own behalf and on behalf of all patients in New York State psychiatric facilities out of concern that under the existing regulations promulgated by the Office of Mental Health, they could be forced "to participate in research, as subjects, without their consent." *Id.*

20. N.Y. CONST. art. I, § 6.

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

22. *Id.* at 187.

23. See *id.* at 185.

*Department of Mental Health*,<sup>24</sup> the court held that “experimental psychosurgery” could not legally be performed on a mentally incompetent person even if a surrogate decision-maker, in this case the patient’s family, consented.<sup>25</sup>

In practice, researchers who seek the participation of decisionally impaired individuals in medical research have relied informally on family consent in these circumstances, rather than routinely, or even occasionally, seeking appointment of a guardian. This practice of relying on family consent finds historical support. For example, the Declaration of Helsinki included 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.”<sup>26</sup>

Researchers’ reluctance to seek judicial approval may in part be based on a belief that such procedures are unnecessary or too time-consuming and costly. Apparently, researchers have generally assumed that the approval of an IRB is sufficient to allow surrogate consent to the participation of incapacitated patients in a research protocol. One successful lawsuit within a state will prove this assumption wrong, with potentially devastating consequences for research conducted in that state to combat psychiatric and cognitive disorders. For example, the result of the court decision in *T.D. v. New York State Office of Mental Health*,<sup>27</sup> may significantly limit research in New York on institutionalized individuals who are cognitively impaired. Based upon the appellate court opinion, residents in a New York State facility operated or licensed by the Office of Mental Health who lack decision-making capacity may 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.<sup>28</sup> Moreover, orders issued by the

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24. 42 U.S.L.W. 2063 (Cir. Ct. Wayne Cty., Mich., 1973).

25. 1 MENTAL DISABILITY L. REP. 147 (1976); see also *State Court Bars Experimental Brain Surgery*, 2 PRISON L. REP. 433, 475 (1973).

26. Declaration of Helsinki (1948), reprinted in Council for International Organizations of Medical Sciences, INTERNATIONAL ETHICAL GUIDELINES FOR BIOMEDICAL RESEARCH INVOLVING HUMAN BEINGS 47 (1993). The statement appears to assume the potential for national legislation allowing relatives to consent to participation in research of an incapacitated individual.

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

28. *T.D.*, 650 N.Y.S.2d at 177.

trial court after its opinion,<sup>29</sup> and a stipulation of the parties entered into prior to the appellate court decision, further stated that such residents may not be subjects of non-federally funded *therapeutic* research that is of greater than minimal risk without court authorization or unless the individual prior to incapacity had consented to the research or had appointed a proxy with authorization to consent to the research.<sup>30</sup>

While the appellate decision stated explicitly that “. . . the large majority of studies, which are therapeutic and/or proceed upon the informed consent of subjects or are Federally funded, will remain unaffected,”<sup>31</sup> issues on appeal in the case include whether the restrictions on non-federally funded research should apply to federally funded research and whether there should be additional due process protections in place for therapeutic research conducted with residents in facilities operated or licensed by the Office of Mental Health who lack decision-making capacity.<sup>32</sup>

### B. *Medical Treatment Statutes*

While most states do not have laws that expressly address consent to conduct research with decisionally impaired patients, during the past two decades, most states have passed statutes that allow individuals to consent to receipt of medical treatment on behalf of another who is cognitively impaired. These proxy consent laws are of two types: “durable power of attorney (DPA) for health care” statutes and “surrogate” statutes. A handful of states, including Maryland, have enacted comprehensive statutes incorporating both guidelines for the execution of advance directives and standards for surrogate health

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29. See 626 N.Y.S.2d 1015, No. 5136/91 (Sup. Ct. Jan. 18, 1996) (order to show cause with temporary restraining order).

30. See also 626 N.Y.S.2d 1015, No. 5136/91 (Sup. Ct. Feb. 9, 1996). Therapeutic research is defined as research “for which an Institutional Review Board has determined that the research holds out a prospect of direct benefit and is important to the health or well being of the patient and is only available in the context of the research.” *Id.* at 10-11. Non-therapeutic research was defined as “all research which is not therapeutic research as that term was defined. . . .” *Id.*

31. *T.D.*, 650 N.Y.S.2d at 177.

32. See 650 N.Y.S.2d 1015, No. 5136/91 (App. Div. 1996) (notice of motion for leave to appeal; support of motion for leave to appeal; grant of motion to appeal).



care decision-making for incapacitated individuals.<sup>33</sup> In Maryland the law is referred to as the Health Care Decisions Act.<sup>34</sup>

DPA statutes allow a competent individual to execute a document appointing an "agent" to make health care decisions for the individual in the event that he or she becomes incapacitated.<sup>35</sup> The agent's authority is generally defined by the individual in the DPA itself.<sup>36</sup>

In many states, surrogate consent statutes apply when no agent has been appointed.<sup>37</sup> These statutes typically allow a family member to make medical decisions for an incapacitated patient based on an assessment of what the patient would have wanted (a substituted judgment standard) or, if that preference cannot be inferred, based upon the patient's best interests.<sup>38</sup> Surrogate statutes generally include a priority ranking of those authorized to make decisions, usually beginning with a person's spouse, followed by adult children, then parents and adult siblings.<sup>39</sup> Some statutes go further down the family chain, and a few include a "close friend" in the list.<sup>40</sup>

These statutes, however, do not explicitly address consent to participation in medical research. The laws generally limit the authority of the agent or surrogate to decisions regarding health care or medical treatment. However, only a few states define the terms "health care" or "medical treatment" in their durable power of attorney for health care and surrogate consent statutes.<sup>41</sup> In Maryland, the Health

33. These states include Arizona, Connecticut, Delaware, Florida, Kentucky, Maine, Maryland, New Mexico, Oregon, and Virginia. See ARIZ. REV. STAT. ANN. §§ 36-3201 to -3262 (West 1994); CONN. GEN. STAT. § 1-43 (1993) and §§ 19a-570 to -575 (1993); DEL. CODE ANN. tit. 16, §§ 2501-2517 (1996); FLA. STAT. ANN. §§ 765.101-401 (West 1994); KY. REV. STAT. ANN. §§ 311.621-643 (Michie Supp. 1994); ME. REV. STAT. ANN. tit. 18A, §§ 5-801 to -817 (West 1995); MD. CODE ANN., HEALTH-GEN. §§ 5-601 to -608 (1994); N.M. STAT. ANN. §§ 24-7A-1 to -18 (Michie 1995); OR. REV. STAT. §§ 127.505-640 (1993); VA. CODE ANN. §§ 54.1-2981 to -2993 (Michie Supp. 1992).

34. MD. CODE ANN., HEALTH-GEN. § 5-602 (1994).

35. See, e.g., MD. CODE ANN., HEALTH-GEN. § 5-602 (1994).

36. See ALAN MEISEL, THE RIGHT TO DIE § 12.22, at 164-65 (2d ed. 1995).

37. See *id.* § 14.4, at 253.

38. See *id.* § 14.8, at 263-66. While virtually all states have a DPA statute, only about two-thirds have surrogate decision-making laws. See Diane E. Hoffmann, et al., *How Close is Enough? Family Relationships and Attitudes Toward Advance Directives and Life Sustaining Treatments*, 3 J. ETHICS, LAW & AGING 5, 18 ("As of January, 1996, 32 states and the District of Columbia had statutes authorizing family members to make medical treatment decisions for an incapacitated relative based on the patient's wishes or his or her best interests.").

39. See MEISEL, *supra* note 36 § 14.4, at 254. In states that lack such statutes, case law generally authorizes family members to make health care decisions for incapacitated patients. See Hoffmann et. al., *supra* note 38, at 19.

40. See, e.g., MD. CODE ANN., HEALTH-GEN. § 5-605(a)(2)(vi) (1994).

41. See, e.g., ANN. CAL. PROB. CODE § 4942 (West Supp. 1997) (defining "health care" as "any care, treatment, service, or procedure to maintain, diagnose, or treat an individual's physical or mental condition"); see also GA. CODE ANN. §§ 31-36-1 *et. seq.* (Supp. 1997) (de-

Care Decisions Act<sup>42</sup> does not define health care; however, the Maryland Attorney General's Office stated in an opinion letter that the term "health care" would be synonymous with "a procedure or course of treatment that relates to the disease state of the particular patient."<sup>43</sup> Thus, as long as the research being contemplated involves potential benefit, that is, "as long as there is an articulable link between the research and a possible improvement in the patient's condition, then a 'health care' decision is possible, and the patient's hypothesized wishes would be the basis for it."<sup>44</sup>

In each state, determining whether the health care decision-making laws encompass research will require attention to the specific definition of health care in the statutes or to an inference from the other parts of the statutes to determine whether they should be interpreted to apply to any type of research, potentially therapeutic or otherwise. The opinion letter by the Maryland Office of the Attorney General may be the first authority to interpret the application of a DPA or surrogate decision-making statute to consent to participation in research. The letter states that Maryland's law "does not authorize an agent or surrogate to consent to a protocol that is expected to have no present or future therapeutic effect on the patient. Even an advance directive that generally consents to participation in future research cannot authorize an agent's or surrogate's decision that is unrelated to potential therapeutic effect on the patient."<sup>45</sup> According to the Attorney General, while "altruism is noble, . . . it is not 'health care.'"<sup>46</sup>

In the *T.D.* case, the defendants argued that the limitations in New York state law on surrogate decision-making for withholding of life-sustaining treatment<sup>47</sup> would not apply to surrogate consent for participation in research for a cognitively impaired individual because the decision to participate in research would not lead to a patient's death.<sup>48</sup> New York state has one of the nation's most restrictive rules regarding surrogate consent to termination or withholding of life-sus-

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fining "health care" as "any care, treatment, service or procedure to maintain, diagnose, treat or provide for the patient's physical or mental health or personal care").

42. MD. CODE ANN., HEALTH-GEN. §§ 5-601 *et. seq.*

43. Opinion Letter from Jack Schwartz, Chief Counsel for Opinions and Advice, Office of the Maryland Attorney General (July 26, 1996) [hereinafter "Opinion Letter"] (on file with the *Journal of Health Care Law & Policy*).

44. *Id.* at 2.

45. *Id.*

46. *Id.*

47. See N.Y. COMP. CODES R. & REGS. tit. 14, § 527.10 (1995).

48. *T.D. v. New York State Office of Mental Health*, 650 N.Y.S.2d 173 (N.Y. App. Div. 1996), *appeal dismissed by* 680 N.E.2d 617 (N.Y. 1997), *leave to appeal granted by* 684 N.E.2d 281 (N.Y. 1997).

taining treatment from a patient who lacks decision-making capacity. In the majority of states that have surrogate consent statutes, surrogates may consent to termination of life support if it would be consistent with what the patient would have wanted, or if that cannot be determined, if it would be in the patient's best interests.<sup>49</sup> In New York, the law, as defined through court opinions, prohibits a surrogate from making a decision to withhold or terminate life-sustaining treatment from an incapacitated patient unless there is "clear and convincing evidence" the patient, when competent, had provided instructions to have treatment terminated should he be irreversibly ill.<sup>50</sup> The case law does not allow the withholding or withdrawing of life-sustaining treatment based on a best interest test.<sup>51</sup> Thus, the defendant in *T.D.* argued that the surrogate consent law regarding termination of life support should not apply in the research context as that law is too restrictive. The court rejected the defendant's argument as "unpersuasive with regard to . . . greater than minimal risk non-therapeutic studies."<sup>52</sup> Rather, the court stated that "similar substantive and procedural safeguards should be provided to these potential research subjects as is provided to patients in life-sustaining treatment settings."<sup>53</sup>

At least one prestigious body has advocated that the framework used in many states for clinical decision-making for decisionally impaired individuals be applied to decisions regarding their participation in research. A position paper by the American College of Physicians concludes that individuals should be able to consent through an advance directive to participation in research at a future time when they may be "cognitively impaired."<sup>54</sup> If an individual has not executed such a directive, the position paper states that a legally authorized surrogate should be able to consent to certain research protocols, using a mixed substituted judgment and best interest test.<sup>55</sup>

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49. See *supra* note 38 and accompanying text.

50. See *Matter of Westchester County Medical Center*, 72 N.Y.2d 517 (N.Y. 1988); see also *People v. Eulo*, 472 N.E.2d 286 (N.Y. 1984).

51. No appellate court in the state has allowed the use of a best interest test, however, there is a trial court opinion in which the best interest test was applied. See *In re Beth Israel Medical Center*, 519 N.Y.S.2d 511 (N.Y. Sup. Ct. 1987).

52. *T.D.*, 650 N.Y.2d at 191.

53. *Id.*

54. American College of Physicians, *Cognitively Impaired Subjects*, 111 ANNALS OF INTERNAL MED. 843 (1989).

55. *Id.* at 844.

### III. THE MARYLAND POLICY INITIATIVE

#### A. *Identifying the Issues*

In light of uncertainty about the authority of agents and surrogates in Maryland 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 Office established what was called a "Working Group" to begin a dialogue on the issue. The Working Group consisted of approximately 15 individuals, including lawyers, ethicists, researchers from academic and government institutions, and advocates for the mentally ill.

The Working Group held its first meeting in May, 1995. By the end of the meeting, the group had set its priorities to include the following:

1. To address the circumstances under which an individual with present decisional capacity might give a legally and ethically valid consent to participation in research, at a time of future decisional incapacity, through an advance directive.
2. To explore whether, under carefully limited circumstances, a legally and ethically valid consent to participation in research might be obtained by a proxy (health care agent or surrogate decision-maker) for a research subject who never had decisional capacity or who had lost decisional capacity before expressing any views about participation in research.<sup>56</sup>

In considering these issues, the Working Group was free to consider whatever changes in the law were thought desirable to adapt it to the research setting. Indeed, there was considerable initial agreement among Working Group members that the Maryland Health Care Decisions Act would best serve as an initial framework for approaching the issue of proxy consent to participation in research involving the decisionally impaired. In its present form, however, the law did not provide sufficient safeguards if it were to be adapted as an inclusive mechanism for consent to research participation.

Courts and legislatures have required additional safeguards for other types of surrogate decision-making for individuals lacking deci-

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56. Letter from Jack Schwartz, Chief Counsel for Opinions and Advice, Office of the Maryland Attorney General to Diane Hoffmann, Asst. Professor, University of Maryland, School of Law (May 31, 1995) (on file with the *Journal of Health Care Law & Policy*).

sion-making capacity.<sup>57</sup> Unlike cases involving refusal of life-sustaining treatment, where courts have deferred to families and placed very few limits on their decisions to terminate life support for a close relative, courts and legislatures have generally required safeguards such as judicial approval in cases involving a decision by a surrogate to sterilize or administer psychotropic medications to a mentally incapacitated individual.<sup>58</sup> While the Working Group did not agree this level of procedural protection was required for decision-making for participation in research, the reasons for additional protection in the research context appeared justified by similar considerations to their need in decisions regarding sterilization and the administration of psychotropic drugs, including:

- 1) a history of abusive decision-making in these areas;

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57. See Philip M. Bein, *Surrogate Consent and the Incompetent Experimental Subject*, 46 FOOD DRUG COSMETIC L.J. 739 (1991).

58. *Rivers v. Katz*, 495 N.E.2d 337 (N.Y. 1986) (holding that in situations where the state's police power is not implicated and a patient refuses to consent to the administration of antipsychotic drugs, there must be a judicial determination of whether the patient has the capacity to make a reasoned decision with respect to proposed treatment before the drugs may be administered pursuant to the state's *parens patriae* power). See, e.g., *People v. Medina*, 705 P.2d 961 (Colo. 1985) (en banc) (holding that antipsychotic medicine may be administered to a nonconsenting mentally ill patient incapable of making an informed treatment decision only after the trial court conducts a full and fair adversarial hearing; the court must be satisfied by clear and convincing evidence that the patient is incompetent, that treatment by antipsychotic medicine is necessary, that a less intrusive treatment alternative is not available, and that the patient's need for treatment by antipsychotic medicine is sufficiently compelling to override any bona fide and legitimate interest of patient in refusing treatment); *In the Matter of Moe*, 432 N.E.2d 712 (Mass. 1982) (concluding that a guardian must obtain a proper judicial order for sterilization of an incompetent ward before he or she can validly consent to it; guardians and parents cannot consent to the sterilization of a ward in their care or custody); *In re Guardianship of Roe, III*, 421 N.E.2d 40 (Mass. 1981) (holding that if an incompetent individual refuses antipsychotic drugs, those charged with his protection must seek judicial determination of substituted judgment); *In the Matter of Grady*, 426 A.2d 467 (N.J. 1981) (holding that an appropriate court must make final determination whether consent to sterilization should be given on behalf of incompetent individual).

Most courts have required that a judicial decision regarding the competency of the individual be made prior to a surrogate decision, and, in some cases, have insisted that the court make the decision for the surrogate or approve the surrogate's decision. See *Rogers v. Commissioner of the Dept. of Mental Health et. al.*, 458 N.E.2d 308 (Mass. 1983) (holding that an involuntarily committed mental patient must be adjudicated incompetent by a judge in order to be deprived of the ability to make his or her own treatment decisions, and if a patient is adjudicated incompetent, a judge, using a substituted judgment standard, must decide whether the patient would have consented to the administration of antipsychotic drugs); *Keyhea v. Rushen*, 178 Cal.App.3d 526 (Cal. Ct. App. 1986) (holding that prisoners are entitled to judicial determination of their competency to refuse treatment before they can be subjected to long-term involuntary psychotropic medication).

- 2) the courts' concern that the family or institution seeking such treatments may possess interests which conflict with the patient's; and
- 3) the intrusive nature of the treatments and their adverse risk to future health or family life.<sup>59</sup>

These factors may also play a role in medical research on human subjects. According to one author, medical research on incapacitated individuals deserves heightened scrutiny and more stringent standards for a number of reasons:

First, the history of medical experimentation has been characterized by significant incidents of abuse, particularly where members of vulnerable populations have been enlisted as subjects. Second, the interest of medical researchers in securing participation in the experiment often conflicts with their duties as treating physicians to inform, advise, and act in the best interest of their patients. Third, experimentation is inherently intrusive and dangerous, as the nature and magnitude of risks involved are largely unknown and unknowable.<sup>60</sup>

The court in *T.D.* clearly agreed that there is a similarity between the administration of psychotropic and antipsychotic drugs to incapacitated patients and the use of cognitively impaired patients in medical research. In fact, the court stated explicitly that

practices for assessing capacity and obtaining consent for such experimentation must, at the very least, provide the same safeguards to the constitutional and common law rights of the incapable patients, who may be potential subjects of these experiments, as provided to patients over whose objection treating physicians seek to administer, solely for therapeutic purposes, medications, that can cause similar side-effects.<sup>61</sup>

The current climate of medical research in particular lends credibility to an argument that additional safeguards are necessary for research on the decisionally impaired:

The 1980s witnessed an unprecedented marriage of science and entrepreneurship. During that decade researchers began holding financial interests in companies whose products

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59. See Bein, *supra* note 57, at 751-52.

60. *Id.* at 747-48.

61. *T.D. v. New York State Office of Mental Health*, 650 N.Y.S.2d 173 (N.Y. App. Div. 1996), *appeal dismissed by* 680 N.E.2d 617 (N.Y. 1997), *leave to appeal granted by* 684 N.E.2d 281 (N.Y. 1997).

they were studying. This practice has created new conflicts for researchers. Where a company developing experimental products is a fledgling start-up enterprise with few existing markets, its stock price usually reflects expectations regarding research on the new products. Rapid disclosure of successful research results would enable early Food and Drug Administration (FDA) approval and higher share prices often resulting in a windfall to the researcher with a financial interest. Conversely, a researcher holding a financial interest in the company would have strong incentives not to disclose information which might suggest the product is ineffective or unsafe.<sup>62</sup>

Against this background, the Working Group proceeded to consider the types of additional safeguards that were necessary in the research context. Initial questions articulated by the group included the following:

1. If an individual authorizes an agent to consent to the individual's participation in medical research protocols, should the law impose limits on the agent's authority, or should the agent be trusted to make a decision consistent with the individual's wishes? If limitations are appropriate, what should they be?
2. Should an agent be authorized to consent to an incapacitated individual's participation in medical research if the individual has not expressly given this authorization in the DPA? Should the standard DPA form include the authority of the agent to consent to the individual's participation in medical research:
  - a) that holds out the potential for direct benefit to the individual?
  - b) that holds out no potential for direct benefit to the individual but that may ultimately benefit others?Should an agent's ability to consent be based on the level of risk associated with the proposed research?
3. Should a surrogate (not legally appointed by the individual) be able to consent to the individual's participation in medical research:
  - a) that holds out the potential for direct benefit to the individual?

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62. Bein, *supra* note 57, at 758.

- b) that holds out no potential for direct benefit to the individual but that may ultimately benefit others?

What criteria or limitations, if any, should be placed on the surrogate's decision-making authority? Should a surrogate's authority to consent depend on the level of risk associated with the proposed research?

4. In either case, agent or surrogate, should the criteria for proxy consent to participation of an incapacitated individual in medical research that does not hold out the potential for direct benefit to the individual ever go beyond substituted judgment (*i.e.*, be based on factors other than the individual's wishes?)
5. Is it ever appropriate to allow surrogate consent for a never-capacitated individual to participate in medical research that holds out no potential for direct benefit to the individual?
6. Is it ever appropriate to honor the wishes of an individual written in an advance directive to participate in medical research that is likely to benefit others, whether or not the research holds out the potential for direct benefit to the individual, if the individual has not appointed an agent and has no legal surrogate?

These questions, based largely on the state Health Care Decisions Act, combined with concepts incorporated into the federal regulations for research on human subjects to form the basis of the Working Group's deliberations.

The Working Group presumed that the federal regulatory standards were applicable to federally funded research. The Working Group recognized that some elements of federal regulations—for example, the concept of “minimal risk”—are subject to debate.<sup>63</sup> However, the Working Group concluded that it had neither the mandate nor the resources to address perceived deficiencies in federal law, apart from the regulatory gap concerning decisionally impaired subjects. Therefore, the Group's recommendations reflected the concepts and categories embodied in federal law.

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63. The federal regulations define minimal risk as risks where “the probability and magnitude of harm or discomfort anticipated in the research are not greater in and among themselves than those normally encountered in daily life or during the performance of routine physical or psychological examinations or tests.” 45 C.F.R. § 46.102(i) (1996). Some difficulties with the concept of “minimal risk” are explored in Benjamin Freedman et al., *In Loco Parentis: Minimal Risk as an Ethical Threshold for Research upon Children*, 23 HASTINGS CENTER REP.13 (1993).



In addition, the Working Group did not explore the important and difficult issue of a researcher's assessment of a potential subject's capacity to give informed consent—in particular, the researcher's process of deciding that an individual with a psychiatric disorder is nevertheless capable of giving ethically valid consent.<sup>64</sup> The Working Group's recommendations proceeded from the assumption that, in every category addressed by the Working Group, the potential research subject is *not* capable of giving informed consent to participation in a research protocol at the time of potential enrollment.<sup>65</sup>

### B. Framing Recommendations on Proxy Consent

The Working Group organized its discussion and preliminary recommendations by reference to five factual "scenarios."<sup>66</sup> These scenarios differed in terms of the situation of the now-incapacitated individual—for example, whether the individual had executed a DPA and, if not, whether a surrogate for the individual is available.<sup>67</sup> Within each scenario, the Working Group considered research protocols with different levels of risks and potential benefits.<sup>68</sup> After an opportunity for public comment, the Working Group issued a draft statute reflecting its preliminary policy recommendations.<sup>69</sup>

#### *Scenario A: Consent by health care agent—DPA refers to research participation*

This scenario involves an individual who, when able to understand the nature of the action, gave broad written authority for the individual's health care agent to consent not only to health care, but

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64. Among the accounts describing concerns in this area, see Paul S. Appelbaum et al., *The Therapeutic Misconception: Informed Consent in Psychiatric Research*, 5 INT'L J. L. & PSYCHIATRY 319 (1982); Paul R. Benson et al., *Informed Consent in Psychiatric Research: Preliminary Findings from an Ongoing Investigation*, 20 SOC. SCI. MED. 1331 (1985); Philip J. Candilis et al., *A Survey of Researchers Using a Consent Policy for Cognitively Impaired Human Research Subjects*, 15 IRB: A REVIEW OF HUMAN SUBJECTS RESEARCH 1 (1993); Evan G. DeRenzo, *The Ethics of Involving Psychiatrically Impaired Persons in Research*, IRB: A REVIEW OF HUMAN SUBJECTS RESEARCH 7 (1994).

65. The Working Group's recommendations on subjects' assent indirectly address concerns about an erroneous conclusion that an individual is incapable of giving informed consent. See *infra* text accompanying notes 83-85.

66. Jack Schwartz, Initial Report of the Attorney General's Research Working Group 7-15 (Oct. 8, 1996) (unpublished report on file with the Attorney General's Research Working Group).

67. See *id.*

68. See *id.*

69. Jack Schwartz, Second Report of the Attorney General's Research Working Group (May 5, 1997) [hereinafter Second Report] (the Second Report is reprinted in the appendix to this issue of the *Journal of Health Care Law & Policy*).

also to the individual's participation in research. DPAs that refer specifically to research participation are presently rare, if not nonexistent. However, if state law recognized this use of an advance directive, presumably some people would want to include such a provision in their advance directives.<sup>70</sup> Therefore, the Working Group considered whether the law should authorize consent by the health care agent under these circumstances, for particular types of research protocols.

- *Type of protocol:* No greater than minimal risk.
- *Working Group recommendations:* Authorize the agent to consent if the agent concludes that the individual would have wanted to participate in the particular protocol, even if the investigator can identify no reasonable prospect of direct benefit to the individual.

For this first type of protocol, consensus was easily reached. The DPA reflects an atypical interest in research participation. The individual also selected a health care agent to further that interest, and the agent may be presumed to have been chosen because of the agent's familiarity with the individual's character and values. Thus, deference is owed to the agent's judgment that the particular protocol is one that the individual would have wished to support through participation. The individual's interest in self-determination, the Working Group believed, deserves respect even after the loss of decisional capacity. In this situation, autonomy interests are at their highest, and the low risk of the protocol minimizes concerns that arise from the principle of nonmaleficence.<sup>71</sup>

- *Type of protocol:* Greater than minimal risk, reasonable prospect of direct medical benefit to the individual.
- *Working Group recommendation:* Authorize the agent to consent if the agent concludes that participation would be in the individual's medical best interest, unless there is reason to believe that the individual would not have wanted to participate in the particular protocol.

The characterization of research in terms of its potential for direct medical benefit to the research subject reflects distinctions drawn in the federal regulations. For example, the IRB is to determine whether the risks to the research subject "are reasonable in relation to

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70. See Rebecca Dresser, *Mentally Disabled Research Subjects: The Enduring Policy Issues*, 276 JAMA 67, 70 (1996).

71. See THOMAS L. BEAUCHAMP & JAMES F. CHILDRESS, *PRINCIPLES OF BIOMEDICAL ETHICS* 189-94 (4th ed. 1994).

anticipated benefits, if any . . . .”<sup>72</sup> The Belmont Report asserts that “[r]esearch and practice may be carried on together when research is designed to evaluate the safety and efficacy of a therapy.”<sup>73</sup> Because participation in research having the potential for direct medical benefit involves “health care,” as that term is used in the Health Care Decisions Act, the Working Group’s preliminary recommendation amounted to maintaining the legal status quo.

- *Type of protocol*: Greater than minimal risk, no reasonable prospect of direct medical benefit to the individual.
- *Working Group recommendation*: Authorize the agent to consent if the agent concludes that the individual would have wanted to participate in the particular protocol and either of the following conditions is met: the protocol involves no more than a minor increase over minimal risk,<sup>74</sup> or if the protocol involves more than a minor increase over minimal risk, a knowledgeable person from outside the research team (for example, a member of an institution’s ethics committee) confirms that the agent understands the goals and risks of the protocol.

This type of protocol poses the greatest threat to vulnerable subjects because it not only holds out no hope of personal benefit, but also exposes the subject to risks beyond those ordinarily encountered. Yet, the research-specific advance directive that is envisioned here marks the clearest possible statement of personal choice. Respect for persons implies respect for self-determination.

There was initial agreement among Working Group members that, at a minimum, the state should allow an agent to consent if the individual had given express authorization for participation in this type of research and the research would involve no more than a minor increase over minimal risk. The issue for the Working Group was whether to go beyond this. Some members felt strongly that agents in this situation should not be so restricted and that there should be a mechanism to allow an agent to consent to participation in research for a decisionally impaired individual, even if the research involved a

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72. 45 C.F.R. § 46.111(a)(2) (1996); *see also, e.g.*, 45 C.F.R. § 46.405 (1996) (referring to research “that holds out the prospect of direct benefit for the individual subject”).

73. 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 4 (1979). Some commentators reject the distinction, however. *See, e.g.*, Nancy M. P. King, *Experimental Treatment: Oxymoron or Aspiration?*, 25 HASTINGS CENTER REP. 6 (1995).

74. The term “minor increase over minimal risk” is used, but not defined, in the portion of the federal regulations dealing with children as research subjects. *See* 45 C.F.R. § 46.406(a) (1996).

sizeable increase over minimal risk, if the agent concluded that the patient would have wanted to participate in the protocol.

The Working Group then considered what safeguards might be imposed in this situation. One recommendation was the use of a "consent monitor"—someone who would meet with the agent, go over the protocol in detail, and make certain that the agent had a clear understanding of its relevant risks and benefits. The basis for this suggestion was the concern that, in many cases, those who consent do not fully comprehend the risks of the protocol.

The idea of a consent monitor did not originate with the Working Group. A report by the National Commission on the Protection of Human Subjects of Biomedical and Behavioral Research, on research involving those institutionalized as mentally infirm, suggested that where appropriate, an IRB "should appoint a consent auditor to observe the consent process and determine whether each subject (I) consents, or (II) is incapable of consenting and either assents or does not object, or (III) objects to participation."<sup>75</sup> The concept is also used in the current federal regulations on research involving human subjects. These regulations state that "[a]n IRB shall conduct continuing review of research . . . at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research."<sup>76</sup>

Some members of the Working Group argued that the involvement of a third party in the consent process was too burdensome a requirement and would, in fact, promote a mistrust of research. One Working Group member commented that the proposed regulations for research on institutionalized mentally ill individuals died, in part, because of the consent auditor provisions. Others expressed concerns about the cost and other difficulties of implementing the concept.

Given the nature of the protocol in question, however—a significant increase over minimal risk and no prospect of direct medical benefit—and the relatively modest role of the monitor, the Working Group ultimately agreed that such a mechanism was appropriate. The members of the group made clear that they were not recommending that the monitor be required to second-guess the decision of the

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75. DeRenzo, *supra* note 64, at 8 (quoting the NATIONAL COMMISSION FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, *supra* note 73, at 8). The consent auditor, unlike the proposed consent monitor, would observe and determine the ability of the potential research subject to consent. The consent monitor would assist the subject's agent to understand the research protocol.

76. 45 C.F.R. § 46.109(e) (1996).

agent, but rather that the monitor would simply ensure that the agent understood the protocol and its risks. Thus, the safeguard would be one of process, not one of substance.

The Working Group also discussed who might serve as a "consent monitor." One suggestion was to have a member of the institutional ethics committee serve in this function.<sup>77</sup> There was some debate about whether a member of an ethics committee or IRB would be most appropriate. Several Working Group participants felt that members of the ethics committee would not be sufficiently knowledgeable about research issues to serve competently in this capacity. Others felt that often the IRB has too great a conflict of interest to adequately perform this role. The debate was not ultimately settled, although the Working Group did identify a member of an ethics committee as an example of someone who might serve as a consent monitor.

*Scenario B: Consent by a health care agent—DPA refers to health care only*

This scenario focuses on an individual who has executed an advance directive designating a health care agent to make health care decisions for the individual, but the document states nothing about consent to participation in research. This was believed to be the far more common scenario, because few existing advance directives include a statement regarding consent to research.

- *Type of protocol:* No greater than minimal risk.
- *Working Group recommendation:* Authorize the agent to consent if the agent concludes that the individual would have wanted to participate in the particular protocol, even if the investigator can identify no reasonable prospect of direct medical benefit to the individual.

The Working Group concluded that, although the DPA does not address research, autonomy interests are nevertheless reflected in the individual's decision to designate a particular person as health care agent. Therefore, the agent's judgment about the individual's preference for participation ought to be honored when the risks of the research are minimal.

- *Type of protocol:* Greater than minimal risk, reasonable prospect of direct medical benefit to the individual.

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<sup>77</sup> In Maryland, every hospital and nursing home is required to have an ethics committee (also called patient care advisory committee) available to consult about ethical issues in patient care. MD. CODE ANN., HEALTH-GEN. §§ 19-370 to -374 (1996). For an argument against the use of ethics committee members in this role, see Berg, *supra* note 8.

- *Working Group recommendation:* Authorize the agent to consent if the agent concludes that participation would be in the individual's medical best interest, unless there is reason to believe that the individual would not have wanted to participate in the particular protocol.

This recommendation preserves the existing authority of the health care agent under the Health Care Decisions Act. When the protocol has the prospect for direct medical benefit, the health care agent can apply the decisional standards of the Act just as the agent would when contemplating other health care alternatives.

A minority of the Working Group members disagreed with this position. The minority position would prohibit an agent from consenting to an individual's participation in a protocol if it might subject the individual to a significant risk of serious harm, for example, "the risk of a marked deterioration in a previously stable psychiatric disorder as a result of placement in the placebo arm of a double-blind, placebo-controlled trial."<sup>78</sup> This view reflected a greater concern for the protection of vulnerable research subjects and greater skepticism of the ability of an agent to truly exercise the autonomy of the decisionally impaired individual.

There was also some discussion of restrictions that might be placed on an agent. For example, an agent who has an affiliation with the institution that is conducting the research might be precluded from consenting to the individual's participation in research conducted at that institution. However, no agreement on this point was reached.

- *Type of protocol:* Greater than minimal risk, no reasonable prospect of direct medical benefit to the individual.
- *Working Group recommendation:* Authorize the agent to consent if the agent concludes that the individual would have wanted to participate in the particular protocol and the agent's conclusion is based on direct and explicit evidence of the individual's wish to participate, as documented in accordance with standards and procedures set by the IRB, and the protocol involves no more than a minor increase over minimal risk.

The Working Group concluded that additional safeguards are warranted when the individual's advance directive does not itself address research participation. It is ethically perilous, the group observed, to expose an unconsenting individual to research exceeding minimal risk based solely on the consent of a health care agent. Yet

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78. See Opinion Letter, *supra* note 43.

the individual's decision to entrust a particular agent with responsibility for crucial health care decisions evidences a special regard for the agent's judgment worthy of respect in this context as well. The Working Group's recommendation sought to balance these considerations by requiring the agent to submit direct and explicit evidence of the individual's wish to participate in this kind of protocol. Moreover, the recommendation capped the risk to which the individual would be exposed: It is to be "no more than a minor increase over minimal risk."

*Scenario C: Surrogate consent*

This scenario addresses the common case in which an individual has not designated a health care agent, but has a family member or friend who is authorized to make health care decisions as a surrogate.<sup>79</sup>

- *Type of protocol:* No greater than minimal risk.
- *Working Group recommendation:* Authorize the surrogate to consent if the surrogate concludes that the individual would have wanted to participate in the particular protocol, even if the investigator can identify no reasonable prospect of direct medical benefit to the individual.

Given the minimal level of risk, the Working Group concluded that the surrogate's "substituted judgment"—that is, the surrogate's conclusion that the individual would have wanted to participate in the protocol—should be honored. When the risks are low, the surrogate's decision may be presumed to be a product of knowledge gained from the family ties or other intimate links between the individual and the surrogate.

- *Type of protocol:* Greater than minimal risk, reasonable prospect of direct medical benefit to the individual.
- *Working Group recommendation:* Authorize the surrogate to consent if the surrogate concludes that participation would be in the individual's medical best interest, unless there is reason to believe that the individual would not have wanted to participate in the particular protocol.

Given the prospect of direct medical benefit, the Working Group decided to follow the model of the Health Care Decisions Act. The group's recommendation generally preserves the existing authority of the surrogate.

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79. See *supra* text accompanying notes 37-40.

The surrogate's authority, however, unlike that of a health care agent, is subject to an important limitation under current Maryland law: "A surrogate may not authorize . . . [t]reatment for a mental disorder."<sup>80</sup> After considerable discussion, the Working Group recommended that the Act's exclusion should be modified for both clinical and research decision-making. The group tentatively favored a provision that would *prohibit* a surrogate from consenting to an individual's admission to a mental facility, as under current law, but would *allow* a surrogate to consent to most treatments for a mental disorder (or to expected-benefit research) once an individual had been admitted through the involuntary commitment process. The Working Group proposed, however, that a surrogate not be authorized to consent to "a behavior modification program involving aversive stimuli."<sup>81</sup>

The group recognized the possibility that an individual's surrogates, for example, adult children, might not agree whether participation in the protocol would be in the individual's "medical best interest." The group felt that, in these circumstances, the researchers should submit the dispute to an institution's ethics committee for a recommendation, as is prescribed under the Health Care Decisions Act when surrogates disagree about the course of treatment for an incapacitated patient.<sup>82</sup>

- *Type of protocol:* Greater than minimal risk, no reasonable prospect of direct medical benefit to the individual.
- *Working Group recommendation:* Participation in the research would not be authorized.

The Working Group concluded that reliance on the surrogate's "substituted judgment" would be insufficient, given the absence of potential for direct medical benefit and the degree of risk. Unlike an agent, a surrogate does not carry the individual's endorsement and implied confidence in the agent's overall judgment and feel for the individual's presumed wishes.

*Scenario D: Consent by a non-surrogate proxy—advance directive guidance*

This scenario would arise where a cognitively impaired individual does not have a guardian or anyone to act as surrogate and had not designated a health care agent (or the designated agent was deceased or otherwise unavailable), but had made an advance directive stating

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80. MD. CODE ANN., HEALTH-GEN. § 5-605(d) (1994). The term "mental disorder" is not defined.

81. Second Report, *supra* note 69, at A-12 and B-3 to B-4.

82. MD. CODE ANN., HEALTH-GEN. § 5-605(b) (1994).



his or her desire to participate in research. At present, this scenario is more theoretical than real.

- *Type of protocol:* No greater than minimal risk.
- *Working Group recommendation:* The individual's participation in the research may be authorized by a monitor who would make an informed and objective decision about both enrollment and continuing participation in the protocol. The monitor would decide on the basis of the advance directive, other relevant information (e.g., the individual's prior participation in like research), and the specific nature of the protocol.

Respect for autonomy suggested to the Working Group that an advance directive expressly identifying the individual's desire to participate in research ought to be honored in appropriate circumstances. One of these circumstances is the minimal risk posed by this category of protocol.

The role of the monitor in this scenario would be more substantive than the role of the consent monitor discussed earlier. Instead of merely observing someone else's informed consent process, the monitor here would actually make the decision.<sup>83</sup>

Given the monitor's expanded role, the Working Group was concerned about the need to safeguard the monitor's objectivity. The group concluded that the monitor, either an individual or a small committee, must not have a stake in the research itself and must be free of undue institutional constraints in performing the assigned tasks. The Working Group reached no consensus, however, on the degree to which the monitor must be independent of the institution in which the research would be conducted. In one view, the monitor ought not to be an employee of the research institution. Another point of view was that mere employment alone was insufficient to disqualify someone from the role envisioned for the monitor. The Working Group deferred for public comment and further discussion the particular connections between the monitor and the sponsoring institution that would be too attenuated to affect the monitor's independent judgment.

- *Type of protocol:* Greater than minimal risk, reasonable prospect of direct medical benefit to the individual.
- *Working Group recommendation:* An independent monitor may consent to the individual's participation in the research if the

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83. In its statutory recommendation, the Working Group refers to a monitor with decision-making authority as a "proxy decision-maker." See Second Report, *supra* note 69, at A-4.

monitor concludes based on the advance directive, that the individual would have wanted to participate in the particular protocol and that participation would be in the individual's medical best interest. The monitor would have responsibility for the individual's continued participation as well.

In the view of the Working Group, the substituted judgment and best interest assessments required when research is of potential benefit to the individual need not be made by a court. Given the potential for benefit, protection of the individual can best be achieved through a less formal process that nevertheless does not rely on the investigators themselves to make crucial judgments about the individual's presumed wishes or the individual's best interests. Rather, under the proposal these responsibilities, both at the time of enrollment and throughout the course of the protocol, would be vested in the monitor.

- *Type of protocol:* Greater than minimal risk, no reasonable prospect of direct medical benefit to the individual.
- *Working Group recommendation:* Participation in the research would not be authorized.

The Working Group concluded that reliance on an advance directive alone under these circumstances would not be ethically justified. It is most unlikely that the document itself would have been written with adequate knowledge of the details of a future research protocol. Moreover, unlike the situation in which the individual's designated agent is available to act as advocate and protector, here no one has intimate knowledge of the individual's values and attitudes. The bare document alone is insufficient to expose the individual to research involving this degree of risk without the prospect of direct medical benefit.

*Scenario E: Consent by a non-surrogate proxy— no advance directive*

Scenario E involves an individual who has not executed an advance directive and who has no family member or close friend authorized to act as surrogate.

- *Type of protocol:* No greater than minimal risk.
- *Working Group recommendation:* Participation in the research would not be authorized unless the protocol presented a reasonable prospect of direct medical benefit to the individual and the individual's participation is authorized by a court pursuant to existing guardianship procedures.

In the absence of any written indication of the individual's wishes regarding research and in the absence of anyone with intimate knowl-

edge of the individual, the Working Group initially concluded that research with no prospect of direct medical benefit should be ruled out, regardless of the degree of risk. Subsequently, however, the Working Group recognized that evidence of the individual's wishes apart from an advance directive might be sufficient to justify participation in minimal risk research. Such participation could be authorized by a court under traditional guardianship procedures and standards.

- *Type of protocol*: Greater than minimal risk, reasonable prospect of direct medical benefit to the individual.
- *Working Group recommendation*: The individual's participation in the research may be authorized by a court pursuant to existing guardianship procedures.

Again, the Working Group concluded that traditional guardianship procedures and standards should be applied.

- *Type of protocol*: Greater than minimal risk, no reasonable prospect of direct medical benefit to the individual.
- *Working Group recommendation*: Participation in the research would not be authorized.

In the Working Group's view, respect for persons absolutely precludes research participation under these circumstances.

### C. *Subject Assent*

The Working Group's recommendations included provisions calling for the *assent* of subjects, even when a proxy is authorized to give *consent* to research participation. This concept has been incorporated into the federal regulations applicable to research involving children. Under these regulations, an IRB "shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent."<sup>84</sup> "Assent" is defined as "a child's affirmative agreement to participate in research."<sup>85</sup>

The Working Group elaborated significantly on this requirement by recommending that decisionally impaired individuals be told that they are to participate in research and that someone else has consented to their participation.<sup>86</sup> Furthermore, as recommended by the Working Group, "an investigator may not compel a decisionally incapacitated individual to perform an action related to the research if the

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84. 45 C.F.R. § 46.408(a) (1996).

85. 45 C.F.R. § 46.402(b) (1996).

86. Second Report, *supra* note 69, at A-9.

individual refuses to take the action after being asked to do so."<sup>87</sup> Through these means, the Working Group sought to allay concerns about coerced research participation discussed in the *T.D.* case.<sup>88</sup>

#### IV. NEXT STEPS

The Working Group's recommendations represent an important way-station in the state's efforts to reach agreement on this issue and put into effect workable procedures and safeguards for the participation of decisionally impaired individuals in medical research protocols. The Attorney General of Maryland, convener of the Working Group, has emphasized the need for a broadly inclusive policy development process. The process includes several steps: First, the Working Group's initial report, containing its preliminary policy recommendations, was sent for comment to more than 70 researchers, ethicists, patient advocates, health facility administrators, and others. These recipients were encouraged to distribute the report to others in their respective communities. In this way, the report gained fairly wide attention among those in Maryland and those elsewhere who are most concerned about research with decisionally impaired subjects.

Second, the Attorney General's Office held two public meetings about the initial report. These were open forums, at which anyone could ask questions or offer comments. After the public meetings, the Working Group studied the comments and revised its initial recommendations.

Third, the Working Group's revised recommendations, in the form of a draft statute, were widely distributed for comments and were critiqued at a public conference. In light of the comments, the Working Group revised the text of the proposed statute and solicited comments once again. This latest draft reflects a significant restructuring of the proposal, intended to achieve greater clarity, but does not depart from the Working Group's main policy recommendations.<sup>89</sup>

Finally, assuming that a fair degree of agreement emerges, the Attorney General will look for legislators to sponsor the proposed legislation in the Maryland General Assembly. Thus the process, with its expanding circles of involvement—first a small working group, then

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87. *Id.*

88. *See supra* text accompanying notes 21-23.

89. Jack Schwartz, Third Report of the Attorney General's Research Working Group (August 1, 1997) (the Third Report is reprinted in the appendix to this issue of the *Journal of Health Care Law & Policy*).

those particularly interested in biomedical research, then the public generally and its elected representatives—will have concluded.

This process has yielded debate on a number of difficult issues. One such issue is the Working Group's reliance on categories of risk. The term "minimal risk," although defined in the federal regulations, leaves much room for interpretation by an IRB and has been criticized for its imprecision.<sup>90</sup> One participant in discussion at a meeting, for example, pointed out that the federal definition does not clearly identify the perspective from which "risk" is to be assessed: that of healthy individuals, or that of individuals with an impairment similar to the research subject's.<sup>91</sup> Proper regard for the welfare of subjects might require a shift in perspective, depending on the nature of the risk. For instance, psychological distress ought to be assessed from the perspective of a person with a cognitive impairment; harms to dignity, however, ought to be assessed from the perspective of a healthy individual.

Other commentators criticized the Working Group's reliance on gradations of risk — "minor increase over minimal risk" and "greater than minor increase over minimal risk" — that are not clearly distinguishable. Federal regulations on the participation of children in medical research use the term "minor increase over minimal risk" but do not define it.<sup>92</sup> Without clarification, local IRBs will define the terms on a case-by-case basis, leaving room for some inconsistency in their application.<sup>93</sup>

Another issue that evoked comment is the application of a "medical best interest test" to participation in research. Conceptually it may sometimes be difficult to apply this standard to research. In general, when an intervention is being tested as part of a research protocol,

90. Berg, *supra* note 8, at 24.

91. 28 C.F.R. § 46.102 (i). The Department of Justice regulations pertaining to protection of human subjects, the definition of "minimal risk" is ambiguous. The standard in § 46.102(i) is "that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests." Protections of Human Subjects, 28 C.F.R. § 46.102(i) (1997). In contrast, the definition of the term in 45 C.F.R. § 46.303(d) (1996), the HHS regulations pertaining to research involving prisoners, implies that, when the research subjects are not generally healthy (as prisoners are presumed to be) risk is to be assessed by reference to the group of subjects, who often will routinely experience medical interventions beyond those experienced by healthy individuals.

92. 45 C.F.R. §§ 46.404-406 (1996).

93. In its most recent recommendations, the Working Group proposed that the Secretary of Health and Mental Hygiene be authorized to issue regulations identifying the risk of particular procedures.

there is considerable uncertainty about its benefit or effectiveness as compared to standard therapy. Although there is also uncertainty about the effectiveness of an intervention in the clinical context, uncertainty in the research setting is of a different scope and type than in the clinical setting. In the clinical context, an intervention presumably has been proven effective for some percentage of individuals. The uncertainty relates to the effectiveness of the intervention on a particular individual and may vary due to the individual's age, severity of illness, other diagnoses, and the general variability of human response to medical interventions. In the research context, the uncertainty is related to whether an intervention is effective for anyone with the particular disorder in question. Some may argue that, while the potential benefits of the intervention in a research setting may be wholly uncertain, there are other benefits to being part of a research protocol that justify participation of a cognitively impaired individual. These may include increased medical attention and better quality medical care. Yet these "benefits" are what might better be termed "indirect," not attributable to the intervention being tested. Should a medical best interest test be broad enough to include such indirect benefits, or should the test be limited to the direct benefits of the intervention?

Also, it will be a significant challenge to apply the test to a protocol involving a double-blind, placebo-controlled study. While the opinion letter of the Attorney General's office indicates that participation in such a protocol might be in the patient's best interest,<sup>94</sup> some question whether a medical best interest test can ever justify participation in research where there is a probability of no benefit. On the other hand, if standard therapy is non-existent or noxious, then the risks associated with participation in a placebo study might be justifiable.

Other comments addressed surrogate authorization for participation in no-expected-benefit research. A few commentators argued that this departure from the principle of informed consent *by the research subject* was not justified and posed an unacceptable risk to vulnerable persons. Yet, other commentators criticized the Working Group for limiting surrogate authority to minimal risk research, because the limitation would inhibit important research aimed at improving understanding of the underlying disease process or its diagnosis.

While the Working Group's recommendations reflect concerns of both the research community and advocates for the decisionally

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94. Opinion Letter, *supra* note 43.

impaired, they are limited by the experience of those on the Working Group. With broad public participation, ideally the ultimate policy recommendation will reflect an appropriate balance between views of these different groups. Finally, the process and outcome may serve as a model for other states as they take up this important issue.