

Testimony of

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Thank you, Mr. Chairman, and members of the Subcommittee. I am Eric Cassell and I serve as a Commissioner on the National Bioethics Advisory Commission (NBAC). I am also a Clinical Professor of Public Health at Cornell University Medical College. I am pleased to appear before you this morning to describe the recommendations NBAC made in its December 1998 report entitled *Research Involving Persons with Mental Disorders that May Affect Decisionmaking Capacity*. The report, which was forwarded to the President on January 8, 1999, has been widely circulated. I have made copies available to the subcommittee as part of my written testimony, and note that it is available on the Commission's website (www.bioethics.gov).

Mr. Chairman, there have been several efforts to extend additional regulatory protections for research involving individuals with mental disorders, but these efforts have not been fully successful. In the late 1970s, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (the National Commission), studied the need for special protections for research subjects with mental disorders in a report entitled *Research Involving Those Institutionalized as Mentally Infirm*. The Department of Health Education and Welfare proposed regulations in 1979, but these were never adopted.

NBAC decided to study this topic as part of its overall mission to advise the National Science and Technology Council (NSTC) and other government entities on appropriate policies, guidelines, and other instruments addressing the bioethical issues arising from research on human biology and behavior. NBAC examined this topic because of the

special needs of these persons serving as subjects of research--including the need for more research--but also because of the weaknesses in federal regulations that have persisted for the past two decades. Several highly publicized incidents involving research subjects in this vulnerable population were also brought to NBAC's attention.

During its 18-month study, NBAC heard testimony at 13 separate meetings from members of the public, scientists, former research subjects, their families, and others; obtained nearly 120 public comments during a 45-day comment period on a draft report; reviewed commissioned papers from leading experts in law, medicine, psychiatry, and ethics; and reviewed a small sampling of research protocols in this field.

NBAC found that the nation's scientists have made much important progress on the causes and treatments of mental disorders, and that opportunities to develop new therapies are likely to continue to emerge. The scope of research on mental disorders is expanding significantly and the research environment has become far more complex, involving both a larger societal investment and a greater role for the private sector.

With regard to the protection of human subjects, NBAC concluded that in addition to the existing Federal Policy for the Protection of Human Subjects (also known as the "Common Rule"), "research involving subjects with mental disorders that may affect decisionmaking capacity should be governed by specific further regulations."

As Dr. Harold Shapiro stated in his letter to the President transmitting the report, "While current U.S. regulations note the need to ensure ethical treatment of human research subjects with mental disorders, they provide no specific guidance for IRBs and investigators regarding vulnerable subjects... We believe that this state of affairs is not satisfactory, and that additional federal protections are needed."

NBAC made 21 recommendations that provide both a set of requirements that NBAC believes must be satisfied in all research protocols involving persons with mental disorders, and several additional or optional protections that may be considered, as appropriate, in particular circumstances. Taken together, these recommendations would both enhance existing protections and facilitate broad public support for continued research on mental disorders.

The recommendations fall under six categories: review bodies; research design; informed consent and capacity; categories of research; surrogate decision making; and education, research, and support. Let me summarize some of these.

1. With respect to the recommendations relating to review bodies, NBAC recommends that all Institutional Review Boards (IRBs) that regularly consider proposals involving persons with mental disorders should include at least two members who are familiar with the nature of these disorders and with the concerns of the population being studied (Recommendation 1).

NBAC was persuaded that for research involving greater than minimal risk but that does not hold out the prospect of any medical benefit, subjects could be involved only under the most stringent conditions. In these cases NBAC recommends that the Secretary of Health and Human Services convene a Special Standing Panel to review these protocols at the national level (Recommendation 2). This Standing Panel would include members representing the diverse interests of potential subjects, the research community, and the public. This Panel would provide a national and publicly accountable review mechanism for research. It would be charged with developing guidelines that could be used by local IRBs. NBAC recommends that all federal agencies subject to the Common Rule use this panel, and that a study of its effectiveness be completed within five years.

2. With respect to research design, NBAC recommends that research should not target people with mental disorders when research can be done with other subjects (Recommendation 3). In addition, researchers should describe efforts to minimize risks to subjects, so that IRBs can make an informed risk/benefit assessment, a determination that is especially important when the studies involve placebo controls, symptom provocation, or rapid medication withdrawal (Recommendations 4 and 5).

3. With respect to informed consent and capacity issues, NBAC recommends that no person who has the capacity for consent may be enrolled in a study without his or her informed consent (Recommendation 6). In addition, NBAC recommends that a subject's objection to participation should be heeded even if he or she is confused or is incompetent (Recommendation 7). NBAC also recognized the importance of assessment

of capacity; we recommend that where research involves greater than minimal risk, IRBs should require that an independent, qualified professional assess the potential subject's capacity to consent (Recommendation 8).

4. With regard to categories of research, we made specific recommendations about which criteria IRBs should use when evaluating certain types of research based on the level of risk and the extent to which the study held out the prospect of direct medical benefit to the subjects (Recommendations 10-12).

5. We made five recommendations relating to surrogate decision making. In cases where it has been determined that a research subject lacks or has lost the capacity to make decisions about research participation, NBAC made a series of recommendations specifying who is able to act as a "legally authorized representative" of a research subject and under what situations such a representative may enroll a subject in a study (Recommendations 13-17).

6. NBAC made several recommendations relating to education, research and support (Recommendations 18-21). For example, NBAC recommends that all research sponsors (government, private sector enterprises, and academic institutions) should work together to make the necessary resources available for implementation of the recommendations in its report (Recommendation 21).

Researchers will likely see some of the other recommendations as too restrictive of research and those concerned with the rights of subjects may view them as too permissive. For example, NBAC recommends that in cases where research involves greater than minimal risk, IRBs should often require researchers to obtain an independent assessment of the subject's capacity to consent (Recommendation 8). Some may see this as too great an imposition on researchers and institutions, while some advocates for patients' rights might have hoped to see this recommendation go further, requiring that all research subjects, regardless of the level of risk in a study, be assessed for their capacity. Some will no doubt consider NBAC's recommendations that subjects who are capable of consenting can, under certain conditions, give a "prospective authorization" to their future involvement in research (Recommendation 13), which is an important method for permitting competent persons to express their wishes for participation in studies in the future when they are no longer able to express their wishes. Others may find that this recommendation permits people to be enrolled in research without their express informed consent.

The NBAC report identified those who should be responsible for implementing the recommendations. These include investigators and IRBs, state legislatures, the National Institutes of Health, the Department of Health and Human Services (DHHS), health professionals, federal agencies subject to the Common Rule, and others responsible for human subjects protections.

NBAC proposed a number of recommendations for regulatory reform, but it did not take a position on whether these reforms would best be accomplished through changes in the Common Rule, or through the adoption of a new Subpart in the Code of Federal Regulations. More importantly, the Commission made clear its belief that some of these changes could be implemented voluntarily at the local level, emphasizing the following statement in the report: “Regardless of which regulatory route is selected, NBAC encourages researchers and institutions to voluntarily adopt the spirit and substance of these recommendations.”

All agencies subject to the Common Rule received a copy of NBAC's report, and were asked by the NSTC for their comments. The report is now under review by both the NSTC and DHHS.

Mr. Chairman, the subject of this hearing comes at an important time in the history of human subjects protections in this country. The opportunity exists to identify and correct deficiencies in the present system, but also to plan for how best to build the system as we move into the next century. In NBAC's view, the enhanced protections recommended in its report will promote broad-based support for further research by engendering greater public trust and confidence that subjects' rights and interests are fully respected.

While this report focused specifically on research involving persons with mental disorders, NBAC's ongoing mandate is to consider the protection of all human subjects in research. We were recently asked by the Assistant to the President for Science and

Technology, Dr. Neal Lane, to return to our original charge from the President to examine the current system of human subjects protections. This report has just started, and we would be pleased to keep the Subcommittee apprised of this work as it proceeds.

I would be pleased to discuss any of the report's recommendations in more detail. NBAC (and its staff) would be pleased to work with you as you continue to address these important issues.

Thank you, Mr. Chairman.