DWECs for acute surface water (4.3 μg/L) and chronic surface water (1.1 μg/L).

v. *Conclusion.* Therefore, based on complete and reliable toxicity data and the conservative exposure assessment, Gowan concludes that there is reasonable certainty that no harm will result to infants and children from aggregate exposure to halosulfuron-methyl residues with respect to the proposed new uses.

F. International Tolerances

Maximum residue levels have not been established for residues of halosulfuron-methyl on any food or feed crop by the Codex Alimentarius Commission.

[FR Doc. 01–22024 Filed 8–30–01; 8:45 am]

BILLING CODE 6560–50–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Notice of Meeting of the Advisory Committee on Minority Health

AGENCY: Office of the Secretary, Office of Public Health and Science, Office of Minority Health.

ACTION: Notice is given of the third meeting.

The Advisory Committee on Minority Health will meet on Thursday, September 20, 2001 from 9 a.m. to 5 p.m., and Friday, September 21, 2001, from 8:30 a.m.–3 p.m. The meeting will be held at the Holiday Inn Georgetown, Mirage I Room, 2101 Wisconsin Avenue, NW., Washington, DC.

The Advisory Committee will discuss racial and ethnic disparities in health, as well as, other related issues.

The meeting is open to the public. There will be an opportunity for public comment which will be limited to five minutes per speaker. Individuals who would like to submit written statements should mail or fax their comments to the Office of Minority Health at least two business days prior to the meeting.

For further information, please contact Ms. Patricia Norris, Office of Minority Health, Rockwall II Building, 5515 Security Lane, Suite 1000, Rockville, Maryland 20852. Phone: 301–443–5084 Fax: 301–594–0767.

Dated: August 23, 2001.

Nathan Stinson, Jr.,

Deputy Assistant Secretary for Minority Health.

[FR Doc. 01–21976 Filed 8–30–01; 8:45 am]

BILLING CODE 4150–29–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Notice of Publication of the Executive Summary of the report, ''Ethical and Policy Issues in Research Involving Research Participants'', by the National Bioethics Advisory Commission (NBAC)

SUPPLEMENTARY INFORMATION: The President established the National Bioethics Advisory Commission (NBAC) on October 3, 1995 by Executive Order 12975 as amended. The functions of NBAC are as follows:

(a) Provide advice and make recommendations to the National Science and Technology Council and to other appropriate government entities regarding the following matters:

(1) The appropriateness of departmental, agency or other governmental programs, policies, assignments, missions, guidelines, and regulations as they relate to bioethical issues arising from research on human biology and behavior; and

(2) applications, including the clinical applications, of that research.

(b) Identify broad principles to govern the ethical conduct of research, citing specific projects only as illustrations for such principles.

(c) Shall not be responsible for the review and approval of specific projects.

(d) In addition to responding to requests for advice and recommendations from the National Science and Technology Council, NBAC also may accept suggestions of issues for consideration from both the Congress and the public. NBAC may also identify other bioethical issues for the purpose of providing advice and recommendations, subject to the approval of the National Science and Technology Council. The members of NBAC are as follows:

Harold T. Shapiro, Ph.D., Chair
Patricia Backlar
Arturo Brito, M.D.
Alexander Morgan Capron, LL.B.
Eric J. Cassell, M.D., M.A.C.P.
R. Alta Charo, J.D.
James F. Childress, Ph.D.
David R. Cox, M.D., Ph.D.
Rhetaugh G. Dumas, Ph.D., R.N.
Laurie M. Flynn*
Carol W. Greider, Ph.D.
Steven H. Holtzman
Bernard Lo, M.D.
Lawrence H. Miike, M.D., J.D.
Thomas H. Murray, Ph.D.
William C. Oldaker, LL.B.
Diane Scott-Jones, Ph.D.
*Resigned on May 10, 2001

Ethical and Policy Issues in Research Involving Human Participants; Summary

Protecting Research Participants—A Time for Change

Introduction

Protecting the rights and welfare of those who volunteer to participate in research is a fundamental tenet of ethical research. A great deal of progress has been made in recent decades in changing the culture of research to incorporate more fully this ethical responsibility into protocol design and implementation. In the 1960s and 1970s, a series of scandals concerning social science research and medical research conducted with the sick and the illiterate underlined the need to systematically and rigorously protect individuals in research (Beecher 1966; Faden and Beauchamp 1986; Jones 1981; Katz 1972; Tuskegee Syphilis Study Ad Hoc Advisory Panel 1973). However, the resulting system of protections that evolved out of these rising concerns—although an improvement over past practices—is no longer sufficient. It is a patchwork arrangement associated with the receipt of federal research funding or the regulatory review and approval of new drugs and devices. In addition, it depends on the voluntary cooperation of investigators, research institutions, and professional societies across a wide array of research disciplines. Increasingly, the current system is being viewed as uneven in its ability to simultaneously protect the rights and welfare of research participants and promote ethically responsible research.

Research involving human participants has become a vast academic and commercial activity, but this country's system for the protection of human participants has not kept pace with that growth. On the one hand, the system is too narrow in scope to protect all participants, while on the other hand, it is often so unnecessarily bureaucratic that it stifles responsible research. Although some reforms by particular federal agencies and professional societies are under way,[1] it will take the efforts of both the executive and legislative branches of government to put in place a streamlined, effective, responsive, and comprehensive system that achieves the protection of all human participants and encourages ethically responsible research.

Clearly, scientific investigation has extended and enhanced the quality of life and increased our understanding of ourselves, our relationships with others,

and the natural world. It is one of the foundations of our society's material, intellectual, and social progress. For many citizens, scientific discoveries have alleviated the suffering caused by disease or disability. Nonetheless, the prospect of gaining such valuable scientific knowledge need not and should not be pursued at the expense of human rights or human dignity. In the words of philosopher Hans Jonas, ''progress is an optional goal, not an unconditional commitment, and . . . its tempo . . . compulsive as it may become, has nothing sacred about it'' (Jonas 1969, 245).

Since the 1974 formation of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research and the activities in the early 1980s of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, American leaders have consistently tried to enhance the protections for human research participants. The research community has, in large part, supported the two essential protections for human participants: independent review of research to assess risks and potential benefits and an opportunity for people to voluntarily and knowledgeably decide whether to participate in a particular research protocol.

The charter of the National Bioethics Advisory Commission (NBAC), a presidential commission created in 1995, makes clear the Commission's focus: ''As a first priority, NBAC shall direct its attention to consideration of protection of the rights and welfare of human research subjects.'' In our first five years, we focused on several issues concerning research involving human participants, issuing five reports and numerous recommendations that, when viewed as a whole, reflect our evolving appreciation of the numerous and complex challenges facing the implementation and oversight of any system of protections.[2] The concerns and recommendations addressed in these reports reflect our dual commitment to ensuring the protection of those who volunteer for research while supporting the continued advance of science and understanding of the human condition. This report views the oversight system as a whole, provides a rationale for change, and offers an interrelated set of recommendations to improve the protection of human participants and enable the oversight system to operate more efficiently.

Respecting Research Participants

Whether testing a new medical treatment, interviewing people about their personal habits, studying how people think and feel, or observing how they live within groups, research seeks to learn something new about the human condition. Unfortunately, history has also demonstrated that researchers sometimes treat participants not as persons but as mere objects of study. As Jonas observed: ''Experimentation was originally sanctioned by natural science. There it is performed on inanimate objects, and this raises no moral questions. But as soon as animate, feeling beings become the subject of experiment * * * this innocence of the search for knowledge is lost and questions of conscience arise'' (Jonas 1969, 219).

How, then, should people be studied? For over half a century, since the revelations of medical torture under the guise of medical experimentation were described at the Nuremberg Trials,[3] it has been agreed that people should participate in research only when the study addresses important questions, its risks are justifiable, and an individual's participation is voluntary and informed.

The principles underlying the Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (Belmont Report) (National Commission 1979) have served for over 20 years as a leading source of guidance regarding the ethical standards that should govern research with human participants in the United States. The Belmont Report emphasized that research must respect the autonomy of participants, must be fair in both conception and implementation, and must maximize potential benefits while minimizing possible harms. The report's recommendations provided a coherent rationale for the federal policies and rules that created the current U.S. system of decentralized, independent research review coupled with some degree of federal oversight. But although the Belmont Report is rightly hailed as a key source of guidance on informed consent, assessment of risk, and the injustice of placing individuals (and groups) in situations of vulnerability, the principles the report espouses and the regulations adopted as federal policy 20 years ago have often fallen short in achieving their overarching goal of protecting human research participants. Moreover, since the Belmont Report was published, additional concerns have arisen that require much-needed attention today.

Ensuring Independent Review of Risks and Potential Benefits

A central protection for research participants is the guarantee that someone other than the investigator will assess the risks of the proposed research. No one should participate in research unless independent review concludes that the risks are reasonable in relation to the potential benefits. In the United States, the Institutional Review Board, or IRB, has been the principal structure responsible for conducting such reviews.

Independent review of research is essential because it improves the likelihood that decisions are made free from inappropriate influences that could distort the central task of evaluating risks and potential benefits. Certainly, reviewers should not have a financial interest in the work, but social factors may be just as crucial. Reviewers may feel constrained because they are examining the work of their colleagues or their supervisors, and they should not participate in protocol review unless they are able to separate these concerns from their task. All reviewers who themselves are members of the research community should recognize that their familiarity with research and (perhaps) their predilection to support research are factors that could distort their judgment.

Truly independent and sensitive review requires more involvement of individuals drawn from the ranks of potential research participants or those who can adequately represent the interests of potential research participants.

A critical purpose of independent review is to ensure that risks are reasonable in relation to potential personal and societal benefits. This is a precondition to offering people the opportunity to volunteer, since informed consent alone cannot justify enrollment. When reviewed for risks and potential benefits, research studies must be evaluated in their entirety. Studies often include different components, however, and the risks and potential benefits of each should also be examined separately, lest the possibility of great benefit or monetary enticement in one component cause potential participants or IRBs to minimize or overlook risk in another. No matter what potential benefit is offered to individual participants or society at large, the possibility of benefit from one element of a study should not be used to justify otherwise unacceptable elements.

In our view, IRBs should appreciate that for some components of a study, participants might incur risks with no personal potential benefit, for example, when a nondiagnostic survey is included among the components of a psychotherapy protocol or when placebos are given to some participants in a drug trial. For these elements, there

should be some limitation on the amount of social and physical risk that can be imposed, regardless of the participants' willingness to participate or the monetary (or other) enticement being offered. Further, the possibility of some benefit from one element of a study should not be used to justify otherwise unacceptable elements of research whose potential benefits, if any, accrue, solely to society at large. If aspects of a study present unacceptable risks, protocols should not be approved until these elements are eliminated. If removing the risky component would impair the study as a whole, then the entire study should be redesigned so that each of its elements presents risks that are reasonable in relation to potential benefits.

Other parts of studies can obscure risks, such as when standard medical interventions are compared in a patient population, leading some participants and researchers to discount the risks because they are associated with known therapies. It is essential that participants and investigators not be led to believe that participating in research is tantamount to being in a traditional therapeutic relationship. Regardless of whether there is the possibility or even the likelihood of direct benefit from participation in research, such participation still alters the relationship between a professional and the participant by introducing another loyalty beyond that to the participant, to wit, loyalty to doing good science. It is too often forgotten that even though the researchers may consider participants' interests to be important, they also have a serious, and perhaps conflicting, obligation to science.

Years of experience with the current system of independent review have demonstrated that there are enduring questions about how to arrive at such impartial judgments and how to go about deciding when potential benefits justify risks that are incurred solely by participants or the community from which they come. In recent years, increasing strains on the system have undermined the practice of independent review. IRBs are over-burdened by the volume of research coming before them, a strain that is compounded by concerns about training of IRB members and possible conflicts of interest. In addition, the constantly changing nature of research challenges existing notions about what constitutes risks and potential benefits.

Because IRBs are so central to the current oversight system, they need better guidance on how to review and monitor research, how to assess potential benefits to research participants and their communities, and how to distinguish among levels of risk. This report provides such guidance in the following areas: determining the type of review necessary for minimal risk research; ensuring that research participants are able to make voluntary decisions and are appropriately informed prior to giving consent; providing adequate protections for privacy and confidentiality; identifying appropriate measures needed when participants are susceptible to coercion or are otherwise placed in vulnerable situations; and monitoring ongoing research. In addition, the report recommends that IRB members and staff complete educational and certification programs on research ethics before being permitted to review research studies.

Obtaining Voluntary Informed Consent

Even when risks are reasonable, however, no one should participate in research without giving voluntary informed consent (except in the case of an appropriate authorized representative or a waiver). Investigators must make appropriate disclosures and ensure that participants have a good understanding of the information and their choices, not only at the time of enrollment, but throughout the research. Engaging in this process is one of the best ways researchers can demonstrate their concern and respect for those they aim to enroll in a study. It also serves as the best means for those who do not wish to participate to protect themselves.[4]

Recommendations from our previous reports are reinforced in this report, which emphasizes the process of providing information and ensuring comprehension rather than the form of documentation of the decision to give consent. Both the information and the way it is conveyed—while meeting full disclosure requirements—must be tailored to meet the needs of the participants in the particular research context. In addition, documentation requirements must be adapted for varying research settings, and the criteria for deciding when informed consent is not necessary must be clarified so that participants—rights and welfare are not endangered.

The decision to participate in research must not only be informed, it must be voluntary. Even when risks are reasonable and informed consent is obtained, it may nonetheless be wrong to solicit certain people as participants. Those who are not fully capable of resisting the request to become participants—such as prisoners and other institutionalized or otherwise vulnerable persons—should not be enrolled in studies merely because they are easily accessible or convenient. This historic emphasis on protecting people from being exploited as research participants, however, has failed to anticipate a time when, at least for some areas of medical research, people would be demanding to be included in certain studies because they might provide the only opportunity for receiving medical care for life-threatening diseases.

Making Research Inclusive While Protecting Individuals Categorized as Vulnerable

Vulnerable individuals need additional protection in research. Although certain individuals and populations are more vulnerable as human participants than others, people whose circumstances render them vulnerable should not be arbitrarily excluded from research for this reason alone. This includes those viewed as more open to harm (e.g., children), more subject to coercion (e.g., institutionalized persons), more ''complicated'' (e.g., women, who are considered more biologically complicated than men), or more inconvenient (e.g., women with small children, who are viewed as less reliable research participants due to conflicting demands on time). Calling competent people intrinsically ''vulnerable'' can be both insulting and misleading. It is not their gender or other group designation that exposes them to injury or coercion, but rather their situation that can be exploited by ethically unacceptable research. That is, it is their circumstances, which are situational, that create the vulnerability. At other times it is the intrinsic characteristics of the person—for example, children or those with certain mental or developmental disorders—that make them generally vulnerable in the research setting.

The response, whenever possible, should not be to exclude people from research, but instead to change the research design so that it does not create situations in which people are unnecessarily harmed. To do otherwise is to risk developing knowledge that helps only a subset of the population. To the extent that the results are not generalizable, the potential societal benefits that justify doing the research are attenuated. Research participants must be treated equally and with respect. Whenever possible, research should be designed to encourage the participation of all groups while protecting their rights and welfare.

To accomplish this, we recommend that rather than focusing primarily on

categorizing groups as vulnerable, investigators and IRBs should also recognize and avoid situations that create susceptibility to harm or coercion. Such situations may be as varied as patients being recruited by their own physicians; sick and desperate patients seeking enrollment in clinical trials; participants being recruited by those who teach or employ them; or studies involving participants with any characteristic that may make them less likely to receive care and respect from others (e.g., convicted criminals or intravenous drug users). In these circumstances, rather than excluding whole groups of people, researchers should design studies that reduce the risk of exploitation, whether by using a different method of recruitment, by using a recruiter who shares the participants' characteristics, or by some other technique. This is not always easy. It requires researchers to consider carefully their research design and the potential pool of participants. At times, it will mean anticipating that otherwise seemingly benign situations may become more complex because a particular participant or group of participants will be unusually susceptible to harm or manipulation in this situation. At other times, the nature of the vulnerability may require using a different research design. Ethical research does not avoid complexity. Rather, it acknowledges the full range and realities of the human condition.

Compensating for Harms

Despite all these precautions, however, some research participants might be harmed. Participants who are harmed as a direct result of research should be cared for and compensated. This is simple justice. The fact that they offered to participate in no way alters the view that mere decency calls for us to take care of these volunteers. Unfortunately, this is a greater challenge than it might appear. For those who endure harm while participating in research, it is often very difficult to separate injuries traceable to the research from those that stem from the underlying disease or social condition being studied. For others, appropriate care and compensation would be far beyond the means of the researchers, their sponsors, and their institutions. Two decades ago, the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research called for pilot studies of compensation programs—a recommendation that was not pursued. It is time to reconsider the need for some type of compensation program and to explore the possible mechanisms that could be used were one to be adopted. Regardless of individual motives, research participants are providing a service for society, and justice requires that they be treated with great respect and receive appropriate care for any related injuries. It should always be remembered that it is a privilege for any researcher to involve human participants in his or her research.

Establishing a Comprehensive, Effective, and Streamlined System

In the United States, government regulations, professional guidelines, and the general principles highlighted in the Belmont Report (1979) form the basis of the current system of protections. In the earliest stages of adoption, the federal regulations were fragmented and confusing. Even today, they apply to most—but not all—research funded or conducted by the federal government, but have inconsistent and sometimes no direct application to research funded or conducted by state governments, foundations, or industry. They apply to medical drugs and devices and vaccines approved for interstate sale, but not to some medical innovations that would remain wholly within state borders. And they apply to other research only when the investigators and their institutions volunteer to abide by the rules.

A comprehensive and effective oversight system is essential to uniformly protect the rights and welfare of participants while permitting ethically and scientifically responsible research to proceed without undue delay. A fundamental flaw in the current oversight system is the ethically indefensible difference in the protection afforded participants in federally sponsored research and those in privately sponsored research that falls outside the jurisdiction of the Food and Drug Administration (FDA). As a result, people have been subjected to experimentation without their knowledge or informed consent in fields as diverse as plastic surgery, psychology, and infertility treatment. This is wrong. Participants should be protected from avoidable harm, whether the research is publicly or privately financed. We have repeated this assertion throughout our deliberations, and recommendations in this regard appear in four previous reports (NBAC 1997; NBAC 1999a; NBAC 1999b; NBAC 2001).

In this report, we recommend that the protections of an oversight system extend to the entire private sector for both domestic and international research. A credible, effective oversight system must apply to all research, and all people are entitled to the dignity that comes with freely and knowingly choosing whether to participate in research, as well as to protection from undue research risks. This is consistent with our 1997 resolution that no one should be enrolled in research absent the twin protections of independent review and voluntary informed consent.

Even when current protections apply, the interpretation of the federal regulations can vary unpredictably, depending on which federal agency oversees the research. Even the most basic, common elements of the federal rules took a decade to develop into regulations, because there was no single authority within the government to facilitate and demand cooperation and consistency. There still is no such single authority.[5] This has slowed the diffusion of basic protections and made it almost impossible to develop consistent interpretations of the basic protections or those relevant to especially problematic research, such as studies involving children or the decisionally impaired. Nor has there been a unified response to emerging areas of research, such as large-scale work on medical records and social science databases or on stored human biological materials.

Today's research protection system cannot react quickly to new developments. Efforts to develop rules for special situations, such as research on those who can no longer make decisions for themselves, have languished for decades in the face of bureaucratic hurdles, and there is no reason to believe that efforts to oversee other emerging research areas will be any more efficient. In addition, the current system leaves people vulnerable to new, virtually uncontrolled experimentation in emerging fields, such as some aspects of reproductive medicine and genetic research.

Indeed, some areas of research are not only uncontrolled, they are almost invisible. In an information age, poor management of research using medical records, human tissue, or personal interview data could lead to employment and insurance discrimination, social stigmatization, or even criminal prosecution.[6] The privacy and confidentiality concerns raised by this research are real, but the federal response has often been illusory. There is almost no guidance and certainly no coordination on these topics. The time has come to have a single source of guidance for these emerging areas, one that would be better positioned to effect change across all divisions of the government and private sector, as well

as to facilitate development of specialized review bodies, as needed.

In this report we propose a new independent oversight office that would have clear authority over all other segments of the federal government and extend protections to the entire private sector for both domestic and international research. A single office would decide how to introduce consistency or reforms, and only that office would develop mechanisms to provide specialized review when needed. We recognize the challenges to such a proposal. For example, an independent office might lack the political support accorded an existing cabinet-level department. Although assigning one department, such as the Department of Health and Human Services (DHHS), the role of ''first among equals'' would allow it to advocate forcefully for uniform rules across the government, without special provisions it would not have the authority to require other departments to comply, nor is it certain to escape the temptation to develop rules premised on a traditional, biomedical model rather than the wider range of research to be covered.

Federal research protections should be uniform across all government agencies, academe, and the private sector, but they should be flexible enough to be applied in widely different research settings or to emerging areas of research. Furthermore, any central coordinating body should be open to public input, have significant political or legal authority over research involving human participants—whether in the public or private sector—and have the support of the executive and legislative branches of government.

Education as the Key to Promoting Local Responsibility

Currently, federal protections depend on a decentralized oversight system involving IRBs, institutions, investigators, sponsors, and participants. We endorse the spirit and intent of this approach, specifically its contention that the ethical obligation to protect participants lies first with researchers, their sponsors, and the IRBs that review their research. Protecting research participants is a duty that researchers, research institutions, and sponsors cannot delegate completely to others or to the government. In addition, merely adhering to a set of rules and regulations does not fulfill this duty. Rather, it is accomplished by acting within a culture of concern and respect for research participants.

It is unrealistic to think that ethical obligations can be fully met without guidance and resources. To help researchers and IRBs fulfill their responsibilities, the federal government should promote the development of education, certification, and accreditation systems that apply to all researchers, all IRB members and staff, and all institutions. These tools should help researchers craft and IRBs review studies that pose few problems and to know when their work requires special oversight. Today, investigators and IRBs are rightly confused over issues as basic as which areas of inquiry should be reviewed and who constitutes a human participant.

Education is the foundation of the oversight system and is essential to protecting research participants. In all of our reports, we have highlighted the need to educate all those involved in research with human participants, including the public, investigators, IRB members, institutions, and federal agencies. In Cloning Human Beings (1997), we recommended federal support of public education in biomedical sciences that increasingly affect our cultural values. In Research Involving Persons with Mental Disorders That May Affect Decisionmaking Capacity (1998), we called for practice guidelines and ethics education on special concerns regarding this population. In Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries (2001), we recommended measures to help developing countries build their capacity for designing and conducting clinical trials, for reviewing the ethics and science of proposed research, and for using research results after a trial is completed.

In this report, we again acknowledge the inadequacy of educational programs on research ethics in the United States. This deficiency begins at the highest level within the federal oversight system and extends to the local level at individual institutions. We recommend that investigators and IRB members and staff successfully complete educational programs on research ethics and become certified before they perform or review research, that research ethics be taught to the next generation of scientists, and that research ethics be included in continuing education programs.

Clarifying the Scope of Oversight

Many areas of scientific inquiry are ''research,'' and many of these involve human participants, but only some need federal oversight, while others might be better regulated through professional ethics, social custom, or other state and federal law. For example, certain types of surveys and interviews are considered research, but they can be well managed to avoid harms without federal oversight, as the risks are few and participants are well situated to decide for themselves whether to participate. On the other hand, certain studies of medical records, databases, and discarded surgical tissue are often perceived as something other than human research, even when the information retrieved is traceable to an identifiable person. Such research does need oversight to avoid putting people at risk of identity disclosure or discrimination without their knowledge. Federal policies should clearly identify the kinds of research that are subject to review and the types of research participants to whom protections should apply. When research poses significant risks or when its risks are imposed on participants without their knowledge, it clearly requires oversight. However, meaningless or overly rigid oversight engenders disdain on the part of researchers, creates an impossible and pointless workload for IRBs, and deters ethically sound research from going forward.

Ensuring That the Level of Review Corresponds to the Level of Risk

Even within areas of research that need oversight, many individual studies will involve little or no risk to participants. Although current federal policies allow for some distinction between research involving minimal risk and research involving more than minimal risk, the distinction operates mostly in terms of how the research will be reviewed—that is, how procedures are to be followed. But the distinction should be based on how the research is pursued, how the participants are treated, and how the work is monitored over time. Overall, the emphasis should be on knowing how to protect participants rather than on knowing how to navigate research regulations. Instead of focusing so much on the period during which a research design is reviewed, oversight should also include an ongoing system of education and certification that helps researchers to anticipate and minimize research risks. Oversight should also make it easier for researchers to collaborate with their colleagues here and abroad without the burden of redundant reviews. Research review and monitoring should be intensified as the risk and complexity of the research increase and at all times should emphasize protecting participants rather than following rigid rules. In addition, the review process should facilitate rather than hinder collaborative research among institutions and across

national boundaries, provided that participants are protected.

Providing Resources for the Oversight System

Creating a system that protects the rights and welfare of participants and facilitates responsible research demands political and financial support from the federal government as well as the presence of a central coordinating body to provide guidance and oversee education and accreditation efforts. The oversight system should be adequately funded at all levels to ensure that research continues in a manner that demonstrates respect and concern for the interests of research participants.

Summary of Recommendations

This report proposes 30 recommendations for changing the oversight system at the national and local levels to ensure that all research participants receive the appropriate protections. The adoption of these recommendations, which are directed at all who are involved in the research enterprise, will not only lead to better protection for the participants of research, but will also serve to promote ethically sound research while reducing unnecessary bureaucratic burdens. Achieving these goals will, in turn, restore the respect of investigators for the system used to oversee research, support the public's trust in the research enterprise, and enhance public enthusiasm for all research involving human beings.

Scope and Structure of the Oversight System

The entitlements due to all research participants of a prior independent review of risks and potential benefits and the opportunity to exercise voluntary informed consent are the most basic and essential protections for all research participants. However, not all research participants receive these entitlements and not all are protected by the existing oversight system. The commitment to protect participants should not be voluntary, nor should requirements be in place for only some human research. Extending current protections to all research, whether publicly or privately funded, and making uniform all federal regulations and guidance cannot be accomplished within the current oversight system, in which no entity has the authority to act on behalf of all research participants. Thus, to facilitate the extension of the same protections to all humans participating in research, a unified, comprehensive federal policy promulgated and interpreted by a single office is needed.

Recommendation 2.1: The federal oversight system should protect the rights and welfare of human research participants by requiring 1) independent review of risks and potential benefits and 2) voluntary informed consent. Protection should be available to participants in both publicly and privately sponsored research. Federal legislation should be enacted to provide such protection.

Recommendation 2.2: To ensure the protection of the rights and welfare of all research participants, federal legislation should be enacted to create a single, independent federal office, the National Office for Human Research Oversight (NOHRO), to lead and coordinate the oversight system. This office should be responsible for policy development, regulatory reform (see Recommendation 2.3), research review and monitoring, research ethics education, and enforcement.

Recommendation 2.3: A unified, comprehensive federal policy embodied in a single set of regulations and guidance should be created that would apply to all types of research involving human participants (see Recommendation 2.2).

Determining whether particular research activities involving human participants should be subject to a federal oversight system has been a source of confusion for some time. No regulatory definition of covered research can be provided that has the sensitivity and specificity required to ensure that all research activities that include human participants that should be subject to oversight are always included and all activities that should be excluded from oversight protections are always excluded. Clarification and interpretation of the definition of what constitutes research involving human participants will invariably be required if the oversight system is to work effectively and efficiently. Moreover, there will always be cases over which experts disagree about the research status of a particular activity. One of the important leadership roles the proposed oversight office should fulfill is that of providing guidance on determining whether an activity is research involving human participants and is therefore subject to oversight.

Recommendation 2.4: Federal policy should cover research involving human participants that entails systematic collection or analysis of data with the intent to generate new knowledge. Research should be considered to involve human participants when individuals (1) are exposed to manipulations, interventions, observations, or other types of interactions with investigators or (2) are identifiable through research using biological materials, medical and other records, or databases. Federal policy also should identify those research activities that are not subject to federal oversight and outline a procedure for determining whether a particular study is or is not covered by the oversight system.

The proposed federal office should initiate a process in which representatives from various disciplines and professions (e.g., social science, humanities, business, public health, and health services) contribute to the development of the definition and the list of research activities subject to the oversight system.

Level of Review

Although the definition of research involving human participants should be applied to all disciplines, the risks differ both qualitatively and quantitatively across the spectrum of research. Therefore, the oversight system should ensure that all covered research is subject to basic protections'such as a process of informed consent'with the exceptions of the specified conditions for which these protections can be waived, including protection of privacy and confidentiality and minimization of risks. Because the proposed oversight system may include more research activities, it is more critical than ever that review mechanisms and criteria for various types of research are suited to the nature of the research and the likely risks involved. More specific guidance is needed for review of different types of research, including appropriate review criteria and IRB composition. For example, procedures other than full board review could be used for minimal risk research, and national level reviews could supplement local IRB review of research involving novel or controversial ethical issues.

Recommendation 2.5: Federal policy should require research ethics review that is commensurate with the nature and level of risk involved. Standards and procedures for review should distinguish between research that poses minimal risk and research that poses more than minimal risk. Minimal risk should be defined as the probability and magnitude of harms that are normally encountered in the daily lives of the general population (see Recommendation 4.2). In addition, the federal government should facilitate the creation of special, supplementary review bodies for research that involves novel or controversial ethical issues.

Education, Certification, and Accreditation

Protecting the rights and welfare of research participants is the major ethical obligation of all parties involved in the oversight system, and to provide these protections, all parties must be able to demonstrate competence in research ethics'that is, conducting, reviewing, or overseeing research involving human participants in an ethically sound manner. Such competence entails not only being knowledgeable about relevant research ethics issues and federal policies, but also being able to identify, disclose, and manage conflicting interests for institutions, investigators, or IRBs. Finally, the oversight system must include a sufficiently robust monitoring process to provide remedies for lapses by institutions, IRBs, and investigators.

Recommendation 3.1: All institutions and sponsors engaged in research involving human participants should provide educational programs in research ethics to appropriate institutional officials, investigators, Institutional Review Board members, and Institutional Review Board staff. Among other issues, these programs should emphasize the obligations of institutions, sponsors, Institutional Review Boards, and investigators to protect the rights and welfare of participants. Colleges and universities should include research ethics in curricula related to research methods, and professional societies should include research ethics in their continuing education programs.

Recommendation 3.2: The federal government, in partnership with academic and professional societies, should enhance research ethics education related to protecting human research participants and stimulate the development of innovative educational programs. Professional societies should be consulted so that educational programs are designed to meet the needs of all who conduct and review research.

Educating all parties in research ethics and human participant protections is effective only when it results in the necessary competence for designing and conducting ethically sound research, including analyzing, interpreting, and disseminating results in an ethically sound manner. Such competence, however, cannot be assumed to follow from exposure to an educational course or program. As the complexion of research continues to change and as technology advances, new and challenging ethical dilemmas will emerge. And, as more people become involved in research as investigators or in roles that are specifically related to oversight, it becomes increasingly important for all parties to be able to demonstrate competence in the ethics of research involving human participants.

Although accreditation and certification do not always guarantee the desired outcomes, these programs, which generally involve experts and peers developing a set of standards that represents a consensus of best practices, can be helpful in improving performance. Therefore, the choice of standards for these programs and the criteria for evaluating whether an institution has met them are critically important. Accreditation and certification programs should emphasize providing education and assuring that appropriate protections are in place, while avoiding excessively bureaucratic procedures.

Recommendation 3.3: All investigators, Institutional Review Board members, and Institutional Review Board staff should be certified prior to conducting or reviewing research involving human participants. Certification requirements should be appropriate to their roles and to the area of research. The federal government should encourage organizations, sponsors, and institutions to develop certification programs and mechanisms to evaluate their effectiveness. Federal policy should set standards for determining whether institutions and sponsors have an effective process of certification in place.

Recommendation 3.4: Sponsors, institutions, and independent Institutional Review Boards should be accredited in order to conduct or review research involving human participants. Accreditation should be premised upon demonstrated competency in core areas through accreditation programs that are approved by the federal government.

Assessing and Monitoring Compliance

Assessing institutional, IRB, and investigator compliance can help to ensure that standards are being followed consistently. Current mechanisms for assessment include assurances of compliance issued by DHHS and several other federal departments, site inspections of IRBs conducted by FDA, other types of site inspections for participant protection, and institutional audits. In addition, some institutions have established ongoing mechanisms for assessing investigator compliance with regulations. However, institutions vary considerably in their efforts and abilities to monitor investigator compliance, from those that have no monitoring programs to those that conduct random audits. Assessing the behavior of investigators is an important part of protecting research participants and should be taken seriously as a responsibility of each institution. Investigators, IRBs, and institutions should discuss the many practical issues involved in monitoring investigators as they conduct their research studies and provide input into the regulatory process.

Recommendation 3.5: The process for assuring compliance with federal policy should be modified to reduce any unnecessary burden on institutions conducting research and to register institutions and Institutional Review Boards with the federal government. The assurance process should not be duplicative of accreditation programs for institutions (see Recommendation 3.4).

Recommendation 3.6: Institutions should develop internal mechanisms to ensure Institutional Review Board compliance and investigator compliance with regulations, guidance, and institutional procedures. Mechanisms should be put in place for reporting noncompliance to all relevant parties.

Managing Conflicts of Interest

A research setting that involves human participants necessarily creates a conflict of interest for investigators who seek to develop or revise knowledge by enrolling individuals in research protocols to obtain that knowledge. Overzealous pursuit of scientific results could lead to harm if, for example, investigators design research studies that pose unacceptable risks to participants, enroll participants who should not be enrolled, or continue studies even when results suggest they should have been modified or halted. Conflicts of interest can also exist for IRB members or the institutions in which the research will be conducted. Thus, it is important to address prospectively the potentially harmful effects on participants that conflicts of interest might cause.

Organizations, particularly academic institutions, should become more actively involved in managing investigators' and IRB members' conflicts of interest and increase their efforts for self-regulation in this arena. IRB review of research studies is one method for identifying and dealing with conflicts of interest that might face investigators. By having IRBs review research studies prospectively and follow an IRB-approved protocol, investigators and IRBs together can manage conflict between the investigators' desire to advance scientific knowledge and to protect the

rights and welfare of research participants. Financial and other obvious conflicts for IRB members, such as collaboration in a research study, are often less difficult to identify and manage than some of the more subtle and pervasive conflicts. Guidance should be developed to assist IRBs in identifying various types of conflict.

Recommendation 3.7: Federal policy should define institutional, Institutional Review Board, and investigator conflicts of interest, and guidance should be issued to ensure that the rights and welfare of research participants are protected.

Recommendation 3.8: Sponsors and institutions should develop policies and mechanisms to identify and manage all types of institutional, Institutional Review Board, and investigator conflicts of interest. In particular, all relevant conflicts of interest should be disclosed to participants. Policies also should describe specific types of prohibited relationships.

IRB Membership

Appropriate composition of IRB membership ensures that research studies are reviewed with the utmost regard for protecting the rights and welfare of research participants. Current federal regulations require that each IRB have ''at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution'' (45 CFR 46.107(d); 21 CFR 56.107(d)). The regulations also require that each IRB include ''at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.'' Some have raised the concern of whether only 1 unaffiliated member on an IRB is sufficient to avoid institutional influence, especially when IRBs have 15 to 21 members on average. In addition, unaffiliated members do not have to be present for an IRB to conduct review and approve research studies. Thus, IRBs can approve research with only institutional representation present as long as a nonscientist and a quorum are also present. IRBs should strive to complement their membership by having clearly recognizable members who are unaffiliated with the institutions, members who are nonscientists, and members who represent the perspectives of participants. However, it is difficult to require that IRBs increase the presence and participation of more unaffiliated members to reduce the influence of institutional interests on IRB decisionmaking, because finding them can be difficult. Currently, there are no rules or guidance that describe criteria for meeting the definition of an unaffiliated member, that specify how long such members should serve, or that provide guidance regarding under what circumstances they may be removed or what payment should be provided. Institutions should be careful to select unaffiliated members who are truly separated from the institution, except for their role on the IRB. Procedures for the selection and removal of unaffiliated members should be established in a way that empowers the independent voices of those members. In addition, providing reasonable payment to IRB members who are otherwise unaffiliated with the institution can be a valuable way to strengthen these members' role.

Recommendation 3.9: Federal policy should establish standards and criteria for the selection of Institutional Review Board members. The distribution of Institutional Review Board members with relevant expertise and experience should be commensurate with the types of research reviewed by the Institutional Review Board (see Recommendation 3.10).

Recommendation 3.10: Institutional Review Boards should include members who represent the perspectives of participants, members who are unaffiliated with the institution, and members whose primary concerns are in nonscientific areas. An individual can fulfill one, two, or all three of these categories. For the purposes of both overall membership and quorum determinations 1) these persons should collectively represent at least 25 percent of the Institutional Review Board membership and 2) members from all of these categories should be represented each time an Institutional Review Board meets (see Recommendation 3.9).

Guidance for Assessing Risks and Potential Benefits

In addition to protecting the rights and welfare of research participants, it is equally important to protect them from avoidable harm. Thus, an IRB's assessment of the risks and potential benefits of research is central to determining whether a research study is ethically acceptable. Yet, this assessment can be a difficult one to make, as there are no clear criteria for IRBs to use in judging whether the risks of research are reasonable in terms of what might be gained by the individual or society. IRBs should be able to identify whether a clear and direct benefit to society or the research participants might result from participating in the study. However, IRBs should be cautious in classifying procedures as offering the prospect of direct benefit. In fact, if it is not clear that a procedure also offers the prospect of direct benefit, IRBs should treat the procedure as one solely designed to answer the research question(s). A major advantage of this approach is that it avoids justifying the risks of procedures that are designed solely to answer the research question(s) based on the likelihood that another procedure in the protocol would provide a benefit.

Recommendation 4.1: An analysis of the risks and potential benefits of study components should be applied to all types of covered research (see Recommendation 2.4). In general, each component of a study should be evaluated separately, and its risks should be both reasonable in themselves as well as justified by the potential benefits to society or the participants. Potential benefits from one component of a study should not be used to justify risks posed by a separate component of a study.

Minimal Risk

Determining whether a study poses more than minimal risk is a central ethical and procedural function of the IRB. The definition of minimal risk in federal regulations (45 CFR 46.102(i); 21 CFR 56.102(i)) provides an ambiguous standard by which risks involved in a research study are compared to those encountered in daily life. However, it is unclear whether this applies to those risks found in the daily lives of healthy individuals or those of individuals who belong to the group targeted by the research. If it refers to the individuals to be involved in the research, then the same intervention could be classified as minimal risk or greater than minimal risk, depending on the health status of those participants and their particular experiences. According to this understanding, the standard for minimal risk is a relative one.

This report recommends that IRBs use a standard related to the risks of daily life that are familiar to the general population for determining whether the level of risk is minimal or more than minimal, rather than using a standard that refers to the risks encountered by particular persons or groups. These common risks would include, for example, driving to work, crossing the street, getting a blood test, or answering questions over the telephone. Thus, research would involve no more than minimal risk when it is judged that the level of risk is no greater than that encountered in the daily lives of the general population.

Recommendation 4.2: Federal policy should distinguish between research

studies that pose minimal risk and those that pose more than minimal risk (see Recommendation 2.5). Minimal risk should be defined as the probability and magnitude of harms that are normally encountered in the daily lives of the general population. If a study that would normally be considered minimal risk for the general population nonetheless poses higher risk for any prospective participants, then the Institutional Review Board should approve the study only if it has determined that appropriate protections are in place for all prospective participants.

Evaluating Vulnerability

All segments of society should have the opportunity to participate in research, if they wish to do so and if they are considered to be appropriate participants for a given protocol. However, some individuals may need additional protections before they can fully participate in the research study; otherwise they might be more susceptible to coercion or exploitation. Individuals might be considered vulnerable within the research context because of intrinsic characteristics (e.g., they are children or have mental illness or retardation) or because of the situation in which they find themselves (e.g., they are impoverished, unemployed, or incarcerated). Recognizing various types of vulnerability and providing adequate safeguards can prove challenging for IRBs.

Appropriate and specific safeguards should be established to protect persons who are categorized as vulnerable. Once safeguards are established, investigators should not exclude persons categorized as vulnerable from research involving greater than minimal risk because this would deprive them of whatever potential direct benefits they might receive from the research and deprive their communities and society from the benefit of the knowledge such research might generate.

Recommendation 4.3: Federal policy should promote the inclusion of all segments of society in research. Guidance should be developed on how to identify and avoid situations that render some participants or groups vulnerable to harm or coercion. Sponsors and investigators should design research that incorporates appropriate safeguards to protect all prospective participants.

Emphasizing the Informed Consent Process

Rather than focusing on the ethical standard of informed consent and what is entailed in the process of obtaining informed consent, IRBs and investigators have followed the lead of the federal regulations and have tended to focus on the disclosures found in the consent form. However, from an ethics perspective, the informed consent process, not the form of its documentation, is the critical communication link between the prospective participant and the investigator throughout a study, beginning when the investigator initially approaches the participant. Informed consent should be an active process through which both parties share information and during which the participant at any time can freely decide whether to withdraw from or continue to participate in the research. It is time to place the emphasis on the process of informed consent to ensure that information is fully disclosed, that competent participants fully understand the research in order to make informed choices, and that decisions to participate or not are always made voluntarily.

Recommendation 5.1: Federal policy should emphasize the process of informed consent rather than the form of its documentation and should ensure that competent participants have given their voluntary informed consent. Guidance should be issued about how to provide appropriate information to prospective research participants, how to promote prospective participants' comprehension of such information, and how to ensure that participants continue to make informed and voluntary decisions throughout their involvement in the research.

Waiver of Informed Consent

Obtaining voluntary informed consent should not be a requirement for every research study. In fact, waiving the informed consent process is justifiable in research studies that include no interaction between investigators and participants, such as in studies using existing identifiable data (e.g., studies of records) and in studies in which risks generally are not physical. In these kinds of research, risks are likely to arise from the acquisition, use, or dissemination of information resulting from the study and are likely to involve threats to privacy and breaches in confidentiality. The criteria for waiving informed consent in such instances should be revised, so that if such studies have protections in place for both privacy and confidentiality, IRBs may waive the requirement for informed consent.

Recommendation 5.2: Federal policy should permit Institutional Review Boards in certain, limited situations (e.g., some studies using existing identifiable data or some observational studies) to waive informed consent requirements if all of the following criteria are met:

(a) All components of the study involve minimal risk or any component involving more than minimal risk must also offer the prospect of direct benefit to participants;

(b) The waiver is not otherwise prohibited by state, federal, or international law;

(c) There is an adequate plan to protect the confidentiality of the data;

(d) There is an adequate plan for contacting participants with information derived from the research, should the need arise; and

(e) In analyzing risks and potential benefits, the Institutional Review Board specifically determines that the benefits from the knowledge to be gained from the research study outweigh any dignitary harm associated with not seeking informed consent.

Documentation of Informed Consent

Although the federal regulations may have been intended to reflect a legal standard for documentation of informed consent, NBAC is aware of no case law in which a signed, written consent form is required. To fulfill the substantive ethical standard of informed consent, depending on the type of research proposed, it may be more appropriate to use other forms of documentation, such as audiotape, videotape, witnesses, or telephone calls to participants verifying informed consent and participation in the research study.

Recommendation 5.3: Federal policy should require investigators to document that they have obtained voluntary informed consent, but should be flexible with respect to the form of such documentation. Especially when individuals can easily refuse or discontinue participation, or when signed forms might threaten confidentiality, Institutional Review Boards should permit investigators to use other means of verifying that informed consent has been obtained.

Protecting Privacy and Confidentiality

Privacy and confidentiality are complex and poorly understood concepts in the context of some research. Privacy refers to the ways and circumstances under which investigators access information from participants. Because privacy concerns vary by type and context of research and the culture and individual circumstances of participants, investigators should be well informed

and mindful of the cultural norms of the participants. In addition, investigators should be aware of the various research procedures and methods that can be used to respect privacy. Needed is a clear, comprehensive regulatory definition of privacy along with guidance for protecting privacy in various types of research.

Like privacy concerns, concerns about confidentiality vary by the type and context of the research. No one set of procedures can be developed to protect confidentiality in all research contexts. Thus, IRBs and investigators must tailor confidentiality protections to the specific circumstances and methods used in each specific research study. Further, IRBs and investigators are encouraged to consider the use of strong confidentiality protections, which can also reduce some of the violations associated with privacy. A clear, comprehensive definition of confidentiality is needed, along with guidance for protecting confidentiality in various types of research.

Recommendation 5.4: Federal policy should be developed and mechanisms should be provided to enable investigators and institutions to reduce threats to privacy and breaches of confidentiality. The feasibility of additional mechanisms should be examined to strengthen confidentiality protections in research studies.

Monitoring of Ongoing Research

Continual review and monitoring of research that is in progress is a critical element of the oversight system. Such review is necessary to ensure that emerging data or evidence have not altered the risks/potential benefits assessment so that risks are no longer reasonable. In addition, mechanisms are needed to monitor adverse events, unanticipated problems, and changes to the protocol. IRBs can do a better job in this area with the appropriate guidance and some restructuring of the review and monitoring process.

Currently, the requirement of continuing review is overly broad. The frequency and need for continuing review vary depending on the nature of research, with some protocols not requiring continuing review. In research involving high or unknown risks, the first few trials of a new intervention may substantially affect what is known about the risks and potential benefits of that intervention. Even if the knowledge does not warrant changes in study design, it may warrant changes in the information presented to prospective and enrolled participants.

On the other hand, the ethics issues and participant protections necessary in minimal risk research are unlikely to be affected by developments from within or outside the research—for example, research involving the use of existing data or research that will no longer involve contact with participants because it is in the data analysis phase.

Continuing review of such research should not be required because it is unlikely to provide any additional protection to research participants and merely increases the burden of IRBs. However, because minimal risk research does involve some risk, IRBs may choose to require continuing review. In these cases, other types of monitoring may be more appropriate, such as assessing investigator compliance with the approved protocol or reporting of protocol changes and unanticipated problems. Clarifying the nature of the continuing review requirements would allow IRBs to better focus their efforts on reviewing riskier research and would increase protections for participants where they are most needed.

Recommendation 6.1: Federal policy should describe how sponsors, institutions, and investigators should monitor ongoing research.

Recommendation 6.2: Federal policy should describe clearly the requirements for continuing Institutional Review Board review of ongoing research. Continuing review should not be required for research studies involving minimal risk, research involving the use of existing data, or research that is in the data analysis phase when there is no additional contact with participants. When continuing review is not required, other mechanisms should be in place for ensuring compliance of investigators and for reporting protocol changes or unanticipated problems encountered in the research.

Recommendation 6.3: Federal policy should clarify when changes in research design or context require review and new approval by an Institutional Review Board.

Adverse Event Reporting

Assessing adverse events reports can be a major burden for IRBs and investigators because of the high volume and ambiguous nature of such events and the complexity of the pertinent regulatory requirements. Investigators have reported frustration in attempting to understand what constitutes an adverse event, the required reporting times, and to whom adverse events should be reported. The regulations need to be simplified, and one set of regulations should be available for safety monitoring. Regulations and guidance should be written so that investigators and sponsors understand what constitutes an adverse event, what type of event must be reported within what time period, and to whom it should be reported. In addition, regulations and guidance should be clear regarding whose responsibility it is to analyze and evaluate adverse event reports and should describe the required communication and coordination channels for these reports among IRBs and safety monitoring entities, such as Data Safety Monitoring Boards, investigators, sponsors, and federal agencies.

Recommendation 6.4: The federal government should create a uniform system for reporting and evaluating adverse events occurring in research, especially in multi-site research. The reporting and evaluation responsibilities of investigators, sponsors, Institutional Review Boards, Data Safety Monitoring Boards, and federal agencies should be clear and efficient. The primary concern of the reporting system should be to protect current and prospective research participants.

Review of Cooperative or Multi-Site Research Studies

One of the greatest burdens on IRBs and investigators is the review of multi-site studies. Requiring multiple institutions to review the same protocol is unnecessarily taxing and provides no additional protection to participants. In addition, such review poses problems in the initial stages of review as well as in the continual review and monitoring stages and is especially problematic in the evaluation of adverse events in clinical research. Innovative and creative alternative mechanisms and processes for reviewing protocols in multi-site research are needed. To allow for such projects and to support a change in the current system toward a more flexible review system, federal policy should be clear about the functions that must be performed, but be less restrictive about who performs each function.

Recommendation 6.5: For multi-site research, federal policy should permit central or lead Institutional Review Board review, provided that participants' rights and welfare are rigorously protected.

Compensation for Research-Related Injuries

Participants who volunteer to be in a research study and are harmed as a direct result of that study should be cared for and compensated. However, no adequate database exists that describes the number of injuries or illnesses that are suffered by research

participants, the proportion of these illnesses or injuries that are caused by the research, and the medical treatment and rehabilitation expenses that are subsequently borne by the participants. It may be argued that regardless of the magnitude of the problem, the costs of research injuries should never be borne by participants. If individuals are injured by research participation, those who benefit from the research (e.g., institutions and sponsors) bear some obligation to compensate those who risked and suffered injury on their behalf. At this time, injured research participants alone bear both the cost of lost health and the expense of medical care, unless they have adequate health insurance or successfully pursue legal action to gain compensation from the specific individuals or organizations that were involved in conducting the research.

A comprehensive system of oversight of human research should include a mechanism to compensate participants for medical and rehabilitative costs resulting from research-related injuries.

Recommendation 6.6: The federal government should study the issue of research-related injuries to determine if there is a need for a compensation program. If needed, the federal government should implement the recommendation of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research (1982) to conduct a pilot study to evaluate possible program mechanisms.

The Need for Resources

Adopting the recommendations made in this report will generate additional costs for institutions, sponsors, and the federal government (through the establishment of a new federal oversight office). Sponsors of research, whether public or private, should work together with institutions carrying out the research to make the necessary funds available.

Recommendation 7.1: The proposed oversight system should have adequate resources to ensure its effectiveness and ultimate success in protecting research participants and promoting research:

(a) Funds should be appropriated to carry out the functions of the proposed federal oversight office as outlined in this report.

(b) Federal appropriations for research programs should include a separate allocation for oversight activities related to the protection of human participants.

(c) Institutions should be permitted to request funding for Institutional Review Boards and other oversight activities.

(d) Federal agencies, other sponsors, and institutions should make additional funds available for oversight activities.

Future Research

This report raises many questions about ethical issues that cannot be answered because of insufficient or nonexistent empirical evidence. Current thinking about ethical issues in research—such as analysis of risks and potential benefits, informed consent, privacy and confidentiality, and vulnerability—would greatly benefit from additional research. Deserving of more study, for example, are questions regarding the development of effective approaches for assessing cognitive capacity, for evaluating what participants want to know about research, and for determining how to ascertain best practices for seeking informed consent. Clearer and more effective guidance could be developed from a stronger knowledge base. In general, understanding the ethical conduct of research would be advanced by increased interdisciplinary discussion that would include biomedical and social scientists, lawyers, and historians.

Recommendation 7.2: The federal government, in partnership with academic institutions and professional societies, should facilitate discussion about emerging human research protection issues and develop a research agenda that addresses issues related to research ethics.

Notes

1. For example, the Office for Human Research Protections is implementing a new process by which institutions assure future compliance with human participant protections. The Institute of Medicine has recently issued a report on accreditation standards for IRBs (IOM 2001). Public Responsibility in Medicine and Research has established training programs and has co-founded a new organization, the Association for the Accreditation of Human Research Protection Programs.

2. To date, NBAC has issued five reports: Cloning Human Beings (NBAC 1997), Research Involving Persons with Mental Disorders That May Affect Decisionmaking Capacity (NBAC 1998), Ethical Issues in Human Stem Cell Research (NBAC 1999a), Research Involving Human Biological Materials: Ethical Issues and Policy Guidance (NBAC 1999b), and Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries (NBAC 2001).

3. United States v. Karl Brandt et al., Trials of War Criminals Before the Nuremberg Military Tribunals Under Control Council Law 10. Nuremberg, October 1946—April 1949. Volumes I–II. Washington, DC: U.S. Government Printing Office.

4. There are, of course, some circumstances in which consent cannot be obtained and in which an overly rigid adherence to this principle would preclude research that is either benign or potentially needed by the participant him or herself. Thus, NBAC endorses the current exceptions for research that is of minimal risk to participants and for potentially beneficial research in emergency settings where no better alternative for the participants exists. NBAC also urges attention to emerging areas of record, database, and tissue bank research in which consent serves only as a sign of respect and in which alternative ways to respect participants do exist (NBAC 1999b; 21 CFR 50.24). In a previous report, the Commission made recommendations regarding persons who lack decisionmaking capacity and from whom informed consent cannot be obtained (NBAC 1998).

5. Porter, J., Testimony before NBAC. November 23, 1997. Bethesda, Maryland. See McCarthy, C.R., ''Reflections on the Organizational Locus of the Office for Protection from Research Risks.'' This background paper was prepared for NBAC and is available in Volume II of this report.

6. See Goldman, J., and A. Choy, ''Privacy and Confidentiality in Health Research'' and Sieber, J., ''Privacy and Confidentiality: As Related to Human Research in Social and Behavioral Science.'' These background papers were prepared for NBAC and are available in Volume II of this report. See also Ferguson v. City of Charleston 121 S. Ct. 1281. (2001).

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Dated: August 27, 2001.

Glen D. Drew,

Acting Executive Director, National Bioethics Advisory Commission

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control and Prevention

[60Day–01–59]

Proposed Data Collections Submitted for Public Comment and Recommendations

In compliance with the requirement of Section 3506(c)(2)(A) of the Paperwork Reduction Act of 1995 for opportunity for public comment on proposed data collection projects, the Centers for Disease Control and Prevention (CDC) will publish periodic summaries of proposed projects. To request more information on the proposed projects or to obtain a copy of the data collection plans and instruments, call the CDC Reports Clearance Officer on (404) 639–7090.

Comments are invited on: (a) Whether the proposed collection of information is necessary for the proper performance of the functions of the agency, including whether the information shall have practical utility; (b) the accuracy of the agency's estimate of the burden of the proposed collection of information; (c) ways to enhance the quality, utility, and clarity of the information to be collected; and (d) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques or other forms of information technology. Send comments to Anne O'Connor, CDC Assistant Reports Clearance Officer, 1600 Clifton Road, MS–D24, Atlanta, GA 30333. Written comments should be received within 60 days of this notice.

Proposed Project

Preventive Health and Health Services Block Grant, Annual Application and Reports (OMB #0920–0106)—Revision—National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP), Centers for Disease Control and Prevention (CDC). In 1994, OMB approved the collection of information provided in the grant applications and annual reports for the Preventive Health and Health Services (PHHS) Block Grant (OMB #0920–0106). This approval expires on November 30, 2001. CDC is requesting OMB clearance for this legislatively mandated information collection until November 30, 2004. The request is to approve the development and adherence to *Healthy People 2010,* the Nation's Health Objectives which was released the Spring of 2000. The PHHS block grant is mandated according to section 1904 to adhere to the Healthy People framework, therefore, the current application and report format was restructured to coincide with 2010.

This information collected through the applications from the official State health agencies is required from section 1905 of the Public Health Service Act. There is a slight change in the proposed information collection from previous years. The changes include more program specific information and the relationship of block funded activities to program strategy. The information collected from the annual reports is required by section 1906. The development of a PHHS block grant web page with data web links from existing federal databases will be used to coincide with the collection of uniform data for the annual report. The availability to collect data through internet accessibility will allow for a more streamlined and efficient use of data processing by the states and will reduce the states burden of duplicate reporting on outcome and risk factor data. The cost to respondents is estimated at $25 per burden hour, a total cost to respondents of $106,750.

Respondents	No. of respondents	No. of responses/ respondent	Average burden per response (in hours)	Total burden (in hours)
Application	61	1	30	1830
Report	61	1	40	2440
Total				4270

Dated: August 23, 2001.

Nancy Cheal,

Acting Associate Director for Policy, Planning and Evaluation, Centers for Disease Control and Prevention.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control and Prevention

[30DAY–46–01]

Agency Forms Undergoing Paperwork Reduction Act Review

The Centers for Disease Control and Prevention (CDC) publishes a list of information collection requests under review by the Office of Management and Budget (OMB) in compliance with the Paperwork Reduction Act (44 U.S.C. Chapter 35). To request a copy of these requests, call the CDC Reports Clearance Officer at (404) 639–7090. Send written comments to CDC, Desk Officer, Human Resources and Housing Branch, New Executive Office Building, Room 10235, Washington, DC 20503. Written comments should be received within 30 days of this notice.