

Executive Summary

ABSTRACT

In response to a request from the Secretary of Health and Human Services, the Institute of Medicine formed the Committee on Assessing the System for Protecting Human Research Subjects to conduct a two-phase study to examine how to improve the structure and function of human research review programs. This report provides the committee's response to the tasks in phase 1. With respect to human research review programs, those tasks are to review and consider proposed performance standards, recommend standards for accreditation, and recommend an approach to monitoring and evaluating the system for protection of human research participants. The committee reviewed and considered available draft standards developed independently by Public Responsibility in Medicine and Research (PRIM&R) and the National Committee for Quality Assurance (NCQA), which is under contract to the U.S. Department of Veterans Affairs (VA). The committee provides a series of findings and recommendations for using performance standards to improve the system for protection of human research participants.

The committee finds that the standards proposed by NCQA for VA facilities appear promising for use in the accreditation of VA facilities. The committee regards the standards prepared by NCQA to be more suitable than those prepared by PRIM&R for not only pilot testing in VA facilities but also, with modification, for the accreditation of other research institutions. The NCQA standards are the strongest basis for use in the accreditation of other research institutions because they pay

specific attention to quality improvement, provide flexibility in achieving performance goals (e.g., increased protection of research participants), and are explicit in their grounding in current regulations.

The committee recommends that pilot accreditation programs should start from the accreditation standards and processes proposed by NCQA for VA facilities and be adapted for use in other organizational contexts by NCQA or other accreditation bodies. In expanding the draft NCQA accreditation standards for use beyond VA facilities, the committee recommends that the standards be strengthened in several specific ways. These include how investigators will be reviewed, beyond the review of protocols by institutional review boards; how sponsors will be assessed; how participants will be involved in setting performance standards; and how oversight mechanisms can ensure participants' safety.

The committee further recommends that (1) the organizations formulating accreditation standards and carrying out the accreditation process be independent, nongovernmental organizations; (2) the formulation of accreditation standards, the accreditation process, and human research participant protection program operations directly involve research participants; and (3) the accreditation process accommodate organizations involved in research beyond the traditional models of academic health centers and VA facilities and be appropriate for research methods other than clinical research.

Only by experience gained through pilot testing can the value that accreditation adds to the current regulatory system, in terms of enhanced protection of human research participants, be adequately assessed.

Beginning in the 1960s, a formal system for ensuring the ethical conduct of research with humans developed in the United States. This system traditionally centered on the institutional review board (IRB). However, the Committee on Assessing the System for Protecting Human Research Subjects and others now envision a broader system with multiple functional elements that will be referred to in this report as *human research participant protection programs* (HRPPPs) (Figure 1). That system is the central element for protecting the interests of those who participate in research, and it has four principal functions: (1) to ensure that research design is sound and that a study's promise for augmenting knowledge justifies the involvement of human participants,¹ (2) to assess the risks and benefits independently of the investigators who carry out the research; (3) to ensure that participation is voluntary and informed; and (4) to ensure that participants are recruited equitably and that risks and benefits are fairly distributed.

¹ See Chapter 1 for discussion regarding the committee's use of the term "participant" versus "subject."

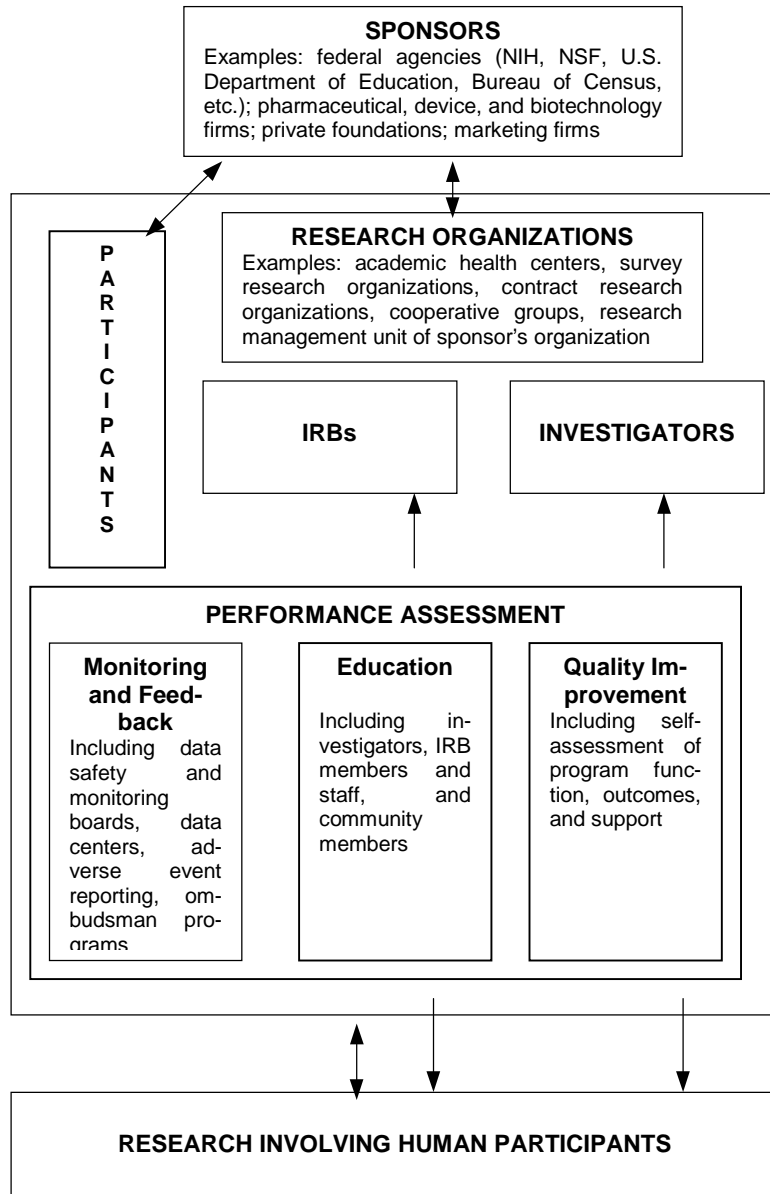


FIGURE 1 Human research participant protection programs. The components in the large box are all parts of an HRPPP. Arrows represent information flow pathways, not organizational responsibilities. All units within HRPPP should have formalized communication procedures.

When the original system for the protection of human participants in research was created, the typical study was done at a single research institution by a single investigator or a small team of investigators. IRBs² were formed to ensure an independent review of proposed research by volunteers at individual sites and remain the centerpiece of HRPPPs. Today, however, some clinical trials involve scores or even hundreds of centers and tens of thousands of participants. With the dramatic increase in privately funded research, a separate system of independent IRBs has also been created; such IRBs typically have professional staff, and their members are often paid for their time and effort. The review system as a whole, however, has not transformed or adapted to the vast growth in the scale and complexity of research.

Research carries with it inherent risk, but it must always be conducted so that risk to research participants is reduced to the minimum necessary and the rights of the volunteers who participate in the research are respected by the entire system of research sponsors, institutions, and investigators (the HRPPP). Trust in the human research enterprise, embodied in an individual consenting to participate in a study, demands that the system responsible for protection be credible and accountable. Yet, the repeated documentation of serious strains on the system has not led to discernable improvement as weaknesses and lapses continue to come to light.

The need to improve HRPPPs has become ever more apparent as report after report highlighting mounting concerns about the ability of HRPPPs to keep up with the evolving research enterprise has been issued (see Chapters 1 and 2). Nearly all of these reports have recommended a reexamination and modernization of the system. In addition, beginning in May 1999 the federal Office for Protection from Research Risks (OPRR) and the Food and Drug Administration (FDA) took action against several major research universities, suspending their human research programs because of apparent noncompliance with federal regulations. In September 1999, Jesse Gelsinger, an 18-year-old research volunteer, died in a gene transfer trial not because of his underlying disease but because of the experimental intervention itself. As the circumstances and events leading up to his death emerged, it became apparent that the system intended to protect him from unacceptable risks in research instead failed him.

In response to these and other events over the last several years, the U.S. Congress, the U.S. Department of Veterans Affairs (VA), and the U.S. Depart-

² IRBs are defined in federal regulations governing human research (45 CFR 46.107–109; 45 CFR 56.102 (g)). Food and Drug Administration (FDA) regulations cover “independent” IRBs that review privately funded research. The majority of IRBs operate under one or both sets of federal regulations. Some nongovernment organizations have formed groups to review and approve research that is not subject to federal regulation. These groups can perform the functions of an IRB overseen by FDA or the Office for Human Research Protections (OHRP) but do so outside the purview of FDA and OHRP.

ment of Health and Human Services (DHHS) began looking at how the system for the protection of participants in human research could be brought into line with the new challenges that it faced without unduly limiting opportunities for advancing knowledge through innovative research. In the spring of 2000, congressional hearings, legislation, and new initiatives announced by the Secretary of Health and Human Services and VA sought to assure the public that policy makers were aware of the fundamental need to ensure access to the great potential offered by research without sacrificing participant safety or well-being. Likewise, organizations within the research community responded to public concern by reaffirming their commitment to the safe and ethical pursuit of research and by establishing focused task forces to examine identified areas of concern (AAMC et al., 2000; AAU Task Force on Research Accountability, 2000; AAUP, forthcoming) Accreditation of HRPPPs was one of the ideas that emerged from these discussions.

THE COMMITTEE'S TASK

One component of the DHHS effort to examine the system for the protection of human research participants was to ask the Institute of Medicine (IOM) to initiate an in-depth study of how to improve the structure and function of activities related to the protection of participants in human research, with an emphasis on the responsibilities and elements of HRPPPs. In this framework, HRPPPs include, but are not limited to, programs that use the traditional IRB model. The complexity of significant and delicate issues that are encompassed in such a task merits an in-depth examination by IOM, and thus, the task is to be conducted in two phases.

This report represents the results of phase 1 of the IOM study. It examines the potential benefits and strengths that an accreditation strategy, such as those under development within the research community and at the direction of VA (see Appendixes B and C), could bring to ongoing efforts to enhance HRPPPs. More specifically, the report addresses the following three tasks:

- 1. review and consider proposed human research review program³ performance standards;**
- 2. recommend standards for accreditation of HRPPPs, considering measures of structure, process, and performance, as well as resource sufficiency; and**

³ In the course of committee deliberations, the term "human research participant protection program" was substituted for "human research review program," as the former term better reflected the system of oversight that the committee hopes will result from its recommendations.

3. recommend steps that the organizations and institutions that conduct research and that the federal government should take to collect and analyze data to monitor and evaluate how well the system for protecting human research participants is operating.

This report therefore provides recommendations for core standards with which to initiate pilot accreditation programs for HRPPPs, specific comments on standards under development, and suggested interim actions that can be used to initiate and monitor the impact of accreditation on the system and its ability to achieve the intended goals. The recommendations, listed below, appear in Box 1, at the conclusion of the Executive Summary, according to how they relate to the three broad categories; that is, whether they respond to the goal of developing an accreditation program, standards, or a system of evaluation. However, all comments are made in the context of the current policy and existing regulatory structures and without the benefit of a full examination of the underlying issues and possible solutions.

The structures and processes constituting an accreditation system are only coming into being and still need to be tested. Therefore, the committee's recommendations are aimed at a moving target. Its recommendations about accreditation standards in particular presume that those standards will evolve substantially, especially with the benefit of feedback from initial pilot tests. The committee recommends standards for pilot testing of accreditation programs, but the committee did not itself formulate those standards. It neither could nor should have done so, for several reasons. First, the accreditation standards should be formulated in a "bootstrap" process, with strong feedback between the formulation of standards and direct experience with the implementation of HRPPP standards. Second, accreditation bodies should be accountable for their standards as well as their accreditation processes. Reliance on "IOM standards" would thus undermine this alignment between authority and responsibility for standard setting at a critical point in the development of an accreditation program(s). Finally, the standards will evolve over time and will evolve rapidly during initial pilot testing. This iterative process would not be possible with a set of IOM standards produced at this time. As the committee formulated its recommendations, no pilot testing had taken place, and reliance on standards in advance of and independent of such testing runs contrary to early experience with the development of new oversight mechanisms in general and past models of accreditation in particular.

MAJOR FINDINGS

In accordance with its task, the committee reviewed available draft accreditation standards at the time of its deliberations. For this purpose, materials developed by Public Responsibility in Medicine and Research (PRIM&R) and,

subsequently, the National Committee for Quality Assurance (NCQA) were provided to the committee. To assess those materials, the committee found it useful to use the following general criteria: (1) their scope and focus; (2) their relationship to the existing regulatory standards; and (3) the extent to which the standards can be consistently implemented, measured, and enforced, as well as their inclusion of various key elements. For more discussion on the review and elements considered, please see Chapter 3.

Finding 1: The standards proposed by NCQA for VA facilities appear promising for use in the accreditation of VA facilities. Those same standards are the strongest basis for use in the accreditation of other research institutions (see Table 1). The committee regards the standards prepared by NCQA to be more suitable than those prepared by PRIM&R for not only pilot testing in VA facilities but also, with modification, for the accreditation of other research institutions.

Finding 2: Neither set of proposed standards applies readily to the full range of research involving human participants or to the diversity of research institutions that conduct it. Both sets of standards understandably and reasonably start from the kinds of research and the types of research organizations where recent problems have been best documented. It is not clear, however, how standards should be applied to nonbiomedical research settings, contract management organizations, clinical trials cooperative groups, independent IRBs, central IRBs, site management organizations, or units of research sponsors that conduct human research (e.g., research units within federal agencies and private pharmaceutical, biotechnology, and device companies).

How the proposed standards can be adapted to the large and growing fraction of research not conducted in the framework of biomedical research institutions will be an important question to be addressed in pilot tests. This is problematic in two respects. First, many institutions performing research with humans are not primarily focused on clinical research, yet the standards have clearly been formulated with medical research in mind. Second, the accreditation system must cover all types of research organizations. A very large fraction, probably a majority, of clinical research is privately sponsored and conducted outside traditional medical research institutions for which both sets of standards were developed. Failure to include privately sponsored research reviewed by independent IRBs would not only exclude a significant fraction of research with humans but would also call into question whether the accreditation process was skewed in favor of academic health centers. It is premature to judge how accreditation can work for these organizations, but it is critical to include them in any credible accreditation system.

TABLE 1 Comparison of Draft NCQA and PRIM&R Accreditation Standards

Organization preparing standards	Strengths	Weaknesses
NCQA	<ul style="list-style-type: none"> • Direct linkage to quality improvement programs • Grounded in baseline regulatory requirements • Measurement criteria and data sources specified • Interpretive guidance provided • Accreditation process specified • IRB decision appeals process specified • Thresholds for compliance specified • Formulation of standards and accreditation of VA facilities by the same organization 	<ul style="list-style-type: none"> • Because of an exclusive focus on VA facilities, will need to be modified for use for organizations for which standards were not originally designed^a • Insufficient standards relating to participant involvement beyond informed consent • Insufficient attention to role of HRPPP accreditation vis-à-vis external research sponsors • Insufficient standards for research monitoring • Uncertain application to nonmedical research
PRIM&R	<ul style="list-style-type: none"> • Grounded in ethical principles of The Belmont Report^b • Reflect strong expertise about IRB operations in academic health centers • Differentiate substandards for IRBs, institutions, and investigators 	<ul style="list-style-type: none"> • Lack of specificity in standards for investigator and institutional obligations • Documentation standards for IRB record-keeping inapplicable to many IRBs • Uncertain application to nonmedical research, independent IRBs, contract research organizations, clinical trials cooperative groups, central IRBs, and other research organizations • Lack of cross-tabulation of standards to regulations

- Inadequate specification of data sources, except documentation standards
- Insufficient attention to role of HRPPP accreditation vis-à-vis external research sponsors
- Insufficient standards relating to participant involvement beyond informed consent
- Insufficient standards for research monitoring
- Lack of specificity regarding measures and thresholds for compliance
- Lack of interpretive guidance
- Lack of specificity regarding accreditation judgments
- Formulated with an inadequate link between responsibility for developing standards (an ongoing process) and responsibility for implementing accreditation process

ⁱ Although it is identified as a weakness in this table, the NCQA standards were designed only for VA facilities, so a lack of more general applicability is not a criticism of the NCQA formulation but is an observation about their use of the NCQA standards for purposes that the committee recommends, that is, for non-VA organizations.

ⁱⁱ National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1979).

In the course of the second, more comprehensive, phase of the committee's work, the committee may or may not revisit HRPPP accreditation. The future report will certainly address other strategies for improvement to supplement this report, such as educating investigators, augmenting resources for research oversight (at both the federal and the local levels), enhancing oversight of ongoing research (including monitoring bodies and reporting mechanisms), and other strategies.

RECOMMENDATIONS

Recommendation 1: Pursue Accreditation Through Pilot Testing as One Approach

Accreditation of HRPPPs should be pursued as *one* promising approach to improving the human participant protection system. The first step is implementation of pilot programs to test standards, establish accreditation processes, and build confidence in accreditation organizations. This effort should be evaluated for its impact on protecting the rights and interests of participants in 3 to 5 years.

The process of establishing an accreditation system typically takes many years, and it must be continually adjusted, particularly in its initial phases. Current efforts to establish accreditation systems are just under way, and the proposed standards are new and untested. The process for the accreditation of HRPPPs is still being configured, and the organizations thus far identified to carry it out are taking on an unprecedented task. Two specific approaches have been presented to the committee. The process that is furthest along is a nascent accreditation process for the VA medical facilities being conducted by NCQA under a contract with the VA. That contract commenced in May 2000. Another organization, the Association for the Accreditation of Human Research Protection Programs (AAHRPP), was originally incorporated in March 2000, but its formal establishment is still under way (see Chapter 2).

These emerging accreditation programs are best viewed as pilot projects that will have to be evaluated in light of experience. Any accreditation system must be constructed as an evolving tool and part of a long-term strategy and cannot be expected to immediately correct deficiencies in the HRPPP system. As a component of a long-term strategy to improve the quality of research oversight, however, a nongovernmental accreditation process has promise and should be tested as soon as possible. The logical first step is to continue the VA accreditation program. The second step is to pilot test accreditation in academic health centers and private research organizations whose HRPPPs conform to the organizational structures for which both sets of draft standards were formulated: those that conduct research, directly employ investigators, and have IRBs. The

NCQA standards appear to be closer to adaptation for such use than the PRIM&R standards do (see Recommendation 9).

Recommendation 2: Establish a Nongovernmental Accreditation Organization(s)

Organizations formulating accreditation standards and carrying out the accreditation process should be independent, nongovernmental organizations. These organizations should include within their programmatic leaderships the perspectives of the relevant stakeholders in the applicant HRPPP community (i.e., institutions, investigators, sponsors, and participants).

An accreditation process is only as credible as the organizations that carry it out. The foremost criterion is independence (Hamm, 1997). Organizations formulating standards and conducting the accreditation process should

1. be national in scope;
2. be familiar with the operations of institutions that apply for accreditation; and
3. incorporate the perspectives of research participants within their programmatic leadership.

An accreditation process should directly involve the kinds of institutions being accredited, but an accreditation organization should not be beholden to any particular stakeholder or interest group. Accreditation bodies for HRPPPs will require input from academic health centers, organizations representing research sponsors, nongovernmental research organizations, private firms developing products and services tested in studies with humans, participants, IRB members and staff from both academic and nonacademic institutions, research administrators in both academic and nonacademic institutions, and individuals from a range of research fields appropriate to the intended range of applicant institutions.

Research participant representatives will be particularly important in formulating the overall goals of the HRPPP systems, and their perspectives should be systematically solicited in both the formulation of standards and the execution of the accreditation process. This involvement will also include representation on groups that set standards and teams that conduct external evaluations and site visits. National accreditation bodies should seek to involve organizations that have both a genuine national constituency that corresponds to the interests of the research participants⁴ and a demonstrated familiarity with the research process and research protection rules and regulations (see Recommendation 8).

⁴ In the case of VA, for example, this would include national veterans organizations; for medical research, this would include health advocacy organizations; and for community-based or population-based research, this would include organizations representing the communities or the full range of subpopulations sampled.

Recommendation 3: Articulate Sound Goals Within Accreditation Standards

The goals of accreditation standards should be to ensure

1. That the proposed research promises to contribute knowledge sufficient to justify research involving human participants;
2. independent review of research by a board knowledgeable about protection standards and the fields of research being reviewed;
3. that the perspectives of participants are represented on IRBs, on research monitoring bodies, and throughout the research oversight system;
4. that IRB members do not review protocols with which they have financial or nonfinancial conflicts of interest;⁵
5. that investigator and institutional conflicts of interest, both financial and nonfinancial, are disclosed to IRBs and participants and are managed responsibly by research institutions;
6. a review process that balances risks and potential benefits, keeps risks to the minimum necessary, and monitors research on a continuing basis;
7. that an effective process for obtaining voluntary informed consent of participants is in place;
8. that policies and procedures are in place to assess the quality of HRPPP operations, enhance accountability, and improve performance;
9. there is fairness in recruitment and selection of participants;
10. that the privacy and confidentiality of research participants are protected; and
11. that the HRPPP is transparent so that participants can judge the research process to be trustworthy.

Recommendation 4: Establish Flexible, Ethics-Based, and Meaningful Standards

Accreditation standards should meet the following minimal criteria:

1. They should be based on sound and widely accepted ethical principles.⁶

⁵ The committee does not mean that any member who could have a conflict with any conceivable protocol coming to an IRB for review should be excluded from service on an IRB but, rather, means that the individual should recuse himself or herself from reviewing such protocols.

2. They should be flexible and adapted to different kinds of research and different research institutions.
3. They should encourage accredited organizations to shift from a culture that relies on external compliance checks to a culture that puts safety and voluntary participation foremost.
4. They should facilitate compliance with federal regulations but should aim to move an organization toward having stronger protection of human research participants.
5. To the extent possible, they should focus on the use of meaningful measures of how well the rights and interests of research participants are being protected rather than simple determination of whether informed-consent statements have been signed or IRB meetings were duly constituted.

The committee believes that the draft NCQA standards are close to meeting the criteria in Recommendations 3 and 4 for pilot testing in VA facilities, and if they are modified as suggested under Recommendation 9, they could be used as the basis for pilot tests of HRPPP standards outside VA facilities.

Recommendation 5: Accommodate Distinct Research Methods and Models Within Accreditation Programs

The accreditation process should accommodate other research organizations in addition to the traditional models provided by academic health centers and VA facilities. The accreditation process should also cover research other than clinical research.

Proposed NCQA standards were designed for VA facilities only. PRIM&R standards were prepared with a broader range of institutions in mind, but the committee heard strong, consistent comments that they do not fully recognize either the diversity of institutions or the full range of research (IOM, 2001). The standards proposed by NCQA and PRIM&R focus on HRPPPs that comprise a research institution, investigators, and IRBs. These elements are present in VA

⁶ The principles laid out in *The Belmont Report* are one foundation (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979). Accreditation standards, however, should also incorporate the recommendations of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research (President's Commission, 1981, 1983), the recommendations of the Advisory Committee for Human Radiation Experiments (ACHRE, 1995), recommendations presented in reports of the National Bioethics Advisory Commission (NBAC, 1998, 1999a,b, forthcoming-a, forthcoming-b) the recommendations of the Office of the Inspector General of DHHS (DHHS OIG, 1998b, 2000b), and the recommendations of the General Accounting Office (GAO, 1996). In addition, recommendations from reports and declarations of private bodies and independent scholars should be incorporated. This presupposes that an advisory apparatus is available to cull this literature.

facilities, academic health centers, and some other research organizations. Many organizations that might reasonably apply for HRPPP accreditation, however, do not conform to the traditional research organization model. Independent IRBs do not directly conduct research, for example, and so entire sections of the proposed standards are inapplicable to them.

To be credible, the accreditation process should expand to include independent IRBs; cooperative groups; contract research organizations; site management organizations; units within federal research agencies that conduct their own research; and units of pharmaceutical, medical device, and biotechnology firms that carry out research with human participants. The accreditation process must be sufficiently elastic to accommodate all major organizational structures involved in research with humans. Failure to cover the full range of research organizations under an accreditation program would undermine the credibility of the accreditation process so essential to the program's success in two ways. First, it would eliminate a large and growing fraction of research with humans, and second, it could be perceived as a subterfuge to protect the competitive advantage of academic health centers to the detriment of private independent IRBs on the basis of categorical exclusion rather than quality. Yet, neither NCQA nor PRIM&R draft standards can be directly applied to many organizations conducting research with humans. Discovering how to do this with one or several sets of standards, whether under one accreditation body or a few, will be an important question to address in pilot tests.

Accreditation of an independent IRB, for example, might use only the subset of standards pertinent to IRBs, but doing so would also require assurance regarding the functions covered by proposed standards that pertain to investigators, research institutions, and research participants, as well as standards not yet incorporated into NCQA or PRIM&R standards (but covered by the guidelines of the International Conference on Harmonisation; see Chapter 3) pertaining to sponsors. Independent IRBs could be accredited with such assurances, perhaps on the basis of binding written agreements between the independent IRB and the research sponsors contracting for its services.

Another approach would be to accredit the organization that does directly control all the relevant elements of an HRPPP (e.g., a contract research organization that has a formal agreement with an independent IRB to review all its protocols, the research unit of a private firm, the unit of a federal agency that performs research, or a clinical trials cooperative group). These approaches are not mutually exclusive, but neither approach is reflected in the NCQA and PRIM&R draft standards. One of the virtues of a nongovernmental voluntary accreditation process is its flexibility, and nongovernmental accreditation bodies should not find it difficult to accommodate disparate organizational structures, but it is not yet clear how the current proposed standards or accreditation processes would do so.

How to apply the proposed standards to nonmedical research institutions⁷ is also controversial and should be explicitly addressed in pilot accreditation programs. Commentary at the committee's January 2001 public forum stressed that proposed HRPPP standards focus almost entirely on clinical research. Although the proposed PRIM&R standards include many that would be used only "if applicable" to a given applicant organization, a set of standards developed for the social and behavioral sciences or for population-based studies *ab initio* would not include many of the "if applicable" standards and would expand or rephrase other standards.

The committee believes that the same principles for protection of the rights and interests of research participants apply to all research, and in that sense the same general standard of conduct should prevail. It is an open question, however, whether the best accreditation strategy would be to use one set of operational standards for all research. That might well prove viable, but it also might prove better to encourage the evolution of different specific standards for different kinds of research institutions. Those in the best position to judge this will be organizations devising the accreditation processes, not this committee or the federal government. Whether to develop one set of standards or a few sets of standards specific to a few different classes of research organizations should not be decided by fiat but should be decided in light of experience gained through pilot accreditation programs that include medical and nonmedical sites.

Accreditation demonstration programs can begin by focusing on the research institutions for which they were designed, but they might evolve in many different ways. In the future, there could be one or a few accreditation bodies and one or a few sets of accreditation standards, and many different kinds of organizations will continue to be involved in research with human participants.

Recommendation 6: Base Standards on Existing Regulations

Accreditation standards should start from federal regulations for the protection of human research participants but should augment those regulations. The process should be iterative and continual, with evolution of both accreditation standards and the operations of accredited organizations, creating incentives for accredited organizations to improve.

⁷ By "nonmedical institutions," the committee refers to organizations that conduct or review research that is not primarily clinical. Some research institutions, for example, concentrate on national surveys or demographic research; others mainly review student research projects. Entire research centers are devoted to epidemiology, population and community-based research, or public health. Some academic and independent private research institutes focus on studies in anthropology, oral history, sociology, psychology, journalism, law, and political science. These fields have widely different norms and methods, and the nature of the risks for participants also differs.

Accreditation standards start from a base of regulations governing research with humans. The regulations, in turn, are based on a set of principles for the ethical conduct of research (see Recommendation 4). The standards proposed by NCQA are tightly coupled to the existing federal regulations, but they also incorporate quality improvement processes that could evolve into a different set of standards over time. The NCQA strategy will therefore focus first on facilitating compliance with existing regulations but, importantly, will provide a means to raise the quality of protection standards over time. By using standards that emphasize processes of continual quality improvement instead of an exclusive focus on regulatory compliance, the way may be open to the development of future standards that center on HRPPP performance, in addition to the current focus on documentation. For example, HRPPP that demonstrates that it can ensure informed consent because it has data showing that participants understand the protocols in which they are enrolled could begin to supplant or augment paper audits of signed informed-consent forms. This strategy therefore has the potential to introduce the desired flexibility and focus on outcomes into the oversight system.

Accreditation will not be successful until it is widely accepted as a mark of excellence. It should also serve as an educational tool to raise the median overall performance. To do this, accreditation standards and the processes in which they will be used must incorporate consistent feedback from the parties involved in the various aspects of an HRPPP. Those who encounter problems in the research system—participants or people who care about them, investigators submitting research for review by an IRB, institutions negotiating agreements to perform sponsored research, anyone who notices something going awry in the course of a study, or data safety and monitoring boards that note a pattern in reported adverse events—need simple, consistent ways to bring their concerns to light. In addition, they need ways to bring relevant information into the procedure for the review of the process, including the functioning of both the HRPPP system and the accreditation process.

One of the chief advantages of a voluntary nongovernmental accreditation system over a mandatory government process is that it can evolve over time without requiring new federal regulations at each step. It took 10 years for 18 agencies to adopt the federal Common Rule governing human research (45 CFR 46, Subpart A), and at least 3 agencies that conduct human research remain outside of the rule.⁸ The current regulatory system is demonstrably unresponsive to dramatic changes in how research is conducted; a nongovernmental accreditation

⁸ OPRR noted three agencies that appeared to sponsor research with human participants but that were not signatories to the Common Rule: the National Endowment for the Humanities, the U.S. Department of Labor, and the Nuclear Regulatory Commission, as cited in a draft report forthcoming from the National Bioethics Advisory Committee (NBAC, forthcoming-b).

system may be more responsive by comparison and would comport with Circular No. A-119 of the Office of Management and Budget, which urges the use of non-governmental “voluntary consensus standards” where possible (OMB, 1998).⁹

The committee envisions an accreditation process that will continually evolve, updating standards over time. The operations of organizations seeking accreditation will also evolve. The parallel evolution of accreditation standards and HRPPP operations should be an iterative process, with the formulation of standards efficiently informed by knowledge acquired in the accreditation process. The formulation of standards, the conduct of accreditation site visits, and external evaluation must therefore be intimately linked.

Recommendation 7: Incorporate Continuous Quality Improvement Mechanisms into Standards

Accreditation organizations should emphasize the process of self-study, evaluation, and continual quality improvement among applicants. They should move beyond documentation of informed consent and protocol review, which, although essential, do not of themselves protect the rights and interests of research participants.

Standards should aim to improve outcomes and should not overly prescribe how to achieve the specified objectives. Rather, they should focus on the core standards that apply across programs and that are essential to a quality HRPPP. Current proposed standards generally reinforce the documentation practices required by federal regulations but do not go beyond these regulatory requirements. In general, both entities seeking accreditation and accreditation bodies should identify exemplary performance and best practices, providing benchmarks for the research community at large and making information on organization performance openly available to the public and policy makers.

Linkage to quality improvement strategies also offers a path to achievements well beyond regulatory compliance. For example, an HRPPP demonstrating a particularly reliable system for the monitoring of participant safety or the reporting of problems in ongoing research, could have a competitive advantage over nonaccredited competitors in seeking support from sponsors or having access to participants, researchers, or students. The committee concurs with this strategy which was incorporated into the standards proposed by NCQA and recommends that it should also be applied to non-VA research organizations.

⁹ Circular No. A-119 was intended mainly for technical standards pertaining to products, but it also contemplates “related management systems practices.”

Recommendation 8: Directly Involve Research Participants in Accreditation Programs and HRPPPs

The formulation of accreditation standards, the accreditation process, and HRPPP operations should directly involve research participants.¹⁰

Accreditation bodies should formally solicit input from and directly involve the groups of people who will be studied in research carried out by the organizations that they will accredit. Participant perspectives are an essential element in research design, especially as it pertains to informed consent and the minimization of risk, and participant representatives should be directly involved in IRB review and should be members of the programmatic leaderships of accreditation review groups, site visit teams, monitoring boards, and oversight and advisory groups in research institutions. Standards should also reflect stronger participant involvement beyond securing signatures on informed-consent documents.

Recommendation 9: Use Modified NCQA Standards to Initiate Pilot Programs

Pilot accreditation programs should start from the accreditation standards and processes proposed by NCQA for VA facilities, as adapted for use in other organizational contexts. In expanding the draft NCQA accreditation standards for use beyond VA facilities, the standards should be strengthened in six specific ways as pilot testing commences.

The PRIM&R standards were prepared for a broad set of potential applicant organizations, which would include but not be restricted to academic health centers. The NCQA standards were explicitly prepared for accreditation of VA medical facilities. In this instance, the applicant pool is defined, and, in fact, pilot tests that will use those standards are being planned as this report goes to press.

As noted throughout this discussion of report recommendations, the committee regards the NCQA standards as an excellent starting point for accreditation of VA facilities. The committee recommends, however, that the NCQA standards be strengthened in six areas, discussed in more detail in Chapter 3, to specify (1) how investigators will be reviewed beyond the review of the protocols that they submit for IRB approval; (2) whether and how research sponsors will be assessed in the accreditation process; (3) how participants will be involved in setting standards and accrediting HRPPPs; (4) how oversight mecha-

¹⁰ By “participants,” the committee refers to those whose background and expertise are credible to a lay constituency external to the research institution and who are knowledgeable about the research process and research protections. The term is further defined in Chapter 1.

nisms can ensure participants' safety in ongoing research; (5) the steps that research institutions and their leadership can take to cultivate a culture that puts the safety and interests of research participants foremost; and (6) mechanisms by which research institutions and, where applicable, research sponsors can be held accountable for ensuring sufficient funding, structural support, and professional rewards for HRPPPs.

The NCQA standards, if improved as recommended, could also be used—by NCQA, AAHRPP, or other accreditation organizations—as the basis for the development of accreditation standards for non-VA research organizations.

Recommendation 10: Begin Collecting Data and Assessing Impacts of Accreditation Now

DHHS should commission studies to gather baseline data on the current system of protections for human participants in the research that it oversees and to assess whether the system is improving over time.

Baseline data are needed on the following:

- a taxonomy of research institutions: the number of institutions conducting research with human participants and the number of studies of different types (e.g., clinical trials, surveys, student projects, and behavioral studies) approved by their HRPPPs;
- a taxonomy of IRBs: the number of IRBs and what fraction of them are primarily devoted to studies of particular types;
- a taxonomy of studies with humans: the number and distribution of investigations with humans under way by type of study, for example, clinical trials of various stages, observational studies, cross-sectional and longitudinal surveys, and social science experiments;
- the number of people involved in research and, among them, how many are involved in research with more than minimal risk;
- the fraction of studies with more than minimal risk that have formal safety monitoring boards and how (and how well) those boards operate;
- the type and number of inquiries, investigations, and sanctions by FDA and the Office for Human Research Protections; and
- the type and number of serious or unanticipated adverse events attributable to research.

DHHS should also commission studies of how the databases for existing clinical trials and other research resources could be used to assess how well the system of research protections is operating and, specifically, whether accreditation is having measurable impacts (e.g., by comparing accredited and nonaccredited institutions or by comparing institutions before and after accreditation).

Other studies are needed to bolster the nascent literature on how well research participants understand the studies that they join, which risks matter most

to them, and what forms of informed consent are most effective. Several new initiatives to enhance clinical research in particular are under way, and the National Institutes of Health has initiated new programs to improve research monitoring. DHHS should evaluate these efforts not only for their primary purpose of improving clinical research but also for how they can improve HRPPPs.

Recommendation 11: Initiate Federal Studies Evaluating Accreditation

The U.S. Congress should request an evaluation of accreditation pilot programs from the General Accounting Office. The Secretary of Health and Human Services should consider requesting a parallel evaluation from the Office of the Inspector General of DHHS.

An evaluation process that is independent of AAHRPP, NCQA, and other accreditation bodies can help policy makers decide on the value of accreditation as an improvement strategy several years hence. Without such an evaluation, Congress and the executive branch will be positioned little better than they are today to make prudent choices about how to improve HRPPPs in 5 years. Research pursued under Recommendation 10 can provide some baseline information, but it cannot substitute for a thorough evaluation of the accreditation pilot projects themselves. Furthermore, the evaluation efforts would benefit in several respects if they were initiated soon, while the pilot projects are getting under way. Evaluators could observe which organizations seek accreditation and which ones do not. They could also conduct interviews with organization officials who are making a particular choice to find out why and what they perceive the benefits or problems of HRPPP accreditation programs to be. If multiple accreditation bodies emerge, the evaluation should compare their effectiveness.

The HRPPP accreditation process should be evaluated not only according to whether it has improved protections for human research participants but also according to whether resources devoted to accreditation could be spent to equal or better effect on other ways to improve HRPPP oversight such as education, research monitoring, and improved feedback mechanisms. Evaluation should take into account both the costs of establishing a national accreditation system and the costs to applicant organizations. The costs to applicant organizations will include direct costs for the accreditation process and also costs for the preparation for and following up on the accreditation process.

CONCLUDING REMARKS

In summary, the committee has addressed through its recommendations what it believes are the fundamental components necessary to initiate and effectively utilize an accreditation process and a set of accreditation standards to enhance participant protection in human research. Box 1 presents the committee's

recommendations according to the three phases intrinsic to the implementation of an accreditation program: development of the process, development of standards, and evaluating the program.

First, to develop the accreditation process, accreditation of HRPPPs should be pursued through pilot programs as one method to enhance the overall protection of participants taking part in research. This effort should be led by nongovernmental accreditation bodies with both the responsibility and the authority to craft and implement accreditation standards. Maintenance of these tasks within one or a few independent entities allows data collection and the experience gained through the process of accreditation to be tethered tightly to the timely evolution of standards. Further, any accreditation standards must encompass an assessment of participant involvement in local research oversight, greater specificity about the responsibilities of research sponsors, and integration of research monitoring, professional education and quality improvement into the oversight system.

Second, with respect to the development of accreditation standards, the committee believes that the NCQA draft standards should be adopted as a starting point. They will, however, require modification to include the components in Recommendation 9 and to accommodate disparate research environments and disciplines. This recommendation stems from the NCQA standard's explicit underpinning in federal regulations, their reliance upon rigorous quality improvement programs, and the resulting potential to move from a system overly focused on administrative compliance to one that emphasizes flexibility in achieving protection of participants in research.

Finally, efforts to evaluate the ability of accreditation programs to improve HRPPP function (i.e., ensure participant protection) should begin now. The committee suggests two complementary strategies: 1) data collection to assess systemic improvement over time; and 2) independent, comprehensive analysis of the effectiveness and relative cost of accreditation programs in achieving desired outcomes.

These recommendations are intended to guide the federal government and research entities in their immediate efforts to ensure that high-quality, innovative research never sacrifices the rights and safety of those individuals who voluntarily assume the risks inherent in research with humans.

BOX 1 Summary of Committee's Recommendations According to the Three Implementation Phases of an Accreditation Process**Development of an Accreditation Program:**

Pursue Accreditation Through Pilot Testing as One Approach

(Recommendation 1)

Establish a Nongovernmental Accreditation Organization(s)

(Recommendation 2)

Accommodate Distinct Research Methods and Models Within Accreditation Programs

(Recommendation 5)

Directly Involve Research Participants in Accreditation Programs & HRPPPs

(Recommendation 8)

Development of Standards:

Articulate Sound Goals Within Accreditation Standards

(Recommendation 3)

Establish Flexible, Ethics-Based, and Meaningful Standards

(Recommendation 4)

Base Standards on Existing Regulations

(Recommendation 6)

Incorporate Continuous Quality Improvement Mechanisms into Standards

(Recommendation 7)

Use Modified NCQA Standards to Initiate Pilot Programs

(Recommendation 9)

Development of an Evaluation Process:

Begin Collecting Data and Assessing Impacts of Accreditation Now

(Recommendation 10)

Initiate Federal Studies Evaluating Accreditation

(Recommendation 11)