

APPENDIX B

PRIM&R Accreditation Standards

© Copyright 2001 by Public Responsibility in Medicine and Research (PRIM&R). All rights reserved. These standards or parts thereof, cannot be used or reproduced in any manner without the written permission of PRIM&R. Contact PRIM&R, 132 Boylston, St., 4th Floor, Boston, MA 02116, 617-423-4112 or email rachlinj@aol.com.

INTRODUCTION

The research community, Congress, and the public have all voiced concerns regarding the adequacy of the system for the protection of human research participants. In response to these concerns, and to suspensions of research at a few institutions around the country, in May 1999 Public Responsibility in Medicine and Research (PRIM&R) began the development of a proposed accreditation program. The accreditation program would be voluntary and educationally-driven, directed toward improving human subject protection programs and thereby promoting the strongest possible system of protections for individuals studied in research.

The planned accreditation program has two phases: The first phase has been the development and planned promulgation of objective, outcome oriented performance standards, which can then serve as the measurement criteria for the new private, voluntary accreditation program described above. Beginning in the fall of 1999, PRIM&R convened a multi-disciplinary group of individuals, all of whom have been leaders in their respective fields, to write these draft Standards. Four writing group “retreats” were held, and the balance of the work was conducted via telephone and email.

Once these standards have been reviewed and accepted, they will be suitable for both self-assessment and formal peer review during the accreditation process. With respect to their self-assessment function, it is expected that the

standards will serve as a guidepost to aid organizations and other entities in building and/or strengthening their programs for the protection of protections for individuals studied in research.

The on-site review portion of the accreditation program is the second phase, and, as mentioned above, be voluntary, educational, and constructive.

Standards are prerequisite to the successful operation of an accreditation system, as they provide a means by which expectations can be stated, and by which performance in accordance with those expectations can be measured.

When evaluating the applicability of these standards to a given research program, the responsible institutional individual(s) should take into account the types of research with which that human research protection program is involved. For example, in light of the continuing increase of multicenter and cooperative studies, organizations participating in such trials must first assess the manner in which the various components of their Human Research Protection Program interact in order to provide appropriate protective mechanisms.

GOALS

The goal of voluntary accreditation is to improve the systems that protect the rights and safeguard the welfare of individuals who participate in research. Secondary goals may include:

- To communicate to the scientific community and to the public a strong declaration of a research organization's commitment to the protection of human research participants;
- To help organizations understand the need to commit adequate resources to maintain quality human research protection programs;
- To enhance an organization's ability to attract students to graduate research training programs; and
- To promote a higher quality of research, which will in turn result in better scientific outcomes and, ultimately, better healthcare.

PRINCIPLES UNDERLYING THE PROTECTION OF HUMANS STUDIED IN RESEARCH

In the United States the conduct of research involving humans is a conditional privilege requiring that research is conducted in keeping with well-established ethical principles, applicable federal, state, and local laws, and/or relevant policies and procedures.

The Belmont Report—Ethical Principles and Guidelines for the Protection of Human Subjects of Research (1979) provides the philosophical basis for current laws governing human subjects research. This Report identifies three fundamental ethical principles that are relevant to all research involving human

subjects: (1) Respect for Persons, (2) Beneficence, and (3) Justice. Application of these principles in the conduct of human research requires: (1) that the process of informed consent be prerequisite to an individual's participation; (2) that additional protections be employed for persons who cannot provide this consent; (3) that risks and benefits be responsibly and ethically assessed; (4) that research populations have been selected equitably; and (5) that equity exists for all individuals in consideration of the burdens and benefits of the research. Each of these principles carries equal moral force, and difficult ethical dilemmas may arise when they conflict.

Careful and thoughtful application of the principles of *The Belmont Report* cannot be exclusively relied upon to resolve particular ethical problems without conflict. The principles, however, do provide an analytical framework that will help guide the resolution of most ethical problems arising during the development and review of research, and that will increase the likelihood that individuals who agree to be studied in research will be treated in an ethical manner.

These voluntary accreditation standards incorporate the ethical principles of *The Belmont Report*. Therefore, seeking accreditation is an organization's public declaration that it endorses and implements the Belmont principles.

GLOSSARY

Accreditation An assessment process in which an agency uses experts in a particular field of interest or discipline to define standards of acceptable and applicable operation/performance for an organization/system and to measure compliance with them.

Data and Safety Monitoring Board (DSMB) A group of experts, independent of the research project, who review the safety data and critical efficacy endpoints of a research protocol at specified intervals and recommend whether to continue, modify, or terminate that research. It should be noted that DSMBs are usually convened in phase three and in large multicenter studies, and not routinely in phase I and II trials. In addition, it should be noted that a DSMB should not be confused with a data and safety monitoring plan, which is required for all NIH clinical trials.

Human Research Protection Program (HRPP) A system that includes all components critical to protecting individuals studied in research and that is managed in accordance with these standards and with applicable federal, state and local laws and regulations. In general, the HRPP has a central authority, Institutional Review Board(s) (IRB), IRB staff, and researchers and research personnel. Some components of the HRPP may be external to the organization seeking accreditation, but the essential components of an HRPP should be identifiable in all cases.

Institutional/Organizational Official An individual within the organization who has the responsibility for and authority over the Human Research Protection Program (HRPP).

Institutional Review Boards (IRBs) Committees or boards that review research to ensure the protection of human subjects. The term includes, but is not limited to Institutional Review Boards (per the Common Rule, 45 CFR 46), Central Review Boards, Independent Review Boards, and Cooperative Research Boards.

Investigator Any individual who has responsibility for the design, conduct, management or analysis of research.

Organization The entity with an HRPP. Organizations include but are not limited to corporations, private research entities, hospitals, universities, colleges, institutions and governmental agencies. The functional arrangement of the HRPP may vary depending upon the type of organization. There are circumstances when the sponsor of the research (e.g., a pharmaceutical firm) may be the logical organization responsible for the HRPP.

Research A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge, or, any experiment that involves an FDA-regulated test article.

Research Participant/Subject/Individual Studied in Research An individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. The term “subject” is traditionally used in the literature and in federal regulations to describe these individuals. In these Standards, the term “subject” will be used when the individual has not had an opportunity to consent to the research, “participant” or “research participant” will be used when the individual has consented to be part of the research, and “individual studied in research” will be used in a general sense when either may be the case.

Sponsor Any entity that provides funds or other resources to support the research. This entity could be a federal agency, corporation, foundation, institution or an individual.

PROPOSED STANDARDS

Section 1—Organizational Responsibilities

1.1 Protection of individuals studied in research must be a core value within the organization.

COMMENTARY on Standard 1.1: Officials at the highest level of the governing body of an organization shall demonstrate to the organization the importance and value of the protection of the individuals studied in

research by the development and support of a system of protections. This principle should become a basic tenet in the organization.

1.2 The organization must uphold ethical principles underlying the protection of individuals studied in research.

COMMENTARY on Standard 1.2: *The Belmont Report—Ethical Principles and Guidelines for the Protection of Human Subjects of Research (1979)* provides the philosophical basis for federal regulatory requirements. It should be noted that the Common Rule in many ways “operationalizes” the principles of the Belmont Report.

1.3 The organization must assure compliance with applicable legal requirements, including state and local laws.

COMMENTARY on Standard 1.3: Organizations must comply with applicable federal regulations including the Common Rule, 45 CFR 46 (DHHS regulations), and 21 CFR 50 and 56 (FDA regulations) in all research conducted within the organization, regardless of the type of study, the source of funding, or the locale.

1.4 The organization must place the responsibility for the HRPP in an institutional official with sufficient standing and authority to ensure implementation and maintenance of the program.

COMMENTARY on Standard 1.4: An organization demonstrates that the protection of individuals studied in research is a priority by investing overall responsibility in an institutional official with demonstrated authority in the organization, with access to adequate resources to support the HRPP, and without conflicting responsibilities in other aspects of the organization’s activities.

1.5 Individuals responsible for the HRPP must identify and minimize conflicts of interest, and/or competing interests, which may compromise the goals of the HRPP.

COMMENTARY on Standard 1.5: Institutional officials responsible for the HRPP should have clearly defined and institutionally supported responsibilities and authority in order to maximize their ability to achieve the goals stated in 1.5 without interference.

1.6 Any delegation of authority for the HRPP by the responsible institutional official (see 1.4 above) must be assigned to qualified individuals and documented in writing

COMMENTARY on Standard 1.6: Any delegation of authority by the responsible institutional official to others requires serious and thoughtful attention. The institutional official must only delegate authority to qualified individuals and in situations that enhance the HRPP. Written documentation of delegation of authority is required to promote clear communication among the organization's constituencies and to establish an organizational record.

1.7 The governance of the organization must assure the independence and credibility of the IRB(s).

COMMENTARY on Standard 1.7: IRBs are one of several critical elements in an organization's HRPP. A successful HRPP requires that IRB members and chair(s) possess knowledge about ethical, regulatory, and institutional requirements. The IRB must be supported by the organization, which would necessarily exclude inappropriate influence by powerful officials, researchers, and potential funding sources. The IRB should have a clear mechanism for managing any influence that blocks or otherwise interferes with its functions.

1.8 The organization must have conflict of interest policies and must enforce those policies to minimize real, potential or perceived conflicts from interfering with the protection of individuals studied in research.

COMMENTARY on Standard 1.8: Organizations must have a mechanism to address real or perceived conflicts of interest that could interfere with the protection of individuals studied in research. Organizational policies need to define conflicts of interest, provide mechanisms for disclosure of conflicts, establish a process for evaluating whether a conflict of interest may interfere with protection of the individuals studied in research, and institute actions to manage conflicts of interest determined to have the potential to interfere with that protection.

Organizations need to disseminate these policies to individuals responsible for the conduct of research involving humans and they need to determine what role the IRB should play in monitoring the application of these policies. The existence and enforcement of the organization's conflict of interest policies further demonstrates its commitment to place the protection of individuals involved in research above financial, professional, and other concerns.

1.9 The organization must have and follow clearly written policies and procedures governing all human research. The policies and procedures must specify applicability. The policies and procedures must be re-

viewed periodically and updated as necessary. The policies and procedures must be disseminated appropriately within the organization to all staff involved with protection of individuals studied in research.

COMMENTARY on Standard 1.9: Mechanisms should be established regarding when new policies and procedures are needed, and how existing policies and procedures should be reviewed and revised. Appropriate intervals for this review and revision must be specified. New research personnel must also be provided with this information and all staff must be kept apprised of any changes.

1.10 The organization must assure that all personnel conducting or supporting human research or involved in the HRPP demonstrate and maintain sufficient knowledge of the protection of individuals studied in research appropriate to their role.

COMMENTARY on Standard 1.10: The organization must assure the provision of acceptable educational activities for principal investigators, other research personnel, IRB chairs, IRB members, IRB staff, appropriate institutional officials, and others in the organization as appropriate.

The organization needs to assure that: (1) Educational programs for professional development in the area of protection of individuals studied in research are appropriate to the investigator's role in the research; (2) Mechanisms exist to provide additional education as needed; (3) Procedures exist for demonstrating the effectiveness of these activities; and (4) Individuals receive ongoing education at intervals determined appropriate in consideration of their research endeavors. Appropriate procedures for these individuals may involve attendance at courses, participation in seminars, and/or completion of computer-based training. Supplemental techniques such as performance feedback, monitoring, supervision, or mentoring are also acceptable. (Please note that the NIH Required Policy for IRB Review of Human Subjects Protocols in Grant Applications [Notice: OD-00-031: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-031.html>] describes the minimum requirement for NIH grantees.)

1.11 The organization must establish the number of IRBs appropriate for the volume and types of human research that the IRBs review.

COMMENTARY on Standard 1.11: The trend in many research organizations is towards establishing more than one IRB. In large organizations conducting many research studies, it may be difficult for one IRB to provide an adequate level of review of the protocols, particularly if they are complex or originate from different disciplines (e.g., biomedical versus social and behavioral sciences). In determining the appropriate num-

ber of required IRBs, the organization should take into account the volume, complexity and types of research it reviews. Organizations with multiple IRBs require additional thought and consideration to ensure that all human research subject protection issues are taken into account in a uniform manner.

1.12 The organization must provide sufficient and appropriate staff, space, equipment, finances, technology, and other resources for the HRPP.

COMMENTARY on Standard 1.12: The organization must determine what constitutes adequate resources. Input from the IRB(s) chairs, members and staff is a critical ingredient in this determination (see further discussion of this issue in Section 2 of these Standards).

In addition to staffing needs, IRB administrative offices require enough space to maintain secure storage of records, to enable private communication, to provide current computer technology and support services, and to provide adequate space for meeting with investigators and IRB members.

1.13 The organization must recruit and retain IRB chair(s), members and staff who have both experience and knowledge appropriate to their respective roles on the IRB team, and who represent all fields of science applicable to their organization.

COMMENTARY on Standard 1.13: The organization must both recruit and maintain a quality IRB by having high caliber chairs, members and staff. The organization's policies must foster the retention of individuals knowledgeable and sensitive to the principles of the organization's human research protection program sufficient to assure continuity of high levels of performance. Appropriate and meaningful recognition, including but not limited to adjustments to compensation or organizational responsibilities, are central to the retention of knowledgeable and committed individuals.

1.14 The organization must have procedures for timely identification and dissemination of new information that may affect the HRPP, including laws, policies and procedures, as well as emerging ethical and scientific issues.

1.15 The organization must have and follow written policies and procedures for addressing allegations and findings of non-compliance with the requirements of the HRPP, and management of research harms. The policies and procedures must be reviewed periodically and updated as necessary.

COMMENTARY on Standard 1.15: There must be a clear and public policy concerning identification and reporting of research harms and for the compassionate and efficient management of such events. These procedures must include a fair and reasonable process for all parties involved. Any accused individual should have the right to appear in person to defend himself/herself. The procedures should also include a mechanism that determines those violations serious enough to inform regulatory agencies and funding sources. The organization must have and follow a written policy that protects from retaliation those who in good faith report allegations of non-compliance. (Please note that the Office for Research Integrity's Notice of Proposed Rulemaking can be found at 65 Fed. Reg. 70830 (2000) and may be accessed by clicking on News on the ORI home page, <http://ori.hhs.gov>.)

- 1.16 The organization must utilize a system for regularly assessing outcomes of and improving the performance of the HRPP. The system developed to examine results or outcomes of the HRPP's activities must also include the identification of problems, implementation of interventions, and measurement or evaluation of the effect of interventions.**

COMMENTARY on Standard 1.16: Performance evaluation and assessment of programmatic outcomes in other disciplines are well known and have become generally accepted as organizational best practice. Until now, they have neither been widely applied nor implemented by HRPPs.

Two reports, one by the Advisory Committee on Human Radiation Experiments (ACHRE) and the other by the DHHS Office of the Inspector General (OIG), concluded that an adequate system of human research protection "would require that the system be subjected to regular, periodic evaluations that are based on an examination of outcomes and performance and that include the perspective and experiences of research [subjects] as well as the research community." The OIG's Report recommended that IRBs be given more flexibility by the FDA and OPRR (now OHRP), with concomitantly a greater accountability for results by taking "concrete actions ... to assess and verify the actual results of their efforts in protecting human subjects." The Report described a small number of creative efforts currently undertaken by some IRBs.

Persistent problems in human research protection and the changing nature of clinical research, public expectation, and organizational best practices have thus necessitated that the organization, IRBs, and investigators regularly evaluate their performance and assess outcomes. An organization seeking accreditation must propose its own methods/procedures for evaluating the performance of all aspects of the HRPP.

As performance evaluation of HRPPs, IRBs, and investigators becomes more routine around the United States, PRIM&R will publicize innovative programs that effectively address these organizational best practices.

- 1.17 The organization must provide evidence of programs, policies or procedures for ongoing communication with representatives of the geographic and/or subject communities studied in research. These communication vehicles should provide for the ongoing discussion of commonalities and/or differences in research portfolios and agendas, goals of interest to either or both parties, and for the sharing of each other's values and concerns.**

COMMENTARY on Standard 1.17: The organization must be aware of the customs and values in the respective research participant populations it serves, including legal requirements as appropriate. This awareness is especially important when research is being conducted or contemplated that involves individuals from that community (geographic, demographic and cultural). For example, organizations conducting research involving Native Americans must understand and appreciate tribal concerns that influence the conduct of such research. Organizations whose IRBs are widely separated geographically from their investigators should detail the manner in which such potentially diverse communities will be engaged and involved.

Section 2—Institutional Review Boards (IRBs)

GENERAL COMMENTARY on Section 2: In fulfilling their mandate to protect the rights and welfare of individuals studied in research, IRBs are intended to be impartial reviewers of research studies. Their responsibilities include the review, approval, or disapproval of protocols, and the recommendation of protocol and/or consent modifications, all of which are designed to minimize the risks to the individuals to be recruited into the study.

- 2.1 The IRB(s) must comply with all applicable laws, regulations and organizational policies and procedures.**

COMMENTARY on Standard 2.1: See Standard 1.2

- 2.2 The IRB(s) must identify to the appropriate institutional officials the resources it requires.**

COMMENTARY on Standard 2.2: The IRB staff, chair(s), and members constitute the relevant source of information concerning the needs for this component of the HRPP.

2.3 Each IRB should be constituted to promote respect for its advice and counsel in safeguarding the rights and welfare of the individuals studied in research.

COMMENTARY on Standard 2.3: The size of the organization and the extent of its research will determine the number of IRBs required. The type(s) of research reviewed by the IRB(s) (*e.g.*, behavioral research, clinical trials, epidemiological research, and research involving vulnerable populations or minority groups) will influence membership requirements. Appropriate expertise of IRB members, chair(s) and staff is required to ensure an adequate review of protocols from varied disciplines. IRBs also need to recognize when consultant expertise is required.

2.4 The IRB chair(s), members and staff must possess sufficient respect within the organization and the leadership skills as a team sufficient to be an authority on the protection of individuals studied in research under the jurisdiction of the HRPP.

COMMENTARY on Standard 2.4: The position of IRB chair is of singular importance, and requires commitment, knowledge, and the necessary leadership skills to serve as an effective steward. The responsibility of the chair should be vested in a highly credible member of the organization, as s/he will then be better able to engender respect for the authority of the IRB.

Attributes which are a measure of an effective IRB team include: (1) the ability to conduct meetings in an efficient, expeditious and fair manner; (2) attentiveness to the details of applicable federal regulations and other legal and institutional requirements; (3) skillful facilitation of contextual interpretations and application of these requirements that will foster ethically and scientifically sound research involving human beings; (4) the ability to encourage dialogue in IRB meetings and within the organization; (5) respect for the contributions of all IRB members and staff, especially the contributions of the non-scientists and community representatives; (6) the confidence and courage to uphold IRB judgments, and (7) investment of adequate time, interest and commitment by the chair, IRB members, IRB staff, researchers and other interested individuals in the organization.

2.5 Knowledge, Skills and Abilities

The IRB administrator, staff, chair(s) and Board members must possess and maintain knowledge, skills and abilities appropriate to their role including:

General ethical principles and concepts underlying the conduct of research involving humans;

Applicable Federal, state, and local laws and regulations;

Applicable HRPP and IRB policies and procedures;

Role of the IRB(s) in the HRPP; and

These Accreditation Standards

COMMENTARY on Standard 2.5: Appropriate activities include education of new members, chair(s) and staff and continuing education for current staff, members, and chair(s) using performance feedback, mentoring and monitoring techniques. These activities should be designed to ensure that IRB chairs, staff and members know and apply the concepts and requirements in this Accreditation Standard.

Continuing education for IRB team is particularly important in light of the breadth and depth of their expected knowledge base. Organizations should support the team's attendance at and/or participation in local, regional and/or national meetings or programs on the protection of individuals studied in research.

Successful IRB administration requires a combination of a working knowledge of protection of those studied in research and skills in administration. Organizations should support appropriate training for IRB administration. This may include their attendance at and/or participation in meetings or programs on the protection of individuals studied in research, acquisition of topic oriented journals/books, and/or professional development such as certification through the ARENA Council for Certification of IRB Professionals (CCIP).

2.6 In the review of protocols, the IRB must recognize when additional expertise is needed and must obtain that expertise (e.g., education in, or consultation on scientific, ethical, community representation, or other issues).

COMMENTARY on Standard 2.6: Some protocols may present new or special considerations beyond the scientific and ethical expertise of the IRB. The IRB should have and follow policies regarding inviting individuals with competence in special areas to assist in the review of protocols that require expertise in addition to that available within the IRB. These individuals can submit comments in writing and they may attend IRB meetings in a non-voting capacity to present their findings. IRB procedures must specify in writing details regarding this process.

- 2.7 IRBs must demonstrate systematic review of research protocols in order to assure that issues, regulations, and other applicable organizational policies and procedures relevant to the protection of individuals studied in research are consistently addressed.**

COMMENTARY on Standard 2.7: IRBs must determine, at a minimum, that all of the following criteria are satisfied: (1) Research risks are reasonable in relation to anticipated benefits; (2) Risks are minimized; (3) The selection of those in the population to be studied is equitable (the IRB should be particularly cognizant of the special problems of research involving vulnerable populations); (4) Informed consent is sought from research participants or their authorized representatives unless waived by the IRB; (5) Monitoring of data is appropriate to ensure safety; (6) Adequate provisions are made to protect privacy and maintain the confidentiality of research data, and (7) When vulnerability to coercion or undue influence may exist, additional safeguards are included in the study to protect the rights and welfare of individuals participating in the research.

- 2.8 The IRB must ensure that consent documents are legible, understandable, well organized, and remain appropriate for the research population.**

COMMENTARY on Standard 2.8: Technical and legal language should be defined and stated in terminology that the research population can understand. Systematic feedback from coordinators, research participants and investigators should be one method for implementing the assessment of the adequacy of the consent documents.

- 2.9 The IRB must determine that the consent process is appropriate for the circumstances under which the research will be conducted.**

COMMENTARY on Standard 2.9: The entire process for obtaining informed consent must be considered in the IRB review including who, when, how and any special circumstances pertinent to the process. The Principal Investigator (PI) of the study is responsible for all aspects of the consent process regardless of any special circumstances.

- 2.10 The IRB must receive evidence that the investigator(s) is qualified through training, experience, and commitment of time and resources, to be responsible and appropriate for the planned research.**

COMMENTARY on Standard 2.10: The IRB should have policies that define acceptable evidence of the qualifications of the principal investigator and research team members as related to the specific protocol.

These policies should also include provisions indicating how students and trainees are covered when the curriculum or training requires that research be accomplished.

- 2.11 The IRB must have written policies and procedures pertaining to the following and which are appropriate and relevant to the types of research reviewed within the organization, including research involving special populations (children, persons who are decisionally impaired, the elderly, etc.) or certain types of research (e.g., social and behavioral research, drug washout studies, double-blinded placebo controlled studies, or research conducted in emergency circumstances).**

POLICIES REQUIRED OF ALL IRBs

(A) Initial IRB review of protocols

COMMENTARY on Standard 2.11 (A): IRB review of protocols must be complete and substantive. IRB members must receive sufficient information to make a determination of each review criterion.

(B) Substantive and meaningful continuing IRB review of protocols, including frequency of review and assuring that design and procedures continue to be appropriate and safe

COMMENTARY on Standard 2.11 (B): When conducting continuing review, all IRB members must receive sufficient information to allow the Board to pass judgment.

(C) Full review requirements (e.g., quorum requirements, asking IRB members who have conflicts of interest to recuse themselves, etc.)

(D) Requirements for the consent process, including the consent forms and their modifications

(E) Expedited review

(F) Exempt research

(G) If appropriate, procedures for the IRB's primary reviewer of the protocol

(H) Investigators' conflicts of interest

COMMENTARY on Standard 2.11 (H): In keeping with Standard 1.8, the IRB implements the organization's written conflicts of interest policies in regard to individuals studied in research. The IRB is responsible for determining whether any potential, real, or perceived conflicts of interest could affect the conduct of research under consideration or that could impact the safety of those individuals studied in research.

(I) Identification and reporting of adverse events (to the IRB and others as required)

- (J) Procedures/rules for the review of PI's response(s) to IRB stipulations and recommendations**
- (K) Noncompliance by researchers or research personnel with protocol requirements and/or with IRB policies/procedures**
- (L) Suspensions or terminations of approvals**
- (M) Collaborative agreements (national and international)**
- (N) Reporting IRB findings to investigators, appropriate institutional officials, and appropriate federal or other regulatory agencies**
- (O) Advertisements and other recruitment-related materials**
- (P) Remuneration to research participants**
- (Q) Investigator record keeping and retention requirements**
- (R) Vulnerable populations**
- (S) Waiver of informed consent, or, of documentation of consent**
- (T) Any other relevant areas**

POLICIES REQUIRED OF IRBs WITH SPECIAL INTERESTS

- (A) Determining the regulatory status of an investigational device concerning the significance of the risk of the device, if needed**
- (B) Emergency use of IND compounds or other investigational interventions**
- (C) Grant review for certification of approval of research**
- (D) Any other relevant areas**

2.12 The IRB protocol records/files must contain at least the below-listed information.

COMMENTARY on Standard 2.12: As the study file contains the details regarding the protocol and the review of that protocol, and as the file is subject to audit, it is necessary that the study file be complete, accessible and archived. The IRB protocol records/files must contain at least the following information:

- (A) A copy of the protocol, including approved consent documents and results of existing related information pertinent to the protocol**
- (B) Scientific evaluations reviewed by the IRB, if any**
- (C) Initial reviews**
- (D) Advertisements and other applicable recruitment materials**
- (E) Payments to be made to research participants (amount of payment, etc.)**
- (F) Continuing reviews and progress reports**
- (G) Adverse event reports with documentation of IRB review**
- (H) All correspondence (including electronic mail) with investigator(s), consultants, and others (institutional officials, sponsors, etc.) about the protocol.**

- (I) Statements of significant new findings provided to research participants
- (J) Reports of non-compliance, if applicable
- (K) Reports of deviations from approved protocols, if applicable
- (L) Protocol modifications/amendments
- (M) Suspensions or revocation of approval, if applicable
- (N) Minutes relative to the protocol review and actions
- (O) When applicable, the investigator's plan to communicate with representatives of the community from which individuals will be recruited in order to share the protocol and learn of community concerns, values and expectations

2.13 IRB minutes, record keeping, and retention requirements.

COMMENTARY on Standard 2.13: IRB minutes are fundamental parts of its record keeping activities. The minutes, together with other IRB documents, should enable a reader who was not present at the meeting to determine how and with what justification(s) the IRB arrived at its decisions. The IRB must also have policies and procedures for retention of minutes and records.

- (A) **The IRB meeting minutes must include at least the following information:**
 - (1) Approval of minutes from the previous meeting;
 - (2) Attendance at meetings;
 - (3) Actions taken;
 - (4) Votes (including total number of members present) for, against, and abstaining, as well as names of abstainers, and reason for abstention, if appropriate;
 - (5) Documentation indicating change or loss of quorum throughout meeting;
 - (6) Summary of the discussion of issues and their resolution (including, when appropriate, minority reports);
 - (7) Basis for requiring changes, deferring, or disapproving protocols;
 - (8) Special findings (i.e., criteria for varying or altering consent requirements or risk categories for children and other vulnerable populations);
 - (9) Discussion of the need for a DSMB or other monitoring procedure(s) when applicable;
 - (10) When applicable, determination of significant/non-significant devices (for studies under the auspices of FDA investigational device regulations); and

- (11) Requirements for frequency of continuing review, if more often than annually.**
- (B) The IRB files must include an IRB roster, members' qualifications, and organizational assurances including any relevant appendices, when appropriate. Documents should be archived for reference.**

Section 3—Investigators and Other Research Personnel

GENERAL COMMENTARY on Section 3: The roles and responsibilities of investigators are influenced by the nature of the environment in which they conduct research (e.g., academic center, private practice/community setting, etc.) and by the type of research in which they are engaged. However, in all circumstances, investigators are an essential element in the protection of individuals enrolled in their respective research studies. Therefore, these Standards should apply irrespective of the manner in which the HRPP is constituted. The presence of an intelligent, informed, conscientious, compassionate and responsible investigator is the best possible protection for all involved in the research process.

- 3.1 The investigator should understand and apply the underlying ethical principles as delineated in *The Belmont Report* when designing, or when evaluating already designed studies, and when conducting human research .**
- 3.2 Investigators must put the rights, welfare, and safety of each individual studied in their research ahead of their professional, academic, financial, personal, or other interests.**

COMMENTARY on Standard 3.2: The investigator's primary attention must be focused on the safety and welfare of the individuals who volunteer to participate and those included without their consent (e.g., use of preexisting data, etc.). Investigators must identify and avoid conflicts of interest that may interfere with the rights and welfare of research participants and the appropriate conduct of research.

- 3.3 Investigators must meet organizational requirements for conducting research with human subjects and comply with all applicable federal, state and local regulations and guidelines dealing with the protection of individuals studied in research.**

COMMENTARY on Standard 3.3: Investigators are responsible for the overall design, development, conduct and analysis of the investigation, whether the investigator personally developed the protocol or if others prepared the protocol (e.g., as in a multicenter investigation). Investigators must have a collegial relationship with the IRB. Although many IRBs may

have information manuals for investigators that cover the requirements, it is the investigator's responsibility to seek out and comply with those requirements even if the IRB does not overtly supply the supportive material.

3.4 Principal Investigators (PIs) must assure that all research involving human subjects is reviewed and approved by an IRB before study initiation and that it remains approved for the duration of the study.

COMMENTARY on Standard 3.4: The IRB should be consulted when questions arise regarding whether a given research activity constitutes human research. The IRB should be accorded the authority within the organization to determine what constitutes human research, as the IRB has specific expertise in making such decisions. The PI should be cognizant of the types of research that may be exempt from IRB review, or which can be processed by expedited review. This determination usually requires consultation with the IRB.

PIs must be familiar with the criteria for IRB review and approval indicated in Standard 2.7 and, at a minimum, be able to provide the IRB with this information as well as any continuing review information relevant to the research protocol.

Appropriate and continuing oversight of a research protocol by the PI includes orderly retention of research records, appropriate level of review, compilation, assessment and appropriate reporting of adverse events. The PI has the responsibility for the prompt reporting to the IRB and sponsor(s) and appropriate federal agencies of any injuries, adverse events, or other unanticipated problems involving risks to subjects and others.

3.5 Principal Investigators must delegate responsibility only to individuals who they determine are qualified through training and experience for their role in the research.

COMMENTARY on Standard 3.5: The qualification of the PI to conduct the proposed research must be submitted to the IRB to provide adequate guidance for review. There should be a documented training and experience for the PI and PIs must assure that all research personnel involved in the protocol are qualified through training and experience to perform their role in the research.

3.6 Principal Investigators must conduct research in which individuals are studied only when supported by adequate resources including staffing, time allocated by the staff to the research, funding, space, record-keeping capability, and back-up for adverse events.

3.7 Principal Investigators should, when appropriate, communicate with potentially concerned sectors of the community or of the specific population to be recruited in their investigation.

COMMENTARY on Standard 3.7: Discussions about research with prospective research participants and/or the community in which the research will be conducted is a regulatory requirement in some circumstances (e.g. FDA and other DHHS Requirements for research conducted in emergency circumstances, etc.). However, investigators should be aware that community involvement in the design and conduct of some research studies may benefit research participants, researchers, and the community. For example, the likelihood of improving informed consent may be enhanced if the community has the opportunity to be included more directly in the decisions made by the organization. Addressing the concerns and values of the community early in the process can help engender a positive attitude in the community for the research organization and/or for the researcher.

3.8 When appropriate, the investigator should explain to, and discuss with, the potential research participants their responsibilities to enhance their protection and to support the integrity of the investigation in ways which include:

- (A) Ensuring that research participants understand the risks and benefits of the study, and alternatives thereto;**
- (B) Ensuring that research participants know who to contact when they feel they have been dealt with inappropriately;**
- (C) Ensuring that research participants know who to contact on the research team if they believe that an adverse event has occurred; and**
- (D) Recognizing that the safety of research participants and the integrity of the research study are enhanced by ongoing and candid communications between research participant and researcher(s).**

PUBLICATIONS CITED IN ACCREDITATION STANDARDS

- U.S. Department of Health and Human Services, Office of Inspector General, "Institutional Review Boards: A Time for Reform," OEI-01-97-00193 (June 1998). Copies are available through the Boston office: (617) 565-1050, or the OIG Web site: <http://www.dhhs.gov/progorg/oei>
- U.S. Department of Health and Human Services, Office of the Secretary, The National Commission for the Protection of Human Research Subjects, *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (April 18, 1979). Copies are available at the following Web site: <http://ohrp.ospphs.dhhs.gov/humansubjects/guidance/belmont.htm>

