Appendix H: IRB Policies and Procedures

Abt Associates Inc. Human Subjects Policies & Procedures Manual

Abt Institutional Review Board

May 2009

Marianne Beauregard
IRB Chair

Abt Associates Inc.
55 Wheeler Street
Cambridge, MA 02138

Contents

Acknowledgements

This manual was originally developed by the Director of Human Subjects Protection at Abt Associates, Malcolm Russell-Einhorn, with assistance from Marianne Beauregard, Chair of the Abt IRB. (It was subsequently updated by Marianne Beauregard.)The authors gratefully acknowledge the guidance and modeling provided by materials and information offered on the Web sites of the Office for the Protection of Research Subjects at the University of California, Los Angeles, and the Office of Regulatory Affairs within the Office of the Dean of Research and Graduate Education at the Georgetown University Medical Center. The design and contents of this manual and the forms used by the Abt IRB were significantly influenced by the approach to human subjects regulation taken by these two institutions and the policy and operational materials used by them.

I. Introduction

This Policies and Procedures Manual is designed to document Abt Associates' commitment and adherence to research practices that are carried out in conformity with the basic ethical principles and Federal regulatory requirements governing research involving human subjects.

A. Scope

The practices described in this Policies and Procedures Manual are to be followed by the Abt Institutional Review Board (IRB), Principal Investigators, and Project Directors on all studies or projects that involve human subjects. This is consistent with Abt Associates' corporate policy on human subjects' protection. See Contract Management (CM) Policy No. CM.02-0309, Institutional Review Board Policy.

1. Definition of Human Subjects and Research

Federal regulations (45 CFR 46.102(d)) define **research** as "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge." Federal regulations (45 CFR 46.102(f)) define **human subject** as "a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual or (2) identifiable private information." **Private information** includes information that an individual can reasonably expect will not be made public, and information about behavior that an individual can reasonably expect will not be observed or recorded. **Identifiable** means that the identity of the individual is or may readily be ascertained by the investigator or associated with the information.

2. Purview of Abt Associates Institutional Review Board

Review of research by the Abt Associates IRB is limited to research studies or projects that are conducted by Abt Associates employees and/or subcontractors and agents. All research involving minimal risk to human subjects, and most research involving greater than minimal risk to human subjects that is funded by the government sector will be reviewed by the Abt IRB. Under certain circumstances, greater than minimal risk research may be referred, in the Board's discretion, to an outside IRB. Work involving greater than minimal risk to human subjects that is funded by the private sector will generally be referred to and reviewed by a commercial IRB. Abt Associates' Federalwide Assurance (FWA) with the Office for Human Research Protections (OHRP) of the U.S. Department of Health and Human Services (DHHS) provides that the company will assure compliance with the Terms of Assurance only for Federally-supported research. Most research reviewed by the Abt IRB involves social and behavioral research, but the Abt IRB will also review clinical research, epidemiological research, and repository research.

I. Ethical and Regulatory Basis for Abt Associates Human Subjects Protection Practices

The ethical foundation on which Abt Associates' practices rests includes the ten principles of the Nuremberg Code (enshrining the necessity of informed consent by human subjects), the Declaration of Helsinki (which calls for prior approval and ongoing monitoring of research by independent ethical review committees), and the Belmont Report (establishing the systematic principles for human subjects protection of respect for persons, beneficence, and justice).

Applicable Federal regulations require specific protections for human subjects.

Department of Health and Human Services (DHHS) Regulations. DHHS regulations at 45 CFR Part 46, Subpart A constitute the Federal Policy (Common Rule) for the protection of human subjects. The DHHS regulations also include additional protections for pregnant women, human fetuses and neonates (Subpart B), prisoners (Subpart C), and children (Subpart D). All human subject research at Abt Associates must comply with all four Subparts of the DHHS regulations. These regulations are enforced by OHRP.

II. Shared Responsibility for Protecting Human Subjects in Abt Associates Research

The ethical conduct of research is a shared responsibility. It requires cooperation, collaboration, and trust among Abt Associates management, investigators, project directors, and their research staff, the subjects who enroll in research, and the Abt Associates IRB. A clear delineation of the responsibilities of each of these parties can help protect the participants who volunteer for research.

1. **Abt Associates Management.** The responsibilities of Abt Associates derives from its research mission as a leading policy and research consulting firm committed to the highest intellectual and ethical standards. Abt's FWA requires the company to comply with regulations governing the protection of human subjects in all Federally-funded research. As part of this Assurance, the company will commit itself to policies and procedures for conducting human subject research in a responsible and ethical fashion, including how research will be reviewed by the Abt Associates IRB, the reporting of unanticipated problems to the IRB and appropriate regulatory bodies, and other issues.

   Abt Associate's Chief Administrative Officer (CAO) serves as the Institutional Signatory Official for Abt's Assurance and is ultimately responsible for overseeing the protection of human subjects within the institution. The Institutional Signatory Official must also maintain open channels of communication between the IRB, research investigators and staff, and the company, and provide the IRB with sufficient resources to support its substantial review, record keeping, and training responsibilities.

2. **The Institutional Review Board (IRB).** An IRB is an appropriately constituted group that has been formally designated to review and monitor research involving human subjects. In accordance with the Common Rule, the IRB has responsibility for approving, requiring modification to (to secure approval), or disapproving research. The Abt IRB also has the authority to suspend or terminate research for continued noncompliance with the Common Rule or its own findings, determinations, and initial and continuing review procedures.

3. **The Project Director/Principal Investigator (PD/PI).** An Abt Project Director bears ultimate responsibility for protecting every research subject involved in Abt research. This responsibility starts with protocol design, which must minimize risks to subjects while maximizing research benefits. In addition, the Project Director and all members of the research team must comply with the findings, determinations, and requirements of the IRB. The Project Director must also be responsible for the adequacy of both the informed consent document and the informed consent process, regardless of which members of the research team actually obtain and document consent. While these responsibilities may be delegated, or may run formally to a formally-designated Principal Investigator if that individual is an Abt Associates employee, the Project Director has ultimate authority for ensuring compliance with all applicable human subjects protection duties.

   In summary, Project Directors (PDs) at Abt Associates have the following responsibilities: (i) that all human subject research that they conduct under Abt Associates auspices has received prospective review and approval by the Abt IRB or an IRB designated by the company; (ii) that continuing review and approval of the research has been secured in a timely fashion; and (iii) that the research is conducted at all times in compliance with all applicable regulatory requirements and the determinations of the Abt or, where applicable, another IRB. No changes in approved research may be initiated without prior IRB approval, except where necessary to eliminate apparent immediate hazards to subjects; and no research may be continued beyond the IRB-designated approval period. PDs must notify the IRB promptly of (i) any unanticipated problems or serious adverse events involving risks to subjects or others, and (ii) any serious or continuing noncompliance with applicable regulatory requirements or determinations of the IRB of which they become aware.

4. **Other Members of the Research Team.** Every member of the research team is responsible for protecting human subjects. PDs/PIs, research assistants, consultants, and all other research staff have a strict obligation to comply with all IRB determinations and procedures, adhere rigorously to all protocol requirements, inform investigators of all adverse subject reactions or unanticipated problems, oversee the adequacy of the informed consent process, and take whatever measures are necessary to protect the safety and welfare of subjects. Researchers at every level are responsible for notifying the IRB

promptly of any serious or continuing noncompliance with applicable regulatory requirements or determinations of the designated IRB of which they become aware, whether or not they themselves are involved in the research.

5. **Research Subjects. Subjects have responsibilities as well.** They can be expected to make every effort to comprehend the information researchers present to them so that they can make an informed decision about their participation in good faith. They should also be willing to comply with protocol requirements (unless they decide to discontinue participation) and inform the investigators of unanticipated problems.

III. Managing Conflicts of Interest

Conflict of interest can be defined in the broadest terms as any situation in which financial or personal obligations may compromise or present the appearance of compromising an individual's or group's professional judgment in conducting, reviewing, or reporting research.

Research personnel, IRB members, or research sponsors may have conflicts of interest in a particular research study. Conflicts of interest may arise from industry-academic partnerships, from financial or other incentives that certain companies may offer researchers for conducting certain studies or enrolling subjects, or due to particular role relationships within particular institutions, as in the case of IRB membership.

Abt Associates' Conflict of Interest (COI) Policy (Abt Policy BE.01-1007) and associated Conflict of Interest Review Procedures govern the management of potential conflict of interest issues within or affecting the company, and extends generally to conflicts that may arise in the context of safeguarding human subjects protection. For purposes of this Policies and Procedures Manual, the company adopts the COI Policy's' (and in turn, the U.S. Government's) definition of a conflict as any situation where, as a result of other activities or relationships with other persons (or entities): (1) a person is unable to render impartial assistance or advice to the Government, (2) the person's objectivity in performing the contract work is or might be otherwise impaired, or (3) the person has an unfair competitive advantage (now or in the future) as a result of the relationship.

In addition to complying with any relevant procedures contained in the COI Review Procedure, Project Directors, Principal Investigators, or any Abt research staff who may suspect the existence of the conflict of interest that would compromise or create appearance problems concerning the protection of human subjects must additionally notify the IRB Chairperson to determine if a conflict exists or potentially exists. This entails forwarding to the IRB Chairperson a copy of Abt's Conflict of Interest Review Checklist Form (contained in the COI Review Procedure). If a possible conflict of interest is discerned, appropriate consultations will be held between the IRB Chairperson, the IRB Administrator, the cognizant Associate Division Manager (ADM), Division Vice President (DVP, the Group Vice President, and where necessary, the CAO and the Chief Financial Officer of the company. The objective of these consultations will be to determine how best to manage, reduce, or eliminate the conflicting interest(s).

Conflicts of interest pertaining to IRB members are specifically addressed in Section III.D of this Manual.

II. Institutional Review Board (IRB) Administration

IV. **IRB Roles and Authorities**

Federal regulations require that institutions engaging in human subject research funded by the Federal government develop processes for protecting human subjects. The regulations require that each institution conducting human subject research file a written "Assurance" of protection for human subjects and designate one or more Institutional Review Boards (IRBs) to review its human subject research.

1. Institutional Authorities

The filing of an Assurance and the registration of the Abt IRB is the responsibility of the CAO and the Chair of the IRB. Acting through the IRB Chair and the IRB Administrator, the CAO is ultimately responsible for administrative oversight and review of the institution's systemic protections for human subjects.

Abt has developed this Policies and Procedures Manual under which its IRB will operate in conformity with the terms of its FWA. These policies and procedures apply to all research involving human subjects in the Government Divisions, regardless of the source of funding.

2. Purpose of the IRB

The IRB's primary responsibility is to protect the rights and welfare of participants involved in human subject research. In doing so, the IRB monitors human subject research to determine that it is conducted ethically and in compliance with Federal regulations, the requirements of applicable law, Abt Associates' Assurance, and the company's policies and procedures. The designated IRB fulfills these responsibilities by conducting prospective and continuing review of human subject research, including review of the protocols, the informed consent process, procedures used to enroll subjects, as well as any adverse events or unanticipated problems reported to the IRB. The IRB will review proposals or grant applications upon request.

3. Scope of Authority of the IRB

All human subject research conducted at Abt Associates or by Abt Associates' employees or agents must be prospectively reviewed and approved by the Abt IRB. No human subject research may be initiated or continued at Abt or by Abt's employees or agents without prospective approval of the IRB.

The IRB is empowered to take any action necessary to protect the rights and welfare of human subjects in research conducted at Abt or by Abt's employees or agents. The IRB has the power to approve, require modifications of, or disapprove any human subject research conducted at Abt or by Abt's employees or agents. The IRB may also suspend or terminate the enrollment and/or ongoing involvement of human subjects in research as it determines necessary for the protection of those subjects. The IRB has the authority to observe and/or monitor Abt's human subject research to whatever extent it considers necessary to protect human subjects.

No Abt committee, official, or PD/PI may set aside or overrule a determination by the IRB to disapprove or require modifications of a research study conducted at Abt or by Abt employees or agents. The IRB will provide investigators with a written statement of its reasons for disapproving or requiring modifications in a specific proposed research project and will give the investigator an opportunity to respond in person or in writing. The IRB will carefully and fairly evaluate the investigator's response in reaching its final determination. There is no limit to the number of times a research project can be revised and re-submitted to the IRB for consideration.

4. Human Subject Protection Education Program

Abt Associates will provide on-site educational programs on human subject protections for PDs/PIs, IRB members, and other selected staff. Off-site educational opportunities and Web-based links to educational resources will also be provided as appropriate. The Chair of the IRB and theIRB Administrator are responsible for developing and implementing this education program.

III. IRB Membership

Pursuant to Federal regulations, 45 CFR 46.107, Abt's IRB will have sufficient expertise to review the broad variety of research in which the company commonly becomes involved, will be knowledgeable about all relevant regulatory requirements, and will remain impartial and objective in its reviews.

V. Appointment of IRB Members, Length of Service, and Duties

Members of the IRB are formally appointed by the IRB Chair. Members vote to approve, require modifications of, disapprove, or defer research submitted to the IRB. Members are expected to attend IRB meetings on a regular basis, serve as primary reviewers for particular research studies, as appropriate, and serve as general reviewers on all research discussed at convened meetings. Members are also expected to conduct expedited reviews on behalf of the IRB when so designated by the IRB Chair.

VI. IRB Chairperson and IRB Administrator

Responsibility for human subjects' protection at Abt Associates rests with the Chairperson and Administrator of the Abt IRB .

1. IRB Chairperson

The Chairperson of the IRB is formally appointed by the CAO and in turn is responsible for appointing the IRB members and the IRB Administrator for the company. In addition to his or her responsibilities as an IRB member, the Chairperson has primary responsibility for reviewing and approving all policies and procedures governing the protection of human subjects involved in Abt Associates research. The IRB Chairperson is also empowered to conduct IRB meetings and provide general direction to the IRB Administrator so as to ensure that the IRB operates within all applicable regulatory requirements. The IRB Chairperson works with IRB members, the IRB Administrator, and PDs/PIs to protect the rights and welfare of research subjects. As a fair and impartial committee head, the Chairperson functions as a role model for how IRB business should be conducted.

2. IRB Administrator

The IRB Administrator for the company is appointed by the Chairperson of the IRB. The IRB Administrator is responsible for ensuring, together with the Chairperson, that the company is in compliance with all applicable Federal regulations and other requirements governing the protection of human subjects in Abt Associates-led research. The IRB Administrator is a professional staff person responsible for documenting that IRB activities and decisions fully satisfy all regulatory requirements. The IRB Administrator must have a detailed, working knowledge of relevant regulatory requirements. In furtherance of these responsibilities, the IRB Administrator has the following specific duties:

- maintaining the official roster of IRB members;
- scheduling IRB meetings;
- distributing pre-meeting materials;
- compiling the minutes of IRB meetings in compliance with regulatory requirements and drafting memos documenting actions taken or requested by the IRB;
- promptly reporting changes in IRB membership to OHRP;
- maintaining all IRB documentation and records in accordance with regulatory requirements;
- assisting new IRB members in completing orientation procedures and meeting required education standards;
- securely and properly archiving all IRB records.

Together, the IRB Chair and Administrator have the following duties:

- facilitating communication between investigators and the IRB;
- serving as a resource for investigators on general regulatory information, and providing guidance about forms and submission procedures;
- maintaining training and reference materials related to human subject protection requirements, and organizing and monitoring training all research staff at Abt;
- developing, maintaining and updating the IRB policies and procedures manual and IRB forms;
- drafting reports and correspondence directed to research officials, federal officials, and others on behalf of the IRB;;

tracking the progress of each research protocol submitted to the IRB, using an electronic database where necessary;

assisting in evaluation, audit, and monitoring of human subject research as directed by the IRB; and

filing assurance documents.

VII. IRB Membership

In compliance with Federal regulations at 45 CFR 46.107, Abt Associates' IRB must meet the following requirements:

- The IRB will have a minimum of five members, which shall include the IRB Chairperson and the IRB Administrator.

IRB members will possess varying backgrounds to promote complete and adequate review of research activities commonly conducted at Abt.

IRB members will be sufficiently diverse relative to race, gender, cultural background, and sensitivity to community attitudes so as to promote respect for the IRB's advice and counsel in safeguarding the rights and welfare of human subjects.

IRB members will include persons able to ascertain the acceptability of proposed research in terms of institutional commitments, regulations, applicable law, and standards of professional conduct and practice.

The IRB will include at least one member whose primary expertise is in a scientific area, and at least one member whose primary concerns are in non-scientific areas.

The IRB will include at least one member who is particularly knowledgeable about the rights of prisoners relative to research, and one member who is particularly knowledgeable about the rights of children relative to research.

The IRB will include at least one member who is not otherwise affiliated with Abt Associates and who is not part of the immediate family of a person who is affiliated with Abt.

B. Conflict of Interest

In accordance with the Common Rule, no IRB member may participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB. IRB members, including the Chairperson, who have conflicting interests are required to disclose such interests and to recues themselves from deliberations, quorum counts, and votes on any relevant protocol. Such absences shall be recorded in the meeting's minutes. Since many IRB members also conduct research, it is their responsibility to disclose adequately any conflicting interests they may have.

VIII. Consultants

IV. IRB Recordkeeping & Required Documentation

The IRB may, at its discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB. Consultants may assist the IRB on an as-needed basis.

IX. **Training, Continuing Education, and Professional Development of IRB Members**

Upon being appointed to the IRB, a member receives comprehensive reference materials (including these policies and procedures) necessary to review research from an ethical and regulatory perspective. At a minimum, all members must complete an initial educational module. Acceptable human subjects training includes PRIM&R's IRB101 and the NIH training module. Members will periodically be provided with continuing education opportunities, and resources will be made available each fiscal year for each IRB member for this purpose.

Federal regulations require that Abt Associates implement written policies and procedures to govern the operations and direct the activities of its IRB. This IRB Policies and Procedures document satisfies that requirement.

B. Record Retention and Maintenance

In accordance with Federal regulations at 45 CFR 46.115(b), IRB records will be retained by Abt Associates Inc. for no less than three years after the completion of the research with which they are associated.

Currently, Abt uses a third party automated information system, IRB Manager, to manage research study records. All studies that were active as of December 2003 are included in the IRB Manager database. As of May 2007, only electronic records are kept. All hard copy IRB records are kept in secure off-site storage. Ordinarily, access to IRB records is limited to the IRB Chairperson, the IRB Administrator, IRB members, and officials of Federal and State regulatory agencies, including OHRP. Research investigators will be provided reasonable access to files related to their research. All other access to IRB records is limited to those who have legitimate need for them, as determined by the IRB Chairperson.

C. IRB Records Generally

IRB records include the following categories of documents organized into appropriate files:

- IRB Written Operating Procedures
- IRB Membership Roster (containing information on members' degrees, specialties, and representative capacities on the Board);

- Training Records (including information on IRB members and company employees who have participated in/passed particular training courses)
- IRB Correspondence (other than protocol-related)
- IRB Research Application Files (including all study-related correspondence by the IRB)
- Research Study Tracking System
- Documentation of Exemptions
- Documentation of Expedited Reviews
- Documentation of Convened IRB Meetings, including all submitted materials and minutes of the Board
- Documentation of Review by Another Institution's IRB (where relevant)
- Adverse event reports

D. IRB Research Application Files

The IRB will maintain a separate virtual file for each research study application that it receives for review. Applications will be numbered sequentially, in the order in which they are initially received. Each IRB research application file will contain the following materials:

The Research Application Form, describing the protocol. (Forms A and B)
Documentation of the type of IRB review obtained
The IRB-approved informed consent document, with the beginning and ending dates of the current approval period clearly displayed
Privacy and/or data security plans or policies
Advertising or recruiting materials, if any
Applications for protocol amendments or modifications (Form E)
Continuing review forms containing progress reports on the research (Form D)
Reports of unanticipated problems involving risks to subjects or others, and reports on adverse events occurring within Abt Associates or involving Abt employees or agents, and reported to any relevant regulatory agency. (Form F)
Scientific or scholarly literature relating to the research, where relevant and available
Results of any internal quality control and monitoring activities, if any.
Documentation of all IRB review and approval actions, including initial and continuing convened (full) IRB review, any expedited review, and all relevant correspondence to and from research investigators.
Documentation of Project Closeout.

All of the above material is stored in the IRB Manager Database for projects that were active after May 2007.

E. IRB Database

Abt Associates will maintain a research study tracking database. At a minimum the database will include the following information:

- Title of the research
- Name of the Principal Investigator and/or Project Director
- Funding source
- Date of initial IRB approval
- Date of most recent continuing approval
- End of current approval period
- Documentation of all Board actions taken and all requests made of the Board, by date
- Current status (Under Review, Approved, Suspended, Closed)

This information is maintained in IRB Manager.

F. Documentation of Exemptions

The IRB Chairperson and IRB Administrator are responsible for reviewing and verifying, on behalf of Abt Associates, whether certain research activities are exempt from Federal human subjects protection regulation. Documentation of the verified exemptions consists of written concurrence by the Board (authored by the IRB Administrator or the IRB Chair) that the activity described in the PD/PI's Human Subject's Information Form (*see* Appendix D) satisfies the conditions of the cited exemption category.

G. Documentation of Expedited Reviews

Expedited IRB review procedures may be employed for (i) minor changes in previously approved research during the specified approval period, or (ii) initial or continuing review of research falling with specific categories enumerated in Federal regulations. Expedited reviews are conducted by the IRB Chairperson and the IRB Administrator or, depending on the circumstances, a qualified IRB member designated by the Chairperson.

Documentation of expedited review and approval consists of (1) the reviewers' notation in the IRB Research Application File that the activity satisfies the conditions (i) for a minor change, or (ii) of the cited expedited review category; and (2) documentation of the review itself, via Board memo.

H. Minutes of Convened IRB Meetings

The IRB Administrator will compile the minutes of IRB meetings. The following specific information will be recorded in the meeting minutes:

- Attendance
- Quorum requirements
- Actions taken by the IRB on the initial or continuing review of research; review of protocol or informed consent modifications or amendments; unanticipated problems involving risks to subjects or others; adverse event reports; reports of continuing noncompliance with the human subject regulations or IRB determinations; suspensions or terminations of research; and other actions.
- Votes on these actions
- Required IRB findings and determinations
- The basis for requiring changes in or disapproving research.
- A summary of any controverted issues.
- A list of research approved since the last meeting utilizing expedited review procedures.

I. Quorum Requirements and Voting at IRB Meetings

IRB minutes will include a statement of quorum requirements based on the following standards:

(i) A majority of the IRB members, including at least one member whose primary concerns are in nonscientific areas and one member who is not employed by Abt Associates or part of the immediate family of someone employed by Abt Associates, must be present in order to conduct a convened meeting. In order for research to be approved, it must receive the approval of a majority of those members present at the meeting.

(ii) Members may be present in person or audio (telephone) or audio-visual teleconference. Members present via teleconference will be noted as such in the meeting minutes, which will also indicate that the members received all pertinent information prior to the meeting and were able to actively and equally participate in all discussions.

(iii) IRB minutes will include documentation of quorum and votes for each IRB action and determination by recording votes as follows: Total Number Voting ( ); Number voting for ( ); Number voting against ( ); Number abstaining ( ).

(iv) Members absenting themselves due to conflicting interests may not be counted toward quorum requirements (i.e., may not be counted among those voting or abstaining).

(v) No individual who is not listed on the official IRB membership roster may vote with the IRB.

J. Required IRB Findings and Determinations

The following specific IRB findings and determinations will be documented in IRB meeting minutes:

(i) The level of risk of the research.

(ii) The approval period for the research, including identification of any research that may warrant review more frequently than annually.

(iii) Identification of any research for which there is a need for verification from sources other than the investigator that no material changes have been made in the research.

(iv) Justification for waiver or alteration of informed consent, addressing each of the four criteria at 45 CFR 46.116(d), *viz.*, that (1) the research involves no more than minimal risk to subjects; (2) the waiver or alteration will not adversely affect the rights and welfare of subjects; (3) the research could not practicably be carried out without the waiver or alteration; and (4) whenever

appropriate, the subjects will be provided with additional pertinent information after participation.

(v) Justification for waiver of the requirement for written documentation of consent in accordance with the criteria at 45 CFR 46.117(c).

(vi) Justification for approval of research involving pregnant women, prisoners, and children, addressing each of the criteria specified under Subparts B, C, and D of the DHHS human subject regulations. The IRB Chairperson is responsible for ascertaining, with the assistance of the IRB Administrator , whether any particular research study may require review assistance by one or more outside experts.

(vii) Special additional protections may be warranted in specific research projects for groups of subjects who are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, regardless of source of support for the research.

V. Types of IRB Review

All human subject research conducted at Abt Associates or by Abt employees or agents must be prospectively reviewed and approved by the Abt IRB. No human subject research may be initiated or continued at Abt Associates or by Abt employees or agents without such prospective approval.

X. Review by the Convened IRB Generally

Federal regulations and the Federal Policy for the Protection of Human Subjects (Common Rule) require that an IRB conduct initial and continuing reviews of all non-exempt research at convened meetings at which a majority of the members are present, unless the research falls into one or more of the categories appropriate for expedited review (see Section V.E below).

A majority of the IRB members, including at least one member whose primary concerns are in nonscientific areas and one member who is unaffiliated with the company or not part of the immediate family of a person affiliated with the company, must be present in order to conduct a convened meeting. In order for research to be approved, it must receive the approval of a majority of those members present at the meeting.

XI. Initial Review by the Convened IRB

Prior to a convened meeting, Abt IRB members will be provided detailed initial review materials describing the research in order to discuss the protocol adequately and determine

the appropriate action during the convened review. These materials will include the proposed informed consent document and the IRB Form B: Application for IRB Review, which includes information about subject recruitment and selection, the research plan, risks and benefits, privacy and confidentiality protections, safety monitoring (where relevant), informed consent procedures, protections for vulnerable subjects, and any other information relevant to the approval criteria described in the regulations.

XII. Continuing Review by the Convened IRB

Abt's IRB will conduct substantive and meaningful continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. Continuing reviews will be conducted by the convened IRB unless the research falls into one or more of the categories appropriate for expedited review (see Section V.E. below).

Prior to a convened meeting, IRB members will be provided with detailed continuing review materials sufficient to conduct substantive and meaningful reviews. These materials will include the currently approved informed consent document and the IRB Continuing Review Application Form, which should include a summary of the research, a status report on the progress of the research, number of subjects enrolled and withdrawn, problems and adverse events, pertinent recent literature, and other relevant information.

As noted above, the IRB is required to conduct substantive and meaningful continuing review of research at least once per year. The regulations permit no grace period and no exceptions to this one year requirement. Research that continues after the approval period expires is research conducted without IRB approval. Consequently, the IRB will automatically suspend the enrollment of new subjects in any ongoing research that does not receive continuing review and approval prior to the end of the stipulated approval period. Previously enrolled subjects may continue their involvement in suspended research only where the IRB determines that continued involvement is in the best interest of the subjects.

In the case of certain multi-site studies or in other circumstances where it may be difficult for the Abt IRB to monitor research progress or problems that may develop between scheduled IRB reviews, the IRB may retain or rely on outside individuals or organizations to verify that unreported changes or problems will not occur between such scheduled reviews.

XIII. Expedited Review of Research

Federal regulations and the Federal Policy for the Protection of Human Subjects (Common Rule) permit the IRB to review research through an expedited procedure if:

(i) the research constitutes a minor change in previously approved research during the period for which approval is authorized; or
(ii) data collection is complete, and the research is in the analysis and reporting stage; or
(iii) the research is not greater than minimal risk and falls within the categories on the November 9, 1998 DHHS list of research eligible for expedited review.

Under an expedited review procedure, the Abt IRB Chairperson and the IRB Administrator or an experienced reviewer designated by the Chairperson may review and approve the research on behalf of the IRB. Documentation for expedited reviews maintained in IRB records will include the category and circumstances that justify using expedited procedures, as well as documentation of the review itself.

The IRB Administrator will keep all IRB members advised of research that has been approved under expedited procedures by listing the research in the minutes of the next IRB meeting.

XIV. **Expedited Review of Minor Changes in Previously Reviewed Research**

PDs/PIs must report to the Abt IRB any proposed changes in IRB-approved research, including proposed changes in informed consent documents. No changes may be initiated without prior approval of the IRB, except where necessary to eliminate apparent immediate hazards to subjects.

The Abt IRB may employ expedited procedures to review a proposed change to previously approved research if it represents a minor change to be implemented during the currently authorized approval period.

A minor change is one which, in the judgment of the IRB Chairperson or other designated reviewer, makes no substantial alteration in (i) the level of risks to subjects; (ii) the research design or methodology; (iii) the number of subjects enrolled in the research; (iv) the qualifications of the research team; (v) the facilities available to support safe conduct of the research; or (vi) any other factor which would warrant review of the proposed by changes by the convened IRB.

XV. **Review of Reports of Unanticipated Problems or Adverse Events**

PDs/PIs are required to notify the Abt IRB promptly of any unanticipated problems involving risks to subjects or others that occur in research conducted at Abt Associates or by Abt employees or agents. The Abt IRB must receive the completed IRB Form F: Adverse Event/Unanticipated Problem Reporting Form from the PD/PI within 5 working days of the event.

All such reports are reviewed by the IRB Chairperson and the IRB Administrator. If the event is determined not to be related to the research or not serious, and if the event does not require a change in the informed consent document or the protocol, the IRB Administrator will document this determination in writing. The report and accompanying documentation will be placed in the IRB Research Application file and noted in the minutes of the next IRB meeting.

If, in the judgment of the IRB Chairperson, the event may warrant more than a minor change in the protocol or informed consent process, the Chairperson will refer the event to the convened IRB for review. In the interim, the Chairperson may require modification or suspension of research activities deemed necessary to eliminate apparent immediate hazards to subjects.

During a convened review, the Abt IRB may determine whether the research will be permitted to continue as proposed, or whether changes are required. If the research will continue, the IRB will also determine whether a consent form revision is required and to what extent re-consenting and/or subject notification about new information is warranted. The IRB also has the authority to suspend the research if it has significant safety or other concerns.

It is the responsibility of the IRB Chairperson to provide prompt written notification to the CAO, the cognizant Division Manager and Group Vice President, the President, and to relevant Federal Agencies, including OHRP of any unanticipated problems involving substantial risks to subjects or others, and of the resolution of those problems.

XVI. IRB Review Determinations

The Abt IRB will notify PDs/PIs in writing of its determinations. IRB actions for initial or continuing review of research include the following.

(i) Approved with no changes (or no additional changes). The research may proceed.

(ii) Approvable with minor changes to be reviewed by the IRB Chairperson, the IRB Administrator or a designated IRB member. Such minor changes must be clearly delineated by the IRB so the investigator may simply concur with the IRB's stipulations. The research may proceed after the required changes are verified and the protocol is approved by the designated reviewer.

(iii) Approvable with substantive changes to be reviewed by the convened IRB. The research may proceed only after the convened IRB has reviewed and approved the required changes to the research.

(iv) Deferred pending receipt of additional substantive information. The IRB may determines that it requires additional or modified information about the research in order to proceed with its review. The research may not proceed until the convened IRB has approved a revised application incorporating all necessary information.

(v) Disapproved. The IRB has determined that the research cannot be conducted at Abt Associates or by Abt employees or agents.

XVII. Suspension or Termination of IRB Approval

All PDs/PIs conducting research at Abt Associates or as Abt employees or agents are required to notify the Abt IRB promptly of any serious adverse events or unanticipated problems involving risks to subjects or others.

In addition, all Abt employees and agents are required to notify the IRB promptly of any serious or continuing noncompliance with applicable regulatory requirements or with the determinations of the IRB.

The IRB may vote to suspend or terminate approval of research not being conducted in accordance with IRB or regulatory requirements or that has been associated with unexpected problems or serious harm to subjects. The IRB will notify the PD/PI in writing of such suspension or termination and will include a statement of the reasons for the IRB's actions. The PD/PI will be provided with an opportunity to respond in person or in writing.

Where the IRB Chairperson determines that such action is necessary to protect the rights and welfare of subjects, the Chairperson may require an immediate, temporary suspension of

enrollment of new subjects or of continued participation of previously enrolled subjects, pending review of the situation by the convened IRB.

It is the responsibility of the IRB Chairperson to provide prompt written notification to the CAO and to relevant Federal Agencies, including OHRP, of the suspension or termination or IRB approval as described in this section.

Federal regulations at 45 CFR 46.111 and the Federal Policy for Human Subjects Protection (Common Rule) delineate specific criteria for the approval of research. The Abt IRB must determine that all of the following requirements are satisfied before approving proposed research.

XVIII. Levels of Risk

The Abt IRB must consider the overall level of risk to subjects in evaluating proposed research, and investigators are required to minimize risks to subjects while maximizing research benefits. In general, the regulations require that the IRB distinguish research that is "greater than minimal risk" from research that is "no greater than minimal risk." Under Federal regulations at 45 CFR 46.102(i), "minimal risk means that the probability and magnitude of harm or discomfort in the research are not greater in and of themselves than those encountered in daily life or during the performance of routine physical or psychological examinations or tests." Under specific circumstances, research that is no greater than minimal risk may be eligible for expedited review, waiver or alteration of informed consent requirements, or waiver of the requirement to obtain written documentation of consent.

XIX. Minimization of Risks

In order to approve research, the IRB must determine that risks are minimized by using procedures that are consistent with sound research design and do not expose subjects to unnecessary risks. The IRB is expected to consider the research plan, including the research design and methodology, to ensure that there are no flaws that would place subjects at unnecessary risk. The IRB may determine that proposed research must be re-designed to enhance subject autonomy, maximize benefits, reduce risks, select subjects equitably, minimize undue influence or coercion, etc. When the research design presents unnecessary or unacceptable risks to subjects without commensurate benefits to the subjects or to others, the research cannot ethically proceed.

XX. Risks That Are Reasonable Relative to Anticipated Benefits

In order to approve research, the IRB must determine that the risks of the research are reasonable in relation to the anticipated benefits (if any) to subjects, and/or the importance of the knowledge that may reasonably be expected to result.

XXI. Equitable Selection of Subjects

In order to approve research, the IRB must determine that the selection of subjects is equitable. In making this determination, the IRB should evaluate the purposes of the research and the research setting, and should be especially cognizant of the problems of research involving vulnerable subject populations.

The IRB should carefully examine inclusion-exclusion criteria and recruitment procedures in order to determine that the burdens and benefits of the research are being distributed equitably. The IRB should be mindful of the importance of including members of minority groups in research, particularly when the research holds out the prospect of benefit to individual subjects or the groups to which they belong.

The IRB should be mindful of the desirability of including both women and men as research subjects and should not arbitrarily exclude the participation of persons of reproductive age. Exclusion of such persons must be fully justified and based on sound scientific rationale.

XXII. Informed Consent Procedures

In order to approve research, the IRB must determine that legally effective informed consent will be sought from each prospective subject or the subject's legally authorized representative (see 45 CFR 46.116), unless informed consent requirements can be waived or altered under Federal regulations. Any such waiver must be consistent with applicable laws. The specific elements required for legally effective informed consent are discussed in detail in Chapter VII. The following informed consent procedures apply to all research conducted at Abt Associates or by Abt employees or agents.

(i) Informed consent may only be sought under circumstances that provide the subject (or the legally authorized representative) with sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.

(ii) Informed consent information must be presented in language that is understandable to the subject (or the legally authorized representative).

(iii) No informed consent process may include any exculpatory language (a) through which the subject is made to waive, or appear to waive, any legal rights as research subjects; or (b) through which the investigator, the sponsor, Abt Associates or Abt's employees or agents are released from liability for negligence, or appear to be so released.

(vi) Informed consent must be obtained prior to initiation of any research screening procedures that are performed solely for the purposes of determining eligibility for research.

XXIII. Documentation of Informed Consent

In order to approve research, the IRB must determine that informed consent will be appropriately documented, unless documentation can be waived under Federal regulations.

As discussed in greater detail in Section VII.G. below, Federal regulations at 45 CFR 46.117 provide two different methods for documenting informed consent, the first of which is recommended to be used in all Abt Associates research.

XXIV. Data Safety Monitoring

In order to approve research, the Abt IRB must determine, pursuant to 45 CFR 46.111(a)(6), that where appropriate, the research plan makes adequate provision for monitoring the data to protect the safety of subjects. For research in which risks are substantial, a general description of the data and safety monitoring plan should be submitted to the Abt IRB as part of the proposal. This plan should, where relevant, contain procedures for reporting adverse events.

A Data and Safety Monitoring Board (DSMB) may need to be established for any clinical research that is blinded, involves multiple sites, targets vulnerable subjects, or employs high-risk interventions. It is the policy of the National Institutes of Health (NIH) to require a DSMB and/or a data safety monitoring plan for certain types of studies conducted with its support. The Abt IRB has the authority to require a DSMB as a condition for approval of research where it determines that such monitoring is needed.

XXV. Privacy of Subjects and Confidentiality of Data

In order to approve research, the Abt IRB must determine that there are adequate provisions to protect the privacy of subjects and the confidentiality of data.

In reviewing confidentiality protections, the Abt IRB will consider the nature, probability, and magnitude of harms that would be likely to result from a disclosure of collected information outside the research. It will evaluate the effectiveness of proposed techniques for rendering collected information anonymous, coding systems, encryption methods, storage facilities, access limitations, and other relevant factors in determining the adequacy of confidentiality protections.

Where research involves the collection of highly sensitive information about individually identifiable subjects, the Abt IRB has the ability to determine that special protections are needed to protect subjects from the risks of investigative or judicial processes. These may be prescribed by the Board based on the specific circumstances that exist in a given study, and may build on particular privacy and data security requirements required by Federal funding agencies.

In certain instances involving research that entails particularly high risks to human subject privacy, the Abt IRB may require that an investigator obtain a DHHS Certificate of Confidentiality (CoC). The CoC protects against the involuntary release of sensitive information about individual subjects for use in Federal, State, or local civil, criminal, administrative, legislative, or other legal proceedings. The CoC does not prohibit voluntary disclosure of information by an investigator, such as voluntary reporting to local authorities of child abuse or of a communicable disease. In addition, the CoC does not protect against the release of information to DHHS for audit purposes. Consequently, it is important for investigators to identify beforehand all conditions under which they will voluntarily release information to third parties. These conditions for release should be stated clearly and explicitly in any informed consent document.

XXVI. Additional Safeguards for Vulnerable Subjects

In order to approve research, the Abt IRB must determine that, where appropriate, additional safeguards have been included to protect the rights and welfare of subjects who are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, persons with mental disabilities, or economically or educationally disadvantaged persons. Insofar as the IRB frequently reviews research involving such vulnerable subjects, the IRB will include among its reviewers persons who are knowledgeable about and experienced in working with these vulnerable subjects.

XXVII. Review More Often Than Annually

The following factors will determine which studies require review more frequently than on an annual basis:

(i) The probability and magnitude of anticipated risks to subjects.

(ii) The likely medical condition of the proposed subjects.

(iii) The overall qualifications of the PD/PI and other members of the research team.

(iv) The specific experience of the PD/PI and other members of the research team in conducting similar research.

(v) The nature and frequency of adverse events observed in similar research at this and other institutions.

(vi) Any other factors that the IRB deems relevant.

In specifying an approval period of less than one year, the IRB may define the period with either a time interval or a maximum number of subjects studied or enrolled as specified by the IRB. If a maximum number of subjects studied or enrolled is used to define the approval period, it is understood that the approval period in no case can exceed 365 days and that the number of subjects studied or enrolled determines the approval period only when that number of subjects is studied or enrolled in less than 365 days.

XXVIII. Advertisements and Recruitment Incentives

The Abt IRB is required to review and approve all advertisements and recruitment incentives associated with the research that it oversees. Approval of the IRB must be obtained prior to the use of any proposed advertisement or recruitment incentive. Advertisements and incentives are directly related to the informed consent process and must be consistent with prohibitions on coercion and undue influence.

Any advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest. When appropriately worded, the following items may be included:

(i) The name and address of the PD/PI and Abt Associates

(ii) The purpose of the research and/or the condition(s) under study

(iii) In summary form, the criteria that will be used to determine eligibility for the study.

(iv) A brief list of participation benefits, if any. The possible benefits should be presented in a conservative manner without any exaggeration or excessive enthusiasm.

(v) The time or other commitment required of the subjects.

(vi) The location of the research and the person or office to contact for further information.

Recruitment procedures should be designed so that informed consent is given freely and coercion or undue influence is avoided. In order to evaluate this aspect of the research, the IRB should know what kinds of subjects are involved, what incentives are being offered, and the conditions under which the offer will be made.

XXIX. Payment to Research Subjects

Abt's IRB will review any proposed payments to research subjects associated with the research that it is charged with overseeing. Payments to research subjects may not be of such an amount as to result in coercion or undue influence on the subject's decision to participate. Payment may be permitted, with prior approval of the IRB, in instances where there is no direct subject benefit (i.e., when the study to be performed does not directly enhance the diagnosis or treatment a volunteer subject) and/or when the standard of practice in other institutions or research contexts is to pay subjects under the same or similar circumstances. The IRB will review all proposals involving the payment of subjects (in excess of reimbursement for travel) in the light of these guidelines.

VII. Informed Consent and Documentation of Informed Consent

Unless informed consent has been formally waived by the Abt IRB, PDs/PIs must obtain the legally effective informed consent of a prospective subject, or the subject's legally authorized representative, before the subject can be included in research.

Informed consent presumes two simultaneous concepts: informed decision making and voluntary participation. Prospective subjects must be given sufficient information about the research and its risks and benefits in order to reach an *informed decision* as to whether they will *voluntarily participate*.

For an effective informed consent process, Federal regulations at 45 CFR 46.116(a)(a) mandate the inclusion of eight basic informed consent elements unless the IRB has specifically approved an alteration or waiver of these elements. The IRB may routinely, or on a case-by-case basis, require that additional information, beyond these eight basic elements, be included in the informed consent.

No informed consent process may include any exculpatory language through which the subject is made to waive, or appear to waive, any of their legal rights or through which the investigator, the sponsor, the institution, or the institution's employees or agents are released from liability for negligence, or appear to be so released.

XXX. Required Elements of Informed Consent

The following elements are required to be included in the informed consent process.

1. Research Statement (required element #1). Informed consent information must include the following:

(i) A statement that the study involves research.

(ii) An explanation of the purposes of the research including its long-term goals.

(iii) An explanation of the expected duration of subjects' participation.

(iv) A description of what procedures will be followed.

(v) Identification of any procedures that are experimental.

In certain kinds of bio-social or epidemiological studies, subjects may mistake their participation in research for therapeutic treatment. By specifying the purpose of the research and describing experimental procedures, subjects should be able to recognize the difference between research and treatment.

2. Reasonably Foreseeable Risks or Discomforts (required element #2). Informed consent information must describe any reasonably foreseeable risks or discomforts associated with the research.

3. Reasonably Expected Benefits to Subjects or Others (required element #3). Informed consent information must describe any benefits to subjects or to others that may reasonably be expected from the research. However, benefits must not be overstated so as to create an undue influence on subjects.

4. Appropriate Alternatives (required element #4, in the case of clinical research only). Informed consent information must include disclosure of any appropriate alternative procedures or courses of treatment that may be advantageous to the subject. Enough detail must be presented so that the subject can understand and appreciate the nature of any alternatives. This requirement may not be relevant for most kinds of social science research.

5. Extent of Confidentiality (required element #5). Informed consent information must describe the extent to which confidentiality of records identifying the subject will be maintained (or not maintained). Research often poses the risk of loss of confidentiality to subjects who participate. Many persons who would not otherwise be privy to identifiable, private information about the subject may be involved in the research process. Consent information should describe any procedures that the research team will use to protect subjects' private records. However, the informed consent information must describe the loss of confidentiality that may occur through certain research or required audit procedures (e.g., through actions of a study sponsor, OHRP, or the IRB) or any other, anticipated or unanticipated loss of confidentiality that might occur despite the best efforts of the investigator. In general, confidentiality will be protected "to the maximum extent provided by law," insofar as there may be Federal and/or state reporting requirements that mandate disclosure of certain information that is otherwise protected (e.g., evidence of abuse or neglect of children, etc.). With particular research studies, a Certificate of Confidentiality (CoC) may further circumscribe the circumstances under which disclosure may be compelled.

6. Compensation or Treatment for Injury (required element #6 if study presents more than minimal risk). If more than minimal risk research is involved, informed consent information must include explanations regarding:

(i) Whether any compensation is available if injury occurs.

(ii) Whether any medical treatments are available if injury occurs and whether there is a charge for such medical treatment.

(iii) A description of any such compensation or treatments or where more information about them is available.

7. Contact Information (required element #7). Informed consent information must include details, including telephone numbers, about whom to contact for two specific situations:

(i) For answers to questions about the research. The project director and/or the principal investigator are appropriate contacts for this information.

(ii) For answers to questions about subjects' rights, PDs/PIs may list the IRB Chair at Abt Associates or a contact at another IRB (where such IRB has jurisdiction), or both, as appropriate.

8. Voluntary Participation Statement (required element #8). Informed consent information must contain clear statements of the following:

(i) Participation in the research is voluntary.

(ii) Refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled.

(iii) The subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

It is particularly important for subjects and prospective subjects to understand and have complete confidence that declining to participate in research will not jeopardize their status, treatment, and/or eligibility to receive certain benefits, as the case may be.

XXXI. Additional Elements Where Appropriate

Where relevant and appropriate, the regulations require that one or more of the following six additional elements be included in the informed consent information.

1. Unforeseeable Risks to Subjects. Some research may result in unforeseeable risks to subjects (or to embryos or fetuses if the subject is or may become pregnant). For research of such a nature, the informed consent information must warn subjects that there may be risks that are not known or not foreseeable.

2. Investigator-Initiated Termination of Participation. There may be instances that would require investigators to terminate the participation of particular subjects (e.g., subject noncompliance with research, subject not benefiting from direct-benefit research). The informed consent information should specify these circumstances.

3. Additional Costs. If subjects must bear any additional costs (transportation, time away from work, health costs, etc.), these must be disclosed in the informed consent information.

4. Early Withdrawal/Procedures for Termination. Subjects have the right to withdraw from the research. However, some studies involve medications or procedures that would be dangerous for subjects to discontinue abruptly. For studies of this nature, the informed consent information must provide subjects with knowledge of the consequences affecting a decision to withdraw. In addition, if there are procedures regarding how to withdraw safely from the research, these must also be described. It is not appropriate for research staff to administer any additional research-oriented questionnaires or interventions that do not affect the safety of subjects who have decided to withdraw.

5. ***Significant New Findings.*** Subjects will be informed of any new knowledge or findings about the medication or test article and/or the condition under study that may affect the risks or benefits to subjects or subjects' willingness to continue in the research.

6. ***Approximate Number of Subjects.*** In certain studies involving greater than minimal risks to subjects, it may be helpful or appropriate to disclose the approximate number of subjects to be enrolled, in order to allow subjects and/or representatives to seek more information regarding a particular research design. This may be particularly important in the case of experimental research with a very small number of participants; subjects can be expected to want to know, and to be provided additional information about, the reasons for a low number of participants or enrollees.

XXXII. Intellectual Property Issues

In addition to these elements, the Abt IRB may, if relevant, require that informed consent information contain information about the rights of subjects should particular research yield commercial products. Such information could include a statement to the effect that "information and/or materials obtained from you in this research may be used for commercial purposes. It is the policy of Abt Associates and its agents not to provide any financial compensation to you should this occur."

XXXIII. Assent by Minors

The Abt IRB must make certain findings and determinations when reviewing research involving children. IRB records must reflect the IRB's understanding and justification for the risks and benefits posed by approved research involving children. In classifying research involving children, the proposed research activity must fall within one of the four categories contained in 45 CFR 46.404, each of which specifies particular conditions involving parental consent and/or child assent that must be met before the proposed research can be approved. Provisions must be made to obtain a child's assent when the IRB has determined that the child is capable of giving assent. Guidelines for determining the capability of a child to provide assent are provided in 45 CFR 46.408(a).

XXXIV. Legally Authorized Representatives

Federal regulations do not specify who may serve as a subject's legally authorized representative. State law makes this determination. Investigators should be aware that the standards under which a subject's representative may provide legally effective consent for research may be more stringent than for medical treatment or other procedures. Abt investigators should consult with the IRB should any questions arise about the use of legally authorized representatives.

XXXV. Guidelines for Conducting an Informed Consent Conversation

Informed consent is an ongoing process of communication with a human subject by the investigator and the research team.

Potential subjects should be given a copy of the informed consent document so they can discuss the research with their family or others and develop questions to ask the research staff.

The context of how, when, and where the investigator obtains the subject's informed consent (or in the case of minors, assent) should also be a consideration. The possibility of undue influence or coercion should be minimized, and informed consent information must be presented in language that is understandable to the subject.

XXXVI. Waiver or Alteration of Informed Consent Requirements

For minimal risk research (see 45 CFR 46.116(d)) , Federal regulations permit an IRB to:

(i) approve a consent procedure that waives or alters the required elements of informed consent, or

(ii) waives the requirement to obtain informed consent altogether.

In the case of minimal risk research, the IRB must formally find and document that:

(i) The research involves no greater than minimal risk to subjects;

(ii) The waiver does not adversely affect subjects' rights and welfare;

(iii) The research could not practicably be carried out without the waiver; and

(iv) Where appropriate, will provide subjects with pertinent information about the research after participation.

XXXVII. Documentation of Informed Consent

Investigators are usually required to document informed consent using a written consent form signed by the subject or the subject's legally authorized representative. The most common way to document informed consent is through a full length, written consent document that embodies all of the required elements of informed consent. The consent document must be signed by the subject (or the subject's legally authorized representative), and a copy must be given to the person signing the form.

Federal regulations also provide another ("short form") method for documenting informed consent. The "short form" method employs a short, written consent document, a written protocol summary, and a witness to the consent process. The "short form" method is occasionally used for obtaining informed consent from subjects who do not speak English (see below). In general, Abt does not endorse use of the "short form".

XXXVIII. Obtaining Consent from Non-English Speakers

Federal regulations at 45 CFR 46.116 require that informed consent be obtained in language that is understandable to the subject (or the subject's legally authorized representative).

In accordance with these regulations, the Abt IRB requires that informed consent discussions include a reliable translator when the prospective subject does not understand the language of the person who is obtaining consent.

Investigators can document informed consent in either of two ways:

(i) A full–length informed consent document written in language understandable to the subject; or

(ii) A "short-form" consent document in the language of the subject that states the general elements of informed consent.

Investigators will be responsible for providing the short form to subjects in a language they understand. Such a form is sometimes used by researchers in circumstances where they are unable or unwilling to produce an accurate written translation of the full informed consent form. It is strongly recommended that Abt researchers use a full translated informed consent

form wherever possible in the case of non-English speakers as a matter of accurate documentation and completeness. If for whatever reasons the production of a full translated informed consent form is infeasible or impractical with respect to certain subjects or groups of subjects, investigators may consult the regulations (45 CFR 46.117(b)(2)) for guidance on how to utilize the alternative "short form" method of obtaining written informed consent.

If investigators use the "short form" to document informed consent, they must also provide subjects with (i) the full-length informed consent document in English, and (ii) a translator who can take part in the oral informed consent conversation to ascertain subject understanding and who may serve as the witness. The "short form" consent document written in the subject's language must be signed by the subject (or the subject's legally authorized representative) and the witness. The full-length English consent document must be signed by the witness and the person obtaining consent. The subject must be given copies of both the "short form" consent document and the English consent document.

Whether or not a full length or a "short form" consent document is utilized, the Abt IRB will require that appropriately translated documents be submitted to the IRB for review and approval prior to their use in enrolling subjects. In addition, the Abt IRB may require that the accuracy of the translation be verified through use of a different translator or through some other method (e.g., a reverse translation).

XXXIX. Waiver of Documentation of Consent

Federal regulations at 45 CFR 46.117(c) permit an IRB to waive the requirement to obtain written documentation of informed consent where:

(i) the consent document would provide the only link to the subject and the principal risk of the research would be breach of confidentiality; or

(ii) the risk to subjects is minimal and consent would not be required outside the research context.

In approving a waiver of documentation, the IRB must formally find and document that one of the above conditions applies.

Where the IRB has waived documentation of consent, investigators must understand that they are still required to (i) communicate all the required elements of informed consent to the subject, and (ii) obtain the subject's active consent before proceeding with the research.

In cases where documentation of consent is waived, the IRB may still require investigators to provide subjects with a written statement regarding the research.