NEW YORK STATE PSYCHIATRIC INSTITUTE PROGRAM FOR HUMAN SUBJECTS RESEARCH

POLICIES AND PROCEDURES OF THE INSTITUTIONAL REVIEW BOARD

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Policies and Procedures of the Institutional Review Board

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Section 1. Introduction and Organizational Structure

These internal operating procedures for the Institutional Review Board (IRB) based at the New York State Psychiatric Institute[1] are intended to supplement the "Manual for Institutional Review Boards: Laws, Regulations, Policies and Procedures Relating to the Protection of Human Subjects of Research" (Manual) http://corporate.rfmh.org/research_compliance), of the NYS Department of Mental Hygiene and the Research Foundation for Mental Hygiene, Inc. (Research Foundation). If there is any inconsistency between the provisions of these procedures and the provisions of the "manual" shall apply.

Note 1: The term Full Board is used to signify the convened IRB throughout this policy manual.

Note 2: Additional operational details, requirements and guidance is found on the IRB's website at http://irb.nyspi.org

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1. **Organizational Structure:**
   The Psychiatric Institute (PI) is essentially comprised of two organizations:

   A. NYSPI
   The New York State Psychiatric Institute (NYSPI) is a research facility owned and operated by the New York State Office of Mental Health; and

   B. RFMH

   I. The Research Foundation for Mental Hygiene, Inc. (RFMH) is a private 501 (c) (3) not-for-profit membership corporation organized for the purpose of assisting and enhancing the research and training objectives of the New York State Office of Mental Hygiene (OMH) and its component agencies including the Office of Mental Health.

   II. Sponsored Research: Through an agreement with New York State, the Foundation has been designated as the organization responsible for administering and directing the conduct of sponsored research programs carried out by scientists at Department of Mental Hygiene (DMH) facilities, including NYSPI.

[1] RFMH IRB-4, formed in July 2009, is comprised of experienced current and former IRB members. It has not yet been convened or asked to conduct review of research. It will follow the same policies and procedures as the main NYSPI---IRB, RFMH IRB---1.

2. Affiliated Institutions:

Columbia University (CU) and the Columbia University Medical Center (CUMC) are affiliated with PI. NYSPI is the home of the Columbia University Department of Psychiatry, and the Director of NYSPI is also the Chairman of that Department.
Researchers at NYSPI ordinarily hold faculty appointments in the Department of psychiatry and are involved in a range of clinical, educational, administrative and research activities in that capacity. Through an Institutional Authorization Agreement (IAA), the NYSPI-IRB reviews research originating in the Columbia University Department of Psychiatry.

3. Other facilities under the NYSPI IRB Assurance:

The NYSPI IRB conducts reviews for other facilities under its Assurance.
It is the IRB of record for the:

A. Buffalo Psychiatric Center,
B. New York City Children's Center, and the
C. Institute of Basic Research

4. The NYSPI-IRB also conducts reviews for other components covered by the DMH/RFMH Federal Wide Assurance when the expertise of the NYSPI-IRB is required or the facility does not have its own IRB.

5. The IRB within the NYSPI Organizational Structure

A. The Program for Human Subjects Research (hereinafter referred to as "the Program") defines a structure with four integrated domains:

I. Humans Subject Research Review and Approval,
II. Human Subjects Protection Training and Education,
III. Psychiatric Research IRB Submission Module (PRISM) training, support and
IV. Research compliance monitoring.

The IRB Executive Director, IRB Co-Chairs, and the Director, Psychiatric Research, oversee the Program.

B. The IRB is situated within the Program, and the reporting structure is as follows:
I. The IRB Executive Director and IRB Co-Chairs report to the Director, Psychiatric Research, NYS Psychiatric Institute.

II. The IRB Executive Director serves as liaison to oversight and compliance functions at affiliated and collaborating institutions and organizations.

III. The IRB Director of Operations reports to the IRB Executive Director. The IRB Director of Operations is responsible for the day to day operations and management of the IRB office.

C. Coordination/Communication:

Close coordination between the IRB and research, clinical and administrative leadership structures promotes the Institute's program of human research protections, creates essential bi-directional communication and places the IRB in a prominent place in the institutional culture.

In order to foster effective communication and coordinated research oversight within the Institute:

I. The Director, Psychiatric Research meets at least weekly with the Director of NYSPI.

II. The Director, Psychiatric Research meets with the IRB Executive Director on a regular basis, typically once a week, to discuss all elements of the Program, including but not limited to: research policy, convened IRB and Subcommittee meeting process and activity, IRB member and staff continuing education and research compliance monitoring activities.

III. The IRB Executive Director, Co-Chairs and Director of Operations hold a monthly meeting with the Director, Psychiatric Research to discuss IRB policy and operations.

IV. The IRB Executive Director and Director of Operations coordinate research conference calls with the Deputy Managing Director of RFMH. These conference calls are typically held twice a month and include OMH House Counsel on an ad-hoc basis.

V. The IRB Director of Operations convenes an IRB Office staff meeting twice per month, attended by the Executive Director and all staff within the Program to discuss IRB policy and operations.

VI. The IRB Executive Director attends the monthly Directors and Chiefs meeting attended by all Institute and Department clinical, research and operations leadership. In addition, the Executive Director provides an annual update on IRB activities to NYSPI's Medical Staff Executive Committee.

To promote clear communication and seamless collaboration between the Program and the CUMC Human Research Protection Program (HRPP):

VII. The NYSPI IRB Executive Director attend twice monthly Executive Committee meeting of the CUMC Human Research Protection Program HRPP), and reports on meeting proceedings to the Deputy Director for Research Administration, Ethics and Policy.

VIII. The IRB Executive Director and Director of Operations meet throughout the year on an as-needed basis with the Executive Director of Columbia's HRPP.

IX. The IRB Executive Director and Research Compliance Monitor attend quarterly meetings convened by Columbia's Clinical Trials Office.

6. Budget

Support for the operation of the IRB is provided by RFMH, the Office of Mental Health and Columbia University. The Director, Psychiatric Research proposes an annual budget with input from the IRB Executive Director. The NYSPI Director and the Director of RFMH at NYSPI provide approval.

7. Space

A suite of offices houses the IRB at NYSPI on the fifth floor of the Herbert Pardes Building. Ample and secure file storage is available. The Full Board meets in the main boardroom at the Institute (Room 6601). Subcommittee meetings are held in the conference room adjacent to the IRB suite (Room 5001). Off-site storage is available for retention of closed files and can be accessed within 48 hours as needed.

8. Information Technology

IRB records are created and maintained electronically through the Psychiatry Research IRB System Module (PRISM), and tracked through the Protocol Management System (PMS). Information technology support related to PRISM, PMS and other database systems and software is provided by NYSPI/RFMH Information Technology (IT) professional staff

Section 2. The Authority of the IRB

Research involving human subjects, as defined at 45CFR46 and 21CFR50, 56, requires the prior review and written approval of the NYSPI-IRB.

Research is defined a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge [45 CFR 46.102 (d)].

A Human Subject is defined as a living individual about whom a researcher obtains data through intervention or interaction with the individual or identifiable private information about the individual [45 CFR 46.102 (f)].

1. The IRB is responsible for the initial and ongoing review of all research which involves human subjects, (e.g., patients, staff, control groups, volunteers) regardless of the source of funding (if any), if:

    A. The research is sponsored by the Institution; or
    B. The research is conducted by, or under the direction of any employee or agent of the Institution in connection with his or her Institutional responsibilities and/or using any patients, staff or facilities of the Institution; or
    C. The research involves the use of the Institution's non-public information to identify or contact human research subjects or prospective subjects; or
    D. The research involves the use of the Institution's patients or facilities.

2. As per a cooperative agreement (see Attachment 1.) with Columbia University Health Sciences Division (Columbia), all research originating in the Department of Psychiatry at Columbia is reviewed by the New York State Psychiatric Institute IRB for CUMC. Research submitted by a faculty member with a joint appointment in Psychiatry and another Columbia Department shall be reviewed by the NYSPI-IRB when:

    A. The research is in a field of Psychiatry or related disciplines, or
    B. NYSPI or RFMH patients, personnel, records, space, or funding is involved.
    C. In other circumstances, the Columbia Health Sciences IRBs conduct reviews of such research for Columbia and when applicable, NYPH.

3. The IRB has the authority to determine that an activity does not meet the regulatory definition of research involving human subjects under 45CFR46.102 (f) and 21CFR 56.102(e).

4. The IRB has the authority to determine that NYSPI is not “engaged in research” (http://www.hhs.gov/ohrp/humansubjects/guidance/engage08.html) and therefore NYSPI-IRB review and oversight is not required.

5. The IRB is responsible for the review of human subjects research that would otherwise be considered “exempt” under the provisions at 45CFR46.101 (b).

6. In accordance with NYS Mental Hygiene Law, the IRB may determine that research which involves review of existing identifiable records, tissues or other materials derived from human subjects is subject to IRB review and NYSPI policies and procedures, even when not required by 45CFR46.

7. The IRB has the authority to approve research, require modifications to research as a condition of approval or disapprove research involving human subjects that falls under its authority.

8. The IRB has the authority to require prospective review and approval of all modifications to previously approved research protocols and/or informed consent documents; the only exception is a deviation in protocol procedures that may be necessary to avert or mitigate imminent harm to a research subject.

9. The IRB has the authority to require, and the responsibility to conduct, review of approved human subject research at intervals appropriate to the degree of risk but not less than once per year. The IRB has the authority to specify the duration of approval and the information required for continuation of approval. The IRB has the authority to observe (or delegate a third party to observe) the consent process and the research if the IRB deems this necessary.

10. The IRB has the authority to review and approve or otherwise specify the qualifications of a study's Principal Investigator, co-investigators, individuals authorized to discuss and document consent. Individuals authorized to assess capacity and research staff involved in implementing research procedures.

11. As part of continuing review of research, the IRB has the authority to require feedback (a "report back" to the IRB) on the progress of the research and the experience of research subjects, to observe or otherwise monitor research activities or consent discussions, and to inspect research records for compliance with regulatory requirements and IRB policies and procedures.

12. The IRB has the authority to suspend or terminate approval of any study, or limit or restrict research or components of research activities, when it determines that such action is warranted due to concerns about risks to subjects or noncompliance with IRB or regulatory requirements.

13. The IRB has the authority and responsibility to promptly report to appropriate Institutional officials to ensure prompt reporting to federal regulatory agencies:

    A. Unanticipated problems involving risks to subjects or others;
    B. Any serious or continuing noncompliance by investigators with the regulations or requirements of the IRB;
    C. Any suspension or termination of IRB approval for research.

14. The IRB has the authority to require investigator education and training in research ethics and human subjects protections.

15. The IRB has the authority, in conjunction with Institute administration, to require special oversight or supervision of research.

Section 3. Key Features of Human Subjects Research Review at NYSPI

1. The Regulatory Notion of Vulnerability and the Requirement for Additional Safeguards:

The NYSPI IRB routinely reviews research involving subject populations described in the Common Rule as "vulnerable to coercion or undue influence," including individuals with serious mental illness, neurological illness, substance dependence, developmental disorders, individuals who are economically and educationally disadvantaged, new immigrant populations, and others who are disadvantaged by limited access to necessary health care.

Our standards for the review and conduct of research seek to address this broad notion of vulnerability that is often, although not universally, present in the subjects who take part in research conducted at NYSPI. First, for many, access to mental health care is limited, especially for those of lower socioeconomic and immigrant status. Limited access to treatment in the community (outside of research) will influence an individual's decision-making because options and alternatives outside the research may not be available. Limited access to mental health care also means that many subjects may have limited access to basic health care, meaning they may more likely have undiagnosed or untreated co-morbid medical problems.

Second, many of the populations that NYSPI researchers study are from immigrant communities and members of these populations may present with cultural, educational and language barriers to meaningful consent and research involvement. Third, many patients with psychiatric illness have impairments in decision-making ability which may impact abilities to understand and/or use information relevant to consent. Many populations will be multiply vulnerable. Fourth, despite improvement in public understanding and acceptance of mental illness as illness, stigma and prejudice remain. Harms related to access to private information and breach of confidentiality require special attention in IRB review. Finally, despite the dramatic advances in the diagnosis and treatment of mental illness and related conditions, standard and "effective" treatments may be only partially effective for only a subset of individuals or both. Therefore, another aspect of vulnerability relates to patients who are resistant or refractory to existing treatments.

For these reasons, the NYSPI IRB's review and approval procedures, and procedures to identify and minimize risk, assume potential vulnerability and tailor protections on a case-by-case basis. IRB precedent and "case-law" reflect protections tailored to the degree and nature of vulnerability of the specific study population and to the degree and uncertainty of study risk.

Examples of additional safeguards in IRB procedure and precedent include (but are not limited to):

A. Minimal risk research that is not limited to routine activities for which IRB standards are well established is reviewed by subcommittee and draws on the expanded professional experience and expertise of reviewers.

B. In addition to the primary and secondary scientific reviewer, a tertiary reviewer who is a non-scientist and unaffiliated Board member, reviews each protocol on the agenda and is asked if he/she has comments in addition to those of the primary and secondary reviewers.

C. No subject currently on treatment that is effective and well-tolerated may be discontinued from that treatment for the purpose of research participation when doing so yields an unfavorable study risk-benefit ratio.

D. Full Board decisions are arrived at by consensus in most instances, but approval requires a two-thirds majority of the members present.

E. The Board considers subject vulnerability in determining what constitutes a "reasonable" risk-benefit analysis.

F. All studies involving treatment interventions must detail operationalized drop-out criteria for subject worsening (and, in some cases, failure to improve, if specified during IRB review).

G. A Federal Certificate of Confidentiality must cover research that creates identifiable records and involves subjects who are HIV positive, research on substance abuse, research involving prisoners and studies involving the collection of specimens for genetic analysis.

H. Studies involving the administration of substances of abuse must carefully screen and exclude individuals who are seeking or are amenable to treatment. Repeated study enrollment in such studies is subject to limits.

I. An assessment of capacity by an appropriately qualified person who is not affiliated with the research is required for more than minimal risk research involving individuals with serious mental illness and for most inpatients of the NYSPI. Consent forms for more than minimal risk studies involving complex or multi-component research require use of a "consent form summary" cover sheet, using criteria indicated by the IRB, emanating from 45 CFR 46.116.

J. Clinical trials other than those in support of a New Drug Application (NDA) are required to disclose each subject's treatment assignment at the conclusion of that individual's study treatment, unless special circumstances/justification exists and is approved by the IRB.

K. All treatment-seeking subjects at NYSPI must be provided with the standard care at NYSPI for a pre-determined period, at no cost, at the conclusion of investigational treatment studies, unless the study offers open label, standard care.

L. The IRB may specify additional requirements for continuing review; including special monitoring and interim reports back from the investigator detailing information about study risk and subject experience once enrollment begins.

2. Determination that IRB Review is Required:

All research fulfilling the definition of human subjects research requires IRB approval. The NYSPI IRB does not recognize any such activities as exempt from the application of the Common Rule and the applicable subparts. Investigators are expected to consult with the IRB Office when there is uncertainty as to whether the work in question fulfills the definition of research, if it involves human subjects, or if NYSPI is engaged in research.

In accordance with State law, certain policies and procedures of NYSPI, OMH and the NYSPI IRB extend beyond those defined in HHS and FDA regulations, and related regulatory guidance. Investigators are expected to consult with the IRB when research involves use of secondary data, biological specimens or records that are not readily identifiable and therefore might otherwise not require IRB review.

3. Composition of the IRB:

The NYSPI IRB research portfolio, while extensive primarily involves research on psychiatric disorders, mental health, and behavior. IRB membership is drawn from the faculty and staff of the Institute and Department. As such the NYSPI IRB is a "specialty" IRB, with a concentration of expertise and experience.

RFMH IRB-4, formed in July 2009, is comprised of experienced current and former IRB members. It has not yet been convened or asked to conduct review of research. It will follow the same policies and procedures as the main NYSPI-IRB, RFMH IRB-1.

A. Composition of the IRB: The IRB is constituted in accordance with 45CFR46.107 and 21 CFR 56.107. Its diverse membership provides expertise in the ethical, regulatory and scientific dimensions of human subjects research.

The membership will include at least one scientist, one physician and one non-scientific member. The membership will also include lay members, as they bring the perspectives of patients, their families, and the community to the Board. In total, the Board includes at least ten voting members.

B. Qualifications of Members: Members must possess the appropriate motivation, education, training, and or experience to contribute meaningfully to the review of human subjects research in mental health and related biological, social, behavioral, and epidemiological fields. (See Section 11. Training and Education).

C. Non-scientific Members: There is at least one voting member at every meeting whose interests and background are primarily non-scientific. A prisoner advocate is on the roster as a non-scientific voting member for prisoner research only.

D. Unaffiliated Members: Each Board includes among its membership at least one individual who has no current or former affiliation with the institute, RFMH or CU (and no immediate family member with an affiliation).

E. Diversity of Membership: The membership of each Board includes individuals from a range of professional disciplines and perspectives. Community members typically represent the perspective of individuals with serious mental illness and their families. Membership is reviewed at least annually.

F. Alternate Members: One or more alternate members exist for members of the Board. Such alternate members are of the same category of membership (e.g., scientific or non-scientific) and meet all other IRB membership requirements.

G. Use of Consultants: The Board, Executive Director and IRB chairs may at their discretion invite individuals to contribute to the review of matters that require special expertise or experience. The Chairs, Board members or IRB staff will usually identify consultants. Consultants do not vote with the Board and do not count towards quorum requirements. Consultants are subject to the same confidentiality and conflict of interest rules as members.

H. Representatives of Research Divisions: IRB members are routinely selected from NYSPI's major research divisions and clinical components (representing distinct clinical and/or scientific expertise). In this way, scientific reviewers contribute to a bi-directional flow of information. They often serve as a liaison from the IRB to the divisions, provide guidance and communicate expectations. Members also represent the breadth of research subspecialties in psychiatry and provide scientific education to the IRB.

I. Appointments and Term Limits: While membership is formally reviewed and appointments are made annually, appointments may be renewed and there are no term limits. The IRB endeavors to maintain appropriate expertise and representative capacity and a balance of senior, midlevel and junior members on the board and to ensure that members who are retained develop expertise and contribute actively in the review process.

4. Review by Subcommittee:

An IRB Subcommittee conducts a first step review of all more than minimal risk new research and major modifications to approved research (unless a decision is made that the modification may go directly to the Full Board). Research involving no more than minimal risk can either be assigned to Subcommittee review, or review by an IRB Chair, or IRB member(s) at the discretion of the Executive Director or Director of Operations. The review focuses on readiness of the submission for review, scientific merit, design and risk/benefit considerations, with an emphasis on minimizing risk. The Subcommittee also provides an opportunity for education and training of IRB reviewers and researchers.

A. Structure and membership: Each of four Subcommittees of the IRB meets monthly for approximately two hours depending on workload. To enhance expertise, three of the Subcommittees focus on adult clinical and biological protocols (the area of greatest volume) and one Subcommittee concentrates primarily on research involving children. There is flexibility, however, to move members with child and adolescent psychiatry experience to any of the other three subcommittees on an as-needed basis.

   The standing membership of the Subcommittee includes IRB scientific members and alternates. Consultants with necessary expertise beyond that available on the IRB may be asked to participate at this stage in review. An IRB Chair or another experienced IRB member chairs the Subcommittee. An IRB administrator assigned to the protocol (the Protocol Analyst) is responsible for advising the Subcommittee on regulatory requirements, taking notes and preparing a memo to be sent to the investigator. The Subcommittee Chair or his/her designee typically reviews and approves the memo. In cases where Subcommittee comments are confined to simple directives, the Protocol Analyst may review and approve the memo.

B. Authority: The Subcommittee may determine that the submitted protocol is incomplete and “not reviewable” as submitted and requires significant revision. It may determine that a protocol is eligible for approval on an expedited basis or eligible for approval “pending revision”, on an expedited basis as per 45 CFR 46.110. Finally, the Subcommittee may determine that, pending revision, the protocol may be reviewed by the Full Board.

C. Communication with Investigators: To answer questions during review, or provide guidance to investigators in addressing/revising problem areas in the protocol, investigators may be asked to participate in a teleconference during the meeting. Generally, within three business days following Subcommittee review, a detailed memo is sent by the Subcommittee Chair or designee to the investigator to summarize the Subcommittee critique and to request protocol and consent revisions, justification of risk and clarification of procedures necessary for approval of studies eligible for expedited approval, or for review at the Full Board for other research.

D. Documentation of Subcommittee Review: Notes are kept by the Protocol Analyst and deliberations are digitally recorded to assist in the development of a detailed memo. The recording is erased after the memo has been drafted. No formal minutes of Subcommittee review are maintained; the memo to the investigator represents formal documentation of Subcommittee review.

E. Conflict of Interest: The same conflict of interest rules applied to Full Board review are operative at Subcommittee review (See Section 8. Conflict of Interest).

F. Confidentiality: All consultants and visitors to Subcommittee are required to sign an IRB confidentiality statement.

G. The IRB Chair or the Executive Director may appoint special ad hoc subcommittees to assist the IRB in reviewing matters requiring consideration by the Board.

5. Use of Primary, Secondary, and Tertiary Reviewers:

Continuity of review enhances quality and consistency of review, and the NYSPI IRB therefore employs a system that enables reviewers to work with a protocol from the point of initial submission through protocol approval and continuing review processes. While all IRB members are expected to review the protocol summary form, consent forms and IRB correspondence during review, the primary and secondary reviewers are expected to have greater familiarity with the protocol and to review the grant application when applicable and other study documents such as Investigator Brochures and Data and Safety Monitoring Board reports, and will often have contact with the investigator in preparation for review to clarify outstanding questions. Tertiary Reviewers are generally non-scientific and/or unaffiliated members of the IRB and are assigned to present their review of new protocols, along with consent form and other documentation, at the Full Board meeting.

A. Assignment of Primary and Secondary Reviewers: Primary and secondary reviewers are assigned to all protocols for Subcommittee review by the Director of Operations or her designee, and are selected from among the Subcommittee roster of members and alternates. Where possible, reviewers with special expertise in the subject matter and subject population proposed for the study are selected to be the primary or secondary reviewers. No reviewer may have a conflict of interest related to the study team or "interested entity" when one is identified by the Ethics Advisory Board.

B. Subcommittee Review: While all Subcommittee members receive the entire protocol submission including a Protocol Summary Form (PSF), Consent Forms (CFs) and supporting documents submitted for review, the primary and secondary reviewers also receive and are responsible for reviewing the entire grant application, investigator brochure, and sponsor protocol where applicable. At Subcommittee, any conflicts of interest among reviewers are identified (conflicted reviewers recuse themselves from the meeting) and the primary reviewer is then asked to summarize the background, aims and methods of the protocol, highlight key questions or concerns relevant to the completeness of the application, scientific justification for the study, and human subjects protections considerations.

   Next, the primary reviewer provides a detailed critique of the study, as presented in the PSF and CF, with a focus on risk minimization and compliance with IRB policies and precedent. The reviewer is expected to comment on whether the PSF faithfully reflects the grant, sponsor protocol and investigator brochure. The secondary reviewer then presents his or her critique. When the IRB Subcommittee Chair is not present at the Subcommittee meeting, primary and/or secondary reviewers may be asked to edit the draft memo to be sent by the Protocol Analysts to the investigator summarizing Subcommittee review and required changes.

C. Full Board Review: Either the primary or secondary reviewer assigned for Subcommittee review will also be asked to present (as a "primary" reviewer) when the protocol is assigned for consideration by the Full Board. In addition to the presentation outlined in (b) above, the Full Board primary reviewer is expected to provide a focused review of the Subcommittee's recommendations as detailed in the memo to the investigator and then present the investigator's response. After the Full Board primary and secondary reviewers present, the tertiary reviewer is asked to provide comment on the protocol and consent form.

D. Continuing Review: At continuing review, the primary or secondary reviewers summarize the protocol and review the key elements of the Application for Continuing Approval of Research (ACAR) as outlined in the checklist for continuing review. The reviewers are asked to make a recommendation with regard to approval for consideration and discussion by the Full Board.

E. Modifications Requiring Full Board Review: Modifications requiring Full Board review are similarly assigned to reviewers for presentation to the Board.

6. Protocol Management:

To enhance the quality of review, streamline IRB processing and improve investigator communication, new research studies are assigned to a specific Protocol Analyst to manage the review process from the point of submission through initial approval. Analysts develop areas of interest, expertise and protocol assignments are intended to permit them to develop a "portfolio" of research from particular investigators, research divisions and study types. This promotes consistency and efficiency in review. A Protocol Analyst is expected to obtain and maintain certification as a Certified IRB Professional (CIP).

Protocol Analysts are primarily responsible for ensuring that administrative, regulatory and procedural requirements are met prior to final study approval. To that end; Analysts are responsible for maintaining complete IRB files and IRB database entries for each protocol. IRB Protocol Analysts are the primary liaison with researchers and research staff, and therefore provide education and communicate IRB expectations with regard to protocol preparation and responses to IRB queries and requests. Analysts attend all Subcommittee and Full Board meetings where their studies are reviewed and are expected to identify and provide regulatory guidance to members regarding specific determinations that the IRB is required to make for the particular study. They prepare Subcommittee and Full Board memos for review, revision and approval by the Chair or Chair designee. Protocol Analysts assist the IRB Director of Operations in the completion of minutes of the Full Board meeting. The Analysts "pre-review" responses to Subcommittee memos, responses to Full Board memos and requests for protocol modification for completeness and consistency with IRB rules, and they present a "Protocol Analyst's note" to focus the Chair's review. Analysts also pre-review the consent documents to ensure that required changes (and no other changes) are made. They generate approval notices along with stamped consent forms for the Principal Investigator.

IRB Review in Emergency Situations

The New York State Psychiatric Institute does not conduct planned research involving emergency use of a test article; and exemption from prior IRB approval for emergency use of a test article does not arise in the context of the clinical care and research conducted at the Institute.

Section 4. IRB Office Staff and Description of Responsibilities

1. **IRB Chairman (Part-Time)**: The NYSPI-IRB has two appointed Chairs (i.e., "Co-Chairs"). The IRB Co-Chairs, in concert with IRB Executive Director and the leadership of the NYS Psychiatric Institute, and the Research Foundation for Mental Hygiene, oversee activities of the Institutional Review Board and compliance with Federal, State, and Institutional requirements related to research with human subjects. The IRB Co-Chairs foster the development of standards related to the ethical conduct of research, and the creation and implementation of Institutional policies and procedures for the protection of human research subjects. Specifically, the IRB Co-Chairs:

    A. Report to the Director of Psychiatric Research, New York State Psychiatric Institute.
    Work in close liaison with the IRB Executive Director and Director of Operations on matters related to human subject research.

    B. Actively participate in the development and implementation of IRB policies, procedures and guidelines related to human subject protections.

    C. Actively participate in the ongoing review of IRB policies and procedures to ensure that they are current, complete and consistent with Federal regulations, regulatory guidance, Institutional policies and evolving best practices.

    D. Contribute towards the development and implementation of education and training requirements in human subject protections for the Institute staff, researchers, IRB members and staff.

    E. Assist the Director of Operations in the assignment of reviewers, alternates and consultants.

    F. Direct the proceedings and discussion of the convened Full Board and Ad Hoc IRB meetings.

    G. Communicate with investigators at all stages of the review process regarding IRB actions, requirements and the rationale for them.

    H. Provide support and guidance to investigators in the design and submission of new research protocols and grants in order to fulfill IRB requirements and streamline review.

    I. Review and revise formal internal and external communications involving substantive review issues drafted by IRB Protocol Analysts on behalf of the Subcommittee and Full Board. This responsibility can also be carried out by the IRB Executive Director and Director of Operations.

J. Provide expedited review or designate qualified reviewers to conduct expedited review.

K. Provide final review and make approval determinations regarding research approved pending specified revisions.

L. Meet with investigators, research chiefs and research staff as necessary to address protocol violations and other matters of non-compliance.

M. May suspend IRB approval of research, components of approved research, or a researcher's involvement in research to ensure the safety and well-being of research participants, or when there is evidence of serious non-compliance with IRB requirements. All such suspension of research is reported promptly to the Director of Psychiatric Research, and to the IRB, at the next convened meeting.

N. May require monitoring, auditing and corrective action, including additional training to ensure adherence to IRB requirements and standards for the ethical conduct of research.

O. Assist and supervise the Executive Director and Program staff in the evaluation and response to subject queries, concerns and complaints.

P. Promptly refers any evidence or allegation of research misconduct to the Chair of the NYSPI Research Integrity Committee.

2. IRB Executive Director: The Executive Director reports to the Director of Psychiatric Research, NYS Psychiatric Institute and:

A. Is responsible for the overall operation of the IRB office and the program for human subjects research.

B. Works closely with each IRB Co-Chair, Director of Operations and the Director, Psychiatric Research on all matters related to human subjects research.

C. May review and revise formal internal and external communications involving substantive review issues drafted by IRB protocol analysts on behalf of the Subcommittee and Full Board.

D. Oversees the general function and activities of the IRB office, including matters related to space, staffing and budget, and routinely discusses these issues with the Director Psychiatric Research.

E. Serves as liaison to Research Foundation Mental Hygiene (RFMH) and the Columbia University Medical Center (CUMC) IRB, responds to queries, and oversees the preparation of required reports as required by RFMH policy and the NYSPI-CUMC authorization agreement.

F. Directly supervises the IRB Director of Operations, and shares in the responsibility of supervision of the IRB research compliance monitor with the director of Psychiatric Research.

G. Oversees the recruitment, orientation, training and retention of IRB members.

H. Works closely with the IRB research compliance monitor to effectively carry out Investigational New Drug (IND) and Investigational Device Exemption (IDE) regulatory oversight and to ensure appropriate monitoring of ongoing research for compliance with IRB and regulatory requirements.

I. Is responsible for the development, implementation and dissemination of IRB policies, procedures and guidelines related to human subject protections and keeps the director of psychiatric research apprised of any changes or problems related to existing policies, procedures and guidelines.

J. Is responsible for the ongoing review of IRB policies and procedures to ensure that they are current, complete and consistent with existing federal regulations, regulatory guidance, Institutional policies and evolving best practices, while keeping the director of psychiatric research apprised of the review activity.

K. Oversees the training and education component of the program for human subjects research. Identifies learning opportunities for IRB office staff, board members, investigators, fellows and students. Ensures that IRB review procedures and documentation of review adhere to the requirements of federal and state regulation, guidance and Institutional IRB policies and procedures.

L. Assists the director of operations, as necessary, in the determination of the level of review of newly submitted studies, whether an activity meets the definition of human subjects research, and whether NYSPI is engaged in research.

M. Assumes primary responsibility for the development, implementation and reporting of “metrics” indicative of IRB productivity and efficiency. The Executive Director will work closely with the Director of Operations in the development of process improvements to streamline IRB office operations and decrease time to study approval. (See Section 14. IRB Quality Metrics).

N. May communicate with investigators at all stages of the review process regarding IRB expectations, actions, requirements and the rationale for them.

O. Provides support and guidance to investigators in the design and submission of new research protocols and grants in order to fulfill IRB requirements and streamline review.

P. Attends all convened Full Board meetings to provide regulatory guidance serve as an alternate voting member, as needed.

Q. Is the Institutional contact person for research subject queries, concerns and complaints.

R. Is responsible for documentation of subject complaints and required follow-up and resolution.

S. Is responsible for the preparation of annual reports for RFMH.

T. Presents an annual report to the NYSPI medical staff executive committee.

U. Oversees the recruitment, orientation, training and retention of IRB members.

3. IRB Director of Operations: The Director of Operations reports to the Executive Director and the Director, Psychiatric Research, NYS Psychiatric Institute, and:

A. Is responsible for the overall operations of the IRB Office including supervision of protocol analysts and office staff, scheduling and organization of IRB meetings, communications with investigators and preparation, dissemination, maintenance and storage of materials related to IRB review and approval.

B. Assists the Executive Director in the preparation of annual report for RFMH.

C. Provide assistance to the institutional official or his designee, currently the Deputy Managing Director, investigators and institutional grants offices in preparing reports and responding to queries from federal agencies.

D. May review and revise formal internal and external communications involving substantive review issues drafted by IRB protocol analysts on behalf of the Subcommittee and Full Board.

E. Supervises the protocol analyst team to coordinate IRB meeting agendas and monitor meeting minutes documenting the Full Board's protocol review activity and determinations.

F. Oversees protocol review and the coordination of research subject protection activities among protocol analysts, including (but not limited to), maintaining compliance with institutional policies, communicating with the study investigator and research staff to facilitate protocol submission, review and approval process.

G. Ensure that protocol analysts are correctly reviewing research protocol submissions. Monitors the quality of work output and the workload of each protocol analyst.

H. Provides leadership and continuing education for protocol analysts to enable them to meet and maintain performance standards.

I. Is responsible for the development, implementation, and dissemination of IRB Office policies and procedures related to day to day operations.

J. Ensures that IRB review procedures and documentation of review adheres to the requirements of Federal and State regulation and guidance, and Institutional IRB policy and procedures.

K. Is responsible for assignment of reviewers, alternates and consultants; consults the Executive Director and/or IRB Co-Chairs for assistance with this task, as needed.

L. Is responsible for the preparation of minutes of the convened Full Board meeting.

M. Conducts review of all new protocol submissions to determine if IRB review is required and if so, to determine if expedited review by the Chair or another experienced IRB member or review by Subcommittee is warranted. Determines the level of review of newly submitted studies, whether an activity meets the definition of human subjects research, and whether NYSPI is engaged in research. Consults with the Executive Director and/or IRB Co-Chairs on this determination on an as-needed basis.

N. Communicates with investigators at all stages of the review process regarding IRB expectations, actions, requirements and the rationale for them.

O. Provides support and guidance to investigators in the design and submission of new research protocols and grants in order to fulfill IRB requirements and streamline review.

P. Attends all Subcommittee and Full Board meetings to provide regulatory guidance including identifying and providing regulatory guidance to members regarding specific determinations that the IRB is required to make for the particular study

Q. Collaborates with Information Technology (IT) Support to offer periodic PRISM training and education seminars for the NYSPI research community.

R. Oversees the use of the Protocol Management System and IRBmail, in collaboration with IT Support staff.

4. **IRB Protocol Analyst:** The Protocol Analyst is responsible for managing the review process from the point of submission through protocol termination for an assigned portfolio of research studies. For these studies, the protocol analyst:

A. Is primarily responsible for ensuring that administrative, regulatory and procedural requirements are met prior to final study approval.

B. Is responsible for maintaining complete IRB files and IRB database entries for each protocol.

C. Is the primary liaison with investigators and research staff for a portfolio of studies.

D. Provides education and communicates IRB expectations with respect to protocol preparation and responses to queries and requests from the IRB.

E. Reviews investigator queries in IRBmail, answers queries and forwards others to the appropriate staff or reviewers for action.

F. Attends all Subcommittee and Full Board meetings where her studies are reviewed and provides regulatory guidance to members regarding specific determinations that the IRB is required to make for the particular study.

G. Prepares Subcommittee and Full Board memos for review, revision and approval by the Chair, Executive Director or the Director of Operations.

H. Assists the director of operations in the preparation and completion of minutes of the Full Board meeting.

I. “Pre-review” responses to Subcommittee and Full Board memos, requests for protocol modification for completeness and consistency with IRB rules, and presents a “protocol analyst’s note” to focus the Chair’s review.

J. Provides review of the consent documents against the requirements of the IRB prior to stamping.

K. Generates approval notices along with stamped consent forms for final review and sign-off by the Chair, Executive Director or the Director of Operations.

IRB Protocol Analysts each have areas of expertise and related additional responsibilities, including but not limited to:

A. Management of the IRB budget: Assist the Director of Psychiatric Research and the Executive Director in annual budget preparation, track monthly expenditures, coordinate billing for IRB fees for commercially sponsored research and prepare related reports.

B. Liaison between the IRB Office and the RFMH and CU grants offices**.**

C. Coordination of the Continuing Review process: Track protocol expiration, organize agenda for Full Board review and send reminders for renewal of study approval to investigators.

D. Development and maintenance of the IRB website, ensuring all content is current and fully accurate.

5. **IRB Research Compliance Monitor**: The Research Compliance Monitor is responsible for monitoring NYSPI IRB approved human subjects research, and is supervised independently the Director, Psychiatric Research and the IRB Executive Director.

The Research Compliance Monitor:

A. Is responsible for the scheduling and completion of routine compliance audits of study records for more than minimal risk research.

B. Is responsible for "for-cause monitoring" and "special monitoring" including consent and procedural observation, at the request of the IRB Co-Chairs, Executive Director, and/or the IRB.

C. Reviews all submitted self-monitoring forms.

D. Is the primary liaison between the IRB and investigators and research staff with regard to research compliance findings and corrective action plans.

E. Communicates with investigators and research staff to educate them about the monitoring program, train them to use the self-monitoring form, inform them of monitoring findings and review corrective action plans.

F. Is responsible for preparing monitoring reports and presenting them at IRB Full Board meetings.

G. Is responsible for pre-review of serious adverse event reports.

H. Is responsible for reviewing reports of protocol noncompliance for triage to the IRB co-chairs and executive director and referral to other institutional officials, including the chair of the research integrity committee when appropriate.

I. Is responsible for tracking and follow-up on special monitoring requirements, AE reports, and "reports back" from investigators.

J. Prepares memos to communicate determinations made by the Chair or IRB regarding monitoring findings, serious adverse events and noncompliance.

K. Maintains files of monitoring reports and related correspondence.

L. Maintains an electronic database of serious adverse event reports.

6. **Senior Administrative Assistant for the IRB:** The Senior Administrative Assistant reports directly to the Director of Operations, and also provides general assistance to the IRB Executive Director, Co-Chairs and IRB Office.

A. Oversees the clerical functions of the office and manages and maintains IRB records and files.

B. Prepares meeting materials, meeting schedules, agendas and attendance, and oversees mailings and related office work flow.

C. Logs in and enters new protocol submissions into the IRB protocol tracking system.

D. Assumes a lead role in tracking study protocol activity and deploying interventions to reduce time to IRB approval.

E. Responds to queries from investigators and staff regarding PRISM and communicates directly with IT to provide technical support.

F. Organizes and prepares educational materials for varied IRB educational activities conducted by the IRB executive director.

G. Directly supervises the Secretary/Administrative Support Assistant.

7. **Secretary/Administrative Support Assistant:** This position reports directly to the Senior Administrative Assistant to the IRB, and also provides general assistance to the IRB Executive Director, Director of Operations and Co-Chairs.

    A. Provides general clerical support to the IRB, Institutional Review Board Office. Duties include data entry and management, filing, mailing, electronic scanning and sending correspondence.

    B. Assembles Subcommittee and Full Board mailings.

    C. Maintains the "Research Study Opportunity" bulletin board on the 5th and 6th floors of the Herbert Pardes Building.

    D. Maintains the storage file room (Basement level of the Pardes Building) to ensure all files are secured, clearly labelled, neatly stored and consistent with building code for storage.

    E. Provides essential administrative backup for the IRB Senior Administrative Assistant.

Section 5. Materials Required for Review

1. **Materials required for submission as part of initial review of new research are submitted electronically through the Psychiatric Research IRB Submission Module (PRISM). This module is accessed through the NYSPI IRB website (http://irb.nyspi.org).**

    A. The protocol summary form (PSF): To evaluate each human subject protocol fully in accordance with 45CFR46.111 and local Institutional policies, information must be organized using a current version and instructions of the NYSPI protocol summary form or "PSF". The attestations must be accepted electronically in PRISM, by the Principal Investigator, a faculty sponsor if one is required for the study and the Principal Investigator's Research Chief.

    B. Informed consent documents: Consent and assent documents, informed consent cover sheets (if required), screening consent documents (unless screening is covered under a currently approved IRB protocol), oral consent scripts, information sheets, and texts of any recruitment material or advertisements. Sponsor and multicenter study consent forms must be revised in accordance with NYSPI-IRB requirements prior to submission.

    C. The complete grant application and supporting materials.

    D. The sponsor protocol (if industry sponsored or part of a multi-center contract) and any other protocol describing the proposed study, e.g. study proposal for investigator initiated studies.

    E. The Investigator Drug/Device Brochure (if industry sponsored).

2. **Materials distributed for review by Subcommittee at least seven (7) days prior to review**

    A. All materials in 1A. through 1E. (Indicated above) are provided electronically to all Subcommittee members approximately one week prior to meeting.

3. **Materials distributed to each member of the IRB six (6) days prior to the convened meeting for review of new research**

    A. All materials in 1A. through 1E. are provided electronically to all Board members.

    B. Any memos to the investigator from the Subcommittee requesting information and revision.

    C. Investigator's point by point response to Subcommittee memos.

D. The revised PSF modified based on Subcommittee review with changes highlighted.

E. The revised consent materials modified based on Subcommittee review with changes highlighted.

F. Other supporting materials requested by the Subcommittee.

4. Material required for submission by the investigator for review by the Chair following Full Board approval pending revision and following expedited approval by Subcommittee pending revision:

A. The memo to the investigator from the Full Board or for expedited research, from the Subcommittee or Expedited Reviewer.

B. The investigator's point-by-point response to the IRB memo.

C. The protocol summary form (PSF) revised in accordance with the stipulations of the IRB with all changes highlighted.

D. Revised consent and recruitment materials highlighted with IRB required changes and finalized ("clean") versions (for stamping).

E. Other materials requested for the IRB file.

5. Materials required for submission by the investigator for continuing review of research

A. A completed and signed Application for Continuing Approval of Research (ACAR) sufficient for the IRB to determine that the criteria for approval of research continue to be met.

B. A memo describing any proposed changes to the approved protocol.

C. A PSF; with any newly proposed changes made and highlighted for review.

D. Consent and recruitment materials; revised and highlighted, if applicable, and "clean" versions (for stamping).

6. Material distributed to each member of the Full Board for review of applications for continuing approval

A. Guidance for Reviewers.

B. Items 5A. through 5D., as above.

C. A description of all protocol amendments approved by the IRB during the prior 12 month approval period (generated from the IRB's Protocol Management System database).

D. A description of any findings by the IRB research compliance monitor as a result of routine or special monitoring (see section 9).

7. Modifications to approved research

A. All requests to modify approved research must be submitted electronically by completing an electronic modification form in PRISM. This form requires the Principal Investigator to describe the proposed change(s), describe the rationale for the change(s), and address relevant risk/benefit considerations.

B. The PSF must be modified as appropriate to describe the changes, and all changes must be highlighted to facilitate review.

C. When consent forms require modification, changes should be highlighted to facilitate review.

8. Reporting of adverse events/unanticipated problems

A. Investigators must complete the Serious Adverse Event reporting form or submit a memo describing the potential unanticipated problem involving risks to subjects or others (See Section 10).

9. Protocol exception requests

A. Protocol exception requests should be described in a memo to the IRB. The specific inclusion or exclusion item(s), study procedure or other component for which the exception is requested should be cited. The memo should include a justification for the exception, a brief description of the subject and the extent to which the exception may place a given individual at increased or decreased risk of harm. When appropriate, the memo should also include the procedure by which the subject will be informed of the exception.

Section 6. Procedures for Review

1. New Research Protocols/Initial Review

A. Submission of new research protocols:

I. All information regarding meeting dates, submission deadlines and required material is available on the IRB website.

II. Research proposals are submitted electronically for review using PRISM, the "Psychiatric Research IRB Submission Module". This electronic system is tailored to the research proposal. This feature facilitates the submission and management of electronic submissions (initial review, continuing review and protocol modifications) to the NYSPI IRB. Upon initial submission, the principal investigator is required to complete a Protocol Summary Form (PSF) in PRISM (See Attachment 1b).

The PSF mirrors a standard research protocol with respect to structure (e.g., Study Aims, Research Design, Sample, Methods, etc.) and also queries investigators about important elements (e.g., funding, categorization as a clinical trial, etc.) of the study.

III. Submission deadlines ensure that material for review at Subcommittee or the Full Board is distributed to reviewers at least six (6) days in advance of scheduled meetings.

IV. With the approval of the IRB Chair and notification of primary and secondary reviewers, additional material for review may be disseminated to the IRB, but no less than three (3) days prior to the meeting.

V. IRB Administrative staff review new submissions to ensure that material required to initiate review is provided. Only protocols submitted by the principal investigator and research division chief are accepted for review.

VI. All new protocols are assigned a unique IRB number. Numbers are assigned consecutively and entered into the IRB database. Protocols submitted for a five-year continuation review are assigned a new number with an "R" suffix. Protocols submitted from the Buffalo Psychiatric Center are assigned a new number with a "B" suffix.

VII. Investigators are sent an email acknowledgment of the receipt of the initial submission that includes the protocol number assigned to the research project and a request for submission of the Conflict of Interest forms. Investigators also are provided with links to IRBMail and to the IRB website.

VIII. The review history in the IRB database is updated to show, "tracking commenced."

B. Determining when IRB review is not required:

I. Information is provided on the IRB website to assist investigators in determining whether their work is "research", whether it involves "human subjects", and if it requires review by the NYSPI IRB. However, investigators are encouraged to seek informal and formal advice from the IRB by writing to IRBmail, or by directly contacting the IRB director of operations or executive director. Most often, Investigators submit a proposed research activity as an application, completing a PSF within PRISM. Following the PRISM submission, the federal definition of human subjects research is employed by IRB administrative leadership to determine whether the proposal meets the federal regulatory definition of human subjects research (HSR), or not human subjects research (NHSR).

II. The distinction between "research" as defined within 45CFR46.102(d) and "clinical investigation" within 21CFR56.102 (c), and related activities that may not require IRB review, often requires input from IRB staff and Chairs prior to submission. The Director of Operations or Executive Director will decide what information is necessary or if the submission of a formal protocol is required to determine if the activity

1) Does not constitute research.
2) Does not involve human subjects.
3) Does not constitute research for which NYSPI/RFMH, other OMH facility for which the NYSPI is conducting a review or CUMC is "engaged".
4) Does not constitute an activity that otherwise requires NYSPI IRB review under our FWA or OMH/RFMH requirements.

III. Investigators are notified in writing of the determination. It is the responsibility of the principal investigator to ensure that the IRB is informed if the scope of the work changes to include activities that could constitute research involving human subjects, and to ensure that no human subjects research is initiated prior to IRB approval.

IV. Projects that do not meet the criteria for human subjects research activity are maintained as individual files and recorded in the PRISM database as "NHSR", Not Human Subjects Research. Unless the Principal Investigator submits a modification that alters the initial determination, no further IRB review is conducted.

V. Studies of Existing Data and Specimens:
Research involving existing data and specimens when human subjects are not readily identifiable does not require IRB review. Readily identifiable means that human subjects can be identified directly or through codes linked to identifiable information. Data/specimens are not considered readily identifiable according to NYSPI IRB when codes cross linked to the identity exist and are maintained by an investigator at another institution, and the NYSPI investigator provides a written assurance that he or she will not have or seek access to subject identity. When such codes are maintained at NYSPI or CUMC, then the information is ordinarily considered readily identifiable.

VI. Review of Training Grants, Center Grants, and K-Awards:
The principal investigator of the project is required to submit a copy of the grant and a written overview of the aims of the grant, including a statement that during the period of the award no human subjects will be involved in any research without prior IRB approval. The IRB assigns a tracking number and the Investigator is informed in writing of the IRB's determination. If required, certification to HHS (formerly "310" form) will note that the activity contains multiple projects, some of which have not been reviewed.

C. Levels of Review

New studies are assigned a level of review by the IRB director of operations in consultation with the IRB Chair, as needed. The level of review is based on risk, subject vulnerability, and the complexity of the proposed work. Research which falls within the category of exempt research under the Federal regulations (45CFR46.101(b)) is reviewed by the IRB as if it were covered by the DHHS regulations (an expedited procedure may be used). The following categories are applied at the time of initial submission;

1) Not Human Subjects Research
2) Expedited Review
3) Review by Subcommittee

I. Expedited by Co-Chairs or designee: New research involving data analysis, record review, survey research, low risk and other low complexity research is reviewed either a Co-Chair, the executive director or other IRB members designated by the Chair have the authority to review and approve research as defined by 45CFR46.110 (a) & (b).

II. Review by Subcommittee: All other new human subjects research is assigned to Subcommittee for review. The Subcommittee retains discretion to send protocols to the Full Board for review, that do not meet criteria for Expedited Review under 45CFR46.110 (a) & (b).

D. Procedures Specific to Subcommittee Review:

I. An IRB Subcommittee conducts a first step review of all new research (except as in cii above) and major modifications to approved research. The review focuses on readiness of the submission for review, scientific merit, design, and risk-benefit considerations, with an emphasis on minimizing risk. The Subcommittee also provides an opportunity for education and training of IRB reviewers and researchers (Section 11).

II. Structure and membership: Each of four Subcommittees of the IRB meets monthly for two hours. Three of the Subcommittees focus on adult clinical and biological protocols (the area of greatest volume) and one Subcommittee focuses primarily on research involving children. A protocol is assigned to a Subcommittee based on its IRB Office receipt date and the next scheduled Subcommittee meeting. For studies involving a pediatric population, members from the Subcommittee expert in reviewing research with minors are sometimes asked to attend an alternate Subcommittee meeting to avoid delays in review of this research.

Each of the Subcommittees has a dedicated Subcommittee Chair, who is also a member or Chair of the Full Board. The standing membership of the Subcommittees includes IRB scientific members and alternates. Consultants with necessary expertise beyond that available on the IRB may be asked to participate at this stage in review. A Protocol Analyst is assigned to a given protocol by the Director of Operations. At the Subcommittee meeting, the Protocol Analyst is responsible for providing regulatory guidance, taking notes and preparing a memo to be sent to the Investigator.

III. Authority: The Subcommittee may determine that the submitted protocol is incomplete and therefore “not reviewable” as submitted and requires significant revision. It may determine that a protocol is eligible for approval on an expedited review or pending revision, on an expedited basis. Finally, the Subcommittee may determine that, pending revision, the protocol may be reviewed by the Full Board.

IV. Communication with Investigators: Following Subcommittee review a detailed memo is promptly sent by the Subcommittee Chair to the Investigator. This memo summarizes the Subcommittee’s critique and typically requests protocol and consent revisions, justification of risk and clarification of procedures necessary for approval of studies eligible for expedited approval, or for review at the Full Board for other research.

V. Documentation of Subcommittee review: Notes are taken and deliberations are audio-taped to assist in the development of a detailed memo. No formal minutes are maintained; the memo to the Investigator represents formal documentation of Subcommittee review. Recordings are maintained only until memos are completed.

VI. Conflict of Interest: The same conflict of interest rules applied to Full Board review are operative at Subcommittee review (See Section 8).

VII. Confidentiality: All reviewers and visitors to Subcommittee are required to sign an IRB confidentiality statement.

E. Procedures Specific to Full Board Review:

I. The convened IRB meets twice monthly typically on Mondays from noon to 3pm. Additional meetings are scheduled as necessary.

II. The schedule of meetings is posted on the NYSPI IRB website along with deadlines for submission of materials.

III. The director of operations assigns research submissions requiring Full Board review and approval to the next scheduled full-board meeting, unless an IRB member with required expertise is unable to attend.

IV. Reviewer Assignment:

1. New research will ordinarily have been reviewed by Subcommittee and is assigned to the primary and/or secondary reviewers involved in the Subcommittee review, where possible.

2. For Full Board review, three reviewers are assigned: a primary reviewer, a secondary reviewer and a tertiary reviewer (a non-scientific member).

V. Agenda Preparation and Distribution of Materials:

1. IRB clerical staff assembles electronic information packets for Board members which include a preliminary meeting agenda and the material to be reviewed. As material is submitted, it is logged into the IRB database and scheduled for review. The agenda is generated from the database.

The agenda is sent to IRB members with a link to each protocol in PRISM with all related review materials contained within an electronic "study folder" for easy access. These study folders are distributed to each member of the Board approximately one week in advance of the scheduled meeting date.

For new studies, the electronic study folder includes a copy of the PSF, the Sponsor protocol (if available at the time of review) or full grant, Informed Consent documents, recruitment materials (e.g., flyers, advertisements, phone screenings, scripts), correspondence from the Subcommittee and the Investigator's point-by-point reply. Any additional relevant correspondence from consultants and others who have contributed to the review is included.

2. The agenda may be revised on the day of the meeting to include any revisions to the reviewer list and any supplemental material that may be distributed at the meeting, for example, material which may have been distributed by email prior to the meeting.

   The agenda includes, but is not limited to:

   (1) The meeting date, time and location.
   (2) Protocols to be reviewed along with discussion items.
   (3) Previous meeting minutes for review and approval.
   (4) A report of previously approved expedited research protocols for the prior month.
   (5) A report of modifications approved on an expedited basis for the prior month.
   (6) A report of continuations that qualified for expedited review/approval for the prior month, and the reporting of compliance monitoring activities.

VI. Verification and Maintenance of a Quorum:

1. The IRB Chair and Director of Operations are responsible for ensuring that at least one member or consultant is present with adequate expertise in the areas of the research presented.

2. A quorum consists of a simple majority of the voting membership, including at least one member whose primary concern is in a non-scientific area. The IRB Chair, with the assistance of the IRB staff, will confirm that an appropriate quorum is present before calling the meeting to order.

To ensure the presence of a quorum, alternate members may be required to participate. Quorum includes those participating by teleconference. Members present via teleconferencing are noted as such in the meeting minutes. Such members receive all pertinent information prior to the meeting and are asked to participate actively and equally in the discussion and vote.

The IRB Chair will be responsible to ensure that the meetings remain appropriately convened.

3. One IRB Administrator (i.e., Protocol Analyst) is assigned to record the attendance of members. If at any time during the meeting, the quorum is not maintained, the assigned Protocol Analyst will notify the Chair and the proceedings of the meeting requiring convened meeting review will be suspended until the quorum is re-established or the meeting will be adjourned.

4. IRB members who have a conflict of interest with a particular protocol, event or issue that is reviewed by the IRB are expected to absent themselves from Board deliberations and votes. This means that the Board member must leave the room during the discussion and vote and will not count toward the quorum for that review. Questions may be asked of the member before the completion of discussion. During the preparation of the agenda the IRB staff identifies those submissions for which a Board member who is expected to be in attendance for the meeting has a conflict; this helps to ensure compliance with the need for any such member to leave the room during the discussion of the protocol for which a conflict exists (See Section 8. Conflict of Interest).

VII. Presentation of IRB Materials and Vote:

1. Each research study is presented separately.

2. The primary and secondary reviewers are asked by the Chair to lead the discussion of the study. The primary reviewer is expected to begin with an overview of the research proposal and then focus on key concerns related to scientific merit, if any, and human subjects protections, then provide a focused review of the Subcommittee's recommendations as detailed in the memo. The Investigator response to the Subcommittee's request is then reviewed.

3. After the primary and secondary reviewers present, the tertiary reviewer is asked to comment on the protocol and consent form. Following open discussion and response to the reviewers' presentation, if there is general consensus, the IRB Chair will call for a vote for approval, approval pending revisions, reconsideration/deferral, or disapproval. The vote of a two-thirds majority of members present will determine the final approval.

VIII. IRB Actions/Determinations:

1. Approved: If the convened IRB determines that the study can be approved as submitted, the Investigator is issued an approval. The date of the convened meeting will serve as the date of initial approval and the date of expiration is based on the date of the meeting (minus one day) unless a shorter approval period is determined by the IRB.

2. Approved Pending Revisions: If the convened IRB decides to approve a research study subject to modifications, the written notification to the Investigator indicates the specific revisions stipulated by the IRB in order to obtain full approval to conduct the research.

   A. **Simple Concurrence**: A study may be approved with explicit conditions when the convened IRB is able to stipulate specific revisions that require simple concurrence by the investigator. If the IRB approves a study pending investigator agreement with explicit conditions, then the IRB Chair, or other qualified IRB member may review the revised research protocol under an expedited review procedure, to determine whether the investigator has incorporated the specified explicit conditions into his or her project (i.e., determination of "simple concurrence").

      This requirement means that the IRB may only request protocol modifications whose review does not require significant judgment on the part of the Chair or other IRB member serving as a reviewer. Such modifications include those that are precisely outlined in the memo from the IRB, changes that require modifications to reflect standard policies, procedures or precedent from other approved research. Changes that do not relate in significant fashion to the criteria for approval and changes to the consent form that do not substantially alter its meaning or require special expertise in its review.

Simple concurrence also means that the Investigator agrees with the Board's request and needs only to provide further elaboration on the matter and revised documents so that the Chair or other reviewer can confirm that the Investigator has made the modifications. In the event that the response is not satisfactory or the Investigator does not agree with the changes, the response is re-reviewed at a convened meeting.

3. Deferral: If the convened IRB is not provided with sufficient information or identifies significant questions or concerns that require revision of the protocol or new information, a decision to defer a vote and table review of the research is made. The Investigator is provided with written notification and a list of the problems and/or questions with instructions to resubmit the research for Full Board review. In some instances, the Full Board may request that the research study be returned to the Subcommittee and then for re-review by the Full Board.

   Proposed research may also be tabled due to loss of quorum or lack of appropriate expertise present at the meeting.

4. Disapproval: If the convened IRB decides that the proposed research has fundamental design problems, presents significant ethical or safety concerns to human subjects, or otherwise fails to meet regulatory requirements for approval and modification is unlikely to give rise to an approvable protocol, the research will be disapproved. The Investigator and his/her Division Chief are notified in writing and provided with information about the concerns that must be addressed before the study can be resubmitted for IRB Full Board review. In addition, a meeting is ordinarily scheduled with the IRB Chair to review the Board's determination. A disapproval can only be issued by the Full Board.

IX. Appeal Against IRB Decisions

When a research proposal is disapproved, or changes are required, the investigator may request a re-examination of the protocol by the IRB. The IRB allows the investigator to present his/her case, in person or in writing, and complies with subsequent requests for re-review if the investigator has made significant changes to the study or has significant new information to present. The IRB assists in this process by supplying the investigator, in writing, with its reasons for disapproval or for requiring changes, and the investigator should be provided the opportunity to address the IRB and to provide additional references and/or consultants' reports which may support his/her case. Every effort should be made by the IRB and the investigator to act in good faith to resolve disagreements.

X. Notification of Board Actions/determinations
Investigators are notified promptly in writing of the Board's actions indicating approval, approval pending revision, deferral, or disapproval of research. This notification is sent electronically to the Principal Investigator.

XI. Meeting Minutes
The minutes for a convened Board meeting will include sufficient information to comply with regulatory requirements and to serve as documentation of meeting attendance and actions taken at the meeting.

1. Each protocol submission reviewed by the Board is listed separately by IRB number, Principal Investigator name, and protocol title. For each research submission, the minutes will address:

   A. The action taken.

   B. Documentation of the numerical vote in favor, against and abstaining.
   C. The risk level of the research.
   D. Additional safeguards for subjects vulnerable to coercion or undue influence.
   E. The IRB approval interval designated by the committee.
   F. Special monitoring designated by the committee.
   G. Pertinent comments or concerns expressed during the open discussion of the research, to include significant new findings to be communicated to research subjects, a summary of controverted issues and their resolution, and recommendations for revisions as conditions of approval.

2. IRB Protocol Analysts are responsible for taking notes to assist in the preparation of correspondence to research Investigators and in the preparation of the minutes.

3. The minutes are submitted by the Director of Operations and reviewed and accepted by the Board at a subsequent convened meeting. The minutes are modified as necessary to obtain the approval of the Board. Investigators are notified should any of the modifications of the minutes affect the approval status of their research.

2. Review by Facility Director

A. All protocols that involve human subjects must be approved by the NYSPI Facility Director (or designee) to certify that:

   i. he research is appropriate to the mission of Institute, and
   ii. the necessary resources, facilities and staff can be committed to the project

B. In accordance with NYS OMH policy, the Director also is required to approve the use of any investigational drugs or devices used in the research.

C. The Director may approve, disapprove or approve with conditions. However, the Director does not have the authority to overturn disapproval by the IRB. The Director may disapprove a study that has been approved by the IRB.

3. Modifications

A. Changes in previously approved research may not be initiated without prior IRB review and approval unless such a change is necessary to eliminate or minimize imminent harm to subjects. Request for exceptions to protocol requirements for individual subjects are reviewed and handled as modifications to approved research.

B. Changes in approved research to eliminate an immediate hazard to subjects when there is not sufficient time for IRB review before the change is implemented, OR that have been discovered to have occurred for other reasons (i.e. protocol violation or deviation) must be promptly reported to the IRB and reviewed by the IRB to determine whether the change is consistent with ensuring the subject's continued welfare and to determine whether any corrective actions or reporting are required.

C. Investigators sign an attestation in the PSF stating "No changes will be made without the prior written approval of the NYSPI-IRB." A statement of the requirement is also included on the IRB approval notice.

D. Submitting modifications in PRISM

   i. The Principal Investigator is required to submit an amendment in PRISM which includes an explanation of the requested change, a rationale for the required change, and a discussion of changes to the risk-benefit analysis, if any.

   ii. Investigators are asked to highlight or "bold" the changes so they can be readily identified by the reviewers.

E. Level of Review

I. Minor Change: Minor amendments to approved studies may qualify for expedited review under 45CFR46.110. Minor changes do not increase the level of risk to patients/subjects and do not involve invasive procedures (including x-rays) or procedures for which Full Board review is necessary. Examples of minor changes to previously approved protocols include the following:

1. We define "Minor" in 45CFR46.110(b) (2) as a "minor change in the overall assessment of the study's risk and benefit.

2. The addition of new interventions which themselves qualify for expedited review under 45CFR46.110 (b) (1) can be reviewed using expedited procedures.

3. For a "more than minimal risk study" originally approved by the Full Board, changes that significantly alter the study's aims or goals may not be expedited.

4. An increase in the number of study subjects may be expedited if it is consistent with the scientific objectives of the study and does not adversely impact the risk-benefit assessment for any subgroup of subjects or the study group as a whole.

II. Expedited review:

1. Review and approval of minor changes in previously approved research during the period (of one year or less) for which IRB approval is authorized may be conducted under an expedited review procedure in accordance with 45CFR46.102 (i).

2. Review and approval may be carried out by the IRB Chair, an IRB Subcommittee, or may be delegated to an IRB member.

3. Modifications approved on an expedited basis are presented and ratified to the Full Board in a monthly report of all amendments approved on an expedited basis and upon continuing review of more than minimal risk research on a study-by-study basis.

iii. Full Board review: Changes that represent more than a minor change to previously approved research require review by the Full Board.
   1. The Protocol Analyst typically consults with the IRB Executive Director or Director of Operations and a recommendation is made regarding whether the changes should first be reviewed by a Subcommittee or whether the modified study can be forwarded directly for review by the Full Board.
   2. Modifications requiring Full Board review are assigned to primary and secondary reviewers for presentation to the Board.

F. Notification of IRB determinations

i. Investigators are informed in writing of the outcome of requests for modifications to a protocol whether from a Full Board or expedited review procedure.

4. Continuing Review

A. The IRB sends notices to investigators whose studies will expire in 60 days, reminding them to submit their continuation applications. If the application has not been received in 30 days, a second reminder is sent. If no response is obtained as a given study approaches a lapse of IRB approval, a phone call is placed to the Principal Investigator by an appointed staff member (e.g. Executive Director) to determine investigator intentions regarding the protocol. Should the study's IRB approval expire prior to investigator contact or response, he/she will then be promptly informed via email that IRB approval has expired, and new enrollment and all research procedures must cease. If there is the potential for subjects to experience harm by ceasing all procedures, the Investigator must apply to the IRB for permission to continue only those procedures that are essential.

B. Elements of an Application for Continuing Review of Research
Continuation review requires submission of the following information into the PRISM continuing review application:
   A. Number of subjects entered, completed and currently enrolled, and the number who withdrew themselves or were withdrawn by the Investigator. Reasons for withdrawal must be included.
   B. Description of any previously unknown risks to subjects, including AEs that have and have not been previously reported.
   C. Significant new information, including a description of any relevant literature or other studies that may alter the relevance of the trial.
   D. The consent forms and updated PSF.
   E. A cover memo describing any modifications.

A. Level of Review
   a. Applications for continuing approval of studies that originally received Full Board review are reviewed by the Full Board; applications for studies that were approved by expedited review are expedited, except as follows:

   b. Even if it would otherwise receive Full Board review, a study that has not yet begun to enroll subjects, and for which no new risks have been identified, may receive expedited review.

I. Similarly, a study in which enrollment and all research interventions are completed, a

II. The IRB reserves the right to conduct Full Board review of any study, even if it would ordinarily be scheduled for expedited review, for any reason but particularly if there are new questions regarding risk to subjects.

III. If there is a change in risk or if additional oversight is considered necessary for any other reason, the length of future approvals may be shortened at the time of review.

IV. The Board may determine, at a convened meeting that a study that had previously received Full Board review is eligible for expedited review in the future, based on a re-assessment or change of the risks.

B. All studies must be re-approved at least annually. Continuing review must be substantive and meaningful.

I. The approval period is determined by the IRB at the time of original approval and at subsequent continuing review.

II. The duration of the approval period and other conditions or limitations on approval depend on an number of factors including the overall risk of the study, the novelty of the investigational agent or intervention (and therefore the availability of information about risk or benefit), concerns about feasibility, and vulnerability or susceptibility of the population.

III. In lieu of limiting the duration of the approval period to less than one year, the NYSPI IRB may request special monitoring or re---review of specific data related to subject safety once subject enrollment begins. Special monitoring or re---review of data is to be conducted by the Research Compliance Monitor, and reported back to the convened IRB. The IRB may impose additional requirements including, but not limited to, the following:

1. That a limited number of subjects be studied to provide pilot data on risk before approval of the larger proposed sample is given.
2. A case-by-case "report-back" on a specified number of subjects enrolled in the study.
3. Special monitoring such as observation of the consent or research procedure by the IRB Research Monitor or an IRB member.
4. Feedback surveys from the subjects on their experience of the consent process or research procedures.
5. Upon review of cases, the IRB may require new information or study modification, continue feedback reporting, or suspend a study.

C. At least every 5 years, a study is reviewed as if it were a new protocol submission. The investigator must submit his/her full protocol in PRISM and include a current Protocol Summary Form (PSF) with all relevant signatures, new consent forms, a copy of the grant/sponsor's protocol/Investigator's brochure, as relevant, and other relevant materials (recruitment materials, non-standard questionnaires, etc.).

Section 7. Approval Criteria

1. Criteria for IRB Approval of Research

The Full Board or in the case of research that qualifies for expedited review, a Co-Chair or Chair designated IRB member, must determine that each criterion found at 45CFR46.111 and 21CFR56.111 and requirements found in applicable Subparts of 45CFR46 are considered and satisfied during the review process before research can be approved.

A. Risks to Subjects are Minimized

- Identification of Risk:
  1. The identification of study risk involves a careful analysis of the proposed study procedures and interventions, the qualifications of staff involved in implementation of study procedures, and the characteristics of the proposed study population.
  2. Reviewers must evaluate the potential for research---related harm and other untoward consequences along many dimensions including physical, emotional or psychological, social/interpersonal, legal, economic, and dignitary.
  3. Risks related to breach of confidentiality are of special concern in research involving psychiatric, substance abuse, and HIV---infected populations commonly studied by NYPSI researchers.
  4. The unique vulnerabilities and susceptibility to risk of children, prisoners, individuals with cognitive impairment and pregnant women require special attention.
  5. Reviewers should evaluate available information on the safety and efficacy of study procedures, particularly novel or investigational interventions, in general and in the proposed study population in particular.
  6. Reviewers should consider the risks associated with research-related delay to treatment associated with the morbidity of underlying primary and co-morbid conditions.
  7. Reviewers should consider risks associated with choice of research design and methodology, outcome measures, and selection of comparison group(s).
  8. Reviewers should consider the training, experience, and supervision of researchers and research staff.
  9. Reviewers should consider whether there are subgroups of subjects who are unlikely or less likely to benefit from study involvement or will be at higher risk.
  10. Reviewers should consider the measures by which common or foreseeable study risks will be assessed.
  11. Research related risk may affect individual research participants but also the communities they represent and to others such as family members.
  12. The possible long-range effects of applying knowledge gained in the research (e.g. the possible effects of the research on public policy) is not within the purview of IRB responsibility 45CFR46.111(a)(2); 21CFR56.111(a)(2). However, the IRB may advise Institute Administration of such concerns if they are identified during the IRB review process.

II. Minimizing Risks: Risks to subjects shall be minimized by:
1. using procedures which are consistent with sound research design
2. using procedures which do not unnecessarily expose subjects to risk, such as reducing or eliminating an exposure
3. whenever appropriate, using procedures already being performed on the subjects for diagnostic or treatment purposes
4. developing clear and justifiable inclusion/exclusion criteria
5. appropriate monitoring of the subjects for earlier detection of risks or harms
6. incorporating explicit drop-out criteria within the study protocol to reduce the risk of harm

III. Points to consider in review include:
1. Risks that are not scientifically justifiable should be eliminated, to the extent possible. Study designs that introduce risk (e.g. randomized placebo controlled trials in a patient population) that are not supported by preliminary clinical data should be preceded by preliminary, lower risk research (e.g. safety and tolerability studies in healthy subjects).
2. Less vulnerable and less burdened groups should be studied first.
3. Eligibility screening and related inclusion and exclusion criteria should be refined in effort to minimize exposure to risk for those at highest risk and those least likely to benefit from participation.
4. In studies involving treatment, drug washout, or other delay to standard care for patients, study drop---out criteria based on worsening or failure to improve should be introduced to limit research related harm.
5. Drug washout periods and research related delay to treatment should be minimized.
6. Safety assessment, monitoring, and emergency procedures should be established and implemented to identify, respond to and limit untoward consequences of research participation.
7. The experience and qualifications of the principal investigator and other members of the research staff must be appropriate to the nature of the study and their specific roles in the study.

B. Risk is Reasonable in Relation to Study Benefit

I. The approval of research under Subpart A requires an IRB to determine "that risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result." [45CFR46.111(a)(2)]. IRBs have latitude in deciding when research offers a reasonable balance of risks to benefits. "Reasonable" may include circumstances in which no direct benefit to the subject is anticipated.

II. The following are some points to consider:

1. The determination that the relationship of risks to benefits is reasonable requires a careful analysis by the IRB of several pertinent variables, including: the degree to which the research introduces risk, presents a risk/benefit profile which departs from standard care, offers a prospect of benefit available only in the research, will yield knowledge that will benefit others, whether the research involves minors, or individuals with diminished capacity, and the extent to which

informed consent by a legally authorized representative can be considered equivalent to that of the research participants (SACHRP Secretarial Letter, July 2009, OHRP Website).

2. In evaluating risks and benefits, the Board should consider only those risks and benefits that may result from the research as distinguished from risks and benefits of therapies that subjects would receive even if not participating in the research.
3. Reviewers should carefully evaluate the risk---benefit ratio in each subject population defined in the study (e.g., intervention versus control group) as well as for the aggregate study population.
4. Benefits related to importance of the research should consider, among other factors, the experience of the investigator, whether the study has been peer reviewed, the soundness of the study design, whether the projected subject accrual is feasible, whether the study is sufficiently powered to answer the questions posed etc.
5. What is "reasonable" may differ depending on the degree of vulnerability of the study population.
6. A risk that is not scientifically justifiable cannot be considered an acceptable risk.

C. Selection of Subjects is Equitable

I. The IRB will determine that selection of subjects in each protocol is equitable, taking into account the purposes of the research and the setting in which the research will be conducted.

II. Points to consider include: At the time of initial and continuing reviews, reviewers should consider the characteristics of the anticipated subject population (e.g., ethnicity, race, gender, and degree and nature of vulnerability):

1. Reviewers should consider whether the selected populations are representative of populations with the condition or disorder being studied, and that significant departures are justified.
2. Reviewers should evaluate whether the study unjustifiably excludes groups that have been traditionally under---represented, or burdens such groups without the likelihood of group or individual benefit.
3. Vulnerable populations should never be called upon to take part in research for reasons of cost or convenience alone.

D. Informed Consent Will Be Sought From Each Prospective Subject

I. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

II. Points to consider during initial and continuing review to ensure that the research satisfies requirements for informed consent at 45CFR46.111 and 116 and at 21CFR50.20, as appropriate:

1. The consent process begins with the process of advertising. Materials and approaches must promote informed decision---making with the direct and honest disclosure of relevant information.
2. The context in which consent is sought should be considered by the reviewer. Circumstances must support decision---making by permitting the subject adequate time to consider the information or to consult with others about the choice, if desired. To the extent consistent with the scientific goals of the study consent should not be solicited when factors such as physical discomfort or pain, medication effects, or acute distress are likely to interfere with reasoning or choice. In those cases where the context may interfere with the consent process the IRB must consider appropriate additional safeguards to mitigate this risk.
3. Reviewers should evaluate whether the recruitment process minimizes the possibility of coercion or undue influence, or the appearance of this. In general, subjects should not be approached directly by researchers or research staff. Instead, the consent should include procedures that provide subjects with the opportunity to first consider if they want to learn more about the research. Direct calls to subjects' homes, and direct approaches to subjects in clinic waiting areas, for example, are strongly discouraged. For research involving students or staff, consent should not be obtained by those in a supervisory role. In other words, the recruitment of study candidates with a direct reporting line to the Investigator is not acceptable.
4. Consent forms must include all the required elements of consent, as per 45CFR46.116 or 21CFR50.25, unless specifically waived. Reviewers should consider when additional elements of consent are required.
5. Subject understanding should be assessed in all instances and the required attestation by the person designated to obtain consent must be present on the consent document.
6. For subjects with severe mental illness, who are likely to have impairment in decision-making, an independent assessment of capacity is required.
7. Individuals designated to obtain consent must be listed on the PSF.
8. Reviewers should consider the qualifications of individuals designated to discuss consent and/or to assess capacity. In general, only a physician may obtain consent for a study involving a somatic intervention or treatment.
9. Consent materials must be written in language understandable to the subject. Consent forms, information sheets, recruitment scripts should be written using simple, direct, and non---technical language. Formatting of documents must facilitate reading and understanding.
10. All studies classified as "more than minimal risk" require a consent form "summary" or "cover sheet" in addition to the consent document. This summary should be written in lay language, such that an individual with limited literacy (i.e., less than 8 grade reading level) will largely comprehend the form text.
11. Consent materials must pay particular attention to and adequately emphasize and explain alternatives and aspects of the research commonly misunderstood by research subjects, such as randomization and blinding.
12. The impact of study---related compensation should be considered carefully in the review to avoid undue inducement.
13. Other guidance as per http://irb.nyspi.org.

E. Documentation of Informed Consent is Appropriate

I. As required by 45CFR46.111 and 45CFR46.117, the signature of the subject or the subject's legally authorized representative on the written consent form approved by the IRB is required to document consent to research unless the IRB has waived the requirement for consent (see viii below) or documentation of consent (see v below). The date of consent must be recorded by the subject.

II. The consent form must include a statement by the person obtaining consent that attests to the subject's understanding of the consent decision and the voluntary nature of that decision. The attestation must be signed and dated by the member of the study team who obtained consent and was so authorized by the IRB.

III. The consent form used must have a NYSPI-IRB approval/date stamp on each page.

IV. The subject must be given a copy of the consent form to keep.

V. The requirement for written documentation of informed consent, parental permission, or assent may be waived, as described below.

1. The requirement that some or all subjects sign a written consent document may be waived if it is determined that 1) the research presents no more than minimal risk of harm to subjects; and 2) the research involves no procedures for which written consent is normally required outside of the research context. If the requirement is waived, the IRB may require the investigator to provide subjects with a written statement describing the research, and providing appropriate elements of consent.
2. The requirement for a signed written consent document may be waived if: 1) the only link between the subject and the research would be the consent document; and 2) the principal risk would be potential harm resulting from a breach of confidentiality. In these situations, the existence of a consent form that describes a study and includes the subject's signature may present a significant risk of harm to the subject, due to the potential for breach of confidentiality.

VI. Consent Obtained from Non-English Speaking Subjects

1. When non-English speaking subjects will be enrolled, the IRB will ensure that subjects are presented with the required information in manner understandable to them.
2. If the inclusion of non-English speaking individuals is reasonably anticipated, the consent document(s) must be translated into the prospective subjects' first language or language of choice.
3. If a non-English speaking individual is unexpectedly encountered who otherwise meets eligibility criteria, a "short form" consent process may be used if approved by the IRB. Use of a short form is allowed when:
   A. Study inclusion criteria include subjects who are not able to clearly understand English;
   B. The NYSPI IRB-approved short form template is used or the IRB has approved a research team-provided short form;
   C. Use is not expressly prohibited by the IRB; and

D. The study sponsor (if applicable) allows use of a short form.

If any of the above conditions are not met, an amendment requesting permission must be submitted and approved by the IRB prior to using a short form.

VII. Enrolling Subjects Who are Unable to Read or Write or Communicate Orally

1. When there is the prospect of enrolling illiterate subjects, NYSPI endorses procedures that incorporate the recommendations of the FDA as articulated in the FDA Information Sheet (9/98).
2. A person who can understand and comprehend spoken English, but is physically unable to talk or write, can be entered into a study if they are competent and able to indicate approval or disapproval by other means. The person may be entered into the study, if:
   A. the person retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained verbally, and
   B. is able to indicate approval or disapproval to study entry.
3. The consent form should document the method used for communication with the prospective subject and the specific means by which the prospective subject communicated agreement to participate in the study. An impartial third party should witness the entire consent process and sign the consent document as a witness.

VIII. Waiver of Some or All of the Elements of Informed Consent

1. The IRB may waive the requirement for informed consent per 45 CFR 46.116 (c) or (d) or allow an alteration of some or all of the elements of informed consent.
2. The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent or waive the requirements to obtain informed consent providing the IRB finds and documents that:
   A. The research or demonstration project is to be conducted by or subject to the approval of State or local government officials and is designed to study, evaluate, or otherwise examine:
      I. programs under the Social Security Act, or other public benefit or service programs,
      II. procedures for obtaining benefits and procedures under those programs,
      III. possible changes in or alternatives to those programs or procedures, or
      IV. possible changes in methods or levels of payment for benefits or services under those programs; and
   A. The research could not practicably be carried out without the waiver or alteration.
3. The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent or waive the requirements to obtain informed consent providing the IRB finds and documents that:
   A. The research is not an FDA-regulated study,
   B. The research involves no more than minimal risk to the subjects,
   C. The waiver or alteration will not adversely affect the rights and welfare of the

subjects,

D. The research could not practicably be carried out without the waiver or alteration, and
E. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

f. Data and Safety Will Be Monitored

I. The IRB carefully considers how the investigator will collect and monitor data relevant to the safety of study subjects. The level of monitoring activity is to be commensurate with the nature, complexity, probability and magnitude of study risk. All research proposals must provide a Data and Safety Monitoring Plan (DSMP). For greater than minimal risk studies, the DSMP submitted to the IRB should describe the procedures for safety monitoring, reporting of unanticipated problems involving risks to subjects or others, and description of interim safety reviews (if applicable). For studies deemed no greater then minimal risk, a monitoring plan is still required, and should delineate how research data will be housed and safeguarded.

II. A formal Data Monitoring Committee (DMC) may be required by study sponsors or requested by the IRB for large clinical trials, or smaller trials involving vulnerable populations, high---risk study procedures or novel therapies. Should the study sponsor require DMC oversight, the DMC charter and roster must be made available to the IRB. Once a study begins accrual, the Principal Investigator is responsible for submitting all subsequent DMC reports to the IRB. For non---sponsored studies, the IRB may request assemblage of a DMC, with recommendations as to membership, meeting frequency, and required data review, as appropriate.

III. The Board will ensure that safety assessment measures and frequency are appropriate to the study design, foreseeable risks, and study population.

IV. The Board may request interim safety data from the Investigator (See Section 9. Research Monitoring) for review as part of the continuing review process.

V. The IRB will receive and review DMC reports and request additional information as needed.

g. Privacy of Subjects and Confidentiality of Data Will Be Protected

I. The IRB carefully considers risks to subject privacy and data confidentiality and reviews the methods by which the investigator plans to safeguard private information.

II. Risks related to breach of confidentiality during recruitment and consent, data collection, data storage, and data sharing are identified and minimized during the process of review.

III. Methods required to protect data and private information will vary greatly depending on the possible harms related to breach of confidentiality, the technologies employed in the collection and use of data, Institutional Data Security Policies, and applicable Federal and State confidentiality regulations.

1. The IRB may involve consultants in the review of the use of new technologies (internet-based data collection and storage) to identify and minimize risk.
2. A Federal Certificate of Confidentiality is required for research involving recording of identifiable data about individuals who are HIV+, substance users, in all studies involving genetic analysis, and in other circumstances in which subject involvement in the research may place them at risk related to breach of confidentiality.
3. When protected health information (PHI) will be created, used or disclosed for research purposes, specific language must be included within the Consent Form or CF addendum , if that consent form will be used to obtain permission from the subject to create, use or disclose PHI . Alternatively, a separate HIPAA Authorization may be used as appropriate.
4. In addition to the above item 3, the IRB may approve a waiver of HIPAA Authorization if the required conditions have been met (See Appendix).
5. For patients who are treated in alcohol or drug abuse programs, there are additional requirements (DHHS 42CFR Part 2) that must be followed.
6. Limitations in the extent to which protection of identifiable information can be provided must be disclosed during the consent process. The consent form and authorization must explain the disclosures that may be made for example, to sponsors, regulatory agencies, the IRB, certain legal advocacy groups authorized under law, etc.

2. Approval of Specific Types of Research

A. Research Involving Pregnant Women, Neonates and Fetuses (45CFR46 Subpart B)

I. In order to have a representative sample, it is necessary that investigators include women of childbearing potential as subjects in clinical research. Unless the research is determined to be unlikely to harm the fetus, pregnant women are not usually included as subjects in research.

II. It is the responsibility of the investigator to ascertain that female subjects between menarche and menopause, and who are not surgically or congenitally infertile, are not pregnant at the time that they enroll in a more than minimal risk study unless the study has been specifically approved for the inclusion of pregnant women. This

can be done by including a standard urine or serum pregnancy test in the baseline screening tests.

III. For studies not approved to include pregnant females, women of childbearing potential are generally required to use effective means of birth control for the duration of their participation. Some studies using particularly toxic drugs may require that women use two methods of birth control, or to continue on birth control for a period of time after the completion of the study, until the drug is cleared from their system. If the drug is anticipated to have an effect on sperm, male participants may also be required to use birth control during their participation, and possibly for a period thereafter.

IV. If a woman becomes pregnant while participating in a study, the IRB should be notified promptly, and the research team must assist the subject in obtaining necessary OB/BYN evaluation, provide the subject with information about risk to the fetus, and provide necessary support. Whether ongoing research involvement is appropriate will depend on the nature of the study, duration of the pregnancy, and other clinical considerations.

V. When the IRB considers research which requires the involvement of pregnant women, neonates or fetuses, it ensures that all requirements of 45CFR46 Subpart B are met prior to approval of the research. In addition to applying the criteria for IRB review identified in 45CFR46.111, the IRB ensures that
   1. There is adequate expertise to evaluate the risks and benefits related to the inclusion of pregnant women, fetuses and neonates, engaging consultants where necessary.
   2. The determinations required by Subpart B are documented appropriately in the IRB records.

B. Research Involving Prisoners (45CFR46, Subpart C)

I. The following definitions apply:
   1. A “prisoner” is defined as an individual who is involuntarily confined or detained in a penal institution”. The term is intended to encompass individuals sentenced to such an institution under criminal or civil statutes, individuals detained in facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial or sentencing.
   2. Parolees may not be considered “prisoners” if they are not “confined or detained” in a facility. Individuals sentenced to a halfway house may be considered prisoners if they are “confined or detained” in the facility or if their coming/going is considered restricted.
   3. The definition of prisoner also applies to subjects already in a study who suddenly become incarcerated.

4. The definition of prisoner includes patients in Office of Mental Health facilities who meet the definition above, including but not limited to the following: (1) Minors transferred from the Division for Youth for treatment (2) Persons who are incapable of assisting in their own defense (3) Pre---trial or Pre---sentencing treatment---Section 508 of the Corrections Law (4) Sentenced persons who are in need of treatment.
5. In addition, the RFMH Central Manual lists classes of OMH patients that are considered prisoners [see: http://corporate.rfmh.org/research_compliance]
6. For research involving prisoners, the definition of "minimal risk" is different than for research not involving prisoners, in that the risk is relative to that encountered in the daily lives of healthy individuals: the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

II. Research with prisoners and in prison or alternative physical settings require special safeguards in the review and approval process.

III. Knowledge of prison/facility rules and culture is essential to the identification and mitigation of research related risk. At least one IRB member or alternate who is a prisoner representative must review the proposed research.

IV. The prisoner representative is an individual who is currently or formerly a prisoner or, alternatively, an individual who has a close working knowledge, understanding and appreciation of prison conditions from the perspective of the prisoner.

V. The prisoner representative is a member of the IRB and will count toward the quorum for those protocols reviewed by the Full Board that involve prisoners.

VI. Before enrollment of prisoners in research can be initiated:
1. The IRB will ensure that the certification requirement described in 45CFR46.305(c) is fulfilled for all federally funded studies.
2. The IRB will ensure that the investigator has obtained approval of the appropriate prison officials/agencies.

VII. When the IRB considers research which requires the involvement of prisoners it ensures that all requirements of 45CFR46 Subpart C are met and documented prior to approval of the research, in addition to applying the criteria for IRB review identified in 45CFR46.111.

VIII. As per 45CFR46.305, Additional duties of the IRB where prisoners are involved:

(a) In addition to all other responsibilities prescribed for Institutional Review Boards under this part, the Board shall review research covered by this subpart and approve such research only if it finds that:

(1) The research under review represents one of the categories of research permissible under §46.306(a)(2);

(2) Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

(3) The risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;

(4) Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

(5) The information is presented in language which is understandable to the subject population;

(6) Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and

(7) Where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

(b) The Board shall carry out such other duties as may be assigned by the Secretary.

(c) The institution shall certify to the Secretary, in such form and manner as the Secretary may require, that the duties of the Board under this section have been fulfilled.

IX. As per 45CFR46.306, Permitted research involving prisoners:

(a) Biomedical or behavioral research conducted or supported by DHHS may involve prisoners as subjects only if:

(1) The institution responsible for the conduct of the research has certified to the Secretary that the Institutional Review Board has approved the research under §46.305 of this subpart; and

(2) In the judgment of the Secretary the proposed research involves solely the following:

(i) Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

(ii) Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

(iii) Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of his intent to approve such research; or

(iv) Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research.

(b) Except as provided in paragraph (a) of this section, biomedical or behavioral research conducted or supported by DHHS shall not provide prisoners as subjects.

X. Add certification to the Secretary for DHHS funded research involving prisoners. See http://www.hhs.gov/ohrp/policy/populations/prisoncertlet.html

C. Research Involving Children (45CFR46, Subpart D)

I. In addition to applying the criteria for IRB review identified in 45CFR46.111, when the IRB considers research which requires the involvement of children it ensures that all requirements of Subpart D of 45CFR46 and 21CFR50 are met prior to approval of the research.

II. Children are a vulnerable population and as such require additional protections when they are research subjects. At the same time, children as a class should not be denied the opportunity to enroll or denied the prospective benefits of participating in appropriate research.

III. The IRB is required to consider the following:

1. the level of risk of the research
2. the potential benefit to the individual subject
3. the requirement that permission for participation is obtained from a parent, both parents or legal guardian unless a waiver of parental/guardian permission is granted.
4. the requirement for assent (a child's affirmative agreement to participate in the research) unless assent of the child is waived by the IRB.

IV. There are four possible categories for research involving children. Most of the research that is reviewed falls into the first three categories. For each, the IRB must make the risk determination based on the following:

1. "Minimal Risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (45CFR46.404; 21CFR50.51).
2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects. For research to be approved under this category, the Board must find that:
   A. the risk is justified by the anticipated benefits to the subjects; and
   B. the relation of the anticipated benefit to the risk must be at least as favorable to the subjects as that presented by available alternative approaches. (45CFR46.405; 21CFR50.52).
3. Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition. For research to be approved under this category, the Board must find that it meets the requirements of 45CFR46.406 and, when applicable, 21CFR50.53, as follows:
   A. The risk represents a minor increase over minimal risk;
   B. The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
   C. The intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the subject's disorder or condition;
   D. Adequate provisions are made for soliciting and documenting assent of the children;

E. Adequate provisions are made for soliciting the permission of both parents of each child unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child (45CFR46.407 and 408).

4. HHS will conduct or fund research that the IRB does not believe meets the requirements of 45CFR46.404, 45CFR46.405, or 45CFR46.406 only if:

(a) the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and

(b) the Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined either: (1) that the research in fact satisfies the conditions of 45CFR46.404, 45CFR46.405, or 45CFR46.406, as applicable, or (2) the following criteria:

I. the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;

II. the research will be conducted in accordance with sound ethical principles;

III. adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in 45CFR46.408.

5. Research that involves children is initially evaluated by the Child Subcommittee which includes a Pediatrician as a member. An exception to this practice would be a minimal risk study involving review of existing records on children. Initial determinations regarding anticipated benefits and the level of risk --- whether the proposed procedures or interventions are consistent with minimal risk, minor increment over minimal risk or more than a minor increment over minimal risk --- are considered. The review also focuses on additional safeguards that are needed, procedures for assent, whether permission from one or both parents is needed or, if appropriate, whether criteria for a waiver of parental permission can be granted. If a waiver of parental permission is appropriate, the IRB will consider additional procedures to inform parents are needed.

Points that are considered in the review:

1.Consent

A. Permission for participation of a minor in research shall be obtained from one or both parents or guardians, contingent on the level of study risk and whether or not the research offers the prospect of direct benefit.
B. For research involving no more than minimal risk and research involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects, the IRB may find that the permission of one parent is sufficient.
C. For all other research, both parents must give their permission unless one parent is deceased, unknown, incompetent, not reasonably available or one parent has legal custody of the child. If no parent or legal guardian is

D. available consent may be obtained from an adult family member who is involved in making treatment decisions for the minor, or from a court of competent jurisdiction.

E. The consent form must be explicit about the thresholds for reporting and disclosure, to who (parent, clinician) information will be disclosed, etc. The IRB requires that the CF explicitly describe the limits of confidentiality so parents can understand what they will and will not be told.

F. If the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the requirement for the permission of the parent(s) or guardian provided that an appropriate mechanism for protecting the minors who will participate as subjects in the research is substituted. [45CFR46.116 (a-d)]. The Commissioner (OMH) or his designee must specifically approve waivers and the specific protective mechanisms. In most instances, this protective mechanism will involve an adult who is familiar to the child and is not associated with the research. The advocate should support the child in asking questions about the research and should ensure that the child understands that he/she does not have to participate, can withdraw once participation commences and will not suffer any penalty or loss of benefits for doing so. A letter of agreement to serve this function should be obtained and should certify that he/she does not have any interests that conflict with this role.

2. Assent

G. Written assent from children aged 8 and above is required when, in the judgment of the IRB, the children are capable of providing their assent. The IRB takes into account the ages, maturity, and psychological state of the children involved (see 45 CFR 46.408(a))

Points that are considered in the review:

3.Consent

H. Permission for participation of a minor in research shall be obtained from one or both parents or guardians, contingent on the level of study risk and whether or not the research offers the prospect of direct benefit.

I. For research involving no more than minimal risk and research involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects, the IRB may find that the permission of one parent is sufficient.

J. For all other research, both parents must give their permission unless one parent is deceased, unknown, incompetent, not reasonably available or one parent has legal custody of the child. If no parent or legal guardian is available consent may be obtained from an adult family member who is involved in making treatment decisions for the minor, or from a court of competent jurisdiction.

K. The consent form must be explicit about the thresholds for reporting and disclosure, to who (parent, clinician) information will be disclosed, etc. The IRB requires that the CF explicitly describe the limits of confidentiality so parents can understand what they will and will not be told.

L. If the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a

M. reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the requirement for the permission of the parent(s) or guardian provided that an appropriate mechanism for protecting the minors who will participate as subjects in the research is substituted. [45CFR46.116 (a-d)]. The Commissioner (OMH) or his designee must specifically approve waivers and the specific protective mechanisms. In most instances, this protective mechanism will involve an adult who is familiar to the child and is not associated with the research. The advocate should support the child in asking questions about the research and should ensure that the child understands that he/she does not have to participate, can withdraw once participation commences and will not suffer any penalty or loss of benefits for doing so. A letter of agreement to serve this function should be obtained and should certify that he/she does not have any interests that conflict with this role.

4. Assent

N. Written assent from children aged 8 and above is required when, in the judgment of the IRB, the children are capable of providing their assent. The IRB takes into account the ages, maturity, and psychological state of the children involved (see 45 CFR 46.408(a))
Written assent documents are reviewed to ensure that minors are provided

O. with as much information as they are capable of understanding, in language appropriate to their age and abilities.

P. As with the consent form for parents, the assent form must specify what information will/will not be shared with parents as applicable (e.g., results of pregnancy or drug testing etc.).

Q. The IRB may also consider verbal assent by the child, with documentation by the investigator.

R. The requirement to obtain the assent of a minor may be waived by the IRB if the capacity of the child is so limited that he/she cannot be reasonably be consulted. This decision may be made on an individual basis or, if appropriate, it may be made for a category of subjects if their age or other characteristics indicate that, as a group, they uniformly lack the ability to provide assent.

S. Objection: A minor's objection to participation in research should be carefully considered. Investigators must be cognizant of and document what would count as non-verbal 'dissent' for children who cannot provide assent.

3. Advocates

T. The IRB reviews protocols involving minors to determine whether the potential subjects are likely to be capable of clearly expressing their objection to participation or continuing participation. When appropriate, the IRB may require that an advocate (e.g. an adult who is familiar to the child and is not associated with the research such as a member of the treatment team) be appointed to observe the research and interpret the behavior of the minor.

U. If the minor's behavior is expressive of objection, the advocate should have the responsibility to object to participation on the minor's behalf.

V. The advocate should also encourage the minor to ask questions about

the research and support him/her in expressing reservations or declining participation.

d. Research Involving Persons Who May Lack Capacity To Consent

I. Participation as a subject in any research project or activity should not deprive any patient of any of the rights, privileges and protections provided to all patients. Included in these rights is the right to consent or withhold consent for proposed research or to have surrogate consent or withhold consent for research involving an incapacitated person.

II. IRB review includes consideration of the inclusion of subjects who lack capacity to consent in any research study to ensure that the investigator has demonstrated the necessity of enrolling incapable subjects and that procedures for assessing capacity to consent initially and on an ongoing basis throughout the study are in place.

III. To participate in research, a person must have sufficient capacity to make an informed decision. When there is reason to believe that some or all of the proposed

subjects may lack capacity, the investigator must fully explain the capacity assessment process to the IRB. Investigators must be confident that any person, including a "normal volunteer," giving consent to participation in a research project has sufficient capacity to give that consent.

IV. Capacity must be assessed in relation to a specific situation. Different research studies will require different levels of capacity. A person may have the capacity to consent to some protocols but not to others and capacity may also change over time.

V. A person's capacity may be increased by adapting the manner in which information about the study is provided. This may mean extending the consent process to allow the essential elements to be broken down into simpler components. Alternatively, it may be necessary to use different methods to inform some participants. For example, potential subjects could be shown equipment that will be used in addition to oral and written descriptions. Respect for the autonomy of individuals requires that investigators expend the time and effort to provide research participants with adequate information in a manner that maximizes understanding.

VI. No adult subject regardless of capacity or lack of capacity shall participate in research over his/her objection.

e. Research Involving Investigational Drugs or Devices

I. For studies involving investigational drugs or devices, or approved drugs used off-label, the IRB will consider, in addition to the review criteria under 45CFR46.111, the specific FDA requirements 21CR50, 21CFR 56 and 21 CFR 812 in its initial and continuing review of research.

II. Investigators who hold an IND or IDE themselves (sponsor---investigators) will be required to work closely with the CUMC Clinical Trials Office IND/IDE Assistance Program, which will provide them with education, guidance and operational support in dealing with submission requirements and regulatory responsibilities.

III. The IRB will be responsible for making the final determinations as to whether an IND or IDE is required for a particular study.

IV. Under DMH/RFMH policy, the authority to approve the use of investigational drugs or devices at NYSPI is delegated by DMH to the Director of the Institute. Therefore, as a condition of final IRB approval, The IRB will forward a copy of the protocol submission to the Director for review and approval.

Section 8. Conflict of Interest

A **conflict of interest** may be defined as: a set of conditions in which an investigator's judgment concerning a primary interest (e.g., subject welfare, integrity of research) could be biased by a secondary interest (e.g., personal or financial gain).
– Daniel K. Nelson, In Conflict of Interest: Researchers. Bankert & Amdur.
Institutional Review Board Management and Function. Jones & Bartlett Leaning, 2006.

1. IRB Member Conflict of Interest

A. Regulatory Basis:

I. 45CFR46.107(e) No IRB may have a member 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.

B. Policy:

IRB members, alternates and consultants may not participate in the review of any research in which they have a conflict of interest. Conflicts of interest include but are not limited to:

I. being a listed investigator, member of the research team, or individual designated to obtain consent (or having an immediate family member listed as such) in the research being evaluated

II. having any financial interest (or having an immediate family member with such an interest) in an "interested entity" (see 2b., below) in the research being evaluated

III. Serving as the head of the division from which the research being evaluated originates

IV. having any other conflict that might be perceived to inhibit a fair and unbiased review of the research

C. Procedures:

IRB Members are instructed at the start of each Subcommittee and Full Board meeting of the IRB's policy regarding conflict of interest. A list identifying any interested entity for the studies under review is circulated at Subcommittee and is included on the Full Board agenda. At both meetings, Protocol Analysts identify reviewers who are investigators or other key personnel on research protocols and remind them to recuse themselves and leave the meeting room during the discussion (and vote). Consultants and members asked to perform expedited review are similarly informed of IRB policy and queried regarding conflict. Reviewers are reminded in writing prior to each Full Board meeting to notify IRB staff immediately in the event that they have been assigned to review a study in which they are conflicted. In this case, the study will be re---assigned to

another reviewer.

I. Evaluations of Potential Conflicts at Meetings:

At the start of each IRB meeting, Board members are asked by the Chair to disclose any conflict of interest (financial or otherwise) with respect to the studies scheduled for review. Should a member indicate a conflict of interest, and it is deemed of sufficient magnitude to prevent objective review of the study, the member has the right to recuse him/herself without having to divulge the details. The IRB Chair should be advised in advance of the meeting and the minutes reflect that the member was not present during the discussion and vote. If a member is uncertain about the presence of a conflict and wishes to contribute to the review, he/she may volunteer the details to the IRB Chair for consideration and resolution.

II. IRB Deliberations:

IRB members and consultants will not participate in any IRB deliberations or decisions relating to a research study in which they have a conflict of interest. An exception is to provide information specifically requested by the committee. In the event that an IRB Chair is in conflict with the research being evaluated, he will be asked to step out of the room during the review, discussion and vote. The Chair without conflict, or the Chair designee will serve as acting chair during that portion of the meeting.

III. Documentation within Board Minutes:

The absence of members or consultants due to a conflict (i.e., a listed investigator, financial or other conflict) during the discussion of the research and the vote is documented in the minutes of the IRB meeting.

2. Investigator Conflict of Interest

A. Regulatory Basis:
Proactive Compliance Oversight Program-Financial Conflict of Interest Requirements for NIH-Supported Institutions. Notice Number: NOT---OD---12---159. Release date: September 21, 2012

I. New York State Ethics Commission Advisory Opinion 97-22

II. New York Public Officers Law §74(3)

1. No officer or employee of a state agency . . . should accept other employment which will impair his independence of judgment in the exercise of official duties.
2. An officer or employee of a state agency . . . should not by his conduct give reasonable basis for the impression that any person can improperly influence him in the performance of his official duties, or that he is affected by the kinship, rank, position or influence of any party or person.
3. An officer or employee of a state agency . . . should endeavor to pursue a course of conduct which will not raise suspicion among the public that he is likely to be engaged in acts that are in violation of his trust.

B. Policy:

42 CFR 50.603(1)(i) currently states that a significant financial interest is when the value of any remuneration received from the interested entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds $5,000.

I. Income refers to salary, stipends, honoraria, gifts and other payments, including travel reimbursement.

II. An interested entity is any non-government entity that (a) provides funding for all or part of an investigator's research, including, but not limited to, the Study Sponsor; (b) provides drugs, devices or other materials for the research; (c) holds an IND or IDE for a drug or device being investigated in the research; (d) manufactures, markets, licenses or has other commercial

III. interests in or directly affected by the technology being investigated in the research; or (e) provides any other support, including gifts, related to the research.

IV. The course of the research is defined as the period of study design, conduct and reporting including the 12-month period of time prior to the investigator's involvement in the study. It extends to 12---months after the termination of the research support or until publication of the primary results, whichever comes later.

V. Other financial and non---financial interests are subject to disclosure, review and management by the Ethics Advisory Board.

VI. Any exception to this policy must be approved by the Ethics Advisory Board through a COI management plan. In the event that the IRB is not in agreement with the proposed COI management plan, the decision to grant IRB approval of the protocol remains with the IRB. The IRB may accept the EAB's recommendation or establish stricter requirements including disapproving the individual's participation in a study.

C. Procedures:

I. The NYSPI Ethics Advisory Board (EAB), in tandem with the Administrative Director, Sponsored Projects Compliance, conducts financial conflict of interest review for all human subjects research originating in NYSPI, RFMH, or CU Department of Psychiatry.

II. At the time of the initial protocol submission and prior to IRB review, the Principal Investigator of each protocol will be prompted by the IRB to have all investigators, principal investigators, co-investigators, consenters, affiliate investigators, consultants and key personnel provide annual disclosure of financial interests. Failure to submit this information delays IRB review.

III. The Administrative Director of the EAB reviews all COI forms with their associated study protocol to confirm the presence or absence of significant financial interests. (1) If financial interested are disclosed in relation to the study, the convened EAB reviews and determines a plan to eliminate or manage the COI. The investigator is notified, and confirms acceptance of the plan, at which point the EAB will forward information on the nature of the conflict identified and resolution to the IRB protocol manager. (2) If no financial interests are disclosed for a given IRB protocol, COI review is considered complete.

1. If an IE is not identified in the worksheet, conflict of interest disclosure is complete and IRB review can proceed.
2. If an IE is identified, all investigators and other key personnel, including those authorized to obtain informed consent, must complete the Conflict of Interest Disclosure Form. If financial interests are disclosed in relation to the study, the convened EAB reviews and determines a plan to eliminate the COI.

3. The investigator is notified, and confirms acceptance of the plan, at which point the EAB will forward information on the nature of the conflict identified and resolution to the IRB protocol manager.
4. When there are no financial interests disclosed for a given IRB protocol, COI review is considered complete.

D. Time Frame:

I. The IRB will prompt completion of disclosure forms upon submission of new IRB protocols.

II. Forms must be submitted for review prior to convened IRB review or for expedited studies, prior to final approval.

III. COI review will either be in progress or completed prior to review at the Full Board.

IV. The COI review process must be complete prior to IRB approval being issued.

E. IRB documentation of COI review:

   I. Correspondence between the Administrative Director, Sponsored Project Compliance and IRB Protocol Analysts regarding the outcome of COI review is added in hard copy to the IRB file.

   II. The file and database checklist item for COI are marked as complete.

   III. The IRB (or IRB reviewer for expedited studies) are informed of the presence or absence of disclosed financial interests during review.

3. Coordination/Communication between EAB and IRB

A. An email request for conflict of interest forms is sent to the Principal Investigator from IRBmail at the time of submission of protocols for initial review.

B. Prior to each IRB Subcommittee meeting, COI information is compiled in a report for consideration by IRB members at the time of review. This includes both the interested entity and the nature and extent of financial interests disclosed by investigators and individuals authorized to obtain consent in the research.

C. If all COI forms have not yet been received, a reminder to submit COI forms is included in the memo from the Subcommittee, as a stipulation to be met before IRB Full Board review and/or approval.

D. Prior to each IRB Full Board meeting, COI information is added to the Full Board agenda.

E. EAB determination regarding the presence of a conflict of interest and management plan is communicated to IRB via memo or email. This may include requirements such as disclosure of the financial interest in the study consent form.

F. Completion of COI review is also recorded in the IRB database. IRB administrators confirm that COI review for a given protocol is marked as complete prior to issuing an approval notice.

G. Proposed study amendments that may change the IE(s) are referred to the Administrative Director of the EAB. If necessary, revised COI forms are requested. Approval of the amendment is held until COI review is complete.

H. The Application for Continuing Approval of Research prompts investigators to update study-related COI disclosures.

4. Director of NYSPI and the Director of Psychiatric Research:

In addition to the requirements described above, all studies for which the Director of NYSPI or the Director of Psychiatric Research is a Principal Investigator will be submitted to, reviewed by, and require the approval of RFMH and the OMH

Commissioner's designee because of the direct oversight and authority that the persons in these two positions have over the NYSPI IRB and the potential conflict of interest that this structure creates. A judgment sample of studies for which these individuals are named as co-investigators will be made by RFMH, and these studies will also be reviewed by RFMH and the OMH Commissioner's designee. Review of research conducted by the Director of NYSPI or the Director of Psychiatric Research will encompass the same criteria as reviews for other studies within OMH/RFMH. (Refer to section 3.6 "Review by the Director, RFMH and Department", Manual for Institutional Review Boards RFMH/DMH).

Section 9. Research Monitoring

1. Purpose

Monitoring enhances human subject protections by promoting regulatory compliance and supporting institute-wide standards for the ethical conduct of research. At NYSPI, monitoring of IRB approved research activities includes a conventional compliance auditing function but also enriches the process of ongoing review of approved research by providing data on the experience of subjects participating in the research. Finally, the monitoring process contributes to investigator education and training.

2. Regulatory Basis

The NYSPI IRB monitoring program satisfies regulatory requirements at 45CFR46.103.4 (b)(ii) [Assurances shall include] "written procedures which the IRB will follow…for determining…which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review," and at 45CFR46.109 (e) "An IRB…shall have authority to observe or have a third party observe the consent process and research."

3. Policy

Information collected during monitoring will inform ongoing review of all approved and actively recruiting research studies. The form and frequency of monitoring is specified in this policy and associated SOPs, or otherwise determined by the IRB at the time of

review. The Director, Psychiatric Research, IRB Co-Chairs, IRB Executive Director, and Research Compliance Monitor may, in addition, request or specify additional monitoring requirements.

4. Categories of Monitoring Activities

A. Record Review (External Auditor)

Research files and medical charts are examined by the IRB Research Compliance Monitor (or others independent of the research team). Record review is aimed at determining compliance with IRB approved recruitment, consent, procedures, eligibility criteria, drop---out criteria, and adverse event reporting requirements. The frequency of the auditing function is contingent on factors such as the level of study risk, the novelty of the proposed intervention, the potential vulnerabilities of the subject population, an investigator's previous record of compliance, and the study sponsor (e.g., FDA).

B. Record Review (Self-Assessment)

Record review, as above, is conducted by a member of the research team and submitted to the IRB Research Compliance Monitor. The Research Compliance Monitor conducts oversight, periodic re-audit, and reporting to the Executive Director and IRB (if deemed necessary).

C. Procedural Observation

The Research Compliance Monitor or another appropriately qualified person selected by the IRB will, at times, observe the subject's participation in a study procedure or component. Procedural observation assesses the subject's experience during the research procedure to ensure that it is consistent with research procedures as specified in the research protocol and described in the

consent form. Further, it permits an observation of the environment of care and the research team's interactions with the subject with regard to privacy, safety, and respect.

D. Consent Observation

The Research Compliance Monitor or another appropriately qualified person selected by the IRB will, at times, observe the consent process to ensure that: (1) the information is presented in a manner that facilitates the participant's understanding of the research and its alternatives, (2) sufficient opportunity is provided for the subject to consider the information presented and ask questions, and (3) the subject's understanding of the study and choice to participate is carefully considered, (4) the consent form is administered to the subject in a language understandable to them. The Monitor may focus the assessment on one component of the consent process, at the request of the IRB, when special emphasis is required. The Research Compliance Monitor may use a standard checklist.

E. Subject Feedback Surveys

The IRB may ask the investigator to create a survey tool or instrument to collect subject level data on their experience in the research study. For example, the survey may assess the level of burden a subject experienced during participation, side effects experienced, or how well the consent process prepared them for what they experienced during the study.

F. Interim Progress Reports

The IRB may require investigators to "report back" as a condition of initial approval. The IRB may require that the Investigator provide information on the experience of the first subjects to take part in the study—on either a case basis or after a defined number of subjects have been enrolled or complete study procedures. The Board regularly requires this information when novel or high-risk procedures are involved.

G. Special Monitoring

Special monitoring refers to any other form of monitoring conducted at the request of the Board, Co---Chair or Executive Director. For example, special monitoring may be requested following the report of an adverse event to document that study inclusion and exclusion criteria or study drop---out criteria were met as per the approved protocol. In the event of a report of a protocol violation, special monitoring may require a systematic audit of study compliance with consent documentation requirements.

5. Focus of Review: protocol specific monitoring

A. While all research is subject to ongoing monitoring, specific monitoring options are considered for each study by the convened board at the time of initial approval.

B. The extent of monitoring (the frequency of monitoring, the number of records reviewed) is determined by the nature of the study, it subjects, and any history of compliance problems in the study.

C. Routine monitoring evaluates compliance with the IRB mandated protocol--- specific safeguards including:

I. Fulfillment of inclusion and exclusion criteria

II. Adherence to study drop-out criteria

III. Monitoring and assessment of subjects

IV. Provision of appropriate aftercare or referrals

V. Confidentiality protections

VI. Assessment of capacity

6. Monitoring Procedures

A. Frequency of Review

I. Studies approved by the Full Board: all studies approved by the Full Board are monitored once during the first approval period after recruitment is initiated and prior to the time of the first continuing review, unless otherwise required.

II. Studies given continuing approval by the Full Board: all studies are reviewed during subsequent approval periods until enrollment of human subjects is complete.

III. Other monitoring: all studies are subject to requirements for special review, consent monitoring, procedural observation, and interim progress reports, when specified by the Board, Co-Chairs or Executive Director.

B. Reporting and Follow-up procedures

I. The IRB Research Compliance Monitor (or Protocol Analyst will discuss the following with the Co-Chairs and Executive Director upon discovery:
1. all findings of non-compliance or previously unreported unanticipated problems, and 2) all investigator reports of protocol violations.

1. The Co-Chairs may request to meet with the investigator, request additional information from the investigator, or request additional monitoring data.
2. The Co-Chairs may request a corrective action plan from the investigator.
3. Incidents and clinical concerns may be referred to the Clinical Director or Director of Quality Management.
4. Administrative concerns may be referred to the investigator's Research Chief for follow-up.
5. The Chairs may suspend research or a component of the research if necessary to ensure the safety and well-being of research subjects. (see OHRP and institutional reporting requirements section 10.6 of this manual)
6. Non-compliance judged by the Chairs to be of minor significance may be resolved with "no further action".
7. Serious or continuing non-compliance will be subject to institutional and federal reporting as outlined in Section 10 of this manual.

8. If an allegation or evidence of possible Research Misconduct is found the Compliance Monitor or Protocol Analyst, as the case may be, shall promptly consult with the Chair of the Research Integrity Committee before any actions, other than those necessary to avoid possible immediate harms to subjects, are undertaken.

ll. The IRB Research Compliance Monitor is responsible for presenting the results of monitoring to Full Board as follows:

1. The Monitor will prepare a periodic summary report of activities. The report will be distributed at convened Board or in advance of each meeting.
2. A summary of significant monitoring findings, if any, will be distributed to the Board at the time of continuing review for each monitored study.
3. The following will be presented at the next scheduled Full Board meeting:
    A. Evidence from monitoring that suggests serious or continuing non-compliance.
    B. Evidence from monitoring that reveals a previously unreported, serious adverse event or unanticipated problem.
    C. Other findings that might have a significant impact on the rights, safety or welfare of study participants.
4. The Board will review matters regarding unanticipated problems or allegations of noncompliance, per 46.103(b)(5) criteria, and make recommendations with respect to external reporting. The IRB Chair or the Executive Director will notify the Deputy Managing Director, as per RFMH/DMH policy, along with the NYSPI Director, Psychiatric Research, regarding such recommendations. The responsibility for the final decision for external reporting rests with the Institution.

7. Corrective Action Plan

A. All findings are forwarded by the IRB Research Compliance Monitor to the study's Principal Investigator for comment and clarification prior to review. The Investigator may be asked at that time to outline a plan or statement of corrective action, which will be reviewed by the research monitor and the IRB Chair or his designee and/or by the Board, as above.

B. Upon review of monitoring findings by the Chair, at the convened IRB, or at an ad hoc Subcommittee convened for this purpose, additional corrective action, monitoring or training may be required.

C. The IRB Executive Director, the IRB Co-Chairs, or the IRB may, depending on the nature of the findings, involve the Principal Investigator's supervisor, research department head, or Institute Director in developing a plan of corrective action.

8. Monitoring and Education

A. Monitoring provides an opportunity for ongoing Investigator education and training with regard to IRB requirements.

B. Memos from the Monitor or Protocol Analysts to the investigator will detail findings with regard to IRB and regulatory standards for educational purposes. Additional guidance will be provided as necessary.

C. Investigators of studies in which there are findings of significant non-compliance will be expected to meet with an IRB Co-Chair and/or the Executive Director.

D. The IRB will, at its discretion, mandate additional human subjects training for investigators and research staff and may conduct specific training for an investigator or larger research group.

V. The IRB will also comply with all provisions of policy regarding use of investigational drugs and devices. It will be responsible for ensuring that appropriate safeguards are in place and that appropriate consent is obtained and documented.

Research Involving PET Scans

Studies involving Positron Emission Tomography (PET) require a multi-step review and approval process in addition to IRB review and approval.

VI. Administrative approval by the NYSPI Director, Psychiatric Research, is required of all investigational drugs (INDs) and devices (IDEs).

VII. PET studies employing radioligands approved for research use under an IND require written approval by the JRSC prior to IRB approval.

VIII. IRB approval is required before subject enrollment can commence.

Section 10. Reporting of Adverse Events and Unanticipated Problems

1. Regulatory Basis

A. 21CFR312.66 *The investigator shall also assure that he or she will promptly report to the IRB…all unanticipated problems involving risk to human subjects or others.*

B. 21CFR812.150(a)(1) *An investigator shall submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.*

C. 45CFR46.103(b)(5) & 21 CFR 56.108(b) *Written procedures for ensuring prompt reporting to the IRB, appropriate Institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others. The purpose of prompt reporting is to ensure that appropriate steps are taken in a timely manner to protect subjects from avoidable harm*.

2. Definitions

A. An *adverse event* (AE) is any untoward event involving the research participant or others that is temporally associated with participation in the research.

B. A *serious adverse event (SAE)* is any event that results in death, life threatening experiences, hospitalization or prolongation of hospitalization, disability or incapacitation, overdose, congenital anomalies or other serious events that may jeopardize the participant or require medical or surgical intervention to prevent any of the outcomes listed in this definition.

C. An *unexpected or unanticipated event* is an event that is not previously known or predicted to result from the interactions or interventions of the research or underlying condition of the human subject. The assessment of the significance and expectedness needs to account for the level of severity and frequency of the event. For example, this would include events that are expected in some subjects, but are determined to be occurring at a significantly higher frequency or severity than expected.

D. A protocol deviation involves a change(s) to the study design/procedures that is considered to be an exception to the approved protocol.

E. Significant protocol deviations are those deviations that increase the risk to participants or others, or decrease the potential benefits of the study, undermine the scientific integrity of the study, or occur more than once.

F. An *unanticipated problem involving risks to subjects or others* (UPIRSO) is any incident, experience, or outcome that meets all of the following criteria:

I. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol---related documents; and (b) the characteristics of the subject population being studied;

II. at least possibly related to participation in the research; and

III. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

3. IRB Policy

A. Internal adverse events:

I. In studies for which the NYSPI-IRB reviewed the protocol and approved enrollment at or for the site of the event, the Principal Investigator is required to report all serious and/or unexpected adverse events using the NYSPI-IRB SAE reporting form (see Appendix).

II. Serious and unexpected adverse events are reported to the IRB as soon as possible, but no later than 5 days after the research team learns of the event. Any event that is judged by the Principal Investigator as likely to have a significant impact on the safety and welfare of other study participants should be reported immediately.

III. The investigator is required to submit an "annual summary" of reported adverse events on the Application for Continuing Review of Research (ACAR) required for continuing review.

IV. DMC summary reports must be submitted for review either: 1) at the time of continuing review, or 2) as the investigator receives them throughout the approval period.

B. External adverse events (for multi-center studies):

The IRB reviews adverse events from other performance sites of the same study (for which involvement in research has not been reviewed and approved by the NYSPI-IRB), only when all three of the following conditions are met:

I. They are judged by the Principal Investigator to be at least possibly related to the study treatment or intervention.

II. They are unexpected in nature, degree or frequency of occurrence.

III. They are judged by the Principal Investigator to impact the risk/benefit assessment or design of the NYSPI-IRB approved study, or require

changes to consent form language. In other words, the event must suggest that the research places subjects or others at greater risk of harm or discomfort related to the research than was previously known or recognized.

C. Adverse event or safety reports received from sources other than a local or other performance site of the research:

The PI-IRB will also review adverse events, IND safety reports, or other new information from a study sponsor or other sources, even if the event does not relate to any research study, or if the event occurred in a different study than the PI-IRB approved study, when:

I. The new information is judged by the Principal Investigator to impact the risk/benefit assessment or design of the NYSPI IRB approved study, or otherwise suggest that changes to consent form language are required. In other words, the event must suggest that the research places subjects or others at greater risk of harm or discomfort related to the research than was previously known or recognized.

II. In such cases, as with any significant new information relevant to human subject participation, the information and proposed changes are submitted promptly to the IRB along with a request for study and/or consent modification.

D. Other incidents, experiences or outcomes that may represent unanticipated problems:

I. The IRB recognizes that other events, experiences, or outcomes may occur during the course of human subjects research that represent unanticipated problems but are not ordinarily considered adverse events (e.g., a breach of confidentiality). The Principal Investigator is responsible for assessing whether the event impacts the risk/benefit assessment of the NYSPI---IRB approved study, or otherwise suggests that changes to consent form language are required. Any untoward event that suggests that the research places subjects or others at greater risk of harm or discomfort related to the research than was previously known or recognized requires review by the IRB.

II. In such cases, as with any significant new information relevant to human subject participation, the information and proposed changes are promptly submitted to the IRB in memo form, along with a request for study and/or consent modification.

4. Investigator Reporting Procedures

A. The serious and/or unexpected adverse event reporting policy and form is found on the IRB website, which is available to all research personnel. The IRB Research Compliance Monitor is the primary liaison with investigators and staff who have questions about whether an event requires reporting.

B. Both the attestation associated with the PSF completed by the Principal Investigator and the IRB approval notice serve to document that Investigators are aware of their reporting responsibilities under this policy. Reporting requirements are also a component of required human subjects protections training for investigators.

5. IRB Review Procedures

A. The IRB Research Compliance Monitor reviews all serious and/or unexpected adverse event reports for completeness. Reports are submitted by email to a dedicated email address. Additional information is requested from the study's Principal Investigator as necessary. A summary of the event is entered into the IRB (PMS) database, and the report is promptly forwarded to the a Co-Chair and the Executive Director for review along with the IRB Research Compliance Monitor's preliminary assessment.

B. All other reported events, experiences or outcomes that may represent an unanticipated problem are pre---reviewed by the IRB Research Compliance Monitor or a Protocol Analyst, and forwarded to a Co---Chair or designee, with comments.

C. The Co-Chair's review of a reported event takes into consideration whether substantive changes in the research protocol or informed consent document or other actions are warranted in order to protect the safety, welfare, or rights of subjects or others.

D. Events that adversely impact the study's risk-benefit determination, or are likely to, are promptly presented to the Full Board. Other reported events are compiled in a summary report and presented to the Board upon continuing review.

E. While the Principal Investigator's assessment regarding the relatedness and expectedness of a reported event, as documented on the SAE reporting form or other memo, is taken into consideration, the final determination of attribution, and of whether or not the event meets the criteria of unanticipated problem, is the responsibility of the IRB. This determination is made by an IRB Co---Chair or the Full Board and may involve consultation with the Director, Psychiatric

Research at NYSPI, the Deputy Managing Director of RFMH and/or the OMH Commissioner's Designee.

6. IRB Reporting Procedures

A. Once the determination is made that an event meets the above definition of an unanticipated problem involving risks to subjects or others, the event is promptly reported by the IRB to the head of the sponsoring Federal department or agency, if any, and to OHRP as required by HHS regulations at 45CFR46.103(b)(5) and to FDA when the study is subject to FDA regulation. Reporting to Federal officials will take place within a few days for a more serious incident, but generally takes place within 7-10 days following this determination.

B. Reports of unanticipated problems include the following information:

I. Study name
II. Principal Investigator name
III. IND/IDE # (if applicable)
IV. The Federal award number
V. Summary of the study
VI. Summary of the event
VII. Summary of the IRB's actions in response to the event and any corrective action plan implemented

C. Possible actions in response to reports of unanticipated problems include but are not limited to:

I. changes to the research protocol initiated by the investigator prior to obtaining IRB approval to eliminate apparent immediate hazards to subjects
II. modification of inclusion or exclusion criteria to mitigate the newly identified risks
III. implementation of additional procedures for monitoring subjects
IV. suspension of enrollment of new subjects
V. suspension of research procedures in currently enrolled subjects
VI. modification of informed consent documents to include a description of newly recognized risks
VII. provision of additional information about newly recognized risks to previously enrolled subjects
VIII. suspension or termination of IRB approval

D. Reports of any serious or continuing non---compliance with federal regulation, IRB requirements or determinations will promptly be reported to Institutional officials, OHRP, the FDA when research is regulated by the FDA, and when federally funded, to the appropriate department or agency head. The report will

include a description of the non-compliance, research title and Principal Investigator, identification of any federal funding, IRB Protocol number and actions taken to address the non-compliance. When complete information about the non-compliance is not immediately available, an initial report will be sent promptly, with follow up report(s) as appropriate when more complete information and/or a corrective action plan are available.

E. IRB suspensions or terminations of approved research will be promptly reported to OHRP, Institutional officials, and the department or agency head of other federal agencies when federally funded. This will include the title of the research project, the name of the Principal Investigator, and IRB protocol number, as well as a detailed description of the reason for the suspension or termination and actions taken by the Institution or plans to address the issue.

Section 11. Training and Education

1. **Overview:**
   NYSPI understands the importance of a creating an Institutional culture that promotes the highest standards of ethical practice of research and demands regulatory compliance. All individuals at NYSPI and the CU Department of Psychiatry who are involved in the design, conduct and oversight of human subjects research are expected to know the historical underpinnings of the current system of research regulation, the principles that guide the ethical conduct of research, and the role of the IRB. In addition, all employees are expected to fulfill ethical responsibilities to those who choose to participate as subjects in research.

2. **Mandated Training:**
   1. The NYS Department of Mental Hygiene and RFMH have mandated the use of a web-based training program, the Collaborative IRB Training Initiative (CITI) for human subjects protections training. NYSPI has obtained a license for the use of CITI.
   2. A score of 90% or better is required on a set of required modules.
   3. CITI refresher training is required every three years.

3. **Requirements for Researchers and Research Staff:**
   1. CITI
      I. All key personnel who play a role in the design and conduct of research involving human subjects are required to achieve a score of 90% or better on the course.
      II. CITI certification is a prerequisite for involvement of all key personnel in human subjects research. Key personnel includes the principal investigator, co-investigators, and all other individuals who participate in study design, subject recruitment, screening, consent, assessment of capacity to consent or research interventions.
      III. The training is valid for 3 years at which time a “refresher” course is required.
      IV. Evidence of equivalent training is considered on a case-by-case basis.

   2. Additional Training
      I. Columbia University Good Clinical Practice certification is required for clinical researchers with Columbia Faculty appointments. All investigators are encouraged to complete the Good Clinical Practice Course offered by CITI.
      II. Researchers who hold an IND or IDE (sponsor-investigators) and Principal Investigators on IRB protocols relying on the IND/IDE are required to complete an online training module on CU’s Rascal system related to sponsor responsibilities in such research.
      III. Investigators are encouraged to attend IRB Subcommittee meetings as

guests/observers to familiarize themselves with the review process and IRB expectations.

IV. The "IRB Apprenticeship Program" provides research fellows, residents and other junior faculty with the opportunity to follow a protocol through the review process including the Subcommittee review and subsequent Full Board review. It is required of the HIV Fellows and Child Research Fellows, and open to all others.

V. All researchers and research staff are encouraged to avail themselves of the rich educational programs in research ethics available at NYSPI and CUMC. All faculty receive regular notifications of programs, seminars, and lectures.

VI. IRB communications are framed to facilitate understanding of IRB expectations and the rules from which they derive.

VII. The IRB's auditing and monitoring activities provide feedback to investigators to enhance compliance and understanding of IRB requirements.

VIII. The IRB Vice Chair for Research Administration, Ethics and Policy teaches courses, seminars and workshops for investigators including:

a) A course on research ethics and the role of IRBs for HIV Center Fellows Applied research ethics for the Child Research Fellows;
b) Applied research ethics for the Fellows in Neurobiology and Behavior; and
c) Research Ethics within the Seminar in Applied Ethics for Residents in Psychiatry.

I. PRISM One-hour Workshops

II. IRB Internship Program with the Columbia Master's Program In Bioethics

III. Human Subject Protection Webinars

4. Requirements for IRB Members:

1. CITI

I. IRB members who are researchers or research staff are required to complete the CITI course for researchers *and* must complete the IRB course in addition. A score of at least 90% on all courses is required.

II. Other IRB members are required to complete a course specified on the IRB website.

III. Refresher training is required every three years.

2. Orientation of New Members:

I. Prior to participation in review, IRB members are required to take part in an orientation workshop led by the IRB Chair and Administrative Director.

The interactive session reviews IRB procedures, the Common Rule and Subparts B-D, and application of the Belmont principles to review. Special emphasis is placed on risk identification and the minimization of risk in psychiatric research, children's research, and research with individuals with impairment in decision---making abilities. Members are introduced to other educational resources including the OHRP website and FAQs.

II. An orientation packet is provided and includes:
   1. Institutional Review Board Member Handbook by Amdur and Bankert.
   2. DHHS 45_CFR_46 (Common Rule)
   4. The Belmont Report
   5. Roberts, Laura Weiss, M.D. Ethical Dimensions of Psychiatric Research: A Constructive, Criterion-Based Approach to Protocol Preparation. The Research Protocol Ethics Assessment Tool (RePEAT). Society of Biological Psychiatry. 1999. p.1106---1119.
   6. Roberts, Laura Weiss, M.D. The Ethical Basis of Psychiatric Research: Conceptual Issues and Empirical Findings. Comprehensive Psychiatry. Vol.39, No.3 (May---June). 1998. pp.99---110.
   7. SACHRP, Recommendations Regarding Research in Individuals with Impaired Decision-making, July 15, 2009
   8. Chart: categories of surrogates who may provide consent on behalf of subjects who lack capacity.
   9. Chart: review requirements for research with subjects who lack capacity.

III. Additional individual meetings are held with non-scientific and unaffiliated members to assess their educational/informational needs and provide necessary assistance.

IV. All new members are expected to observe at least one Subcommittee and one Full Board meeting prior to taking part in review.

V. New members review responsibilities are phased in gradually. Feedback and additional supervision is provided by the Chair as needed in an ongoing basis.

3. Continuing education:

I. Members receive copies of the journal IRB.

II. Journal articles are distributed, and news and new developments in the field of human subjects protections are presented for discussion.

III. Full Board and Subcommittee meetings are structured to include member education. The Chair frames IRB discussion and deliberations in terms of core regulatory and ethical criteria, IRB precedent and "case---law."

5. Institute Leadership:

CITI training is required for Institute leadership (Director, Clinical Director, who are not otherwise required to complete training. A score of 90% on the course for institution

officials is required. Refresher training is required every three years.

6. New Employee Orientation:

a. All new employees of NYSPI and RFMH at NYSPI, regardless of position or title, are required to attend a new---employee orientation. This includes a session, led by the Director, Psychiatric Research or the IRB Executive Director, on the research ethics and the role of the IRB at NYSPI. The session reviews seminal events in the history of human experimentation with emphasis on the syphilis studies at Tuskegee and the studies at Willowbrook. The role of the IRB within the Federal regulatory framework is described and the core principles of Belmont are explained. The institution's commitment to high standards in ethics and regulatory compliance is communicated. Staff members are encouraged to bring questions or concerns to NYSPI's IRB Executive Director, IRB Co---Chairs or ethics committee.

b. A copy of the Belmont Report is provided to all new employees.

7. IRB Staff Training:

a. IRB administrators/protocol managers are expected to pass the written examination for certification by the Council for Certification of IRB Professionals and to maintain current "CIP" certification.

b. All IRB Staff must complete the required Basic CITI course requirements for IRB members and the refresher training every three years thereafter.

c. IRB Administrators attend annual PRIM&R conferences at least once every two years. They are expected to attend conferences and workshops sponsored by RFMH, Columbia University and other local universities and organizations.

8. Documentation and Verification of Training:

a. Investigator training is verified by protocol managers who have access to CITI's online database.

b. CITI certification is tracked in the investigator profile in our Protocol Management System.

c. IRB member and Institute Leadership training is tracked by the Administrative Director.

Principal investigators or department heads are expected to maintain documentation of staff certification.

Section 12. Record Retention and Documentation Requirements

The IRB office maintains the following records and reports:

1. IRB Administration

A. List of IRB members, member confidentiality agreements, CVs, and annual appointment letters.

B. Written procedures and guidelines. Written procedures are reviewed periodically to ensure appropriate functioning of the IRB. If amendments are necessary the Executive Director and Co-Chairs shall discuss and develop appropriate amendments. Substantive revisions, as determined by the Chair, will be brought to the Full Board for approval. Dates of revisions will be documented in the manual.

C. Minutes of Full Board meetings, including attendance, reports to the IRB of expedited reviews, monitoring reports, adverse events, discussions of each protocol and decisions reached. The minutes are prepared in accordance with all applicable Federal regulations and are signed by a Co-Chair or designee. A copy of the minutes is provided to all IRB members for review and approval.

D. Protocol files for each project are maintained electronically in within the Psychiatric Research IRB Submission Module (PRISM) system. In addition, the Protocol Management System (PMS), a custom-designed database is maintained within the IRB Office. PMS tracks protocol activity by its unique study number.

2. Protocol Information

A. Each protocol and all accompanying study and approval documents, including but not limited to, consent forms, recruitment material, grant information, Investigational Brochures, sponsor protocols, restrictions (e.g. suspensions, contingencies) and related correspondence from IRB reviewers, Subcommittee and Full Board.

B. Continuing review applications and progress reports. These are requested at least annually from each investigator as long as the study is still active. At least every 5 years, a new protocol application must be submitted as the basis for any further continuation.

C. Amendments to approved studies, including all documents submitted to support the amendment and documentation of review and approval by the IRB.

D. Statements of significant new findings provided to subjects.

E. Reports of injuries to subjects, unanticipated problems and reports of noncompliance.

3. Record Retention Term

A. Records relating to each project reviewed by the IRB must be kept for a minimum of 3 years, and records of research conducted must be kept for at least three years after the research is completed.

B. The files include all the documentation received or produced by the IRB in relation to the research.

4. Confidentiality of Records

A. IRB records including records related to specific research protocols are kept confidential to the extent possible and allowed by law.

B. Authorized representatives of sponsors, Federal regulatory agencies and State and other regulatory oversight agencies with legitimate access may review and inspect records.

C. Requests for photocopying records and release of any IRB records must be received in writing and approved by the IRB Chair or Administrative Director.

5. Off –Site Storage of Records

A. There is provision for off-site storage if the research study has been terminated and no submissions for the file are pending review. A record is kept in the IRB office of all files transferred to off---site storage.

B. Retrieval of a file can be completed promptly after a request is made, usually within 24-48 hours.

6. Electronic Records

A. The Protocol Management System (PMS) is an electronic database in which all pertinent study information is recorded by and accessible to IRB staff. This includes, but is not limited to:

- Investigator-provided study information
    1. Investigators
    2. Abstract of the research
    3. Study locations

4. Medications under study
5. IND/IDE information
6. Subject sample description
7. List of all protocol amendments
8. List of reported serious or unexpected adverse events
9. Funding information

ii. IRB actions
    1. Assigned Protocol Analyst
    2. Level of review
    3. A review history
    4. Key dates (submission, review, approval, expiration)
    5. Current study status
    6. Special requirements
    7. Completion of COI review
    8. Relevant regulations for approval

iii. PMS data is used to produce a number of reports for the day---to---day operations of the office, for example, reminder notices of impending expiration of IRB approval. The system is also used to assign primary and secondary reviewers, schedule studies for Subcommittee and Full Board review, and generate meeting agendas.

B. Psychiatric Research IRB Submission Module (PRISM) is an online electronic form submission and process management system for the IRB and NYSPI research community.

i. Through PRISM, research personnel may log in using their unique username and password, complete IRB forms, attach relevant documents, and submit forms for IRB review. IRB forms have been re--- created in the system as 'smart forms', which are tailored to the research being conducted (e.g. questions are generated to apply to the specific populations and procedures involved and the current study status). These forms are dynamically linked to a database of IRB guidance, which is intended to assist investigators in study design, form completion, and compliance with IRB and other policies.

ii. Once forms are completed online, the entire workflow takes place electronically, including attestation and electronic signature by Principal Investigator and research chief, submission to IRB, assignment of IRB number and protocol manager, pre---review by the Protocol Analyst, correspondence both within the IRB office and between the IRB and investigators, scheduling for review, and review by Chair or committee. Once a study is approved, the IRB protocol and consent forms are

electronically stamped with approval dates. The system allows for an audit trail, as the form history will capture date, time and user involved, at important junctions in the submission and review process.

To date, all forms and correspondence submitted through PRISM have been retained in hardcopy within IRB Office files. Over the past few years, the IRB Office has been moving towards a paperless file system. All new research submissions are electronic. Protocol continuations and amendments are also primarily electronic, with a few exceptions. Adverse event reports continue to be relayed via email, although an electronic form for this reporting in PRISM is now in development.

Section 13. Subject Outreach

1. The NYSPI---IRB website (http://irb.nyspi.org) includes a section specifically for research subjects. This section can be accessed directly from the home page of the website without a log in or password, and includes information about research in general, emphasizing the fact that study participation is voluntary, confidential, and that informed consent is an intrinsic aspect of research participation. There are also links to NAMI, the FDA and NIMH, along with contact information for the IRB. The community is invited to contact the IRB by phone or email for general or specific questions.

2. IRBMail is a dedicated IRB office e---mail address that can be used by research participants to pose questions directly to the IRB. IRBMail is monitored during business hours by the IRB Senior Administrative Assistant and Protocol Analysts, who can either answer questions themselves or direct them to the appropriate person for response.

3. Every consent form is required to include an emergency contact number for the Principal Investigator. In addition, the consent form instructs the study participant to contact the Principal Investigator for questions regarding any aspect of the research study. For study---related complaints or questions regarding subject rights and welfare, individuals are provided the phone number of IRB Executive Director and advised to call.

4. The Executive Director maintains a file of all subject calls involving concerns or complaints about studies conducted at NYSPI. All calls to the Executive Director are returned either the same day or within the next business day. For a call received directly from a study participant, the Executive Director contacts the complainant by phone, identifies the issue, and assures the individual that their concern is important and a response will be forthcoming. All correspondence, with the complainant, study investigator, and other parties, is documented and maintained in secured IRB Office files. Calls of a clinical nature are discussed with the Principal Investigator and IRB Chair immediately. If the complaint is one that is clearly deemed not of a serious nature, does not involve an adverse event, or does not involve an allegation of research noncompliance or misconduct, the Executive Director generally contacts the Principal Investigator and offers suggestions for problem resolution. Complaints deemed to be non-serious and resolvable are not presented to the convened IRB.

Should a study participant contact the Executive Director about an adverse event, alleged research misconduct, or an ethical breach, the Principal Investigator and IRB Chair are immediately notified. The Chair and Executive Director speak with the Principal Investigator to discuss the allegation.

NYSPI Institutional officials are also consulted (e.g. the Director, Psychiatric Research, the Director of Quality Assurance, and the Psychiatry Clinical Director).

All complaints involving unanticipated problems, serious adverse events, allegations of research misconduct or an ethical breach, are promptly presented to the IRB for consideration. Should a complaint or allegation suggest the need to report to OHRP, the FDA and/or other entities, the Chair will present the case to the Board for discussion and a vote will be taken as to appropriate action/reporting. Board decision---making around serious adverse events and/or allegations of research noncompliance are also reviewed by the Director, Psychiatric Research and the Deputy Managing Director of RFMH to ensure consensus regarding action and reporting.

5.

6. NYSPI currently has a Patient and Family Library (Herbert Pardes Building, floor 6). This resource is designed to meet the needs of mental health consumers and their families. The library provides information on mental health disorders, treatments, community resources and coping.

Section 14. IRB Quality Metrics

The Program for Human Subjects Research performs continuous quality improvement activities to meet the highest ethical and regulatory standards for human subjects protection. These activities are implemented to evaluate the effectiveness of the IRB Office, Subcommittees and Full Board with respect to operations, protocol review, and decision-making. IRB quality metrics are essential for the assessment of efficiency and effectiveness, as they enable the HSR Program to identify its strengths and limitations in order to promote best practices.

Program quality metrics encompass three specific domains: 1. Evaluation of IRB Structure, 2. Evaluation of IRB Process, and 3. Evaluation of Review Outcome.

1. Evaluation of IRB Structure.
   This domain involves the evaluation of Subcommittee and Full Board composition and expertise. IRB member composition is routinely reviewed to ensure adherence to regulatory requirements. Other structural indicators for measure include IRB costs, the ratio of IRB Office staffing levels to workload, and the measure of Committee and Chair activity/workload.

2. Evaluation of IRB Process.
   In order to systematically evaluate IRB processes, select protocols are monitored and quality indicators measured. The IRB Research Compliance Monitor, under direction from the IRB Chairs, Executive Director and Director of Psychiatric Research, proactively identifies and monitors protocols deemed as significant risk, involving vulnerable populations, and/or involving investigational drug and devices. Studies involving experimental interventions, drug washout or delay to treatment are routinely monitored. The Compliance Monitor may be asked to closely monitor research led by a new or inexperienced Investigator, or by an Investigator believed to be noncompliant.

   Metrics pertaining to the evaluation of IRB process include, but are not limited to: the timeliness (i.e., total number of days to approval) of review of new protocols, the total number of days from submission to approval of protocol modifications, and the number of days to process protocol continuations. These processes are further analyzed with respect to time attributed to the IRB Office versus time attributed to Investigator activity.

   With respect to informed consent, significant process indicators include: adherence to program requirements for the consent form summary page, the observation of the informed consent process for designated studies, adherence to IRB policies and procedures with regard to the consent of patients with limited capacity, and adherence to policy regarding the qualification of research staff engaged in the process of informed consent and capacity assessment.

   Our Program also employs indicators addressing appropriate and sufficient IRB documentation, for example, the quality and comprehensiveness of IRB minutes. For industry sponsored studies, documented evidence of IRB review of the Investigator Brochure and drug company protocol is evaluated, as is Board discussion of any significant variations between the submitted and sponsor protocol

3. Evaluation of Review Outcome.
Quality metrics assessing the outcome of protocol review include indicators of comprehensive, expert decision-making. Metrics in this domain include documentation of IRB deliberation, reflected in the IRB minutes, as well as protocol correspondence indicating subcommittee feedback to the Investigator and full board stipulations for approval.

The performance indicators across these three domains serve to provide valuable data and insight for the Program, providing a venue for IRB self-assessment and continuous quality improvement.