# Columbia University

## Institutional Review Board

## Standard Operating Procedures

## Effective June 12, 2012

Version 4

## Introduction to the Columbia Human Research Protection Program

Columbia University (CU or Columbia or the University) has developed and implemented a comprehensive Human Research Protection Program (HRPP; hereafter referred to as the Columbia HRPP) in accordance with the recommendations in the Institute of Medicine Report entitled Responsible Research: A Systems Approach to Protecting Research Participants (October 3, 2002). The HRPP is charged with the responsibility of ensuring that all human subjects research conducted by Columbia faculty, employees, and students is conducted ethically and in a manner that promotes the protection of human subjects in research. Protections for human participants in all such research must not only be in compliance with institutional policy, state law, and federal regulations, but must also meet or exceed the standards of accreditation as set forth by the Association for Accreditation of Human Research Protection Programs (AAHRPP).

The Columbia HRPP covers all entities, offices, and individuals engaged in and/or responsible for the review and conduct of human research at Columbia and NewYork-Presbyterian Hospital (NYP). CU has two Federalwide Assurances (FWAs): one for Columbia University Medical Center (CUMC) and one for the main campus at Morningside Heights (CU-MS). NYP has its own FWA and is a separate legal entity from CU. The respective FWAs cover the components of each institution, e.g., the individual schools of CU-MS and CUMC, and the facilities that comprise NYP at Columbia[1]. Although there are three FWAs, the Columbia HRPP is responsible for all human subjects research conducted at CUMC, CU-MS, and NYP, or by any affiliated faculty, students, or staff of CU and NYP regardless of location. Please see Section II.A.5 for the criteria used to determine whether activities conducted by affiliated faculty are covered by these policies and procedures.

The Columbia research enterprise is extensive in size and broad in the scope and nature of its activities, including biomedical, behavioral, social science, and epidemiological research, as well as studies in the area of health services. Subjects may include healthy volunteers as well as patients and other individuals who may be considered vulnerable due to medical, cognitive, emotional, economical, educational, age, or other factors. Although much of the research is conducted in the New York City area and on Columbia campuses, faculty members also actively conduct research at other sites both domestic and international. Furthermore, many Columbia faculty members collaborate on projects with investigators at other institutions. The Columbia HRPP accounts for approximately 1,500 new human research studies each year, and manages approximately 4,500 studies that have been approved or determined to be exempt.

### A. Institutional Leadership

[1] NewYork-Presbyterian Hospital has facilities that are affiliated with either Columbia University or Cornell University. At Columbia, the primary facilities are Allen Pavilion, Columbia University Medical Center, and the Morgan Stanley Children's Hospital of New York (MSCHONY). For simplicity, the Columbia affiliates ("NYP at Columbia") will be referenced as "NYP".

In accordance with the organizational structure of the Office of the Executive Vice President for Research (EVPR), the Columbia HRPP is managed by the Executive Director, Human Research Protection Program (ED), who is also responsible for the management of all Institutional Review Board (IRB) operations at CU. Sections I of these written procedures outline and summarize the Columbia HRPP.

The ED reports to the EVPR, through the Vice President for Research Operations (VPRO), and the Institutional Officials (IOs) designated on the FWAs of CUMC, CU-MS, and NYP. The EVPR, reporting directly to the President of the University, has overall responsibility for the University's research enterprise. The Office of the EVPR establishes and administers the policies governing the conduct of research at the University and oversees the management of its research programs.

In 1966, Columbia established its first IRB under the authority of the Dean of the College of Physicians and Surgeons of Columbia University. Because of changes to the University administrative structure since 1966, including centralization of administrative functions and the establishment of the Office of the EVPR, the functions of and charge to the IRB are now under the purview of the EVPR.

The EVPR is responsible for central oversight of the entire Columbia HRPP and also serves as the IO on the FWA for CU-MS. Individuals with an appropriate level of authority reporting to the Executive Vice President for Health and Biomedical Sciences and Dean of the Faculties of Health Sciences and Medicine (EVPHBS), and to the President of NYP, are designated as the IOs for CUMC and NYP, respectively. Each IO is responsible for ensuring that all research under his/her FWA is conducted ethically and in compliance with all regulatory standards. The EVPR, together with the IOs of CUMC and NYP, the VPRO, and the ED provide a team approach for oversight of the protection of human subjects in research.

## B. Institutional Culture

Essential to the success of the Columbia HRPP is the institutional culture or conscience that permeates all components of the program. Research is one of the key missions of Columbia, which prides itself on its commitment towards excellence in all research activities. Columbia and NYP recognize that the ethical conduct of research is not only vital for the success of the research enterprise and the public trust in our research programs, but more importantly that the institutions have a moral responsibility to act accordingly. Towards these ends, the EVPR and the IOs of CUMC and NYP lead the Columbia HRPP in many different ways, including: 1) instilling the above described culture; 2) supporting the Columbia HRPP with the necessary funds, resources, and intellectual support; and 3) providing the necessary authoritative leadership and support for ensuring the integrity of Columbia's program for the handling of alleged noncompliance incidents.

## C. Standard Operating Procedures

### 1. Development

Columbia University has adopted these Standard Operating Procedures (SOPs) to ensure the ethical conduct of research and the protection of the rights and welfare of human subjects participating in research conducted under the authority of the University. This manual describes the means by which research with human subjects will be reviewed, approved, and monitored.

The IRB Standard Operating Procedures (SOPs) comply with the U.S. Department of Health and Human Services (DHHS or HHS) and the U.S. Food and Drug Administration (FDA) regulations on research with human beings. To the extent that they are consistent with federal law and regulations, the written procedures also comply with the International Conference on Harmonization (ICH) "Guidance for Industry- E6 Good Clinical Practice: Consolidated Guideline".

Policies and procedures are developed within the IRB by one of the two standing committees described in Section I.A.3: the Policy Committee or the Accreditation Committee.

The IRB SOPs will be reviewed regularly, and minimally once per year. Any necessary revision to these policies must be made through the process described in the following section.

### 2. Process for Revising Standard Operating Procedures

a. A proposed revision to an SOP must be submitted to either the Policy or Accreditation Committee, through the respective Chair, for consideration.

   1) More significant changes that may have broader implications should be handled by the Policy Committee.

   2) Minor or less significant changes can be handled by the Accreditation Committee.

b. If necessary, the Chairs of each Committee discuss jurisdiction of any proposed revision and decide which Committee will consider the revision. The ED has the authority to make the final decision.

c. Once a proposed revision is considered by either Committee, a draft is forwarded to the ED, the Associate Director (AD), the Assistant Director for IRB Operations (ADO), all IRB Chairs, the VPRO (when appropriate), and staff for review and

consideration. After a designated review period, all comments are considered by the Committee that drafted the proposed revision.

1) If no substantive changes have been made during the review period, the final draft version is forwarded to the ED for approval. Approval of revised policies is documented with the date and signature of the ED.

2) If substantive changes are made during the review period, a revised version is again circulated to the IRB Chairs and staff. This process continues until the final revised policy is approved. The ED has the authority to revise and approve the policy at a point when all remaining concerns are editorial or grammatical.

3) As necessary or appropriate, draft policies are circulated between CU and NYP, and to other individuals or entities within the institution, e.g., Office of the General Counsel (OGC), EVPR, Clinical Trials Office (CTO), Sponsored Projects Administration (SPA), and the Office of Research Compliance and Training (RCT).

d. Approved policies and changes to these SOPs are announced via the IRB list serv, at a minimum, and posted on the CU IRB websites. Appropriate individuals (e.g., research personnel, IRB staff, IRB members and Chairs, VPRO, IOs, EVPR) are notified of new policies and changes to these written procedures.

Revisions to the SOPs may be made on a section or item basis. This process allows more timely updates to an SOP rather than requiring re-approval of all SOPs with each revision.

At the discretion of the ED or the AD, any change to the SOPs may be implemented immediately without following this process if a determination is made by the ED or AD that the change is necessary for the immediate protection of human subjects or to address an urgent regulatory compliance concern.

**D. Requirement for Submissions**

All protocols for human subjects research to be conducted by Columbia faculty, employees, and students must be submitted for review in Rascal, Columbia's research and administration compliance Information Technology Rascal (IT) system. Non-exempt projects must be prospectively approved by the appropriately designated IRB under one of Columbia's FWAs. Exempt determinations at CUMC are made by an Administrative Review Committee (ARC) within the IRB office or any IRB Chair or Vice Chair; at CU-MS, exempt determinations are made by the IRB Chair or Vice Chair. Per Columbia policy, investigators may not make the final determination of exemption, i.e., protocols that appear to meet federal criteria for exemption must be submitted to the IRB for confirmation of exempt status. Certain pedagogical activities conducted by students must also be submitted for review, in accordance with the IRB Students as Researchers Policy (Reference Document #304), even though the regulatory definition of research may not be met.

## E. Definitions of *Research* and *Human Subject*

Throughout these written procedures, "human subjects research" (HSR) is defined as those activities that meet the criteria articulated in applicable U.S. DHHS regulations to be considered as both "*research*" and as involving "*human subjects*".

> *Research*: a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. [Title 45 of the Code of Federal Regulations (CFR) Part 46.102(d); hereafter, regulatory citations will include only "CFR" and the numbers.]
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> *Human subject*: a living individual about whom an investigator (whether professional or student) conducting research obtains
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> (1) Data through intervention or interaction with the individual, or
>
> (2) Identifiable private information. [45 CFR 46.102(f)]

When an activity involves a drug, device, or biological product that is subject to U.S. FDA regulations, the following definitions also apply:

> Research: The FDA has defined *"clinical investigation"* to be synonymous with *"research"*. *"Clinical investigation"* means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA...or the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. [21 CFR 50.3(c)]
>
> *Test Article*: any drug (including a biological product) for human use, medical device for human use, human food additive, color, adaptive electronic product, or any other article subject to regulation under the jurisdiction of the FDA. [21 CFR 50.3(j)]
>
> *Human subject*: an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient. [21 CFR 50.3(e)]

## F. Rascal

Rascal was developed at Columbia to facilitate the management, review, and oversight of its research administration and compliance. Columbia requires that all research protocols

involving human subjects research be submitted in Rascal for review by the IRB and other administrative offices. This system provides a high level of accountability for all research protocols, as it allows for tracking of research, systematic administration of reviews by the IRBs and other committees, processing and accounting of human research educational training, and management of conflicts of interest.

# I. Human Research Protection Program

A brief overview of the Columbia HRPP is provided below.

## A. Institutional Review Boards and IRB Office

The mission of the CU IRBs and the CU IRB Office, which form the core of the Columbia HRPP, is to enhance and facilitate the ethical conduct of human subjects research that is conducted: a) at Columbia; b) through the support of Columbia funding; and/or c) by Columbia faculty, regardless of location. The CU IRBs perform this mission through their review of human subjects research, and are supported in this endeavor by the IRB Office educational and training initiatives, and compliance oversight and quality improvement programs.

The IRBs are not solely responsible for the integrity and conduct of such research, nor are they responsible for the programmatic development or decisions as to what research should or should not be conducted at Columbia. These considerations also fall under the purview of the EVPHBS, the President for NYP, and the EVPR, who have the authority to restrict research that cannot be supported by resources, principles, or policies of their respective institutions, regardless of whether it has been approved by one of the CU review panels.

Columbia review boards and those of other institutions play a crucial role in the effective protection of the human subjects who are involved in research that comes under the purview of the HRPP. A detailed description of the Columbia IRBs, including scope of authority, constitution, organization, membership, and use of consultants, and an explanation of the role that non-Columbia IRBs fulfill for the HRPP, is provided in Section II.

The IRB Office is the central administrative office for the Columbia HRPP. This Office serves as the central repository of all information affecting the protection of human subjects in research. The IRB Office is responsible for the management and oversight of all IRBs at CU-MS and CUMC. In addition, the IRB Office is responsible for ensuring that all relevant information affecting the safety and welfare of human subjects in research, and noncompliance issues, are reported to the IRBs, and as appropriate to the IOs, federal regulatory agencies, sponsors, and AAHRPP.

Leadership within the IRB office is a team that consists of the ED, AD, ADO, and the manager of each team within the IRB. The IRB Office has two locations: a) on the CUMC campus, and b) on the CU-MS campus, (see Reference Document #160, IRB Contact Information, for current addresses).

The IRB Office convenes ad-hoc meetings that involve the heads of other HRPP units as necessary to address any incidents or issues that may require additional consideration or more immediate action. As necessary for prompt notification, the IRB Office sends communications of relevant information regarding the ethical conduct of human research and the protection of human subjects to all heads of Columbia HRPP units. The ED participates

in monthly meetings that are convened by the EVPR and include the heads of all units under his authority.

The IRB Office also leads bi-weekly meetings of the IRB Executive Committee (IEC). This Committee is comprised of the Chairs and Vice Chairs of all IRBs, the VPRO, the ED, and the AD. The purpose of these meetings is to improve the quality and consistency of the work performed by the IRBs and to address overarching issues and challenges that may face the collective IRBs. Once a month, all IRB officers (professional level staff) also attend this meeting.

Four other committees within the IRB office support initiatives to improve the ethical conduct and review of research: 1) Education and Training Committee; 2) Policy Committee; 3) Accreditation Committee; and 4) Rascal Committee. The purpose of each committee is discussed in more detail below (Sections I.A.3.a-I.A.3.d). Additional committees may be constituted as necessary to support office initiatives.

### 1. IRB Administrative Staff

The ED and the AD are responsible for the management of all CU IRBs and the IRB Office staff. Oversight of the performance and management of all CU IRBs is delegated to the AD. Each IRB Chair and IRB Manager are responsible for daily management of their respective Board.

The IRB Office provides sufficient professional and administrative support, and adequate resources, to ensure compliance with federal and state regulations and institutional policies for the protection of human subjects in research. The commitment of staffing resources for the IRB Office is evaluated internally by the ED and AD, in conjunction with the IRB Managers, and ADO, on a continual basis and additional support is provided as needed. Through regular meetings with the VPRO and CUMC IO, the ED and AD communicate office-wide requests for additional support as warranted.

Adequate meeting and office space are provided for the IRB and staff. Office equipment and supplies, including file cabinets, computers with Internet access, and copy machines, are available to the IRB and staff.

#### a. Organization

##### 1) Administrative Support to Review Panels

Each IRB is administered by a team of staff comprised of an IRB Manager and at least one other officer. Each team is responsible for: a) ensuring that all research reviewed by its IRB is in compliance with all applicable standards and that all reviews are handled efficiently and at a high level of quality; b) providing its IRB members with the necessary information to conduct their reviews; and c) preparing all communications to the research team.

Submissions (i.e., new protocols, modifications, renewals, reports of unanticipated problems, and closure requests) are triaged upon receipt and undergo a thorough administrative, preliminary review ("pre-review") utilizing a detailed pre-review form based on the type of submission. The pre-review process is designed to help ensure that each study is submitted with the necessary information to proceed for review by an IRB member and that each study will receive all relevant regulatory considerations. Once a study has received a pre-review it proceeds to an IRB (for CUMC non-exempt and all CU-MS studies) or to the ARC or a Chair (for CUMC exempt studies) for review.

**2) Compliance Oversight Team**

The Compliance Oversight Team (COT) is comprised of the COT Manager and IRB auditors and reports directly to the ED. The COT is responsible for investigating and handling all allegations of serious and/or continuing noncompliance, concerns about research conduct, and complaints with respect to the protection of human subjects in research, and the tracking of all minor non-compliance. Allegations of noncompliance, concerns, or complaints may be received from anyone, e.g., the IRBs, IRB staff, faculty, research staff, IOs, departmental administrators, research subjects, federal and state regulatory agencies, the media, or the general public, and may be reported anonymously. All such allegations, as well as any other event that must be reported to federal regulatory agencies (e.g., certain unanticipated problems, suspension of IRB approval, etc.) are logged into a tracking system by the COT, which promptly notifies the ED and AD of such reports (if the ED/AD have not already been advised of the allegation). The COT also works with the Privacy Office regarding any concern or finding of Health Information Portability and Accountability Act (HIPAA) noncompliance in research, with the ultimate goal of bringing the study back into compliance.

Alleged incidents of noncompliance are handled in accordance with the Columbia Noncompliance with Human Subjects Regulations Policy (Reference Document #89). When a determination of serious noncompliance has been made, an appropriate corrective action plan is developed. A follow-up report of serious or continuing noncompliance is then filed with the respective IRB, the appropriate IO(s), the EVPR, and when appropriate, with the relevant regulatory agency and sponsor. If necessary, the COT monitors studies where it is deemed necessary to perform follow up reviews of corrective action plans.

The COT also conducts not-for-cause audits as part of the IRB's compliance oversight initiatives. Details of the IRB Oversight Monitoring program, which includes follow-up to allegations of noncompliance, monitoring procedures, and not-for-cause audits, are provided in Section IX.

**b. Duties**

Staff members are categorized as either officers or support staff. Duties for all staff are described in the job description for the specific position held by each individual (Reference Document #91).

To improve quality, performance and efficiency, periodic performance evaluations are conducted for officer-level staff, while regular feedback is provided to support level staff. The current 1199 SEIU United Healthcare Workers East, Supporting Staff Association Area (SSA) and Local 2110 UAW (i.e., unions for support-level staff at CUMC and CU, respectively) Collective Bargaining Agreements with the University guide the supervision and employment of support staff.

### c. Education and Training

IRB staff members complete the same core educational program that is required for research personnel. This includes training relating to relevant laws and regulations and the Columbia IRB policies and procedures. The IRB staff are also provided ongoing and continuing educational opportunities (IRB seminars and workshops; distribution of continuing education information; and access to the IRB website and library). Details of education and training initiatives are provided in Section X.C of these SOPs.

### d. Confidentiality and Conflict of Interest

All IRB staff members are required to sign a Confidentiality and Conflict of Interest Statement (Reference Document #76), the concepts of which are reinforced during training sessions. The statement also articulates the need and expectation for Board deliberations and details of the protocols that are submitted to the IRB to remain confidential.

## 2. Committees within the IRB Office

### a. Education and Training Committee

The Education and Training Committee, one of several standing committees established in 2003 within the IRB Office, holds regular educational sessions for IRB staff, members of the CU research community, and IRB members. The Committee is chaired by an experienced officer on the IRB staff. Committee membership is comprised of IRB staff, each of whom contributes to an active, year-round schedule of events that includes monthly IRB-investigator meetings, an annual IRB conference, "IRB 101" sessions for researchers, Rascal training sessions for IRB members and researchers, orientation for new IRB members, outreach to the community, and staff training sessions on a variety of topics.

Efforts by staff to expand their knowledge of the ethical and regulatory bases for human subject protection by completing online tutorials, attending local and national conferences, and obtaining Certified IRB Professional (CIP) status are strongly

encouraged. Education and training activities for staff include both mandatory and voluntary initiatives.

### b. Policy Committee

The Policy Committee, also established in 2003 within the IRB Office, is responsible for the formulation and drafting of policies relating to: 1) the ethical conduct of human research; 2) the protection of human subjects in research; and 3) IRB review and processes. The Committee meets at least monthly and is chaired by an experienced officer on the IRB staff. Committee membership is comprised of IRB staff, but may include individuals from outside of the IRB.

### c. Accreditation Committee

The Accreditation Committee, which was established in 2004 within the IRB Office, is chaired by the AD, and is charged with preparation for and maintenance of accreditation of the Columbia HRPP. The Accreditation Committee also has the authority to develop and draft new IRB Policies and Procedures or IRB processes that generally do not have broader implications (e.g., policies that do not also impact the research community). The Committee is charged with the added responsibility and authority for the monitoring and oversight of internal IRB processes so that accreditation can be obtained and maintained.

### d. Rascal Committee

The Rascal Committee was established in 2004 within the IRB Office and is charged with working with the Rascal IT Team for further development and enhancement of the Rascal system as it relates to the Human Subject and Consent Form modules. The Rascal Committee is the central repository of all suggestions for improvement of the IRB module. The Committee is responsible for prioritizing all requests for Rascal improvements with the input of the IRB Chairs and staff. Meetings are held on an ad-hoc basis as necessary to accommodate the current needs of the Rascal system and evaluate any new processes being tested. The Committee is chaired by an experienced officer on the IRB staff, and is comprised of IRB staff. An executive subcommittee consisting of the ED, AD, and ADO meets regularly with the Rascal development team.

## B. Privacy Board

The Columbia University IRBs serve as the Privacy Boards for the review of protected health information that may be used by Columbia investigators, and for ensuring compliance with the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA) of 1996. The implementation of policies and processes to ensure such compliance is the responsibility of the Privacy Officer (PO), who reports to the Billing Compliance Officer within the Office for Billing Compliance (OFBC). The PO coordinates such efforts with the ED and/or AD of the IRB, and the COT. See Reference Document #115 (CU IRB Policy on

Research and the HIPAA Privacy Rule) and Reference Document #116 (CUMC IRB Procedures to Comply with Privacy Laws that Affect Use and Disclosure of Protected Health Information for Research Purposes) for additional information.

## C. Office of Sponsored Projects Administration

SPA, together with the CTO described below, are responsible for the administration of all sponsored research conducted by Columbia. SPA works closely with the IRB staff to ensure that all human subjects research has obtained appropriate IRB approval. Any potential noncompliance with the regulations for human subjects protection that is identified by a SPA staff member is promptly reported to the ED.

## D. Clinical Trials Office

The CTO is responsible for the administration of all clinical trials conducted by the College of Physicians and Surgeons. The CTO fosters the ethical conduct of research by establishing important provisions and policies that are relevant for the protection of human subjects. For example, in its contract negotiations, the CTO addresses issues such as ensuring prospective IRB review, payment for research procedures and test articles, compensation for research related injuries, and the protection of confidentiality of research data. Any potential noncompliance with the regulations for human subjects protection that is identified by a CTO staff member is promptly reported to the ED. The CTO also administers the Research Pharmacy (RP), the Investigational New Device (IND)/Investigational Device Exemption (IDE) Assistance Program (IAP), the Clinical Trials Monitoring Assistance Program for FDA Regulated Human Subjects Research (CTMAP), Clinical Research Coordinator Training (CRCT), and the Spanish Translation Center (STC).

### 1. Research Pharmacy

The RP is responsible for the storage, handling, accountability, and dispensing of investigational drugs to research investigators. The RP is overseen by the CTO, and research pharmacists serve on one or more CUMC IRBs. This close working relationship between the RP and the IRB not only provides pharmacy input to the IRBs, but also helps ensure that the handling of investigational drugs is in compliance with federal and state regulations as well as institutional and IRB policies. Any potential noncompliance with the regulations for human subjects protection that is identified by the RP is promptly reported to the ED.

### 2. IND/IDE Assistance Program

The IAP was established in 2010 to assist, at all stages of a clinical investigation, Columbia investigators who hold an IND or IDE. The IAP provides the following to the research community: guidance and education to investigators regarding the responsibilities of sponsors of INDs or IDEs; guidance in the preparation of all documents submitted to the FDA; assistance in the maintenance of an IND or IDE; and consultation in all regulatory matters. The IAP and IRB have developed institutional

policies to assist investigators implement an effective IND or IDE for their research. Any potential noncompliance with the regulations for human subjects protection that is identified by the IAP is reported to the ED.

### 3. Clinical Trials Monitoring Assistance Program

The CTO has established a program to assist Sponsor-Investigators (S-Is) in meeting FDA requirements with respect to monitoring of S-I studies. From the design and development of a monitoring plan to periodic review of adherence, assistance to Columbia faculty and clinical research coordinators is available from CTMAP. Details of the Program are available on the CTO website and in the Clinical Research Handbook.

### 4. Spanish Translation Center

The STC provides translation into Spanish of research documents such as consent forms, recruitment letters, and advertisements for potential research subjects. The STC serves a vital role in Columbia's human research protection program because CUMC and NYP are located in a community with a predominantly Hispanic population, many of whom are non-English speaking. The STC works with the IRB to fulfill requirements of the IRB Enrollment of Non-English Speaking Subjects in Research Policy. Any document that will be translated by the STC for IRB approval must first be approved in English by the IRB. Final approval by the IRB of translated document(s) is granted after review and approval by the STC. Any potential noncompliance with the regulations for human subjects protection that is identified by the STC is promptly reported to the ED. The STC was previously known as the Hispanic Translation Center; reference to the Center by this name may be found on historical documents and in the STC approval stamp.

## E. Office of Research Compliance and Training

RCT develops and provides educational training initiatives for all Research Administration Offices that do not have their own education training program. RCT works with the Columbia IRB office on an ad hoc basis to complement the educational training initiatives of the IRB office.

RCT also provides several compliance oversight efforts. One such effort is to administer and manage the handling of any noncompliance involving research integrity (i.e., fabrication, falsification, or plagiarism). RCT also provides administrative assistance to, and works closely with, the CUMC Conflicts of Interest (COI) Committee in accordance with Columbia's COI policy. All Columbia faculty must complete a COI form when they are hired and must update this form annually. In addition, all Principal Investigators, co-Investigators, and other key personnel on human research proposals must complete a protocol-specific conflict of interest form prior to submission of a research study for IRB approval. The Rascal system facilitates the management of conflicts of interest by identifying any positive response for conflicts in either the Columbia annual COI disclosure statement or the protocol specific COI form. RCT works closely with the Columbia IRB office to foster the ethical conduct of research at Columbia.

## F. Joint Radiation Safety Committee, Radioactive Drug Research Committee, and the Radiation Safety Office

The Joint Radiation Safety Committee (JRSC) oversees the radiation safety program for CUMC, CU-MS, NYP, and New York State Psychiatric Institute (NYSPI). The JRSC, in accordance with New York City (NYC) regulatory requirements, oversees the use of all sources of radiation and licensed radioactive material, whether for research or clinical purposes, and is responsible for approving any individual as an Authorized User or Responsible Investigator.

The Columbia Radioactive Drug Research Committee (RDRC) has been authorized by the FDA to review and approve the use of radioactive drugs in certain research studies. Such use is limited to obtaining basic information regarding human metabolism, physiology, and biochemistry.

The Radiation Safety Office (RSO) is the professional, technical and administrative arm of the JRSC. In accordance with NYC regulatory requirements, the RSO: assists the JRSC in the performance of its duties; establishes, implements and maintains written policies and procedures for the safe use of radioactive materials; and generally oversees the day to day operations of the joint radiation safety program.

The JRSC, RDRC, and RSO work closely wit the IRB in both protocol review and compliance matters. Any study using radiation in human subjects is approved by both the IRB and the JRSC or RDRC, working collaboratively. Likewise, any potential noncompliance with the regulatory requirements for the use of radiation or radioactive materials in research involving human subjects must be promptly reported to the: JRSC or RDRC; the RSO; and the ED. Likewise, any potential noncompliance with the regulations for human subjects protection that is identified by the JRSC, RDRC, or the RSO is also promptly reported to the ED.

## G. Institutional Biosafety Office

The Institutional Biosafety Committee (IBC) is responsible for the review and approval of the handling of hazardous materials in research, such as potentially infectious tissues or bodily samples, and research involving gene transfer. Rascal prompts researchers to identify potential hazardous materials during the creation of an IRB protocol and does not permit a protocol that requires IBC approval to be approved by the IRB prior to IBC approval. Any potential noncompliance with the regulations for human subjects protection that is identified by the IBC is promptly reported to the ED.

## H. Protocol Review and Monitoring Committee

The Protocol Review and Monitoring Committee (PRMC) serves as the scientific review committee for the Herbert Irving Comprehensive Cancer Center (HICCC) on the CUMC

campus. Any research proposal involving cancer in any manner at CUMC requires review and approval by the PRMC prior to review by the IRB. The PRMC conducts an initial review of all cancer research, a review of all modifications to the research study, and an annual re-review of the research. The PRMC forwards notification of its scientific reviews to the IRB for consideration during the IRB review of cancer-related protocols. Any potential noncompliance with the regulations for human subjects protection that is identified by the PRMC is promptly reported to the ED.

## I. Irving Institute for Clinical and Translational Research

The Columbia Irving Institute for Clinical and Translational Research (IICTR) has been awarded an National Institutes of Health (NIH) Clinical and Translational Science Award (CTSA), and provides resources to foster and support new, collaborative, multidisciplinary human subjects research at Columbia. Some of the resources provided include consultation for biomedical informatics, research design and biostatistics, and regulatory considerations. The Institute also administers the Clinical Research Center (CRC) that allows investigators to conduct both inpatient and outpatient studies involving adults and children. All research conducted at the CRC is first reviewed by a scientific review committee called the CRC Advisory Committee. The ED serves as an ex-officio member of the CRC Advisory Committee. Any problems or concerns raised during the CRC scientific review are forwarded to the IRB, as appropriate. Likewise, any potential noncompliance with the regulations for human subjects protection that is identified by the CRC is promptly reported to the ED.

## J. NYP Pharmacy

The NYP Pharmacy works closely with the CUMC Research Pharmacy and the IRB Office to ensure that all investigational drugs, including those administered for emergency use, are administered in accordance with federal regulations, accreditation standards, and IRB and institutional policies. Towards this end, the NYP Pharmacy, the RP, and the IRB Office work together to develop policies for the proper dispensing and handling of investigational drugs, as well as the documentation of such processes. The NYP Pharmacy promptly reports any potential noncompliance with the regulations for human subjects protection, and/or dosing errors involving investigational drugs to the ED.

## K. NYP Patient Services Administration

The NYP Patient Services Administration (PSA) staff is available to: 1) ensure that patient rights are upheld; 2) assist with the resolution of problems or concerns; 3) provide information about hospital services and policies; and 4) connect patients with appropriate departments. As a result, this office serves as a possible repository of concerns expressed by research subjects. The PSA and the CU IRB Office have established a close working relationship to ensure that any concerns from research subjects who participate in human research conducted at NYP on the CUMC campus are addressed satisfactorily. Each office will inform the other promptly of any concerns expressed by such research subjects or any potential noncompliance with the regulations for human subjects protection.

## L. Center for Bioethics

The Center for Bioethics (CBE) provides an inter-disciplinary, inter-professional forum to advance scholarly work on, and public understanding of, contemporary issues in biomedical ethics. One direct benefit for investigators and research administrators is that the Center provides educational training conferences and seminars in the area of bioethics. The Executive Director of the Center for Bioethics also serves as an ad-hoc advisor to the IRB Policy Committee.

## M. Department Chairs, Investigators, and Departmental Administrators

Department Chairs and Investigators are responsible for ensuring that all research involving human subjects is conducted in accordance with ethical principles, institutional policies, and federal and state regulations. The leadership provided by the Department Chairs, Investigators, and Departmental Administrators helps to ensure that research at Columbia is conducted with high quality and in an ethical manner.

The research investigators and staff are at the forefront of human research protections, as they are best positioned to directly ensure that research is conducted ethically. Principal Investigators (PIs) have particular responsibility for conducting research in accordance with the approved protocol and in such a manner that subjects are protected to the extent possible. Additional information relating to PI eligibility, roles and responsibilities, and training is provided in Section III.C and X.D.

Department Chairs are notified whenever serious and/or continuing noncompliance with such policies or regulations occurs within their department. Likewise, any potential noncompliance with the regulations for human subjects protection that is identified internally is promptly reported to the ED.

# II. Institutional Review Boards

## A. Columbia IRBs and Administrative Review Committee

### 1. Guiding Principles, Regulations, Statutes, Standards, Policies

All CU IRBs are governed by the principles of the Belmont Report, applicable statutes, standards, and policies, and the federal regulations for the protection of human subjects in research as codified by:

a. the U.S. DHHS regulations, 45 CFR Part 46, Subparts A (Common Rule), B, C, and D;
b. the U.S. FDA regulations, 21 CFR Parts 50, 56, 312, 600, and 812;
c. the Department of Education (DOE) Family Education Rights and Privacy Act (FERPA);
d. applicable Department of Defense (DoD) regulations;
e. New York State Laws 2440/441 and Article 7, Section 79-1 (Confidentiality of Genetic Tests);
f. The HIPAA Privacy Rule of 1996;
g. Columbia institutional policies; and
h. the AAHRPP Accreditation Standards.

The Boards are subject to regulation by federal oversight agencies, including the FDA and the Office for Human Research Protections (OHRP). Other federal, state and local agencies may have authority to oversee specific aspects of individual research projects or the research program in general.

### 2. Structure

There are six review panels in the Columbia HRPP. Five IRBs (commonly referred to as "Boards") are responsible for the review of non-exempt human subjects research conducted by faculty, employees, and students at CUMC and NYP, and one IRB is responsible for human research (exempt and non-exempt) conducted by faculty, employees, and students at CU-MS. Of the five CUMC IRBs, one is designated to review all cancer-related research that initially required review at a convened meeting (IRB 4), and one manages all research that initially qualifies for expedited review (IRB Exp).

Exempt research and projects that do not meet the regulatory definitions of *research* or *human subject* are reviewed at CUMC by IRB officers with sufficient expertise or by IRB Chairs; collectively they comprise the IRB ARC. Additional IRBs may be added as necessary to ensure adequate and timely review of research proposals.

### 3. Scope of Authority

All CU IRBs are charged with the responsibility of providing review, approval, and oversight monitoring to ensure that all human research under the auspices of the Columbia HRPP is conducted: 1) ethically; 2) in a manner that protects human subjects, and 3) in accordance with the above mentioned regulations, laws, policies, and standards.

The Boards have the responsibility and the authority to:

- review all human subjects research described in Section II.A.5. for prospective IRB approval;
- review progress of studies at least yearly and more often when deemed necessary;
- observe or have a third party, whom the Boards determine is qualified and appropriate, observe the consent process or any aspect of the research;
- suspend or terminate approval of any study that has an unanticipated problem involving risks to human subjects or others, serious or continuing noncompliance with any federal regulation, or serious or continuing noncompliance with the requirements or determinations of the IRB; such actions will generally be determined at a convened meeting of the full Board with a quorum present and will be incorporated into the minutes of the meeting;
- restrict any study it determines to warrant such action, including situations in which one aspect of a study fails to comply with federal regulations or Board requirements or determinations; and
- review research that was initiated without IRB approval for compliance with federal and state regulations and/or institutional policy.

### 4. Autonomy

The IRBs act independently and consider research proposals from the perspective of protection of the subjects who may be involved. While approval from other CU offices or committees may be necessary per institutional policy, the decision whether to approve or disapprove a submission is made autonomously by the IRBs and is not influenced by potential funding, prestige, or other benefit that may accrue to the University. Copies of meeting minutes that document IRB actions are routinely forwarded to the IOs who represent CUMC, CU, and NYP, not only for informational purposes, but also for their consideration of whether the approved studies may appropriately be conducted under the auspices of these institutions.

### 5. Research Conducted by Columbia faculty, employees, and students

Columbia has given the Boards the authority and responsibility to take appropriate action, in accordance with the terms of the FWAs, to protect all human subjects involved in research that is conducted by investigators who are affiliated with Columbia, and in all

other activities which even in part involve such research, regardless of sponsorship, if one or more of the following apply:

1. the research is sponsored by Columbia;
2. the research is conducted by or under the direction of any employee or agent (faculty/student/staff) of Columbia, in connection with his or her institutional responsibilities;
3. the research is conducted by or under the direction of any employee (i.e., faculty or staff), student, or agent (e.g., visiting scientist/scholar, contractor, business associate) of this institution using any property or facility of Columbia; or
4. the research involves the use of Columbia's nonpublic information, e.g., to identify or contact human research subjects or prospective subjects, for data review or analysis.

"Agent" in the preceding statements is defined as an individual or entity that has an agreement or obligation with the University to perform specific tasks or provide defined services and is not an employee.

For some activities that do not meet the federal regulatory definition of *research*, review by the IRB may be required per institutional policy. These activities include student projects as described in the IRB Students as Researchers Policy, and genetic testing on anonymous samples as described in the IRB Guidance on Research Involving Genetic Testing.

Reliance by Columbia on the review of a non-Columbia IRB is appropriate in some situations. Submission in Rascal is required in these situations, for tracking purposes and if applicable, to satisfy the terms of the reliance agreement. The role of non-Columbia IRBs in the review of research that falls under the scope of authority defined above is described in detail in Section II.B.

Any Columbia faculty, employee, student, or agent who proposes to conduct human subjects research must obtain prospective approval from the appropriately designated Columbia IRB under the applicable FWA prior to the initiation of such research. All human subjects research that qualifies for exemption under the federal regulations must also be submitted in Rascal for confirmation of the exempt status.

### 6. Constitution of the Columbia IRBs

The system of human subjects protection at Columbia functions with the number of IRBs necessary to conduct quality and timely reviews of all human subjects research. Columbia will periodically evaluate the number of Boards, and their composition, and make the necessary modifications, including constitution of additional Boards, to ensure adequate review.

Each IRB will ascertain the acceptability of proposed research in terms of institutional commitments, federal regulations, applicable laws, and standards for professional conduct and practice.

Once a Board has reviewed a protocol, all additional oversight and actions will, whenever feasible, be performed by that same Board (i.e., continuing review, review of modifications, and unanticipated problem considerations). The Board will delegate compliance oversight activities for serious or continuing situations to the COT for purposes of conducting investigations, in accordance with the Noncompliance with Human Subjects Regulations Policy, but will receive and act on the COT reports as discussed in Section IX.F.

Each Board will be distinct and completely separate from the other Boards in that it will act independently on protocols assigned to it. If an issue affects more than one Board (e.g., an investigator with studies open under more than one Board is failing to comply with regulations), each Board may address the issue separately or defer the issue to the IEC.

Each Board has its own Chair. The Chairs on the CUMC campus are administratively responsible to the Senior Vice Dean, who is the IO at CUMC, and to the EVPR; the Chair on the CU-MS campus is administratively responsible to the EVPR. The Chairs have direct access to the EVPR, IO-CUMC (as applicable), and the EVPHBS for discussion of IRB issues.

The EVPR is responsible for providing adequate support and resources for the overall operation of the IRB. Coordination of Board activity is achieved by the IEC.

a. Membership

The Columbia IRBs are comprised of three non-specialized Boards on the CUMC campus, two specialized Boards on the CUMC campus (one for oncology and one for minimal risk protocols initially eligible for expedited review), and one non-specialized Board on the CU-MS campus, each of which, except the Board designated to conduct only expedited reviews, meets an average of two times per month. Each Board is constituted to meet the regulatory requirements mandated by DHHS and FDA, and institutional needs, i.e., individuals with the necessary expertise to evaluate the type and volume of protocols submitted for review.

b. Qualification of Members

The membership of each Board includes individuals with varying backgrounds who possess the appropriate professional competence to review the diverse types of protocols that are received or provide awareness of considerations of the local community.

Each IRB includes among its membership at least one individual who has no affiliation with CU (and no immediate family member with an affiliation with CU) other than his/her IRB membership, at least one scientist, and at least one non-scientist. There is at least one voting member at every meeting whose interests and background are primarily non-scientific (lay person). One IRB member may fulfill both non-scientific and unaffiliated criteria. In addition, each Board that reviews FDA-regulated products (drugs, biologics, and devices) has at least one member present at meetings who is a physician. A prisoner advocate is on the roster for CUMC IRBs 1, 2, 3, and Exp, and the CU-MS IRB, either as a full member or as an alternate who counts towards quorum and as a voting member for prisoner research only.

c. Membership Diversity

Membership is selected to assure appropriate diversity, including representation by multiple professions, appropriate scientific disciplines and specialties, varied ethnic backgrounds, and both genders, and to include both scientific and non-scientific members.

d. Alternate Members

One or more alternate members exist for each regular (i.e., primary) member of each IRB. Such alternate members must be of the same category of membership (i.e., scientific or non-scientific), and meet the afore-mentioned guidelines. Alternate scientific members need not be of the same discipline as the primary member(s) for whom they may serve. Alternate members may be necessary for quorum purposes or to provide requisite expertise. Use of alternate members for quorum purposes is separate from review assignments, which are based on area of expertise.

e. Use of Consultants

The Boards may, at their discretion, invite individuals with specific expertise or experience to assist in the review of complex issues that require expertise beyond or in addition to that available on the Boards. These individuals may not vote with the Boards.

Consultants will be required to sign a Confidentiality/Conflict of Interest Statement (Reference Document #76). Conflict of Interest information, including current policies, definitions of “financial interest” and “family member”, and disclosure forms, may be found on the “Conflict of Interest and Research” page of the RCT website.

Efforts are made to select consultants who do not have a conflict of interest with the issue being considered. The Board may ask consultants questions related to the protocol prior to completion of the discussion, after which the consultant will leave the room for the remainder of the discussion and vote.

When consultants are utilized, the terms of the service that will be provided, description of deliverables (e.g., written report, verbal presentation, review of investigator responses), and explanation of confidentiality agreements (e.g., whether name of consultant will be provided to the PI, whether the consultant's report will be released to the PI, whether the PI may contact the consultant) should be documented in writing.

Consultants will usually be identified by Board members or IRB staff, although in some cases, the PI or his/her department may be asked to suggest an individual with appropriate expertise. A list of consultants will be maintained by the IRB office.

## 7. Appointments, Terms, and Responsibilities of IRB Chairs, Vice Chairs, and Members

a. Chair/Vice Chair

1) Selection and Appointment

The IO listed on the CUMC or CU-MS FWA appoints the Board Chairs and Vice Chairs, after consultation with the ED and/or AD, and for Vice Chairs, the relevant IRB Chair. CU faculty who are Officers of Research or Officers of Instruction, and have sufficient expertise and experience, will be considered for these IRB positions. Other experienced IRB members will be considered on a case by case basis, taking into account their expertise and suitability for the position. A curriculum vitae will be required upon appointment, and a request for an updated version will be made periodically by the IRB.

An appointment memo is prepared by IRB staff for approval and signature of the appropriate IO. Copies of the signed memo are sent to appropriate individuals, including the IO, ED, AD, ADO, and Manager of the relevant IRB. A copy is retained in the IRB member file.

A letter that documents the appointment and describes member responsibilities is generated, signed by the ED, and sent to the appointee. Copies are sent to appropriate individuals, including the IO, ED, AD, ADO, and Manager of the relevant IRB. A copy is retained in the IRB member file.

2) Length of Term/Service

Board Chairs and Vice Chairs are appointed to serve a three-year term, which may be renewed. The terms correspond with the University's fiscal year (July 1 to June 30). If a Chair is appointed mid-year, his/her term will be calculated from the following July 1. The IO and/or the ED, considering input from Board members, investigators, and other administrators, will evaluate the Chairs on a regular basis (see Reference Document #113 for process) and renew terms

accordingly. Shorter terms may be considered in special circumstances. Chairs may be granted an extended leave due to medical, personal, or professional reasons, then return to complete their term.

Board Chairs and Vice Chairs receive substantial compensation for their service. In accordance with the "Recognition of Service by IRB Members" memo (Reference Document #109), IRB Chairs and Vice Chairs will receive a token of appreciation upon completion of their service, or as otherwise determined. Recognition by other means (e.g., mid-term letters of appreciation for service, or appreciation events) may also be considered.

3) Duties

Each Board Chair has the responsibility to ensure the compliance of the Board with all federal regulations, and manages his/her Board and the matters brought before it according to DHHS and FDA regulations pertaining to the rights and welfare of research subjects, other applicable statutes, and institutional policies.

Each Board Chair is responsible for conducting the Board's meetings, as well as processing, in Rascal, submissions that are assigned to his/her respective IRB. Assignment of primary reviewers and distribution of submissions to those reviewers is performed by the Chairs or Vice Chairs. Decisions to use consultants when specific expertise is not available among Board members are made by the Chair, generally in consultation with the respective Manager. The signatory responsibility for IRB correspondence is designated by the Chair, in accordance with IRB policies (see Section V.E.1).

A Vice Chair will be appointed for each Board, and will run the meeting and process submissions in the absence of the Chair. In the event of the temporary and short term absence of both the Chair and the Vice Chair, an experienced IRB member will be selected by the ED or designee (e.g., AD, ED, or Chair with concurrence of the ED or AD) to serve in this role. An IRB may have more than one Vice Chair; a hierarchy for serving as Acting Chair in the absence of the Chair will be established when there is more than one appointed Vice Chair.

Approvals by an expedited review process may be issued by a Chair or Vice Chair after designation of the submission as eligible for expedited review. Chairs and Vice Chairs may also make exempt determinations, although reviews of exempt research at CUMC are generally conducted by IRB staff.

Chairs and Vice Chairs are members of the IEC and accordingly are expected to attend semi-monthly IEC meetings or to make arrangements to be apprised of IEC discussions and decisions.

4) Resignation/Removal

Resignation from the Board may occur at the end of or during a term. Notice should be provided to the AD and ED as far in advance as possible to facilitate identification, appointment, and training of a qualified replacement.

After consultation with the ED, the EVPR or the IO designated on the applicable FWA may remove a Chair or Vice Chair mid-term (i.e., at any time during the appointed term).

Prior to the start of each fiscal year, the EVPR and/or respective IO, in consultation with the ED, may determine that the appointment of any Chair or Vice Chair whose term is expiring should not be renewed.

Individual termination letters are prepared by IRB staff and signed by the IO. Once signed, copies are distributed to appropriate individuals, including the IO, the IRB Chair or Vice Chair being terminated, ED, AD, ADO, and Manager of the relevant IRB. A copy is retained in the IRB member file.

5) Education and Training

Chairs and Vice Chairs are expected to participate in initial (i.e., one or more orientation sessions) and continuing education initiatives to understand relevant institutional policies, laws and regulations, and the Rascal system, and to keep abreast of changes to or evolving interpretation of such policies, laws, and regulations. Details of education and training initiatives and requirements are provided in Section X.B.

6) Liability Coverage for IRB Chairs and Vice Chairs

IRB Chairs and Vice Chairs are protected from personal liability under the Columbia insurance policy, which protects individuals serving on all University committees.

7) Confidentiality and Conflict of Interest

All Board Chairs and Vice Chairs are required to sign a Confidentiality and Conflict of Interest Statement (Reference Document #76), the terms of which are reinforced during the orientation session for new members. The statement also articulates the need and expectation for Board deliberations and details of the protocols that are submitted to the IRB to remain confidential.

Chairs and Vice Chairs who have a conflict of interest with a particular protocol, event, or issue that is reviewed by the Board must recuse themselves from relevant Board deliberations and may not participate in related voting.

a) For convened meetings, this means that the Chair who is presiding over the meeting must leave the room during the Board discussion and vote; the Chair will not count towards quorum for that review. The Board may ask the conflicted Chair questions related to the protocol prior to completion of the discussion. IRB staff, during preparation of the agenda for full Board meetings, will identify those submissions for which a Chair who is expected to be in attendance has a conflict; this helps to ensure compliance with the need for any such members to leave the room during discussion of the protocol for which a conflict exists.

b) In the case of expedited reviews, a Chair who has a conflict of interest in relation to a specific protocol is expected to distribute the protocols to a different member or ask the Vice Chair to do so. IRB staff who conduct the administrative review and identify a conflict will include that information in the Notes for the protocol.

c) For both full Board reviews and expedited reviews, Rascal will not allow an individual who is named as Study Personnel on a submission or as an Approver to act in a Chair, member, or reviewer capacity.

d) To the extent possible, IRB staff will not assign a protocol, for which an IRB Chair is the PI, to the IRB of which the PI serves as Chair.

Conflict of Interest information, including current policies, definitions of "financial interest" and "family member", and disclosure forms, may be found on the "Conflict of Interest and Research" page of the RCT website.

b. IRB Members

1) Selection and Appointment

The Chairs and/or IO, in consultation with the AD (or ED when necessary), recommend candidates for appointment as IRB members and the IO named on the FWA makes the appointment to the Board via signature on an appointment memo. Members will be selected in a manner that will ensure that all requirements of these IRB procedures and federal regulations are met. A curriculum vitae, which is generally reviewed during the recruitment process, will be required upon appointment, and a request for an updated version will be made periodically by the IRB.

A letter of appointment is prepared by IRB staff for approval by the appropriate IO. Upon being signed, copies of the appointment memos and letters are distributed to appropriate individuals, including the IO, ED, AD, ADO, and Manager of the relevant IRB. A copy is retained in the IRB member file.

2) Length of Term/Service

Members are appointed to a term of up to three years, which may be renewed, and will be evaluated periodically (see Reference Document #114 for process). If a member is appointed mid-term, his/her term will be calculated from the following July 1. Shorter terms may be considered in special circumstances. Board Members may be granted an extended leave due to medical, personal or professional reasons, then return to complete their term.

IRB members are compensated for their service. In accordance with the "Recognition of Service by IRB Members" memo (Reference Document #127), IRB members will receive a token of appreciation upon completion of their service, or as otherwise determined. Recognition by other means (e.g., mid-term letters of appreciation for service, or appreciation events) may also be considered.

3) Duties

Members independently evaluate project submissions that require full Board review prior to the IRB meeting, participate in appropriate discussions, and vote to approve, disapprove, defer to Chair (i.e., require specific changes, RASCAL status "pending"), defer to Board (i.e., substantive revision required, RASCAL status "return"), or defer (table) each submission during the IRB meeting. These actions apply to: (a) initial reviews, (b) continuing reviews, (c) modifications (amendments), (d) unanticipated problem reports; e) protocol deviations; and f) closure requests.

Members also review and vote on other pertinent business, including compliance oversight activities, which the Chair includes on the agenda.

Experienced members may be assigned by the Chair or Vice Chair to review research activities that qualify for expedited review.

4) Attendance Requirements

Members are usually provided with notice of meeting dates several months in advance and are expected to regularly attend meetings of the IRB to which they are appointed. Members are expected to notify IRB staff affiliated with their respective IRB sufficiently in advance of known absences for the staff to substitute registered alternates, at the discretion of the Chair and Manager, whenever possible; use of an alternate member is a requirement if the absence will affect quorum. When a situation arises that will result in an unanticipated absence, the member is expected to notify the staff at the earliest opportunity.

At the discretion of the Chair and in consultation with the relevant IO designated on the applicable FWA, excessive absences by a member, or a pattern of absences

that affects the functioning of the Board (e.g., three consecutive, or frequent unscheduled), may result in removal.

5) Removal, Resignation

Resigning members must notify the Board Chair and/or the ED, or designee of their intentions in writing. The AD (or ED) will notify the appropriate IO.

Prior to the start of each fiscal year, the Chair of each IRB, in consultation with the ED, AD, respective Vice Chair(s), and/or respective IRB Manager, may determine that the appointment of any regular or alternate member whose term is expiring should not be renewed.

Members may be removed in mid-term by the IO designated on the applicable FWA, or the EVPR. Recommendations for removal by the Board Chairs, other members of the Board, investigators, or other university officials will be considered.
Individual termination letters are prepared and signed by either the ED, or an IO. Once signed, copies are distributed to appropriate individuals, including the IO, respective IRB Chair, ED, AD, ADO, and Manager of the relevant IRB. A copy is retained in the IRB member file.

6) Liability Coverage for IRB Members

IRB members are protected from personal liability under the Columbia insurance policy, which protects individuals serving on all University committees.

7) Education and Training

Members are expected to participate in initial and continuing education initiatives to understand relevant institutional policies, applicable laws and regulations, and the Rascal system, and to keep abreast of changes to or evolving interpretation of such policies, laws, and regulations. Details of education and training initiatives and requirements are provided in Section X.B of these written procedures.

8) Confidentiality and Conflict of Interest

All Board Members are required to sign a Confidentiality and Conflict of Interest Statement (Reference Document #76), the terms of which are reinforced during the orientation session for new members. The statement also articulates the need and expectation for Board deliberations and details of the protocols that are submitted to the IRB to remain confidential. IRB members should not disclose the results of IRB reviews to investigators or others without the expressed permission of the IRB Chair, IRB Manager, or the ED.

Board members who have a conflict of interest with a particular protocol, event, or issue that is reviewed by the Board are expected to recuse themselves from relevant Board deliberations and may not participate in related voting.

a) For convened meetings, this means that the Board member must leave the room during the Board discussion and vote; the conflicted member will not count towards quorum for that review. The Board may ask the conflicted member questions related to the protocol prior to completion of the discussion. IRB staff, during preparation of the agenda for full Board meetings, will identify 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 members to leave the room during discussion of the protocol for which a conflict exists.

b) In the case of expedited reviews, a Board member who has a conflict of interest in relation to a specific protocol is expected to notify the Chair if a submission for that protocol is assigned to the member for review. IRB staff who conduct the administrative review and identify a conflict will include that information in the Notes for the protocol.

c) For both full Board reviews and expedited reviews, the RASCAL system will not allow an individual who is named among study Personnel on a submission or as an Approver to act on submission in a member or reviewer capacity.

d) Whenever possible, IRB staff will not assign a protocol, for which an IRB member is the PI, to the IRB on which the PI is a member.

Conflict of Interest information, including current policies, definitions of "financial interest" and "family member", and disclosure forms, may be found on the "Conflict of Interest and Research" page of the RCT.

Primary reviewers are assigned by the Chair or Vice Chair based on expertise and availability. No investigator has any authority to appoint an IRB member as a primary reviewer.

## B. The Role of Non-Columbia (External) IRBs in the Columbia HRPP

### 1. Reliance Agreements

Columbia University may enter into an IRB Authorization (IAA) with other FWA entities to delegate IRB review to a non-Columbia IRB or to conduct the review for non-Columbia entities. Reliance relationships include reliance on a non-Columbia IRB for review of multiple projects meeting defined criteria, reliance by Columbia on a central IRB, reliance of one or more non-Columbia entities on review by a Columbia IRB, Columbia serving as a central IRB, and reliance by Columbia on a non-Columbia IRB for a single project.

The decision to enter into an agreement with another institution for reliance of both institutions on one of the IRBs is made, depending on the risks of the study, after consideration of one or more of the following:

- evaluation of the non-CU institution's IRB policies and procedures (when CU will delegate review);
- whether regulatory compliance and CU standards may be upheld through the relationship;
- analysis of whether an efficient process may be implemented to conduct the reviews;
- discussions between IRB administrators from each institution;
- the level of risk from study procedures; and/or
- consultation with IOs and/or the OGC.

### a. Reliance on a Non-Columbia IRB

Prior to executing an IAA in which Columbia will rely on the review of another IRB, the ED or AD will determine that the quality of their reviews and system of regulatory compliance is appropriate for Columbia's HRPP, and that the reviewing IRB complies with applicable federal and state statutes in their reviews and operating procedures. These determinations may be made through various means, including review of operating procedures, attendance at IRB meetings, discussions with IRB administrators, assessment of whether federal regulatory agencies have restricted or suspended the IRB's operations, and consideration of accreditation status.

When Columbia relies on an external IRB, processes are in place to ensure that Columbia requirements are satisfied prior to commencement of the research. The administrative review by IRB staff includes these considerations although individual agreements may also require additional levels of review, e.g., by a member of the IRB or by a team comprised of an IRB staff member and an IRB member.

CUMC and NYP, collectively, have multiple-project IAAs with the NYSPI, the Weill Medical College of Cornell University, the National Cancer Institute (NCI) Central IRB (CIRBs; both adult and pediatric) and CU-MS, to rely on their IRBs' reviews for certain types of research projects. Agreements with Weill Cornell Medical College and NYSPI also include their reliance on reviews conducted by CUMC. Details regarding each agreement are provided later in this manual (Section III.E.14).

The CU IRB management meets on an ad-hoc basis with representatives from each external IRB to consider issues relevant to the review of human subjects research at Columbia, unless all local issues are the responsibility of Columbia, per the respective agreement. An example of the latter is the NCI CIRB process, which requires that an IRB member conduct a facilitative review for local considerations.

Columbia may also enter into agreements pursuant to which Columbia relies on another institution's IRB review for a single project.

Except for research reviewed by the NYSPI IRB, Columbia IRB approval is required before implementation of any research involving human subjects, including review of records, tissues, or other derived materials. Depending upon the terms of the reliance agreement, the review at Columbia may be purely administrative (e.g., verification that PI eligibility criteria are met, that training requirements are satisfied, or that approval by the PRMC, IBC, or JRSC has been issues), or may require a limited review by an IRB member.

**b. Reliance on a Non-Columbia IRB for a multicenter study, consortium, or study program**

Columbia and (as applicable) NYP may enter into agreements through which the reviews of multiple projects are delegated to the IRB(s) of another institution that is serving as the central IRB for multiple institutions. For each such case, details of the review processes and responsibilities of each institution will be described within the agreement. Examples include the NeuroNext Consortium for which the Partners IRB is the IRB of Record, and certain studies for which the Fred Hutchinson Cancer Center IRB is the IRB of Record.

Unless otherwise directed by the ED in writing (other than the NYSPI, NCI, NCI-Pediatric, or the Weill Cornell IRB), the following procedures will be followed for every protocol that will be reviewed by a Central IRB. The protocol must be submitted in RASCAL and the submission must specify the designated IRB of record. The Columbia IRB will review the submission to ensure compliance with all institutional policies related to the protection of human subjects (e.g., conflict of interest, radiation safety, institutional biosafety committee, etc.).

The Columbia IRB may develop additional procedures/processes that will be applied to specific studies or research programs that rely on IRB review by a Central IRB.

The processes that the Columbia IRB will follow to ensure appropriate review for each protocol are listed below. All new studies, modifications, and continuing review submissions will be reviewed according the following processes; continuing review submissions must provide a summary of unanticipated problems involving risks to subjects that occurred during the past approval period.

1) Pre-review by a Senior IRB Administrator and an IRB Member with appropriate expertise (three teams of such members will be formed and protocols will be assigned a protocol by either the Associate Director of the IRB or the Executive Director of the IRB).
2) Protocol reviewed by Central IRB with the input from the Columbia IRB.
3) The Central IRB-approved protocol and consent is sent to the Columbia IRB and the PI to determine if they agree to conduct the study at Columbia; the

same team that that conducted the pre-review in step 1 will conduct the final review and provide a recommendation to the ED or in the absence of the ED, the AD for whether or not Columbia should permit the study to be conducted at Columbia.

4) Columbia will issue a final approval letter permitting the study to begin only if the Columbia IRB has confirmed that all institutional policies will be followed.
5) The Columbia letter of approval to the Columbia site PI will include the following statements:

   "All research conducted under this protocol must be conducted in compliance with all relevant Columbia University research policies and procedures including but not limited to policies regarding surrogate consent, genetic testing, and the collection and release of social security numbers (found on the Policy Page of the IRB website. Actualization of this protocol constitutes acknowledgement by the investigator that the research will comply with Columbia policies and procedures.

6) The IRB will establish a QA process for internal protocols reviewed by this process, including but not limited to the IRB's existing not-for-cause audit program.

**c. Columbia Serving as IRB of Record for Non-Columbia Entities**

The situations in which Columbia may serve as the IRB of Record for a non-Columbia institution vary widely, ranging from coverage of collaborating investigators who will only perform analysis of identifiable specimens or data, to serving as the central IRB for multiple projects at multiple institutions.

In situations whereby Columbia researchers collaborate with researchers from other institutions, Columbia may act as IRB of record for the collaboration for some low risk research. The ED or AD will review each such situation and make a determination that such reliance on the Columbia IRB is appropriate.

Decisions to enter into agreements that are broad in scope, and/or involve research that presents greater than minimal risk of harm to subjects require consultation with relevant IOs, the VPRO, the EVPR, and/or OGC. All IAAs must be signed by the appropriate IO. In all cases, whether Columbia or another IRB is responsible for review of the research, there must be a submission in RASCAL for tracking purposes.

Coverage by Columbia and/or NYP of collaborating individuals who will be engaged in non-exempt research but are not affiliated with an institution that has an IRB must be formalized through execution of an Individual Investigator Agreement (IIA). Through the terms of the IIA, the collaborator agrees to abide by specific ethical principles while engaged in the Columbia-directed research.

## 2. Research Conducted at CU by Investigators Affiliated with Other Institutions

Columbia University officials and faculty are often approached by investigators at other institutions for cooperation in their research, e.g., through assistance with recruitment, or to perform specific tests or analyses. In addition, investigators at other institutions may propose a study to be conducted, all or in part, at Columbia.

The need for review by the CU IRB will depend upon the nature of the involvement of the individual who is affiliated with CU in the former situation, and the proposed use of CU facilities, resources, and/or non-public data in the latter circumstance. Therefore, the protocol and supporting documents for the proposed research should be submitted to the ED or AD for administrative review and a determination as to whether formal CU IRB review (i.e., review by a CU IRB in accordance with these SOPs) is also needed. Supporting documents include: a) the informed consent document(s) or justification for waiver of consent; b) study instruments if applicable; and c) a copy of the IRB approval from the external IRB.

CU IRB review is not generally required if, in the case of proposed collaboration, the individual who is affiliated with CU is not engaged in human subjects research, i.e., the individual will not: a) intervene or interact with living individuals for research purposes; b) obtain individually identifiable private information for research purposes; or c) receive a direct federal award. For example, department Chairs or Deans may be asked to assist in the distribution of surveys to faculty or students. Because these individuals would not be considered to be engaged in the research, IRB approval is not required for University offices or officials to inform members of the University about research or provide them with information about contacting investigators if they wish to participate. A detailed explanation of when an institution is engaged in research can be found in the OHRP October 16, 2008, "Engagement of Institutions in Research", which provides the basis for the Columbia engagement philosophy and can be found online at <http://www.hhs.gov/ohrp/humansubjects/assurance/engage.htm>.

However, even though "formal" CU IRB review may not be required because Columbia is not engaged in the research, the administrative review by the ED or AD will be conducted to ensure that the research has been appropriately reviewed by an external IRB for the protection of subjects at Columbia or NYP.

For those protocols that the ED or AD determine will require review by the CU IRB, submission in Rascal is required, and a collaborator at CU who meets the University criteria to serve as a principal investigator must be identified.

CU IRB review of research by investigators from other institutions is generally required, (i.e., the research falls under the jurisdiction of the CU IRB), if:

1. University officials, faculty, staff, or students are actively engaged in or actively cooperate with or encourage participation in the research;

2. University officials, faculty, staff, or students intend to use the findings or results of these studies for their own purposes;
3. Private, confidential information about members of the Columbia University community will be released for purposes of the research; or
4. The research is sponsored by Columbia University.

The ED and AD serve in an advisory capacity to University officials and faculty with regard to research conducted by investigators from other institutions at Columbia University that does not fall under IRB jurisdiction (i.e., the ED can provide advice on such matters as the risks and benefits of the proposed research, informed consent, etc.).

## III. Preparation of Submissions to the IRB

This section describes the types of information and documentation that must be submitted to the IRB for the review of new protocols, modifications, unanticipated problem reports, renewals, closure (i.e., voluntary termination) requests (each of the foregoing, an "Event"), and varying types of research (e.g., drug study, international trial, collaborative project). It also describes the particular information that is required when vulnerable populations are involved in a study.

Each variable is described individually and is provided as guidance for use in the preparation of a submission. If, for example, a submission is for a new protocol that involves an investigational drug administered to children, the information described in each of the relevant sections (i.e., new protocol, drug study, and minors) should be reviewed and the relevant materials included in the submission.

The Study Description is a text field in Rascal in which the protocol is described. The "Help" link for the Study Description field describes the 16 elements of a research protocol that should be provided for review.

### A. Preparation of Event Submissions

Researchers create protocols electronically in the University's web-based research administration and compliance IT system, Rascal. Various options exist in the Rascal IRB protocol for incorporation of pertinent information about the research proposal, to accommodate the various types of documentation that are needed for review. Information may be entered in fields that appear on a composite Data Sheet or in the Study Description field, documents may be attached electronically (e.g., scanned copies of paper forms or electronic documents), and there is also a feature that facilitates construction of consent documents, the "Consent Form Builder" Rascal.

Step by step instructions for creating a protocol and consent document within Rascal may be found in Reference Documents #64 and #71 (Creating a Rascal Protocol and Rascal Consent Form How-To), respectively. In addition, a comprehensive manual for using Rascal, entitled "User's Guide to the Rascal IRB Module", focuses on preparing submissions and is posted on the CUMC and CU-MS IRB websites.

Rascal accommodates the various Events that may occur during the active life of a protocol.

Information and material being entered for new Events is accessible only to study personnel listed on the protocol while the Event status is "creating", i.e., prior to initial submission of the respective Event to the IRB.

All actions related to a specific submission, including information entered, material submitted, correspondence generated, internal IRB notes and documents, history and status, are stored together electronically within the Rascal "protocol file" for each project. IRB staff and members may view all entries and attachments for a given Event once the Event has been submitted and may attach documents to the submission, but may not otherwise modify

the submitted material. Attachments by staff and members are clearly labeled with the name of the individual who attached the document, and the date they are attached. If the IRB modifies an attached document (to decrease returns by making changes which involve standard text), when the revised document is reattached, Rascal will document that the IRB staff member attached it. In such instances, IRB correspondence will explain that the document has been revised, and advise the study team that they should immediately advise the IRB if the changes are not acceptable.

The researcher has access to all parts of the Rascal file for each of his/her protocols except the internal IRB notes and documents, the identity of the reviewer(s), Meeting History (i.e., minutes and dates of convened meetings), and correspondence transmitted between IRB staff and/or between IRB members and staff. The submission is locked against changes by the research team when it is in the IRB queue.

IRB review is based on the material submitted electronically by the researchers via Rascal. Literature reviews by members and notes entered by staff or IRB members to document conversations with members of the research team may also be considered during the review.

Annual financial conflict of interest statements and evidence of satisfactory completion of Columbia-developed training courses in the Rascal Training Center are documented electronically in accordance with Rascal procedures and reflected on the Data Sheet of the submission. Documentation regarding completion of required training modules in the online Collaborative IRB Training Initiative (CITI) program is uploaded into Rascal and appears on the Data Sheet. Training requirements are described in detail in Section X.D.

An electronic protocol-specific conflict of interest statement is also required for the PI, all co-investigators, study coordinators, and regulatory coordinators as part of the submission approval process.

## B. IRB Abbreviated Submission Process

The IRB supports an abbreviated submission process for some types of research, when there is a separate, complete protocol available. This is often the case for multicenter industry-supported studies, grant-funded projects, and student research.

The abbreviated process eliminates the need to summarize the complete protocol in the Study Description field. All other applicable or required Rascal fields must be completed, including but not limited to Personnel, Abstracts, Subjects, Investigational Product, Human Specimen, and Research Procedures fields. Additional information related to the Abbreviated Submission Process is posted on the IRB website and in Reference Document #305, “Abbreviated Submission Process”. Details related to preparation of submissions for three types of projects to which the abbreviated process may be applicable are provided below.

1. Industry-sponsored multicenter studies:

   A statement such as "The *(sponsor's protocol, investigational drug brochure, device manual)* is/are attached" should be entered into the Study Description field, and the referenced document(s) should be attached. In addition, any of the 16 protocol elements that are not included in the attached documents should be described in the Study Description. The following elements will most likely need to be described in detail: a) local recruitment; b) informed consent process; c) protection of privacy and confidentiality at the local site; and d) Columbia's function as a lead institution.

2. Student-initiated research:

   A statement such as "A complete description of the *(dissertation, thesis, capstone project)* is attached" should be entered into the Study Description field, and the referenced document(s) should be attached. In addition, any of the 16 protocol elements that are not included in the attached documents should be described in the Study Description. The following elements will most likely need to be described in detail: a) local recruitment; b) informed consent process or request for waiver of either informed consent or written documentation of consent; c) manner of data storage, e.g., identifiable, coded, de-identified, or anonymous; and d) protection of privacy and confidentiality.

3. Grant-funded research:

   If a proposed study is supported by a detailed grant application, e.g., Public Health Service (PHS) 398 or a National Science Foundation (NSF) application, the abbreviated submission process may be utilized. A statement such as "*(NIH grant application, NFS application)* is attached" should be entered into the Study Description field, and the referenced document(s) should be attached. In addition, any of the 16 protocol elements that are not included in the attached documents should be described in the Study Description. The following elements will need to be described in detail: a) local recruitment; b) informed consent process; c) protection of privacy and confidentiality at the local site; and d) Columbia's function as a lead institution. The abbreviated submission process may not be used for externally sponsored research when the funding application lacks sufficient detail to address a majority of the 16 protocol elements.

## C. Personnel

The Rascal Personnel section solicits information about the individuals who will be involved with conducting the study. It is important that accurate information about each individual's role is entered, because of related eligibility and training requirements. Non-Columbia collaborators should generally not be listed in the Personnel section.

## 1. Principal Investigators

### a. Eligibility

A Columbia University Officer of Instruction, with a full-time appointment at the rank of instructor or higher, may serve as a Principal Investigator (PI) on a protocol. Full-time Officers of Research at the rank of Research Scientist (or equivalent) or higher may also serve as a PI. Exceptions will be considered by the appropriate authority on the relevant campus (Reference Document #13). Criteria for serving in the role of PI are determined by Columbia and articulated in the Faculty Handbook, Principal Investigator section.

For research that will be conducted at NYP by an employee of NYP who is not also affiliated with Columbia, clearance from NYP Administration is required in lieu of satisfaction of the criteria articulated in the Faculty Handbook. IRB staff facilitate the review by NYP Administration.

In general, only one individual may be named as PI. Exceptions may be made when two individuals at Columbia are co-PIs on a grant, or are each the PI for a different site or population (e.g. CUMC vs affiliated hospital as sites, or children vs adults as subjects). In addition, CUMC requires that oncology studies managed through the Cancer Center Regulatory Management Office (CRMO) name a second individual as co-PI to ensure clinical coverage for when the PI is traveling or otherwise unavailable. The roles of each PI named on these studies, i.e., whether the individual is the primary or backup, should be explained in the respective Experience field of the Personnel section in Rascal. The IRB may determine that other higher risk studies also provide a co-PI for similar reasons.

A student may not serve as the PI on a protocol. Appropriately qualified students may have a substantial role in a research project, but supervision by a faculty advisor is required. In most cases, the faculty advisor also serves as the PI for the project. When this is not the case another qualified individual must be identified to serve in this role.

### b. *Research* and *Human Subject* Determinations

No studies involving human subjects may be conducted without IRB approval or IRB determination of exempt status, the latter in accordance with 45 CFR 46 by designated IRB staff or Chairs. Although a PI may make a determination of "Not Human Subjects Research" (i.e., the regulatory definitions of both "research" and "human subject" are not met) on his/her own without submission to the IRB, if that decision is later found to be incorrect, the PI will be responsible for any noncompliance that results. Consultation with IRB staff or submission of the protocol to the IRB via Rascal is recommended whenever it is not clear if the regulatory definitions of "research" and "human subject" are met.

### 2. Roles and Responsibilities

The PI has ultimate responsibility for his/her research project and all official IRB correspondence is addressed to the PI. Rascal correspondence is sent to the PI as well as those members of the research team designated per Rascal procedures (Reference Document #95). Responsibility for the ethical conduct of all study procedures conducted under the auspices of Columbia University, from initial recruitment efforts, through completion of data analysis and closure, rest with the PI, who may delegate tasks but retains responsibility for them.

Personnel who are named on a protocol must be assigned a role. Careful consideration should be given to role assignment as some carry specific responsibilities, have additional requirements for training, or require signoff by the individual before the protocol can be submitted. If an individual is listed in one role (e.g., as a Consent Form Administrant), and duties change such that he/she will be performing duties beyond that role (e.g., moving from only obtaining consent to also conducting other procedures), a modification should be submitted to revise his/her role.

Research personnel who will be affiliated with Columbia on a temporary basis and are engaged in human subjects research conducted by Columbia investigators must adhere to the requirements of the University's Short Term Visitor Policy.

### 3. Training

Before a protocol will be approved by a CU IRB, the PI must complete required training as described in Section X.D. Study personnel must complete applicable training prior to participation in the research.

- Training certifications are valid for three years, after which time continued education requirements are effective.

- All required training modules must be accessed via the Rascal Training Center. Evidence of completion is maintained electronically within Rascal.

## D. Documents/Information Needed for Each Type of Event

### 1. Submission materials: New protocol

The General Information (Reference Document #35), Personnel, Subjects, Funding, and Location screens (found within Reference Document #70, "User's Guide to the Rascal IRB Module") collect the data that will constitute the basic protocol for review.

The following information or documentation should be included or attached for ne protocols:

a. list of personnel (members of the Columbia research team) involved in the research, with certification of any required disclosure/training;

b. justification for exemption, if applicable;

c. research objectives and hypothesis(es), as applicable;

d. description of the anticipated study population, including demographic information regarding anticipated age, ethnicity, and gender;

e. consent documents (e.g., consent form, parental permission form, assent form, information sheet, oral script) and description of the consent process, or request for waiver of consent and/or written documentation of informed consent, with justification for the waiver(s);

f. funding information and, for supported projects, the grant, contract (if available), or other documentation of the supported research, e.g., sponsor's protocol, investigator's brochure;

g. any other information or material pertinent to assessment of the potential risks and benefits of the proposed research, e.g., mechanisms incorporated to minimize risk;

h. plans for maintaining privacy of participants and confidentiality of data, as applicable;

i. data and safety monitoring plan, as appropriate to level of risk presented by study procedures;

j. completion of the Human Specimens section if any tissue or fluid will be obtained from subjects or stored specimens will be used;

k. completion of the Investigational Products[1] section if a drug, device, or biologic is under investigation as part of the research;

l. recruitment material, if applicable (e.g., recruitment flyer or letter, letter to clinicians to notify their patients about the study, text for Internet advertisement);

m. study instruments, if applicable (e.g., survey, focus group guide, interview script, questionnaire); and

n. approvals from other institutions, if applicable and available.

The IRB needs a detailed description of all study procedures in order to meet regulatory review criteria. If there is no separate complete description of the research (e.g., sponsor's protocol, NIH grant application, dissertation), all elements should be described in the Study Description.

As described in Section III.B, the IRB supports an "abbreviated" submission process when there is a separate complete description of the research available. In these cases, a statement such as "The complete protocol *(state type in parentheses, e.g., sponsor's protocol, NIH grant submission, dissertation)* is attached" should be entered into the Study Description, and the protocol should be attached. Columbia-specific information

[1] The FDA considers an investigational product to be one that is the focus of a clinical investigation. Accordingly, if a drug, device, or biologic that is already approved by the FDA is the focus of the protocol being submitted, it should be described in the Investigational Products section.

(e.g., recruitment, informed consent process, confidentiality of study data at Columbia, and plans for monitoring data and safety) should be provided in the Study Description. In addition, any of the 16 protocol elements that are not included in the separate protocol or grant application should be described in the Study Description.

The abbreviated process described above eliminates the need to summarize a protocol in the Study Description field. All other applicable or required Rascal fields must be completed, including but not limited to Personnel, Abstracts, Subjects, Investigational Product, Human Specimen, and Research Procedures fields. Additional information related to the Abbreviated Submission Process is posted on the IRB website and in Reference Document #305, "Abbreviated Submission Process".

Additional information and/or documentation may be required for specific types of research (e.g., drug studies, research with pregnant women). Details are in the applicable subsection presented later in Section III.

**2. Submission materials: Modification**

Any proposed change or modification to a protocol that was approved by the IRB must first receive prospective IRB approval, unless such a change is necessary to eliminate or minimize an imminent harm to subjects.

If the protocol was eligible for expedited review, and the proposed change(s) are such that the protocol remains eligible for expedited review, the modification may also be reviewed under an expedited review process.

If the overall protocol requires review by the convened IRB, and the change is non-substantive in nature, the IRB may approve such a change by expedited review. Full Board review of the modification is required if the proposed change(s) are substantive in nature (e.g., increase risk, add a treatment arm, expand the study population to include vulnerable subjects, etc.).

If it is discovered that there is the potential for imminent harm to subjects, the investigator should implement any change(s) necessary to reduce or remove such harm and subsequently submit a modification to the IRB so that such change(s) are documented and approved by the IRB for all subsequent research activities under the protocol. Changes made without prospective IRB approval, to address imminent harm to subjects, must be submitted to the IRB as a modification at the earliest possible opportunity after the change is made.

Any change in the protocol that is necessary for the enrollment of a specific subject (i.e., deviation from the approved inclusion/exclusion criteria) also needs prospective IRB approval. If a subject who does not meet the enrollment criteria is enrolled, even if the sponsor has agreed to such enrollment, this would be considered a protocol deviation (if the study team identified and submitted the change for IRB review before enrollment) or violation (if the study team did not identify the change and submit it for IRB review

before enrollment) by the IRB. Protocol deviations and violations that occur during the study should also be submitted as modifications, unless the violation involves an unanticipated problem involving risks to subjects; the latter should be submitted using the unanticipated problem reporting module. See Section III.D.6 for additional information regarding submission of reports of deviations and violations.

The Modification Information Form (Reference Document #69) must be completed in Rascal when changes to the approved protocol are requested. This form solicits the following information:

a. summary of and explanation for the requested modification or addendum to the approved protocol;
b. if the submission includes a protocol deviation or violation, and if so, how many of each are included;
c. number of subjects currently enrolled; and
d. study enrollment status (e.g., enrollment ongoing, study closed to enrollment).

The following information or documentation must be attached or included:

a. clean and highlighted copies of revised documents, or a clean copy with a clear explanation of what has changed, if documents have been revised;
b. supporting documentation of modification from the sponsor, if applicable;
c. updated personnel list, if personnel change is involved;
d. updated Study Description and applicable fields in submission, if previously submitted information has changed; and
e. plans to obtain updated consent from enrolled subjects if new information that may affect their willingness to continue participation is involved, or justification for not obtaining updated consent when new information is available.

**3. Submission materials: Renewal (Continuing Review)**

Notification that continuing review is required will be sent automatically by the Rascal system to investigators at 90, 60, and 30 days prior to the expiration date of the current IRB approval. Investigators are required to submit renewal requests in Rascal and are encouraged to submit appropriate reports for ongoing research activities 60 days prior to the expiration date of the IRB approval for the study.

The Renewal Information Form (Reference Document #61) must be completed in Rascal. This form solicits the following information:

a. study enrollment status, (e.g., enrollment ongoing, study closed to enrollment);
b. date enrollment began at CU site;

c. whether a Certificate of Confidentiality (COC) is required;
d. if a COC exists, the date it expires;
e. whether Social Security Numbers (SSNs) will be collected and if so, whether they will be released outside of Columbia;
f. summary of any relevant recent literature or interim findings;
f. explanation for any change including a change to risk/benefit ratio;
g. list of papers pending or published about this study;
h. synopsis of the results to date;
i. If the submission includes a protocol deviation or violation, and if so, how many of each are included; and
j. If the renewal includes a modification, a summary of the proposed change(s).

In addition to completing the Renewal Information form, the Subjects section in Rascal must be updated to reflect, at a minimum:

a. original number of participants anticipated;
b. number of participants enrolled to date at CU site;
c. number of participants enrolled last year at CU site;
d. number of participants who completed the study at CU site;
e. number of participants expected to enroll next year;
f. number of, and explanation for, participant complaints at CU site;
g. number of, and explanation for, participants removed by physician;
h. number of, and explanation for, participants who withdrew from the study;
i. number of participants enrolled to date at other sites;
j. demographic information for subjects enrolled at CU site;
k. if enrollment is less than anticipated, the reasons for, and strategies to remedy, this situation;
l. if any subjects were enrolled using the Short Form Consent Process, and if so, how many for each language;
m. subject population justification;
n. subject compensation and justification, if applicable;
o. consent waiver or alteration requests, if applicable; and
p. recruitment URL, if applicable.

The following information or documentation must be attached:

a. a summary of all Unanticipated Problems that occurred during the review period and since the beginning of the study; details of the elements that should be included in the summary are articulated in the Columbia Reporting to the IRB of Unanticipated Problems Policy (Reference Document #02), as are options for submitting a monitoring entity report in lieu of the summary;

b. recent Data Safety Monitoring Board (DSMB) or other relevant multi-center trial reports, if applicable;

c. for studies that are open to enrollment, a copy of the current informed consent document(s), and any newly proposed revisions to the consent document(s);

d. documentation to support changes to the protocol, consent document(s), study instrument(s), or other study-related material, if a modification is submitted with the renewal;

e. any withdrawal of subjects from the research or complaints about the research since the last IRB review;

f. any other relevant information, especially information about change in risks associated with the research, notifications to research participants of new findings which may affect their willingness to continue participation, and continuing protection under a COC, if applicable; and

g. for federally funded, multiple year projects, or any other externally funded project for which one is produced, a copy of the most recent Progress Report. For all sponsored projects, if changes in the terms or type of funding have occurred, the Funding section should be updated and the appropriate documentation attached.

**4. Submission materials: Report of unanticipated problems involving risks to subjects or others**

The Unanticipated Problem (UP) Report (Reference Document #188) in Rascal must be completed to report incidents, experiences, and outcomes that are UPs in accordance with the CU Reporting to the IRB of Unanticipated Problems Involving Risks Policy (Reference Document #02). This form collects information pertinent to the incident, experience, or outcome being reported, including the following:

a. subject identifier and UP keyword;

b. date, location, and description of the UP;

c. relationship of the UP event to the study;

d. evaluation of whether the UP was unanticipated, related to participation in the study, and suggests an increase in risk to subjects or others;

e. date and means by which the PI became aware of the UP;

f. entities to which the UP was reported;

g. if the monitoring entity determined that the event was unanticipated, at least possibly related, and may place subjects or others as a greater risk of harm than was previously known or recognized;

h. if the submission includes a protocol deviation or violation, and if so, how many of each are included; and

i. evaluation of whether changes are required to the protocol and/or consent document(s).

Supporting documentation may be attached electronically to the Report. If changes to the consent form or protocol are required, a modification must be submitted as a separate event in Rascal.

Protocol violations that result in UPs should be submitted via the Unanticipated Problems Report module.

Reports of Unanticipated Problems for protocols reviewed in accordance with the terms of an IRB Authorization Agreement, when Columbia is not the IRB of Record, should be submitted to the IRB as designated in Reference Document #118, "Processes for Review and Monitoring of Protocols Subject to IRB Authorization Agreements".

**5. Submission materials: Termination (Closure)**

A Termination (Closure) Report form (Reference Document #67) must be submitted when all study procedures are completed, including analysis of identifiable data collected from the study, and IRB oversight of the project is no longer required. For multicenter studies, termination is appropriate: a) when all study procedures are completed at CU, if CU is not the lead institution with responsibility for other sites; or b) when all study procedures are completed at all sites, if CU is the lead institution with responsibility for other sites.

The Termination/Closure Report form solicits varying details depending on the type of review performed by the IRB (e.g., expedited review, full Board review, etc.). Studies that were last reviewed by a full Board process will require the following information:

a. changes or amendments since the most recent approval (including changes in personnel since the most recent approval and additional information about risk associated with the study);

b. total number of participants in the study;

c. number of participants since the most recent approval;

d. number of participants who withdrew from the study;

e. number of participants who complained about the study;

f. summary of any recent literature or findings; and

g. brief summary of results.

**6. Submission materials: Report of Protocol Deviation or Violation**

All deviations from and violations of Columbia policies or IRB determinations, including the requirement for adherence to the approved protocol, must be reported to the IRB. A protocol deviation is defined as a change in the protocol for one or more subjects that is identified by the research team before the change is implemented and should be approved by the IRB before implementation. A protocol violation is defined as a protocol change or modification that is identified by the research team after the change was implemented and was not approved prospectively by the IRB. Protocol violations may be considered as non-compliance with the federal regulations for the protection of human subjects.

The IRB recognizes that some deviations regarding inclusion/exclusion criteria are identified shortly before the subject is scheduled for randomization or entry into the study and that a quick review by the IRB is important for the study. For funded studies, the sponsor's concurrence that the individual may be enrolled should be provided with the submission. In time-sensitive situations, the investigator should follow his/her submission to the IRB with an e-mail outside of Rascal to the Manager of the IRB that approved the study.

If the Protocol Violation is unanticipated and involves risks to subjects or others, it should be submitted to the IRB within one week (5 business days) as an Unanticipated Problem Report in Rascal. Protocol violations related to medication dose errors should also be discussed with the subject, in accordance with the underlying philosophy of NYPs Disclosure Policy (Policy #E145).

Protocol Deviations/Violations that do not involve risks to subjects or others should be submitted promptly as Modifications in Rascal.

The description of the circumstances surrounding the deviation/modification should be clearly stated in the Unanticipated Problem Report (Reference Document #188), in the summary section of the Modification Information form (Reference Document #69), or in the Renewal Form (Reference Document #61) as applicable.

The following information should be included:

a. a complete description of the deviation/violation;

b. an explanation of why the deviation is necessary, or why the violation occurred;

c. whether the deviation affects, or the violation affected, the risk/benefit ratio for subjects, integrity of the research data, and subjects' willingness to continue study participation; and

d. for protocol violations, a description of the corrective measures that will be taken to prevent a recurrence of the same or similar violations.

Supporting documentation may be attached electronically, and should be provided whenever available or pertinent.

### 7. Submission materials: Emergency Use Report

FDA regulations permit use of an investigational drug or device, without IRB approval, in very limited circumstances. Such use is considered to be an emergency clinical use, and FDA requirements for the research use of an investigational agent do not apply. The involvement of the IRB prior to the administration of the agent is to serve as a facilitator for shipment of the investigational product and initiation of a monitoring process. The FDA must be notified of all emergency use situations by the manufacturer or sponsor. A follow-up report must be submitted to the IRB within five (5) working days if all information is not provided in advance of the use.

Only emergency life-threatening situations that will be treated with an investigational agent, for which an approved protocol is not available, in an effort to save a patient's life or loss of a part of the body (e.g., eye, limb, etc.) are to be considered for the emergency use exemption. None of these situations will be considered research and therefore data collection for research purposes is not permitted. Physicians are encouraged to contact the IRB office immediately if such a situation arises.

Consent options for emergency use situations are defined below; proposed procedures must be described in the emergency use request to the IRB prior to the emergency use:

a. If the consent form is prepared at the time of submission of the emergency use request, it should be attached and submitted with the Emergency Use (EU) request;

b. If consent will be obtained, but the form is not yet available, this should be so stated, and a copy of the form submitted with the follow-up report within 5 days of the use of the test article; and

c. If waiver of consent is requested, documentation that the criteria for waiver codified at 21 CFR 50.24 have been met must be included.

In addition, CU policy requires documentation to be provided that the patient's condition is life-or limb-threatening, and there is no effective alternative treatment available. Concurrence by a physician who is not otherwise involved in the use of the investigational product is also required by Columbia policy regardless of whether consent was obtained. If this certification is not available at the time of the request for emergency use, it must be provided in a follow-up report within 5 days of the use of the investigational product.

An EU report must be submitted to the IRB in hard copy when an investigational product has been administered in accordance with the emergency use provisions identified in 21 CFR 56.104(c) and 21 CFR 50.23, if all required information was not provided with the emergency use request. The following information should be included:

a. product name and type (i.e., drug, device, biologic);

b. if a device, product model/version number, if applicable;

c. IND or IDE number, if one has been obtained for this use;

d. description of product;

e. name, affiliation of non-participating physician, and date of affirmation;

f. number and submission date of protocol submitted for IRB review of this article, if applicable; and

g. date of notification to FDA.

## E. Material Needed for Review of Particular Types of Research or Situations

### 1. Submission materials: Drug research

Research that involves a drug or drugs may vary in design, from investigation of the safety and/or efficacy of investigational agents, to comparison of two approved agents, to the evaluation of approved drugs for indications other than those for which they were approved.

A drug is defined in the current federal Food, Drug and Cosmetic Act as:

a. articles recognized in the official United States Pharmacopeia, official Homeopathic Pharmacopeia of the United States, or official National Formulary, or any supplement to any of them;

b. articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals;

c. articles (other than food) intended to affect the structure or any function of the body of man or other animals; and

d. articles intended for use as a component of any articles specified in clause a, b, or c; but does not include devices or their components, parts, or accessories.

In addition to the material listed in the preceding Section III.D relating to the type of Events, the following material and/or information is required for all research involving drugs:

a. sponsor protocol, if industry-sponsored;

b. Investigator's Drug Brochure (IDB), if industry-sponsored;

c. package insert, if approved drugs are administered;

d. documentation of current FDA status, if an IND exemption is indicated;

e. completion of the Investigational Products[2] section (Reference Document #92) for each agent involved;

f. data and safety monitoring plan; and

g. FDA Form 1572.

When drugs that are not yet FDA-approved will be used for research purposes, plans for handling of the investigational agent should be included in the submission to the IRB. These should be in accordance with the CUMC Research Pharmacy procedures (Reference Document # 172) and NYP Policy P168, Investigational Drugs: Use and Control; a statement that the relevant policy(ies) will be followed is sufficient for the IRB submission.

When a PI is acting as a Sponsor-Investigator (S-I: i.e., the IND is held by a member of the Columbia faculty), additional consideration must be given as to how compliance with FDA requirements will be maintained. The Columbia FDA Compliance Program for FDA-regulated Human Subjects Research [Working Practices Document #311] outlines the institutional oversight of S-I research. An IAP [Working Practices Document #314] has been established within the CTO to provide education, training and support to S-Is with respect to FDA regulations to S-Is, and help ensure appropriate documentation and trial monitoring to satisfy regulatory requirements. S-Is are encouraged to consult with CTO early in the development of their protocol. The CTMAP provides support with respect to monitoring S-I research.

When any study is conducted by an S-I, the submission for IRB review must include a letter from the Director, Regulatory Affairs and Clinical Development, IAP, CTO that documents that the Department Chair and the S-I both have provided commitment that adequate resources will be provided that will permit the conduct of the study in compliance with FDA regulatory requirements.

In addition, the submission for IRB approval must include a plan for monitoring of the study in accordance with 21 CFR 312.

**2. Submission materials: Research with Biologics**

Protocols that involve research with biologics require similar submission materials and are reviewed similarly to research with investigational drugs.

A biologic is defined as any virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or analogous product, or arsphenamine or its derivatives, applicable to the prevention, treatment or care of diseases or injuries of man.

[2] The FDA considers an investigational product to be one that is the focus of a clinical investigation. Accordingly, if a drug, device, or biologic that is already approved by the FDA is the focus of the protocol being submitted, it should be described in the Investigational Products section.

Review and approval by the IBC is required for biologics that involve recombinant deoxyribonucleic acid (DNA). When gene transfer is involved, documentation of a decision by the NIH Recombinant Advisory Council (RAC), when their review is required, is expected.

In addition to the material listed in the Section III.D relating to the type of Event, the following material and/or information is required for all research involving biologics:

a. sponsor protocol, if industry-sponsored;
b. IDB, if industry-sponsored;
c. package insert, if approved drugs are administered;
d. documentation of current FDA status, if an IND for a biologic (BB-IND) is indicated;
e. completion of the Investigational Products[3] section (Reference Document #92) for each agent involved; and
f. data and safety monitoring plan.

If the study constitutes S-I research, additional consideration must be given as to how compliance with FDA requirements will be maintained, as described in Section III.E.1above. Documentation from the PI and department chair as described in Section III.E.1 must also be provided.

### 3. Submission materials: Device research

Research that involves a medical device may vary in design, from investigation of the safety, efficacy and practicality of investigational devices, to comparison of two approved devices, to the evaluation of approved devices for indications other than those for which they were approved.

A medical device is defined in the current federal Food, Drug and Cosmetic Act as an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

a. recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them;
b. intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
c. intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through

[3] The FDA considers an investigational product to be one that is the focus of a clinical investigation. Accordingly, if a drug, device, or biologic that is already approved by the FDA is the focus of the protocol being submitted, it should be described in the Investigational Products section.

chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

In addition to the material listed in the preceding Section III.D relating to the type of Event, the following material and/or information is required for all research involving devices:

a. device manual, if industry-sponsored;
b. documentation of current FDA status, (e.g., FDA approval letter with terms if an IDE is indicated, printout of approved indications from FDA website if 510(k) approval, etc.);
c. completion of the Investigational Products[4] section (Reference Document #92) for each device involved;
d. data and safety monitoring plan;
e. device management plan;
f. Clinical Investigator Agreement; and
g. Notice of National Government Services (NGS) approval or disapproval, if the study meets the requirements for device studies that must be submitted for a determination of NGS billing clearance.

If the study constitutes S-I research, additional consideration must be given as to how compliance with FDA requirements will be maintained, as described in Section III.E.1 above. Documentation from the PI and department chair as described in Section III.E.1 must also be provided.

A sponsor's determination of non-significant or significant risk, and basis for the determination, is recommended for studies that do not already have an approved IDE. If this information is not provided, the IRB will make its determination absent this input; if additional information is needed, the determination, and hence the overall review, may be delayed. Ultimately, after review of all material and justification provided by the sponsor and investigator, the IRB's determination is final.

When devices that are not yet FDA-approved will be used, plans for handling of the investigational article should be included in the submission to the IRB. The following factors should be addressed:

a. When recruitment and ordering of devices will begin (i.e., that no patients will be contacted or recruited, and no investigational devices will be ordered, until IRB approval has been obtained and applicable contracts have been signed);

[4] The FDA considers an investigational product to be one that is the focus of a clinical investigation. Accordingly, if a drug, device, or biologic that is already approved by the FDA is the focus of the protocol being submitted, it should be described in the Investigational Products section.

b. That the PI is responsible for ordering, and proper accountability, handling, and storage, of devices, as follows;
   1) How and by whom devices will be ordered (i.e., ordering will be done in accordance with the terms of the protocol and contract, and only after IRB approval is obtained);
   2) By whom devices will be received (i.e., devices will be received only by the PI or designee, or NYP personnel when there is an NYP policy or procedure for device management (e.g., in Operating Room));
   3) How device accountability will be documented including receipt from the manufacturer, method for labeling and tracking individual devices date of use, subject identifier, and lot number of the device, and return of (or destruction of in accordance with manufacturer's instructions/protocol) unused devices to the manufacture or sponsor. The spreadsheet or dispensing log for device accountability should be included with the plan for handling investigational devices;
   4) By whom devices may be handled (i.e., devices will be handled only by individuals listed on the protocol or by NYP personnel when there is an NYP policy or procedure in place (i.e., in the Operating Room));
   5) Who will ensure the sterility of the device prior to use with a subject (i.e., either the product is shipped to the PI in sterile condition or the device will be sterilized on the premises per the protocol and NYP policies).
   6) In what manner will devices be stored to ensure accountability, sterility, and integrity of packaging (i.e., a plan for storing devices securely to ensure physical stability of packaging and appropriate temperature, and separate from similar commercial and/or investigational devices will be implemented);
   7) Procedures by which disposition of devices will occur (i.e., devices will not be destroyed, devices will be disposed of in accordance with the manufacturer's or sponsor's (as applicable) requirements (i.e., returned to sponsor)).
   8) If the device will be explanted from the subject, plans to first send the device to Pathology for its review in accordance with standard practice.

c. That the manufacturer and/or sponsor representatives who are involved with use of the device at a study site under the direction of a Columbia investigator will abide by site requirements and policies regarding privileges and access to facilities, patients, and confidential information. The Columbia Guidelines for Short-term Visitors in Research-Related Activities (Reference Document # 306) should be reviewed for applicability. If vendor representatives will be present in operating or procedure rooms at NYP, requirements of the NYP Vendor (PERIOP/ BUS 14, Reference Document #145) and Vendor Representative (P230, Reference Document #307) policies must be satisfied.

**4. Submission materials: Planned emergency research**

Planned emergency research refers to the study of acute, life threatening clinical situations. Often, informed consent from the subjects is not feasible because the subject lacks the capacity to provide his/her own consent (e.g., unconscious) and/or there is

insufficient time because treatment must be promptly administered. The conduct of planned research in life-threatening emergent situations requires special consideration by the IRB, including consideration of whether consent by an individual subject may be waived. The specific conditions under which prospective consent of the subject may be waived are provided by 21 CFR 50.24.

If waiver of consent is proposed for those subjects who are not capable of providing consent, and do not have a legally authorized surrogate present, the research plan must include not only public disclosure of the study to the community in which the research will be conducted, but also community consultation. The purpose of the community consultation is to assess whether members of the local population at large would approve of the conduct of the emergency research, i.e., whether they are in favor of such procedures being performed on them if they were in a particular emergency situation. The community consultation should include individuals that represent the targeted subject population that will be enrolled in the study. The community consultation must be completed before IRB approval. It is recommended that the research team meet with the IRB staff to discuss the plan for community consultation prior to its initiation.

The plan for the emergency research study, including the plan for community consultation and public disclosure, must also be approved in advance by the FDA if the research involves an investigational or FDA-approved product. The plan must be submitted to the FDA under an emergency IND/IDE by the sponsor or S-I responsible for the IND/IDE. If the emergency research study is federally-supported or conducted and does not involve an investigational or FDA-approved product, approval must be obtained from OHRP (on behalf of the DHHS Secretary). The community consultation and the public disclosures, however, generally do not have to be completed but should be started prior to submission for FDA or OHRP approval. Therefore, the recommended sequence of events would generally be: a) consultation with the IRB; b) development of a plan for community consultation; c) start community consultation to provide some data for the IRB and FDA or OHRP submissions; d) submit the protocol to the IRB; and e) submit the IND/IDE to the FDA or OHRP for approval.

The IRB may approve the study prior to FDA approval of the IND/IDE. When this occurs, the IRB approval will specifically restrict enrollment of subjects as appropriate until the IRB receives notice of FDA approval of the IND, and all outstanding concerns have been adequately addressed.

In addition to the material listed in the preceding Section III.D relating to the type of Event, the following material and/or information is required for all studies involving emergency research:

a. justification for conducting the research in the proposed context, including enough information for the IRB to make all determinations required in Section VI.D.10;

b. detailed process for obtaining consent for subjects who are able to consent;

c. for those subjects who are not able to provide informed consent, a description of efforts to identify an appropriate surrogate, family notification of research participation, when possible, and plans for informing the patient of participation if/when the patient regains cognitive capacity;

d. plans for identifying and contacting family members after participation if such contact could not be done prior to participation;

e. procedures for determining who is a legally authorized representative, when permission will be sought from someone other than the parent of a minor child;

f. description of the efforts by which the community has been advised of the planned emergency research.

The Surrogate Consent section of the IRB Informed Consent Policy provides detailed information about options for surrogate consent.

At the time of continuing review, unless required sooner by the IRB, the investigator will need to summarize efforts made to contact family members of those subjects who were not able to provide their own consent.

Planned Emergency Research must be distinguished from emergency use of an investigational FDA-regulated product for an individual patient. The former is considered research but the latter is considered clinical care. Both may involve waiver of informed consent through the provisions of 21 CFR 50.24.

**5. Submission materials: Research involving pregnant women, fetuses, and neonates**

In addition to the material listed in the preceding Section III.D related to the type of Event, the following material is required for all research involving pregnant women, fetuses, and neonates:

a. information to support the findings required by Subpart B of 45 CFR 46 for participation of pregnant women and fetuses in research; and

b. a description of the additional precautions that will be taken to ensure that legally effective informed consent is obtained, when women in labor will be enrolled. Institutional guidance (Reference Document #10) on when it may be acceptable to approach women in labor for purposes of research participation should be considered when developing this information.

**6. Submission materials: Research involving prisoners**

In addition to the material listed in the preceding Section III.D relating to the type of event, the following material is required for all research involving prisoners:

a. information to support the findings required by Subpart C of 45 CFR 46 for participation of prisoners in research;

b. a rationale for including prisoners in the research, or limiting research participation to prisoners; and

c. approval or letter(s) of support from applicable departments or facilities, if already obtained.

**7. Submission materials: Research involving children**

In addition to the material listed in the preceding Section III.D relating to the type of Event, the following material is required for all research involving children, i.e., information to support the findings required by Subpart D of 45 CFR 46:

a. a description of procedures used to obtain assent, or justification for not obtaining assent;

b. when assent will be obtained, identification of the ages for which assent will be required, and a description of the method used to document that assent was provided, e.g., written documentation on an assent form, verbal agreement documented by researcher in the research record;

c. description of procedures for obtaining, and forms used to document, parental permission;

d. the investigator's initial assessment of risk level and potential for benefit to subjects or others;

e. sufficient information for the IRB to determine the level of risk, and whether there is the prospect of direct benefit to the individual subject;

f. a statement regarding the inclusion of wards if the research involves greater than minimal risk without the possibility of direct benefit, i.e., whether wards will be included and if so, what procedures have been developed for identifying an advocate for each ward; and

g. procedures for determining who is a legally authorized representative, when permission will be sought from someone other than the parent of a minor.

The Child Involvement section in Rascal, which solicits the information described above, must be completed by the investigator if he/she has indicated that children will be involved in the study. This section is designed to remind the investigator of information required, depending upon the level of risk and prospect of benefit to subjects.

Researchers who anticipate that children will be included among their study subjects are advised to review the Columbia policy, Research Involving Children (Reference Document #107), which articulates the institution's expectations for parental permission, assent, risk/benefit analysis, and related issues. The policy is posted on the CUMC and CU-MS IRB websites.

### 8. Submission materials: Research involving other vulnerable adults

In addition to the material listed in the preceding Section III.D relating to the type of Event, the following material is required for all research involving vulnerable populations:

a. a description of procedures incorporated into the protocol to ensure that the rights and welfare of individuals with decreased autonomy will be protected;

b. a description of procedures that will be utilized to obtain legally effective consent;

c. where applicable, a description of procedures that will be utilized to determine competency to provide consent initially or during the course of participation, the latter for studies in which it is expected that cognitive capacity may become diminished;

d. procedures for determining who is a legally authorized representative or appropriate health care proxy, when one is needed to provide consent;

e. description of procedures that will be utilized to minimize risks related to the vulnerability of the prospective subjects; and

f. description of procedures that will be in place to eliminate elements of undue influence or coercion.

### 9. Submission materials: Research involving non-English speaking individuals

If the inclusion of non-English speaking individuals is anticipated, the consent document(s) must
be translated by an acceptable translator, as defined in the CU IRB Enrollment of Non-English Speaking Subjects in Research Policy (Reference Document #101), into the prospective subjects' first language or language of choice. Certification of the translation, as described in the Policy, must be provided. It is not sufficient in most cases to rely on verbal translation of English consent documents during the consent process.

If a non-English speaking individual is unexpectedly encountered who otherwise meets eligibility criteria, and the trial involves an intervention that offers the prospect of direct benefit, the short form consent process may be used and use of the process must be documented. The summary document (in English) and the participant's attestation (in his/her first language or language of choice) must be approved by the IRB. Efforts to translate the entire approved English consent document are encouraged, whenever possible.

Details of translation options are provided in Reference Document #101, Enrollment of Non-English Speaking Subjects in Research Policy.

In addition to the material listed in the preceding Section III.D relating to the type of Event, the following material and description of procedures are required for all research in which the involvement of non-English speaking subjects is anticipated:

a. a description of procedures to obtain consent in the subject's language of choice;

b. plans for communicating with Non-English speaking subjects throughout their participation.

c. a statement that consent and recruitment documents will be translated after the English version is approved (if this is not included in the submission, the IRB approval letter and correspondence will articulate the need for translation); and

d. after the English version is approved, submission of translated documents as a modification (if submitted with additional changes), or via email for the administrative review process, with certification of exact translation.

At the time of continuing review, if previously approved consent and recruitment documents have not changed, the same translation may be submitted for review.

**10. Submission materials: Research involving students or employees as subjects**

Ethical concerns may arise if a study recruits individuals in positions subordinate to the PI. At times, however, recruitment of individuals in this situation may be necessary to accomplish study objectives. In those cases, the investigator must justify the use of this population and identify how elements of coercion or undue influence will be addressed. The Board will consider whether proposed procedures to minimize such elements are adequate, and request revisions or additions if necessary.

These measures are not, in general, intended to apply to research conditions under which subjects are recruited by flyers or other advertisements posted publicly to which individuals subordinate to the investigator may elect to apply. There may, however, be instances in which the IRB must consider whether enrollment of subordinates is not appropriate, even if recruitment is via flyer and initiative by the prospective participant is required, i.e., when there is the potential that the student/employee may feel that they must participate in order to be seen as favorable or cooperative to their instructor/employer.

In addition to the material listed in the preceding Section III.D relating to the type of Event, the following material is required for all research involving students or other individuals in a subordinate position to the researcher:

a. justification for use of this population;

b. description of procedures that will be utilized to avoid elements of coercion or undue influence;

c. explanation of other options for obtaining course credit if research participation offers such incentives; and

d. explicit instructions for advising subjects of the voluntary nature of participation.

When students will be recruited, the "Students as Research Subjects" guidance (Reference Document #128) should also be reviewed for applicability.

If research will be conducted in NYC public schools, approval from the NYC DOE IRB is required.

**11. Submission materials: International research**

IRB review of international research raises additional considerations relating to local laws, institutional commitments and regulations, standards of professional conduct and practice, cultural norms, and local community attitudes (relative to the study site). Physical, social and psychological risks may vary from those in the New York City communities within which the Columbia campuses reside, i.e., from the area "local to" the CUMC and CU-MS IRBs. Challenges may be raised when assessing the risks and benefits of research conducted internationally if adequate knowledge of the local setting is not provided. Care must be taken to ensure that the cultural norms of the host country are respected and that the participants will not suffer adverse consequences from participation, such as being subjected to retaliation from local authorities or the local community.

To that end, evaluation of the protocol by a review board local to the study site, consultation with an expert in the respective country, and/or other means to obtain knowledge of the local context is required.

If sufficient information about the proposed research site, to satisfy the IRB's requirement for knowledge of the local context, is not provided in the submission, it will be requested as part of the administrative pre-review.

In general, if local ethics committee approval is required, it should be obtained after review by the CU IRB. If local ethics committee review is conducted before the CU IRB review, the approved consent document(s), explanation of issues raised by the local committee during its review, if available, and approval letter from the local committee, should be considered in the CU IRB review.

If CU IRB review occurs before the local ethics committee review, CU approval to commence study procedures would be contingent upon receipt of the approval by the local ethics committee, which should employ standards that are appropriate for Columbia's HRPP.

Investigators conducting research in foreign countries must be aware of and abide by all applicable Columbia polices related to international activities. The website maintained by the Office of RCT provides additional information.

In addition to the material listed in the preceding Section III.D related to the type of Event, the following material or considerations are required prior to approval by the IRB:

a. documentation of knowledge of local context, i.e., details of the local context to provide a basis for the IRB review;

b. local IRB/ethics committee approval, evaluation by a consultant, or input from an individual or entity with adequate knowledge of the study site should be submitted with the application (if this documentation is available at the time of the CU IRB submission), obtained by the IRB during the renewal process, or in the case of local approval, provided after approval (if the local review board requires CU approval first);

c. agreement that consent documents will be translated after the English version is approved, if the study population is expected to include non-English speaking individuals;

d. identification of local individuals, if any, who will participate in conducting the research, and a description of their roles; and

e. where appropriate, letter(s) authorizing conduct of the study at the international institution or organization.

**12. Submission materials: Substudies**

Substudies may be defined as projects that are developed to answer a research question that has arisen as a result of an ongoing study, i.e., there is a logical evolution or expansion of the initial research hypothesis, or auxiliary studies are offered to participants in a study, e.g., optional pharmacokinetics or genetic procedures.

The determination of whether a substudy should be submitted as a separate, new Rascal submission, or as a modification to an approved protocol, is dependent on the relationship of the new procedures to the existing protocol, e.g., objectives, subject population, consent procedures, study instruments, risk and benefit. In general, if the population, consent procedures, and objectives vary significantly from the approved study, such that the IRB can no longer make one set of required determinations for the entire Rascal protocol, the substudy should be submitted separately. In such cases, the approved main study should be referenced in the new submission so that, where feasible, both can be reviewed by the same IRB and primary reviewers.

In addition to the material listed in the preceding Section III.D relating to the type of Event, the following material is required for all substudies:

a. an explanation of the relationship between a previously approved, or recently submitted, protocol and the substudy that is being submitted for review;

b. a description of the modifications, if any, that will be made and submitted to the IRB for review, to recruit from the main study, if applicable;

c. if subjects from the main study will be recruited for the substudy, a description of how the substudy will be introduced to the subjects; and

d. consent procedures for the substudy, and additional consent forms, if applicable;

e. details of data use and sharing, if applicable, between studies.

**13. Submission materials: Collaborative research that will not be conducted under an IRB Authorization Agreement**

Researchers affiliated with Columbia may collaborate with individuals from other institutions on a specific research project involving human subjects. When this occurs, the IRB needs to know enough about the activities at each site to be able to accurately determine the risks and benefits of the activities for which CU has oversight, and the documentation, if any, required from each site.

In addition to the material listed in the preceding Section III.D relating to the type of Event, the following material/information is required for all collaborative research:

a. For all collaborative projects:

   1) the name and title of, and contact information for, the individual (identified by role) who is responsible for the conduct of the project at the collaborative site(s);

   2) the procedures that will be conducted at each site (level of detail will be dependent upon CU role, e.g., whether CU is the lead institution, one of the study sites, coordinating center, etc.);

   3) the funding mechanisms involved;

   4) identification of the individual who will serve as the overall PI for the project;

   5) a clear description of what the CU personnel will be doing as well as what will be done, in relation to the research study, at CU;

   6) proposed use of consent forms, i.e., whether CU forms or the other institution's forms will be used, and for which site(s) each consent form will be used , if each institution has one or more; and

   7) appropriate authorization for research at the site, and IRB approval, as applicable;

b. In addition, if CU is the lead institution:

   1) the status of IRB approval at each site or arrangements previously made or in progress to delegate authority for review;

   2) description of services provided by coordinating centers, and identification of the coordinating centers, if applicable;

   3) a written plan explaining how regulatory compliance will be ensured for each site engaged in the research. The plan should include:

a) details on how local IRB approval will be obtained and maintained at each site;

b) a description of procedures in place to ensure that the informed consent document approved by the local IRB does not have substantive changes in the purpose, procedures, and risks sections from the form approved by the CU IRB;

c) a plan for ensuring that UPs involving risks to subjects or others will be reported to the local and CU IRBs;

d) a plan for data and safety monitoring, including review of reports of unanticipated problems that involve risks to subjects or others, ensuring confidentiality of study data at local sites, during transmission, and at CU, analysis and dissemination of interim results;

e) a process for implementing protocol modifications.

c. In addition, if the research is non-exempt and will be federally conducted or supported:

1) the name and FWA number for each site engaged in the research;

2) an IIA for any individual who is engaged in the research, but is not working under the auspices of an institution or organization.

Processing multi-site projects, some of which may require IRB review for funding purposes long before procedures for inclusion of human subjects have been developed, requires special consideration by the administrative staff and IRB. Although projects for which CU serves multiple roles may be submitted as one protocol for IRB review, it is often beneficial for the components to be submitted separately. This approach facilitates focused review of each component, and management of each role as appropriate to that role, e.g., the protocol for CU as a clinical site could be closed out when study procedures for all subjects are concluded, while the related repository or data coordinating center protocol for the overall project continues at CU. Consultation with IRB staff early in the development process is recommended, to identify and guide the most efficient approach.

### 14. Submission materials: Collaborative Research that will be conducted under IRB Authorization Agreements

Federal regulations permit an IRB at one entity to rely on the review of an IRB at another entity in specific situations, and require that the terms of the reliance agreement be described in an executed IAA. IAAs may exist between institutions for multiple projects that meet specific criteria, between legally separate components of one institution for multiple projects, or for individual projects. All IAAs that involve CU must be approved by the appropriate IO on the CU or NYP FWA(s), as applicable, and the ED or AD.

Several multiple project Agreements exist that describe the conditions under which: a) Columbia may rely on the IRB of another institution; Columbia will conduct reviews for another institution; or a combination thereof. Information about the terms of the specific agreements, and the material(s) required to be submitted to the Columbia IRB for a protocol that is subject to one of these Agreements, is contingent upon the relevant IAA and may be found in Reference Document #05.

When Columbia relies on another IRB to review protocols, there may or may not be a subsequent review by the Columbia IRB. When such a review is conducted by the Columbia IRB, it will often be a facilitated review, i.e., a review by an IRB Chair or an experienced member of the IRB to determine whether the protocol is appropriate for the local environment. Regardless of whether the relevant Agreement requires a facilitative review, protocols reviewed by other IRBs under IAAs generally need to be submitted to the Columbia IRB via Rascal for tracking purposes and for confirmation that institutional requirements (e.g., training and COI disclosure) are met.

**15. Submission materials: Domestic research conducted at non-CU sites**

As with international sites, some domestic sites may have characteristics (e.g., socioeconomic, literacy, culture) that are significantly different from those at CU and in the surrounding areas, and consequently present a challenge in ensuring that IRB review criteria are satisfied because IRB members may not have adequate knowledge of the local context. In some cases, such research will also be reviewed by a local IRB if collaboration between CU and local researchers is involved, and in those situations, documentation of such review should be obtained.

If local IRB review is not obtained, and a need for additional knowledge about local context is identified, the IRB may opt to obtain this information through one or more sources, including the following: a) use of a consultant who has extensive knowledge of the environment and/or population, as appropriate; b) input from a local community board or similar committee comprised of individuals who represent the locale and/or citizens; or c) literature review. Selection of the source of information should be based upon the level of risk of study procedures to participants, i.e., while literature review may be acceptable for a minimal risk survey, use of a consultant or feedback from a local committee may be more appropriate for a study that poses greater than minimal risk.

Justification for selection of the particular study site should also be provided. Authorization from facilities at which study procedures will be conducted may be necessary in addition to knowledge of local context described above.

**16. Submission Materials: Research Conducted at External Sites by CU Researcher**

Columbia investigators who conduct research at non-Columbia sites have additional responsibilities for ensuring that all appropriate approvals from the study site(s) are obtained, and that procedures have been developed to ensure that the study may be conducted in compliance with the protocol at the external site.

In addition to the material listed in the preceding Section III.D relating to the type of Event, the following material/information is required:

- contact information for each site;
- documentation that each site has granted permission for the research to be conducted at the facility; and
- IRB/ethics approval:
  - whether each site has an IRB and if so, whether it has approved the research; or
  - plans to enter into, or attachment of an executed, IAA whereby the site relies on the Columbia IRB.

Additional guidance:

- If the external sites are international, please refer to Section III.E.11 of these procedures for additional guidance.
- If there will be collaboration with investigators from other institutions, please refer to Section III.E.13and/or III.E.14 of these procedures for relevant guidance.
- If the external sites are in the U.S., but not local, please refer to Section III.E.11. of these procedures for guidance on obtaining adequate knowledge of the local context.

### 17. Submission Materials: Transfer of Research when PI is leaving Columbia

If the PI of a study that is approved by the IRB will be leaving Columbia, plans for closure of the study or continuation with another PI at Columbia must be considered. A submission to the IRB is required, the nature of which will be determined by the decisions that are made about the future status of the study at Columbia. Common situations and options for IRB submissions are described below. IRB staff should be consulted about appropriate action for other circumstances.

For active research:

1. If the study(ies) will be transferred to another institution, an intervention is involved, and subjects will be offered the opportunity to continue participation at the new institution, a modification that describes plans for notifying subjects, determining whether they will continue participation, and safely transferring or ending subject participation should be submitted to the IRB;
2. If the study(ies) will be transferred to another institution, subjects are not currently enrolled or all subjects have completed study procedures or have withdrawn, but identifiable data will be transferred, a modification should be submitted to describe how confidentiality of data will be maintained in accordance with the terms to which the subjects agreed; and
3. If the study(ies) will not be transferred to another institution, a qualified individual must be identified to serve as PI, and a modification submitted to implement the change.

For research that has not yet started or for which all activities have concluded, but the study remains open while awaiting publication, the study should be closed out with the IRB.

# IV. Processing of Submissions to the IRB: Pre- and Post-IRB or ARC Review

## A. Preliminary review of submitted events

Upon submission, a preliminary review ("pre-review") by experienced IRB officers is conducted. This section provides an overview of the pre-review process. Complete details of the process, including the criteria on which the review is based, will be found in the Review section (Section VI) of these procedures.

The nature of the pre-review is contingent upon the type of Event and is described in more detail in the Review section (Section VI) of these procedures.

As a result of the pre-review, the submission is either logged in to the Chair's queue in Rascal or returned electronically to the researcher. If the submission is returned, it will have another staff review upon resubmission. Details of the routing process can be found in Reference Document #24.

New protocols undergo a cursory review upon submission to assess the proper level of review so they may appropriately be routed for pre-review. Upon completion of each pre-review of new protocols submitted for the first time, the staff reviewer completes a reviewer form (Reference Document #34a, "Reviewer Form: New Protocols (Biomedical)" or #34b, "Reviewer Form: New Protocols (Behavioral)") and enters comments in the Notes field for the Event. The protocol will be assigned to the appropriate review panel depending upon the level of review required: CUMC IRBs 1-3 for full board non-oncology studies; CUMC IRB 4 for full board oncology studies; CUMC IRB Exp for protocols eligible for expedited review; the CUMC ARC for exemption or determination of Not Human Subjects Research (NHSR); or MS IRB for protocols originating from CU-MS researchers.

A reviewer form is also completed by staff during pre-review of renewal submissions (Reference Document #110, "Renewal Pre-review Form"), and the termination review is guided by specific criteria (Reference Document #111, "Termination Return Criteria"), followed by a summary entry in the Notes field. A template for notes about modifications, and a review form (Reference Document #308) are being developed and will guide, in a consistent manner, the administrative review of modifications to approved protocols. The outcome of staff pre-review of other Events is entered in the Notes field.

At the conclusion of the pre-review for renewals, terminations, and unanticipated problem reports, the reviewer takes appropriate action to facilitate the Event being logged in (i.e., accepted for review) or returned to the researcher for revision or additional documentation/information. The format for the commentary that is entered in the Notes section can be found in Reference Document #20.

## B. Routing of submissions to IRB per level of review required

Submissions are routed electronically to the Chair's queue after being logged in by IRB staff. Individuals designated as Chair or Vice Chair (either, a "Chair") review pre-review comments entered in the Notes field relevant to each Event to obtain a synopsis of the Event,

facilitate awareness of regulatory considerations, and document the recommended level of review. Depending upon the level of review required, the Chair will review the submission for the Event him/herself or distribute it to an experienced IRB or Committee member for review. To the extent possible, reviews after the initial approval of a protocol will be conducted by the IRB or Committee that originally approved the study and by the IRB or Committee member who originally presented the study.

### 1. Level of Review: Not Human Subjects Research

During the course of the review of submitted new protocols, and with consideration given to the recommendations of the preliminary reviewer, a determination may be made that the project does not meet the definition of research as defined in the applicable federal regulations, or the involvement of humans is such that the definition of a human subject is not met. In such cases, the designated reviewer may label the protocol as either NHSR, i.e., definition of research is not met, or "Not Human Subjects Research per 45 CFR 46" (NHSR per 45 CFR 46), i.e., definition of human subject is not met.

At CUMC new protocols for which the recommended determination per the pre-review is "NHSR" are assigned to the ARC, which is made up of IRB staff, for documentation of the determination. At CU-MS, the Chair makes the NHSR determination. Although IRB Chairs or staff must review the protocol in order to make a NHSR determination, these projects are not subject to the requirements of the federal regulations for the protection of human subjects or to continued oversight by the IRB.

Justification that the project does not meet the criteria to be considered human subjects research must be provided, if the PI is seeking such a determination. If the staff reviewer is able to derive, from submitted materials and information, or through interactions with the study team, that the project is NHSR or NHSR per 45 CFR 46, even though such a determination was not requested, staff may recommend that the study be considered NHSR, or NHSR per 45 CFR 46. Only a Chair or a member of the ARC may select one of the NHSR options in Rascal.

If it is unclear whether research with human subjects is involved, an investigator may request an administrative review of a proposal outside of the system to determine whether review by the IRB is required. In those cases, an IRB officer will request a copy of all available materials, and based on that information, make a determination as to whether a submission to the IRB is required, i.e., whether the proposed activities constitute *research* with *human subjects*. The determination is documented in writing to the investigator, and includes a statement to the effect that the determination is applicable only to the materials/information that were submitted and reviewed, i.e., upon which the decision was based.

IRB staff and Board members may use the Research Decision Chart (Reference Document 29), or other similar tools, such as the OHRP decision charts, to assist them in making the appropriate determination.

## 2. Level of Review: Exempt determination

Research that falls into one or more of six specific categories of research defined in the federal regulations (45 CFR 46.101(b), 21 CFR 56.104(d), and 21 CFR 56.104 (c)) may be determined to be exempt from the requirements of 45 CFR 46. Protocols for which the investigator has entered an exempt declaration and justification are reviewed by a designated reviewer (i.e., Chair at CU-MS, and staff at CUMC), who may to approve the project as exempt, designate the protocol as eligible for expedited review (if more appropriate than exemption), or return the protocol to the investigator. The protocol will be returned if revisions, additions, or deletions are required. The designated reviewer also has the authority to either remove an exempt declaration that was entered by the PI, or designate a protocol as exempt even if the PI has not entered an exempt declaration. When an exempt declaration entered by the PI is removed by a designated reviewer, the information that was in the exempt declaration is automatically exported to the IRB notes by the Rascal system.

At CUMC new protocols for which the recommended determination per the pre-review is Exemption are assigned to the ARC. At CUMC the staff reviewer on the ARC, and at CU-MS the Chair/Vice Chair, attaches or removes the Exempt Declaration, as appropriate.

As a function of the Rascal system, a Chair or other designated reviewer may not electronically distribute Events that include an Exempt Declaration. Therefore, if the Chair or ARC member decides that the protocol requires review by another member, he/she may request that another IRB or ARC member review the material by retrieving it in Rascal by the IRB number rather than by accessing it in his/her reviewer queue. The selected reviewer may enter comments in the Notes section upon completion of their review. Rascal labels exempt determinations as approvals; only a Chair or an ARC member may electronically "approve" an exemption.

If there is any information that needs to be verified with the investigator, the designated reviewer or staff may initiate this contact. Communication via Rascal correspondence is recommended. If e-mail communication is used, the messages should be copied and pasted into the Notes section, attached, or otherwise documented within the Event submission, for the Event being reviewed. Phone calls should be documented in the Notes if other than routine procedural information is discussed.

The DHHS exemptions apply to research with children, with certain limitations. Exemption (2) at 45 CFR 46.101(b)(2) for research involving survey or interview procedures or observations does not apply to research involving children, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed. Surveys and interviews with children are acceptable under exemption (1) at 45 CFR 46.101(b)(1) if the questions are directly related to evaluations of standard educational practices in accepted educational settings.

Research involving prisoners is not eligible for exemption. Except for exemption (6), which is reflected in the FDA regulations as 21 CFR 56.104(d), the exemptions at 45 CFR 46.101(b) do not apply to research that involves an investigational drug, device, or biologic, (i.e., are subject to FDA regulations).

As noted in the Columbia Informed Consent Policy (Reference Document #10), in the spirit of the principles of the Belmont Report, in which autonomy of the individual and the voluntariness of participating in research are fundamental ethical principles, the IRB strongly recommends that informed consent be obtained for certain exempt studies. For exempt studies that allow for direct interaction between the investigator and human subjects, participants should minimally be informed of the following: that the activity is research, the procedures that are involved in the study, the nature of the risks (e.g., little, if any expected inconvenience or harm), that participation is voluntary and that they may withdraw from the study at any time.

Exempt decisions are communicated to the research team via Rascal correspondence by both the CUMC and CU-MS IRBs, and, in the case of approvals, also by electronic Letter of Approval (LOA) (Reference Document #93).

Exempt determinations are valid for a period of two years. At the end of the two-year period, an abbreviated renewal application must be submitted for tracking purposes. Unless the research has changed in such a manner that the project is no longer exempt, approval will be provided for an additional two year period (Reference Document #9).

A list of exempt determinations is generated via the Rascal IRB minute function. Copies of approved minutes are forwarded to the IOs. Although not required from a regulatory perspective, such notification affords the IOs the opportunity to be aware of, and if warranted, provide input about all human subjects research that may be conducted under the auspices of the institution.

The FDA allows four exemptions from IRB review of activities under FDA purview:

a. Any investigation which commenced before July 27, 1981 if specific conditions are met;
b. Any investigation which commenced before July 27, 1981 and IRB review was not required;
c. Emergency use of an investigational article; and
d. Taste and food quality evaluations and consumer acceptance studies if specific conditions are met.

### 3. Level of Review: Expedited

The IRB may utilize an expedited review procedure as authorized by 45 CFR 46.110 and 21 CFR 56.110.

At CUMC, new protocols for which the recommended level of review per the pre-review is expedited are assigned to CUMC IRB Exp. The CU-MS IRB conducts expedited reviews of protocols originating from CU-MS researchers.

Upon review of a submission, if the criteria for expedited review appear to be met, a Chair will designate the protocol as eligible for expedited review by selecting the appropriate expedited review category(ies) in Rascal. The Chair will then distribute the protocol for review by selecting a primary reviewer and sending the protocol electronically to the reviewer's queue. The reviewer has access, electronically within Rascal, to all information and documents that were submitted by the study team. A qualified member of the Board (in general, one who has one year or more of IRB experience) or the Chair may serve as the primary reviewer. If necessary to ensure the necessary reviewer expertise, additional reviewers may be selected.

In accordance with federal regulations, the designated reviewer(s) may act for the Board to approve or require changes to an Event under review, and ensures that all review criteria are met. To facilitate this process, reviewers are routinely provided with tools and information to guide their review, including a primary reviewer form, decision charts, and educational information, as part of the CU IRB educational initiatives. Board action is required, however, for a decision to disapprove a study.

The IRB may utilize the expedited review process for the following types of research (45 CFR 46.110; 21 CFR 56.110):

a. Minor changes in research previously approved by the convened IRB or through an expedited review process during the period for which approval is authorized; a guidance document (Reference Document #112) has been drafted to assist in determining whether a change is minor; in addition, minor modifications are addressed in Section VI.C.2. of these SOPs;

b. Research activities involving no more than minimal risk for which the only involvement of human subjects will be in one or more of the categories identified on the list as published by the FDA and DHHS.

In reviewing the research, the reviewer may exercise all of the authority of the Board except disapproval. If the reviewer finds that the protocol does not meet the criteria for expedited review, he/she will refer it to the full Board for action.

As with the review of exemptions described in the preceding Section, if there is any information that needs to be verified with the investigator, the designated reviewer or staff may initiate this contact and should document it in Rascal.

The reviewer who is conducting the expedited review may enter comments in the Notes section of Rascal and make non-Rascal documents such as handwritten or typed comments available to the IRB staff as documentation of the review and to assist in preparation of correspondence. These documents will not be considered part of the official file unless they are attached to the protocol in Rascal.

A list of research that has been approved under an expedited procedure, including PI and title, is provided to the members of IRB Exp as soon as practical after such expedited approval, via IRB minutes. Members who participated in the expedited review will respond to questions, if raised, from the members concerning the Events approved in this manner.

The Board will not use the expedited procedure if its use has been suspended or terminated by the FDA, OHRP or the University.

Decisions made by expedited review are communicated to the research team via Rascal correspondence, and, in the case of approvals, also by electronic LOA (Reference Document #93).

**4. Level of Review: Facilitative/Administrative/118**

Three functional categories exist in Rascal in the expedited review option list: Facilitative Review, Administrative Review of certain types of awards to support multiple projects involving numerous investigators, and review per 45 CFR 46.118. The first was developed to allow processing of protocols subject to IIAs when CU is not the IRB of Record (additional detail in following section), the second was implemented to permit processing of submissions for programs for which human research exists only in individual studies that will each receive IRB approval, and the third was instituted to facilitate processing of protocols for which procedures involving human subjects were not defined at the time of IRB submission (but IRB approval is required by the funding agency). See Reference Document #108, email from George Gasparis to CU IRB Chairs and staff, "Addition of new expedited review category in Rascal", for additional information regarding the Administrative Review category.

a. Facilitative review

A facilitative review is conducted when the IRB has agreed to rely on the review of an IRB from a non-Columbia institution, via an executed IAA. The specific review process is contingent upon the relevant Agreement.

The Boards may act in liaison with the IRBs of other institutions as necessary to assist in the approval of joint and cooperative projects involving multiple sites and/or investigators. The ED or AD may agree to permit another IRB listed on a CU FWA to act as the IRB of Record for studies to be conducted by, or with the assistance of Columbia personnel, at the facilities of another institution. In addition, a CU IRB may agree to function as the IRB of Record for another investigator and/or institution if the project involves material collaboration with Columbia personnel.

The IAAs will require written letters of agreement and may necessitate the completion of an FWA, an IIA, or an IAA. Specific criteria for, and procedures for

implementing, each of these agreements, which CU has adopted, can be found on the OHRP website.

Details of the level of, and criteria for, review of protocols that are subject to an IAA can be found in Reference Document #05.

Approvals under these categories are reported to members of the IRB that conducted the facilitative review via approved minutes.

b. Administrative review

This Columbia-specific expedited review category is utilized for submissions that describe a funding mechanism for human subjects research, but do not, in and of themselves, describe specific research projects. Examples are center grants and training grants. Each project that will involve human subjects and be supported by the award will be submitted individually within Rascal. For each individual submission, IRB review will be conducted and all necessary IRB determinations made.

CU pre-award research administrative offices require an IRB approval prior to creation of an account for the funds. This category of expedited review was created to accommodate, within Rascal, the technical need for an approval. At the time of continuing review, a list of all projects that are funded through one of these awards should be attached. The IRB will confirm that the necessary approvals are in place for the supported projects before approving the continuing review submission for the infrastructure grant.

c. "118" reviews

This Columbia-specific expedited review category is utilized for funded research that anticipates the involvement of human subjects within the funding period, but not until preliminary procedures that do not involve human subjects are completed, i.e., research conducted in accordance with 45 CFR 46.118. Examples are projects for which study instruments will be developed with grant funds in the first phase of the research, and studies for which personnel need to be hired and trained before human subject involvement commences.

When the involvement of human subjects is fully defined, a modification that describes the procedures in which human subjects will be involved, and provides applicable study-related instruments, must be submitted for review. The involvement of human subjects may not commence until the modification is approved. The level of review will change as warranted by the level of risk and type of procedure.

### 5. Level of Review: Full Board

Full Board review is required for any protocol that involves research with human subjects and does not qualify for exemption, expedited review per the federally defined categories, or a facilitative, administrative, or "118" review as described in Section IV.B.4.4.

Each protocol that requires full Board review will be assigned to a primary reviewer (explained below) who is an IRB member, will be responsible for a full review of all materials, and will lead the discussion of the protocol at the meeting. Additional primary reviewers may be designated by the Chair. Review criteria are explained in more detail in the Review section (Section VI) of these procedures. All members of the Board to which a review is assigned have access in Rascal to all materials submitted by the study team, Notes entered by IRB staff and Chair, and Internal Documents attached by IRB staff or Chair.

Complete documentation of all submissions to a specific IRB is available electronically, from the time of the initial submission, for review by all members appointed to the respective Board.

Board members are also notified electronically of the protocols to be considered at each meeting, to facilitate online review.

## C. Primary Reviewer system

### 1. Primary reviewer system: Initial review

The CU IRBs use a primary reviewer system for research that requires full Board review. Each research activity is assigned to at least one primary reviewer, based on related expertise. A reviewer who has a conflict of interest with respect to the protocol, (i.e., is a co-investigator, has provided consultation for, or has a financial interest in the sponsor or product being tested), will not be assigned as a primary reviewer, but may be asked to provide information to the Board during the review. IRB members who are listed among the personnel on a submission do not have access to the Notes entered by IRB staff and members, Internal Documents, or reviewer assignment.

When making reviewer assignments, the Chair or designee considers the type of research and any recommendations from IRB staff, then selects a reviewer with expertise in the relevant area. It is especially important that individuals with appropriate scientific expertise serve as primary reviewers or otherwise have input into the IRB review if a project has not been peer-reviewed, either by a funding agency (e.g., NIH, NSF) or intra-departmentally (e.g., HICCC, Department of Pediatrics).

Protocols are distributed electronically within Rascal. Consultants who do not have Rascal access will receive material by other means.

When necessary to ensure a substantive review of the protocol, more than one reviewer may be assigned to evaluate a given protocol. An individual Board may elect to assign more than one primary reviewer for all protocols.

When additional expertise is needed that is not available among members of the Board conducting the review, consultants may be used, or the protocol may be assigned for review to another Board that has the appropriate expertise.

If vulnerable populations are involved in the research, and considering the risk level of the study, the Chair attempts to assign the protocol to an IRB member with the requisite experience to make appropriate determinations for the target population or, in the case of full Board reviews, ensures that an individual with such knowledge or experience will be at the meeting at which the submission is reviewed. The Chair may assign a protocol to him/herself, another primary member, or an alternate member.

A prisoner representative is assigned to review each protocol that involves prisoners as subjects. The Chair may determine that protocols involving subject populations for which the potential for incarceration during the course of participation in the trial is high should be reviewed as a prisoner protocol, to avoid disruption of participation or the need for re-review if a subject should become a prisoner. The reviewer is guided by the Prisoner Research review form (Reference Document #94).

Primary reviewers are responsible for conducting an in-depth review of all available documentation and presenting the study to the Board, if the submission requires full Board review. All members have electronic access to the complete submission of all protocols assigned to the Board of which they are a member, whether regular or alternate.

**2. Primary reviewer system: Continuing review (renewal)**

The Chair selects a primary reviewer (him/herself, another regular member of the IRB, or an alternate member) and distributes the renewal request within Rascal to that individual. As with new protocols, the Chair selects a primary reviewer who has the appropriate expertise to review the submission. The Chair may distribute the renewal electronically to a consultant who has RASCAL access but the consultant would be considered to be a secondary reviewer. Information that is available electronically, and should be reviewed by a primary reviewer, is provided by the most appropriate means (e.g., in hard copy or electronically) to any consultant who would not normally have access in Rascal.

An attempt is made to assign the protocol to the Board member who reviewed the initial submission or the most recent renewal request.

The reviewer has access to the complete historical file (i.e., where applicable, the paper file that was in existence before the conversion to Rascal) for the study as well as all renewal information during his or her review and may request that specific information be provided to all Board members prior to the convened IRB meeting (for those studies

that require full Board review). All members have electronic access to the complete renewal submission in Rascal and all preceding submissions for the protocol that are in Rascal.

A prisoner representative is assigned to review each renewal that involves prisoners as subjects. The Chair may determine that protocols which involve subject populations for which the potential for incarceration during the course of participation in the trial is high should be reviewed as a prisoner protocol, to avoid disruption of participation or the need for re-review if a subject should become a prisoner. The reviewer is guided by the Prisoner Research review form (Reference Document #94).

### 3. Primary reviewer system: Modifications, Unanticipated Problem reports

The Chair selects a primary reviewer (him/herself, another regular member of the IRB, or an alternate member) to receive the electronic submission. As with new protocols, the Chair selects a primary reviewer who has the appropriate expertise to review the submission. The Chair may distribute the modification electronically to a consultant who has RASCAL access but the consultant would be considered to be a secondary reviewer.

An attempt is made to assign the Event to a Board member who reviewed the initial submission or the most recent renewal request.

Consultants may also be used when the requisite expertise to assess the information provided cannot be provided by available Board members.

Information that is available electronically, and should be reviewed by a primary reviewer, is provided by the most appropriate means to any consultant who would not normally have access in Rascal.

All Board members have electronic access via Rascal to the complete modification or Unanticipated Problem Report submission: the Report of the Unanticipated Problem or modification summary, protocol Data Sheet, Study Description, current consent documents, Notes field affiliated with the event (which includes pre-reviewer notes), and supporting documentation attached by the researcher.

Board members also have access to the complete historical file (i.e., prior submissions and IRB actions) for the study for their review.

The Board determines, based in part on the primary reviewer's recommendation, whether the report is complete or additional information is required. In addition, a determination is made as to whether the protocol and/or consent document(s) should be revised, if this is necessary as a result of the UP or modification and has not already been initiated by the study team. When revision to the consent form(s) is deemed necessary, the Board determines whether currently enrolled subjects also need to be informed. Finally, the Board may impose restrictions on the research (e.g., more frequent reporting, suspension of enrollment, suspension of the study, termination, etc.) if review of an unanticipated

problem report or modification results in a determination that the risk/benefit ratio has become less favorable.

Details of all review processes are in Section VI, IRB Review of Human Subjects Research, of these procedures.

#### 4. Primary reviewer system: Terminations (closures)

The IRB Chair selects a primary reviewer (him/herself, another regular member of the IRB, or an alternate member) to receive the electronic submission. An attempt is made to assign the event to a Board member who reviewed previous submissions for the protocol. The Rascal system routes all closure requests to a Board meeting; Board members have access to the complete historical file (i.e., prior submissions and IRB actions) for the study during their review. Closure reports are voted upon as a group when presented at a convened meeting. Any Board member may request discussion of an individual closure report.

Requests for closures of protocols that are assigned to IRB Exp are listed on an agenda after which members of IRB Exp are notified that these items are available for their review until a specific date. If an IRB member has a concern about any closure request, the appropriate action, which may include obtaining additional information or recommendation to the study team that the protocol remain open, is taken. When all issues are resolved, IRB staff subsequently process the closure submissions. A similar process is followed for closure requests for exempt protocols that are assigned to the Administrative Review Committee, with staff members conducting the reviews.

### D. Post-Review Procedures

Minutes will be generated to reflect actions taken by the Board during convened meetings. The minutes of IRB meetings will document separate deliberations, actions, and votes for each event undergoing review by the convened IRB, as well as a summary of any Board discussions of controverted issues.

Notification to the IRB members of actions taken by the Chair or designated reviewers in-between meetings occurs via inclusion in the agenda and minutes of subsequent meetings. Details of the process by which minutes are generated can be found in the Minutes Section (VII.E.) of these procedures.

### E. Notification to Researcher: General Process

Outcomes of all reviews will be communicated to researchers as expeditiously as possible after the review is complete. Minutes of full Board meetings will usually be approved in their entirety prior to transmittal of the correspondence, via Rascal, related to the outcome of an Event reviewed at the meeting.

Minutes for the entire meeting need not be approved before the correspondence for an individual Event is sent, provided the minutes for that Event are approved (through documented contact with the Chair outside of Rascal or via use of the Immediate Action feature in Rascal). An electronic LOA (Reference Document #93) is also generated to document IRB approval.

The Boards will follow DHHS and FDA regulations for reporting its findings and actions to the investigator, and when applicable, to the institution (45 CFR 46.108; 46.103(b)(4); 46.103(b)(5); 21 CFR 56.108 (a)(1)). Hard copies of minutes are provided to IOs with a cover memo highlighting items that may require additional institutional consideration. In cases where the protocol is not approved as submitted, specific requests and concerns of the reviewer and/or Board, as appropriate to the level of review, will be communicated to the study team via Rascal. Wherever possible, guidance as to an acceptable response and the basis for the requests or concerns are included.

### 1. Notification: Approval and Outcome of Review

All requests and concerns of the IRB, whether from a full Board or expedited review, or evaluation to determine whether exemption is appropriate, must be addressed satisfactorily by the research team before a protocol may be approved or receive an exemption determination.

For expedited and exempt reviews, correspondence to the research team will initially be generated and transmitted in Rascal via the correspondence function for each action taken by the Board, Chair, or designated reviewer. IRB staff will evaluate the correspondence for completeness and accuracy, revise as necessary to include regulatory or institutional requirements, and release the correspondence for electronic transmittal to the research team. See Reference Document #95 for an explanation of the members of the research team to whom correspondence is sent within Rascal.

For Full Board reviews, correspondence for each individual event that was indicated on the agenda will be automatically transported from the minutes, when approved, to the correspondence queue, where IRB staff will then conduct an evaluation for completeness and accuracy, add regulatory or institutional requirements, if necessary, and forward the correspondence to the research team.

Approval of a non-exempt research activity will also be documented and communicated by means of an electronic LOA that will be posted in Rascal. The LOA will reflect the approval provided electronically by the Chair/designee or authorized expedited reviewer, and must be signed by a designee with signing authority. This authority is limited to IRB Chairs, the ED, AD, ADO, Managers, and other experienced officers.

Letter templates (Reference Document #93) are used to ensure consistency of format and inclusion of specific elements.

The LOA used for initial and continuing approval of a protocol will contain information about the study and its approval status. This document includes:

a. title of the research project;
b. name of PI;
c. for funded projects, funding award number and protocol version number, if available;
d. level of IRB review;
e. approval and expiration dates;
f. consent requirements;
g. approved study-related material that will be provided to subjects;
h. conditions to the approval, e.g., requirement to translate consent documents;
i. approved HIPPA forms; and
j. information regarding continuing review requirements, reporting of UPs, and the need to submit modifications for approval prior to implementation.

The LOA for changes in an approved research project will include, in addition to the items noted above:

a. a description of the modification;
b. consent requirements and forms, if revised from the originally approved procedures; and
c. HIPPA requirements and forms, if revised from the original approved procedures.

All LOAs will indicate to whom copies (if any) will be sent. Letters for research approved under an IAA may be copied to the IRB office of the institution with which the agreement was signed, depending upon the procedures applicable to the respective Agreement.

If recipients of copies do not have Rascal access, they will receive electronic copies by other means. It is noted that the Cancer Center protocol office receives correspondence on all cancer-related protocols and is so informed of IRB actions.

**2. Notification: Disapproval**

Correspondence will be sent to the research team electronically via the Rascal correspondence function. See Reference Document #95 for an explanation of the members of the research team to whom correspondence is sent within Rascal.

Disapproval of research may only be determined by the convened Board, and the action will be documented in the minutes for the meeting. Documentation of the outcome of the review will be communicated by means of Rascal correspondence and an electronic Letter of Disapproval (LOD) (Reference Document #96) which will be posted in Rascal. A hard copy letter may also be issued. The LOD will reflect the disapproval issued electronically by the Chair/designee (through the status change in Rascal) and must be

signed by a designee with signing authority. This authority is limited to IRB Chairs, the ED, AD and Managers.

The LOD must include the reason that the research, or research procedures, was/were disapproved. This document will also include:

a. title of the research project;

b. name of PI;

c. description of the process through which the investigator may address the Board in person or in writing regarding its action;

d. contact information for the IRB.

A letter template (Reference Document #93) is used to ensure consistency of format and inclusion of specific elements.

All LODs will indicate to whom copies (if any) will be sent. Letters for research approved under an IAA may be copied to the respective institution's IRB office with which the agreement was signed, depending upon the procedures applicable to the respective Agreement.

If recipients of copies do not have Rascal access, they will receive electronic copies by other means. It is noted that the Cancer Center protocol office receives correspondence on all cancer-related protocols and is so informed of IRB actions.

**3. Notification: Suspension**

Correspondence relating to suspensions will initially be sent to the PI either by email or hard-copy letter, and may follow via Rascal correspondence. See Reference Document #95 for an explanation of the members of the research team to whom correspondence is sent within Rascal. Documentation of the non-Rascal notification will be entered in the Notes section of the protocol or as an attached document in Rascal.

The PI's Department Chair and/or Division Chief, as appropriate, and the relevant IO will be copied on the letter.

Notification of all suspensions will also be forwarded to OHRP and, as appropriate, to any other regulatory agency(ies).

## F. Documentation of review and approval

Documentation of actions taken by the Chair or other authorized reviewer(s) in Rascal will be retained electronically within the Rascal system.

All IRB members are provided with a checklist of the IRB review criteria (45 CFR 46.111 and 21 CFR56.111) to guide them through reviews, as these must be satisfied before a new,

ongoing, or modified non-exempt protocol may be approved. See Reference Document #109 for a copy of this checklist. The approval of a new, ongoing, or modified protocol via an expedited review process indicates that the reviewer has considered all of the criteria and ensured that they are met. When full Board review is required, the affirmative vote of the IRB to approve a protocol, either outright or when specific items have been addressed, reflects that the primary reviewer's comments have been considered and the IRB review criteria have been satisfied.

Correspondence related to IRB actions that is generated within Rascal will also be stored electronically within the electronic system.

Consent documents generated within Rascal, using the consent form builder function, will be stamped as approved electronically when the status of the event changes to "approved". Please refer to Reference Document #161, Exceptions to Automatic Consent Form Stamping, for a current list of situations for which a consent form will not automatically receive an approval watermark when the event to which it applies is approved.

Consent documents, including recruitment material and study instruments that are generated outside the system but attached in Rascal will be stamped electronically with the IRB approval stamp; the stamped copy will be available in Rascal to the study team.

Both the Rascal and electronic approval stamps indicate that the document has been approved by the Board, and shows the expiration date. The stamp is only used on finalized documents, and will appear on each page of the consent form and recruitment material; study instruments, if voluminous, will only be stamped on the first page of the document. The electronic stamp will also include the IRB number, the initials of the staff member who affixed the stamp, and the approval date.

The approval stamp will be applied to the document only when the Board action has been completed. Documents may not be stamped in advance of the approval.

## V. IRB Pre-review and Review Criteria

This section describes how the IRB determines whether an Event that has been submitted should be approved. Each variable (e.g., type of Event, type of research) is described individually as guidance for use in the review process. Investigators should be familiar with the criteria for review for their particular type of research and Event submitted, to facilitate the inclusion of all necessary information in the submission. The IRB will consider all applicable factors for a given submission. For example, if a submission is for a new protocol that involves an investigational drug administered to children, the information described in each of the relevant sections (i.e., new protocol, drug study, and minors) will be evaluated.

The IRB will conduct a review of non-exempt research in accordance with 45 CFR 46, New York (NY) state law, and institutional policies, and ensure that all elements of 45 CFR 46.111 are met prior to approval of the research. When the research involves FDA regulated drugs, devices or biologics, the IRB will also consider the applicable parts of Title 21 of the Code of Federal Regulations [21 CFR 50, 56, 312, 600, 812].

Review of all research involving human subjects, including exempt research, must ensure that all new personnel have completed the appropriate web-based human subjects training course available through the Rascal Training Center. Individuals must complete both the Human Subject Protection (HSP) and research-related HIPAA courses if they are affiliated with the CUMC campus or are conducting research that involves the creation, use, or disclosure of Protected Health Information (PHI). Additional training requirements for specific types of research are detailed in Section X.D.

Specific details regarding review of each type of Event are in the Event-specific sections of these procedures (Section VI.A).

Protocols that meet the criteria for exemption and those for which the definition of *research* or *human subject* are not met, will initially be pre-reviewed by IRB staff, then reviewed by the IRB Chair at CU-MS, or by a member of the Administrative Review Committee at CUMC.

Research involving procedures that fall within one or more of the allowable categories for expedited review will initially be pre-reviewed by IRB staff, and then reviewed by the IRB Chair, or an experienced Board member designated by the IRB Chair. In accordance with federal regulations, the designated reviewer(s) may act for the Board to approve or require changes to a study under review. Board action is required, however, for a decision to disapprove any study.

Protocols that do not meet the criteria for exemption or expedited review will initially be pre-reviewed by IRB staff, and then reviewed at a convened meeting of the IRB. This process is described more fully in Section VI.

At each step of the review process, the Event under review is assigned a specific status (e.g., approved, pending, returned, deferred) to reflect the action of the researcher, staff, or Board, as

applicable. See Reference Document #04, Actions of the IRB, for specific terms and the description of each.

"IRB review" in these SOPs, unless specified otherwise, refers to: a) review by the convened Board when full Board review is warranted; and b) review by an experienced IRB member when submissions undergo an expedited review. Similarly, in reference to review processes, "IRB" means the convened IRB for full Board reviews and an experienced IRB member for expedited reviews. "Panel" refers to an IRB (also referred to as a "Board") or the ARC (labeled "Admin" in Rascal).

## A. Pre-review of Submitted Events

Upon submission of an Event in Rascal, a pre-review by IRB staff is conducted. Depending upon the nature of the Event, the process may differ but will result in all cases in a decision to accept the submission for review ("log in" the submission), or return it to the PI to obtain missing information, clarification of information, and/or missing documentation. An overview of the process was provided in Section IV.A. Details of the process for each type of Event are described below.

During the pre-review, IRB staff will attempt to obtain missing information, clarification of information, or missing documentation through contact with the study team before returning the submission in accordance with the return criteria described in the following sections. When it is determined to be most efficient or necessary, however, the submission will be returned. Reasons for return include, but are not limited to: information must be entered in Rascal fields, requests are numerous and a return would be more productive, and/or contact with the study team outside of Rascal has not been successful or effective.

### 1. Pre-review: New Protocols

New protocols are pre-reviewed for completeness and compliance with applicable policies and statutes. The staff reviewer determines whether the protocol is complete and should be logged in or returned, enters comments about the protocol in the Notes section of Rascal for consideration by the Board reviewer, completes a reviewer form, attaches the reviewer form to the protocol in Rascal as an internal document, and recommends a level of review based on federal regulations and institutional policy.

At this stage, protocols will be returned for the following reasons:

a. The PI is not qualified, no one is named as PI, more than one PI is named, or the PI's privileges have been suspended by the IRB;

b. The sponsor's protocol, investigator's brochure, device manual or other component of the formal description of the research is missing;

c. The grant application or other documentation of funded procedures is not included, if the study is externally funded;

d. consent documents are not included, and a waiver of informed consent is not requested;

e. study instruments (e.g., surveys, questionnaires, interview or focus group guides, etc.) are referred to but are not provided;

f. plans for recruitment are not provided;

g. there is no data and safety monitoring plan, if the study is greater than minimal risk;

h. the Child Involvement section is applicable but not completed;

i. the Investigational Product section is applicable but not completed;

j. the protocol is cancer-related but does not include the Cancer Center in the Research Facilities field;

k. Appendix A (for recombinant DNA), B (for infectious agents) or C (for gene transfer) is required but is not attached;

l. there is not enough information to conduct an adequate review; or

m. the Event is eligible for expedited review or exemption, and is in "approvable condition" except for minor items that need to be revised or added.

Additional details of the pre-review process are included in Reference Document #20 and in Section IV.A. of these procedures.

**2. Pre-review: Renewals (Continuing Review)**

Renewals are pre-reviewed for completeness, progress since initial approval, and compliance. The staff reviewer determines whether the renewal is complete and should be logged in or returned, assesses whether enrollment is ongoing, determines whether previous IRB conditions have been met, enters comments about the progress of the study in the Notes section of Rascal for consideration by the Board reviewer, completes a reviewer form, attaches the reviewer form to the renewal in Rascal as an internal document, and recommends a level of review based on federal regulations and institutional policy.

At this stage, renewals will be returned for the following reasons:

a. enrollment status is not provided, and/or information regarding enrolled subjects is not included;

b. enrollment is ongoing, consent forms are not attached, and a waiver of informed consent is not requested;

c. the PI is not qualified, no one is named as PI, more than one PI is named, or the PI's research privileges have been suspended by the IRB;

d. the sponsor's protocol, investigator's brochure, device manual, grant, or other component of the formal description of the research is missing;

e. a summary of UPs, recent reports from a data and safety monitoring body, or Progress Report, is not included, where applicable;

f. the Oversight Monitoring/Unanticipated Problems section applies but was not completed;

g. the Child Involvement section is applicable but not completed;

h. Cancer Center review is required, but the Cancer Center is not included in the Research Facilities field;

i. Appendix A (for recombinant DNA), B (for infectious agents) or C (for gene transfer) is required, but is not attached;

j. Investigational Product section is applicable but not completed; or

k. information that is necessary to adequately address IRB review criteria is missing.

IRB staff will use their professional judgment in evaluating whether there is sufficient time prior to the expiration of IRB approval to obtain missing information by returning the submission to the investigator. When the IRB review may proceed with enough information to evaluate the progress of the study and the IRB approval for the study has expired, or will expire in the near future, the IRB staff will not return the submission to the investigator, but rather attempt to obtain the missing information outside of Rascal. Whenever missing information cannot be obtained for studies with imminent expiration of IRB approval, the IRB staff will note the missing information and the IRB will proceed with a review, at a minimum for subjects who are currently enrolled.

Additional details of the pre-review process are included in Reference Document #20 and in Section IV.A of these procedures.

### 3. Pre-review: Modifications

Modifications are pre-reviewed initially by staff and a brief summary of the requested modification is entered in the Notes section. The staff reviewer also indicates whether the consent form has been modified, assesses whether enrolled subjects need to sign new consent forms, and makes a preliminary assessment as to whether the modification can be reviewed by expedited review (if changes are not substantive, or the protocol in its entirety is eligible for expedited review) or requires full Board review.

The intent of the summary is to provide the Chair with the basic information to decide whether he/she or another Board member can process the modification. If the submission is incomplete, i.e., all necessary information or documentation to support the changes or additions is not submitted, it will be returned by the staff reviewer.

Guidance is provided on what constitutes a substantive change in Reference Document #112, “Modifications: What Constitutes a Substantive Change?”

### 4. Pre-review: Unanticipated Problem Reports

The Rascal system uses a screening process for UP Reports to ensure that researchers submit only those Events that meet the criteria for UPs in the CU Reporting to the IRB of Unanticipated Problems policy (see Reference Document #02).

UP Reports that are submitted but are determined during the pre-review to not meet the UP criteria are returned with instructions to withdraw the Report or provide an explanation as to why it does meet the criteria and therefore should be reviewed by the IRB.

UP Reports that meet the criteria will be logged in. The staff reviewer may also review the current consent document to recommend whether changes need to be made to satisfy regulatory review criteria, if the researcher has not provided such an assessment, or the assessment appears incomplete or inaccurate. The staff reviewer will enter comments in the Notes field to reflect the pre-review findings.

Board members have access to UP Reports as well as all material previously submitted for the protocol, in addition to the pre-review comments. At the Board meeting, the primary reviewer's recommendations, based on a comprehensive review of all available information and the pre-review comments, will be considered by the convened IRB. Determinations regarding the completeness of the Report, and whether changes to the protocol or consent documents are necessary, will then be made.

Additional details of the pre-review process are included in Reference Document #20 and in Section IV.A of these procedures.

### 5. Pre-review: Termination (Closure) Requests

Termination (Closure) Requests are pre-reviewed by IRB staff to verify that all information requested in the Rascal Termination screens has been submitted, and to make a preliminary assessment as to whether there are any outstanding issues that need to be addressed prior to termination of IRB oversight. Outstanding issues may include: receipt of new information that must be provided to subjects, a final report has not yet been provided, harms to subjects occurred for which resolution has not been reached, or decisions related to research that may have been conducted during a lapse in IRB approval. Incomplete submissions will be returned.

The staff reviewer may use the Termination Return Criteria (Reference Document #111) to guide the pre-review, and enters comments in the Notes field to reflect the pre-review findings.

Additional details of the pre-review process are included in Reference Document #20 and in Section IV.A of these procedures.

## B. IRB Criteria for Review

Each Board, or authorized reviewer (in the case of expedited reviews), must determine that the following requirements are satisfied before non-exempt research can be approved.

These criteria, as defined in 45 CFR 46.111 and 21 CFR 56.111, will be considered during the review process for each non-exempt Event submitted for review. A detailed discussion of how each criterion is evaluated is provided immediately after the list of review criteria.

1. Risks to subjects are minimized: (i) by using procedures which are consistent with sound research design and that do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

2. 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 from the study. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (i.e., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

3. Selection of subjects is equitable: In making this assessment, the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative (LAR), in accordance with, and to the extent required by, 45 CFR 46.116.

5. Informed consent will be appropriately documented, in accordance with, and to the extent required by, 45 CFR 46.117 and 21 CFR 50.27.

6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

In addition, IRB review will consider the following, as applicable:

8. Recruitment methods and advertising material are appropriate.

9. Additional protections are in place for vulnerable subjects.

10. Potential conflict of interest of investigators is eliminated, mitigated or managed.

The following section provides details on how the Boards will review each element described above.

**1. Risks to Subjects are Minimized (applies the principle of beneficence)**

This criterion is met by first determining all potential risks (including physical, social, emotional, and those related to breach of confidentiality) in the research study based on prior data or other relevant information. The review of risks begins with contemplation of the potential harms described by the investigator in the Rascal submission. The IRB reviewer must also consider, based on his/her knowledge and experience, risks that may not be described in the protocol submission. In particular, for all studies that involve greater than minimal risk, the IRB will consider whether the protocol includes provisions by which risks to subjects are minimized and any methods that may decrease risk.

Risks to subjects may be minimized by:

a. using procedures that are consistent with sound research design;
b. using procedures that do not unnecessarily expose subjects to risk, such as reducing or eliminating an exposure;
c. whenever appropriate, using procedures already being performed on the subjects for diagnostic or treatment purposes (45 CFR 46.111(a)(1); 21 CFR 56.111(a)(1));
d. increasing monitoring of the subjects for earlier detection of risks or harms; and
e. adding endpoints to the study to reduce further exposure.

The IRB process may also minimize risk through requirements for reporting, e.g., authorizing an approval period of less than one year or after a specific number of subjects, or requiring period reports of the progress of the research.

At the time of initial review, an IRB will classify the risk level of each protocol reviewed at a convened meeting, based on information provided in the submission and knowledge/experience of Board members, as minimal risk or greater than minimal risk. Consideration is given to all measures taken to minimize risk when making the risk level determination.

By definition, protocols that are approved via expedited review under one or more of the federally designated expedited review categories may present no more than minimal risk to subjects. (NB: Based on OHRP guidance, CU IRBs interpret expedited review category 8.a. as allowing greater than minimal risk research to be approved via this mechanism, if all other criteria for the category are met.)

At each subsequent continuing review, the Board will also consider the status of the protocol and reported UPs, and will carry the initial determination forward unless noted otherwise in the IRB record. Changes proposed in modification submissions must also be evaluated for effect on the risk level of the overall study.

Level of review required may change upon subsequent reviews if the risk level changes, i.e.:

a. if the initial submission qualified for expedited review, and a modification increases the risk level to greater than minimal, the protocol would then require full Board review;

b. if the initial submission required full Board review, and procedures were limited to data analysis of long-term follow-up at the time of continuing review, the protocol could then be reviewed under an expedited review procedure.

**2. Risk/Benefit Ratio is Acceptable (applies the principle of beneficence)**

The IRB will approve a protocol only after it is assured that the risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and to the importance of the knowledge that may be expected to result from the study.

The analysis of risks is described in the preceding section. The analysis of benefits is based on the information submitted by the investigator as well as reasonable potential benefits that may be considered by the reviewer, or Board.

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. The Board should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility (45 CFR 46.111(a)(2); 21 CFR 56.111(a)(2)).

Evaluation of the scientific design of a proposal is not the primary function of the IRB. The extent to which a Board will consider the soundness of the design is dependent upon a number of factors:

- When a protocol has undergone a peer review or equivalent process (e.g., for NIH or NSF funding), the IRB will generally accept that the design is sound.
- For some units within CU, scientific design is conducted internally, and the IRB may accept the approval of those internal review committees as evidence of sound scientific design.
- When there is an IDE or IND for the study, the IRB may consider the scientific scrutiny of the FDA as confirmation of scientific merit, and the recommendations of the IAP.

For investigator-initiated unfunded projects, which inherently lack such a process, unless they have been reviewed by the FDA for the purposes of an IND or IDE application, the IRB must consider the design, to the degree necessary to ensure that statistically valid results may be possible.

In all cases, where the design is such that no generalizable results may emerge, and subjects are placed at risk due to participation, the IRB may not approve the protocol until the design is revised to bring about an acceptable risk/benefit ratio.

**3. Selection of Subjects is Equitable (applies the principle of justice)**

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

At the time of initial review, the characteristics of the anticipated subject population (e.g., ethnicity, race, gender, or vulnerable population) must be considered to ensure that one group does not assume the risks of the research while another group accrues the benefits.

Special consideration must be provided for the recruitment of vulnerable populations such as children, prisoners, pregnant women, and mentally disabled persons, so that their enrollment and participation in the study is not adversely affected, or risk of procedures increased, by their vulnerability. IRB policies for Enrollment of Children (Reference Document #107), Enrollment of Non-English Speaking Subjects (Reference Document #101), Clinical Research Involving Pregnant Women (Reference Document #103), Surrogate Consent (within the Informed Consent policy, Reference Document #10), and Same Day Consent for Elective Procedures (Reference Document #309) provide additional guidance.

Renewal submissions must include demographic information for enrolled subjects, or a clear rationale for exclusion of this information. With this information, the IRB may assess whether recruitment procedures need to be revised to ensure that the initially proposed demographics are met, or consider whether the demographic characteristics of the total anticipated study population should be revised. In the latter situation, the IRB must also determine whether the objectives of the study may still be met.

**4. Informed Consent Process is Appropriate (applies the principle of autonomy)**

Legally effective informed consent must be obtained from every participant in human subjects research unless the requirement has been waived by the IRB in accordance with 45 CFR 46.116(c) or (d), or 21 CFR 50.24. Legally effective informed consent is not fully defined by federal regulations and therefore, state law must also be considered. The definition of human subjects research differs in the federal regulations and New York State law in a manner that the state law more narrowly defines human research activities.

Columbia's policy for obtaining legally-effective informed consent for participation in human research is based on HHS regulations (45 CFR 46), FDA regulations (21 CFR 50), New York State law, and the ethical principles articulated in the Belmont Report.

Both the DHHS and FDA regulations for the protection of human subjects require that legally-effective informed consent be obtained from every subject enrolled into a study. The federal regulations require that each subject provides informed consent in a process that includes an understanding of the purpose, procedures, risks, benefits, alternatives to participation, confidentiality, compensation for research related injuries (for research greater than minimal risk), contacts for questions regarding the study, injuries, and rights as a research subject, and that participation is voluntary. Effective March 7, 2012, the FDA requires that a statement regarding posting of clinical trial information into a databank be included in consent documents for certain clinical trials. CU IRBs evaluate each consent form in light of the federally postulated elements of consent.

The regulations further state that additional elements should be included as appropriate. For clinical trials that involve greater than minimal risk, the CU IRBs generally require the inclusion of a statement that significant new findings developed during the course of the research, which may relate to the subject's willingness to continue participation, will be provided to the subject.

Also, when study subjects will be compensated for their participation and study procedures involve more than one session or visit, the IRBs will evaluate the payment schedule to ensure that participants do not feel pressured to remain in a study to completion solely to obtain the compensation. Pro-rating of the compensation per study visit is the standard method of distributing the compensation fairly. Regardless of the number of study visits, the amount of compensation must be described in the consent process and reflected in consent documents, as applicable.

Further details of the elements of consent and related information about the process of informed consent can be found at CUMC's IRB website.

The regulations require that "an investigator shall seek such consent only under circumstances that provide the prospective subject or the representative with 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."

New York State law for human research, like the regulations, also requires that written informed consent must be obtained prospectively from every subject involved in research. There are no provisions for waiver of informed consent in the New York State law. However, New York State law defines human research as only that that involves medical experimentation, medical procedures, or treatment on humans. Therefore, research that solely involves questionnaires, surveys, or epidemiological methodology is not covered under New York State law; hence, informed consent is not required. (However, these types of research procedures may be included in research that meets the

criteria to be considered human subjects research per the federal regulations for the protection of human subjects. Informed consent, in accordance with the applicable federal regulations, would be required in these situations unless appropriately waived.)

The IRB will consider both the process of obtaining consent and the content of the process as provided in the consent form, information sheet, verbal consent script, or assent form, as appropriate.

Informed consent will be sought from each prospective subject or the subject's LAR, in accordance with 45 CFR 46.116, 21 CFR 50, New York State law, including the Family Health Care Decisions Act, and as outlined in these procedures.

During the review process for protocols with study populations that may include individuals who lack the capacity to provide consent for themselves, if the IRB submission does not include specific information about surrogate consent issues, attempts to obtain this information may include accessing hard copy or online resources, asking the study team to obtain the necessary information, securing a consultant with expertise about surrogate consent or the study location, or contacting IRB administrators at institutions located near the study site. When necessary, the CU OGC, other appropriate legal sources, or a legal authority local to the study area will be contacted for clarification regarding age of majority or qualifications to serve as a legally authorized representative. The Surrogate Consent section of the IRB Informed Consent Policy (Reference Document #10) provides guidance based on current New York State statutes.

The investigator will submit a draft consent form for the Board's review as part of the initial submission, when appropriate to the research procedures. The Board or designated expedited reviewer will indicate any necessary changes to the consent form at the Board meeting or will document them within Rascal, as appropriate to the level of review. If revision is necessary, IRB staff members notify the investigator in Rascal of the changes that should be made to the consent form. The investigator will make the required changes to the consent form, and return the corrected consent documents to the Board for confirmation. The confirmation may be made by the Chair or by an assigned IRB reviewer, if the changes were specific and the Event was deferred back to the Chair or primary reviewer. If the changes are substantive, and the Event was deferred back to the Board, the consent will be reviewed at a Board meeting. At any time, the Chair or Board member who is conducting an expedited review, or is reviewing a resubmission of an Event that was deferred back to the Chair or primary reviewer, has the authority to require that consent forms be discussed at a full Board meeting.

### a. Special Consent Situations

#### 1) Consent from Non-English Speaking Subjects

When non-English speaking subjects will be enrolled, the Board must ensure that each subject is presented with the required information in a format that he/she can understand. Specific information regarding the requirement for

translation of consent documents may be found in the "Review of Research involving Non-English Speaking Subjects" section of these procedures.

It is noted that when a professional interpreter (e.g., an interpreter hired by NYP) assists during a consent process that uses a short form, a second bilingual person is not required to be present.

**2) Consent for Audio- and Video Recording**

To ensure informed consent when study procedures involve audio- or videorecording, subjects must be advised of this detail during the consent process. The confidentiality, use and storage of the recording must be included in the consent form and, depending upon whether the recording is a required or optional procedure, a separate signature may be required. See Reference Documents #16 and #17, Audio- and Videotaping Policy and Sample Audio-/Videotaping Addendum, respectively.

**3) Consent for Live Case Procedures**

When study procedures propose real-time video recording of an invasive research procedure for educational purposes, as a modification to an approved protocol, the IRB must review the modifications promptly and carefully. Given the nature of the situation, i.e., that an eligible subject must be identified and has indicated tentative agreement to the recording, with the procedure timed to coincide with an educational Event, the need for approval is generally time-sensitive. Nonetheless, the rights and welfare of the subject must be protected.

To facilitate prompt and consistent review of requests for approval for live cases that involve FDA regulated devices, the following process has been developed, after careful consideration of the unique factors involved:

a. Submissions should state clearly, in the modification summary, whether the protocol involves an IDE issued by FDA;
b. If an FDA-issued IDE is involved, **either** written FDA approval for the live case(s) **or** the date that the sponsor sent a request to the FDA for approval of the live case(s) should be provided, and if documentation is available of the request, it should be attached;
c. The consent form for the live case should be attached, and the date when the live case consent form will no longer be needed (e.g., when a conference has ended) should be included in the modification summary;
d. IRB approval will state that conduct of the live case may not occur until FDA approval is obtained and documented in writing, unless FDA approval was provided with the modification;
e. If not previously provided, FDA approval of the live case must be provided to the IRB; ideally this would be prior to the live case being conducted, but minimally it should occur promptly afterwards;

f. The live case consent form should be detached/archived/deleted, as appropriate, as soon as possible after the date identified in item #c above.

With the appropriate documentation provided, including HIPAA and media release forms that are developed through consultation with the applicable NYP or CUMC external relations office, modifications that involve only a request for approval of a live case transmission usually qualify for expedited review.

Live case procedures that do not involve FDA regulated devices should follow a similar process with the exception of the IDE steps.

**4) Same Day Consent for Elective Procedures**

The IRB aims to avoid seeking consent for research on the same day as elective procedures when possible, and provide adequate protections when such consent is necessary. Guidance for these situations is provided in the IRB policy, "Same Day Consent for Elective Surgery" (Reference Document #309) which is available on the CUMC IRB website.

**5) Consent from Women in Labor**

Guidance for obtaining consent from women who are in labor can be found in the IRB policy, Clinical Research Involving Pregnant Human Subjects, which is posted on the CUMC IRB website. The policy describes the circumstances and safeguards surrounding the appropriate participation of pregnant human subjects in clinical research studies performed at NYP and CUMC, and provides procedures by which women in labor may appropriately be enrolled into clinical research studies.

**6) Enrolling Illiterate Subjects**

When there is the prospect of enrolling illiterate subjects, Columbia endorses procedures that incorporate the recommendations of the FDA as articulated in the FDA Information Sheets (9/98), from which the following excerpts are provided:

A person who can understand and comprehend spoken English, but is physically unable to talk or write, can be entered into a study if he/she is competent and able to indicate approval or disapproval by other means. If (1) 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 (2) is able to indicate approval or disapproval to study entry, they may be entered into the study. 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. A video recording of the consent interview is recommended.

A person who speaks and understands English, but does not read and write, can be enrolled in a study by "making their mark" on the consent document, when consistent with applicable state law.

### 7) Enrolling Individuals with Physical Limitations Related to Writing

When an individual with decision-making capacity meets enrollment criteria for a study that requires written documentation by the participant of informed consent, but the individual is unable to provide a written signature due to physical limitations, alternatives to the requirement for a signature may be considered on a case-by-case basis. These may include application of a thumbprint or mark in conjunction with the signature of an impartial witness, videorecording of the individual's verbal consent, signature on the consent form of an impartial witness to the individual's verbal consent, and/or an electronic signature by the individual. Whenever possible, approval from the IRB for a deviation of this nature should be obtained in advance. If timing does not allow prospective approval from the IRB, the professional judgment of the PI may be sufficient, and the violation should be reported to the IRB as soon as possible. For externally funded studies, approval from the sponsor may also be required in advance of the use of alternative procedures.

### 8) Obtaining Consent for Future Use of Specimens

When it is anticipated that specimens or data collected for a study may be used for a future study, consent for the storage and potential future use should be described in the consent form to the extent possible. Because the nature of the future use may include various options (e.g., in an identifiable manner, after de-identification, for research on similar conditions as the initial study, for research on conditions unrelated to the condition under investigation in the initial study), several statements regarding potential future use may be necessary. It is recommended that each statement have a yes/no selection option and include space for the participant's initials next to each statement.

If future genetic testing on stored specimens is anticipated, the requirements of the IRB Genetic Testing Policy must be considered when developing the consent form.

### 9) Obtaining Consent for Future Contact for Research

When it is anticipated that future contact with study participants either for studies related to the initial study (e.g., substudies, or subsequent phases) or for research unrelated to the initial studies (e.g., use of identifiable data or specimens from the initial study) may occur, a statement regarding potential future contact may be included. The statement should have a yes/no selection option and include space for the participant's initials.

If agreement to future contact (e.g., long-term follow-up phone calls at specified time points) is a requirement of participation, this should be clearly stated in the consent form and should not include yes/no options.

**b. Waiver of Some or All of the Elements of Informed Consent**

For research that does not involve FDA-regulated drugs, devices, or biologics, the Board or expedited reviewer may waive the requirement for informed consent per 45 CFR 46.116 (d) (or allow an alteration of some or all of the elements of informed consent) if all of the conditions of one of the two allowable options is met:

Option 1:
To waive consent, the Board or expedited reviewer must find and document that:

1) the research involves no more than minimal risk to subjects;
2) the waiver or alteration will not adversely affect the rights and welfare of the subjects;
3) the research could not practicably be carried out without the waiver or alteration; and
4) whenever appropriate, the subjects will be provided with additional pertinent information after participation (45 CFR 46.116(d)).

Option 2:
To waive consent, the Board or expedited reviewer must find and document that:

1) 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:
    a) public benefit or service programs;
    b) procedures for obtaining benefits or services under those programs;
    c) possible changes in or alternatives to those programs or procedures; or
    d) possible changes in methods or levels of payment for benefits or services under those programs; and
2) The research could not practicably be carried out without the waiver or alteration (45 CFR 46.116(c)).

Informed consent may also be waived in emergency use situations involving investigational (non-approved) FDA-regulated products that meet the criteria described in 21 CFR 56.104 (see Section III.E.4). The regulatory citation for waiver in these situations, which are considered clinical applications and from which research data may not be collected, is 21 CFR 50.24. OHRP guidance dated October 31, 1996 clarifies OHRP's position regarding waiver of the applicability of the 45 CFR Part 46 requirement for obtaining and documenting informed consent for a

strictly limited class of research, involving research activities that may be carried out in human subjects who are in need of emergency therapy and for whom, because of the subjects' medical condition and the unavailability of legally authorized representatives of the subjects, no legally effective informed consent can be obtained. This waiver, which provides a third route through which IRBs may approve research in this class, took effect November 1, 1996. This guidance is posted online at the U.S. Department of Health & Human Services website.

In situations where some or all elements of informed consent are waived, IRB records will document the waiver and the basis for the waiver. For full Board reviews documentation will be in the minutes of the IRB meeting at which the review took place, and for expedited reviews, documentation will be in the Notes, the reviewer approval correspondence, or in an attached document. When justification for a waiver is provided in the submission by the study team, and the submission is approved without notations that indicate the waiver is not approved, approval will serve as documentation that the reviewer(s) concurred with the rationale and approved the waiver.

Waiver of informed consent is different than waiving the requirement of documentation of informed consent, described in item 5.

**5. Documentation of Informed Consent is Appropriate (applies the principle of autonomy)**

Use of a written consent form that requires a signature from the subject is the usual means of documenting agreement to participate in studies that involve human subjects. The form generally includes information about the consent process (i.e., describes that the prospective subject should have the opportunity to ask questions and have them answered prior to agreeing to participate), in addition to required elements of consent, and the signed document, which represents the subject's decision, becomes a record of that agreement for both the research team and the subject. Procedures usually provide for subjects to receive a copy of the consent form as well. In clinical studies that involve in-patients, documentation of the subject's agreement to participate in a research study should also be documented in the medical record. The IRB will determine that the protocol includes procedures to ensure that informed consent will be appropriately documented in accordance with and to the extent required by 45 CFR 46.117 and 21 CFR 50.27.

In certain specific situations, the requirement for written documentation of informed consent, parental permission, or assent may be waived, as described below.

**a. Waiver of Written Documentation of Consent**

The Board or expedited reviewer may waive the requirement that some or all subjects or the subject's representative sign a written consent document 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 the research context (46 CFR 45.117(c)(2); 21 CFR 56.109(c)(1)).

If the Board waives the requirement of documentation of informed consent as identified above, it may require the investigator to provide subjects with a written statement describing the research and providing appropriate elements of consent (46 CFR 45.117(c)(2); 21 CFR 56.109(d)(2)). This decision will be documented in IRB records.

For research under HHS jurisdiction that does not involve an FDA-regulated product, the Board may also waive the requirement for a signed written consent document 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 (46 CFR 45.117(c)(1)).

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. The IRB has the option to approve a consent procedure that utilizes either an information sheet or oral presentation of information to the subject rather than a signed consent form.

In these cases, IRB records will document that the requirement to obtain written documentation of informed consent was waived. For full Board reviews, documentation will be in the minutes of the IRB meeting at which the review took place, and for expedited reviews, documentation will be in the Notes, the reviewer approval correspondence, or in an attached document. When justification for a waiver is provided in the submission by the study team, and the submission is approved without notations that indicate the waiver is not approved, approval will serve as documentation that the reviewer(s) concurred with the rationale and approved the waiver.

**6. Data and Safety will be Monitored (applies the principle of beneficence)**

The Board will determine that there are adequate provisions in the research plan, where appropriate, for monitoring the data collected to ensure the safety of subjects (45 CFR 46.111(a)(6); 21 CFR 56.111(a)(6)).

Plans for interim monitoring of cumulative reports of UPs, including adverse events, will be assessed at the time of initial review.

For research involving therapeutic intervention(s), the IRB will evaluate the safety monitoring plan. If the research is greater than minimal risk, the IRB will also consider whether a DSMB or a Data and Safety Monitoring Committee (DSMC) should be required. In some cases, a committee constituted by the research team or sponsor is acceptable; in others, the IRB may find that a monitoring body comprised of individuals with no affiliation to the researchers or sponsors is necessary. Level of risk, potential for financial gains, and ability of the researchers and/or sponsors to objectively monitor the safety and data are factors that must be considered. It is noted that the HICCC has developed a Data and Safety Monitoring Program (CC-DSMP) that is applicable to clinical trials conducted under the auspices of the HICCC and for which there is no other data and safety monitoring plan.

The following general guidelines* provide a framework for determining the appropriate level of monitoring, but are not intended to be absolute or proscriptive. Adequacy of the monitoring plan will need to be determined relative to the specific protocol under review.

| Monitoring Type | Study Characteristics |
|---|---|
| Individual Investigator | • Study population is small<br>• Narrow range of factors that could have a significant impact on risks and benefits<br>• Continuous, close monitoring by the study team is possible<br>• Phase I and some Phase II trials |
| Data Monitoring Committee or equivalent<br>(More than Individual Investigator but less formal than a Data and Safety Monitoring Board as described by the NCI in 1999) | • Death or severe disability is not a likely consequence of participation<br>• Low to moderate risk research<br>• Many industry-sponsored multicenter trials |
| Data and Safety Monitoring Board | • Moderate to high risk research<br>• Multiple sites or large numbers of subjects<br>• Double-Blind study design<br>• Inclusion of vulnerable populations<br>• Definitive Phase III trials |

*The table above was derived from information presented in Chapter 5-10 of *Institutional Review Board: Management and Function* (editors Robert Amdur and Elizabeth Bankert, 2002 edition).

During the course of the research, UPs must be reported to the IRB in accordance with the CU Reporting to the IRB of Unanticipated Problems policy dated January 24, 2008 (Reference Document #02).

At the time of continuing review or when they are submitted as modifications, interim reports from data and safety monitoring bodies and a summary of UPs to date will be reviewed by the IRB if applicable to the study. The IRB may suspend or terminate research for which the risk/benefit ratio has shifted from acceptable to unacceptable due to the type, frequency, or severity of adverse events or other problems encountered during the conduct of the research.

**7. Privacy and Confidentiality will be Protected (applies the principle of beneficence)**

The Board will determine that there are adequate provisions to protect privacy of subjects and to maintain the confidentiality of data, where appropriate (45 CFR 46.111(a)(7); 21 CFR 56.111(a)(7)).

At the time of initial review, the IRB will ensure that each protocol includes provisions for protecting the privacy of subjects and maintaining the confidentiality of study data. The IRB will consider privacy and confidentially protections that will be in place during recruitment (e.g., by review of the recruitment plan), enrollment (e.g., by considering whether the subject being seen by others in association with the researcher could result in harm to the subject), and participation (e.g., by examining the extent of electronic security measures to be used to protect data).

Details of where paper records will be stored, and/or how electronic data will be protected from unauthorized access, are required in the submission. In addition, consideration will be given to who has access to the data. Awareness of CU IT policies related to security of electronic research/patient data is the responsibility of the PI who must also ensure that the entire research team is aware of these policies. When applicable, the IRB review will include consideration of whether these requirements are met.

Reports generated by CUMC or NYP IT staff from any NYP database(s) require approval from the NYP DISCOVERY Committee. This approval should be requested after IRB approval is issued. The purpose of the DISCOVERY Committee review is two-fold: a) to ensure that IRB approval has been obtained and proposed use of data is in accordance with NYP policies; and b) to ensure that requests for reports are prioritized appropriately, per nature and timeline for the project and to maximize efficiency of IT resources. Reference Document #310 provides additional information.

At times, research may involve the collection of data that is especially sensitive due to the risk of emotional, financial, legal or other harm that may be incurred if the data were disclosed outside of the context of the research. For some of these cases, the Board may require that the study team obtain a Certificate of Confidentiality, which protects against

compelled disclosure and is obtained from the federal government, or that other additional protections are put in place.

When Social Security Numbers (SSNs) will be collected, adherence to University policies related to collection of SSNs is essential. If collected for purposes other than reimbursement or compensation, the IRB submission should include a description of why they are necessary and how they will be safeguarded. If release of SSNs outside of the institution is proposed, the requirements of the CU Policy for Disclosure of Social Security Numbers Outside of Columbia for Research Purposes, must be satisfied. The policy, Reference Document #313, is posted on the IRB websites.

Cash payments to subjects for participation or reimbursement for expenses must also be processed in accordance with the CU Petty Cash policy (Reference Document #98) to protect the confidentiality of subjects to the extent possible. When subject names will be released to institutional departments other than the IRB for the purpose of providing compensation, reimbursement, or replenishing petty cash accounts that are used for subject payments, this disclosure must be described in the consent document.

At CU, requirements of the Privacy Standard of HIPAA are managed by the IRBs, which serve as the Privacy Board when such review is required, in conjunction with the efforts of the Privacy Office. The PO or designee acts as an agent of the IRB for processing of all HIPAA forms and approval of all forms other than waiver requests. HIPAA language is not routinely included in the consent form for the respective study, but is provided in a separate Authorization Form. Combined consent/authorization forms may be utilized if requested by a sponsor or in other situations where a single form is preferable.

The CU policy, "CU IRB Policy on Research and the HIPAA Privacy Rule", describes the relationship of the Privacy Officer to the IRB and delineates responsibility for processing of HIPAA forms (Reference Document #115). Specific procedures for review of each form are described in (Reference Document #116, "CU IRB Procedures to Comply with Privacy Laws that affect Use and Disclosure of Protected Health Information for Research Purposes").

Additional information may also be obtained via Rascal or from the website maintained by the Privacy Office.

**8. Recruitment Methods and Advertising Material are Appropriate (applies the principles of autonomy and justice)**

The IRB will review proposed methods of recruitment, to ensure that the process is not affected by elements of coercion or undue influence, and that the principle of justice, as it relates to availability of innovative practices and sharing of both the burdens and risks of research, is upheld. In addition, the IRB will be mindful that patients coming to CUMC for clinical care, and the physicians who are responsible for their care, expect that the integrity of the clinical relationship will be respected and taken into account in the research process.

Acceptable recruitment methods, when patients are involved, and the treating physician is not the researcher, include:

- This may be done in writing or verbally, depending on the specific circumstances of the study.
    - If it is done by letter, the letter should be signed by the treating physician. If the research is conducted in a setting, such as the Emergency Department or an intensive care unit, where the treating physicians work in shifts, or in a resident-based clinic, the medical director of the setting may sign the letter. Again depending on the specific circumstances of the study, the IRB may permit the letter to be structured using an "opt out" format, such that the patient is given a telephone number to call and a time window to make the call, if he or she does NOT wish to be contacted by the study team about the research study, or the letter may be structured using an "opt in" format, in which the patient calls the study team if he or she wishes to learn more about the study.
    - If the initial information about the study is provided verbally by the treating physician, the patient should be provided with a written brochure or description of the study at the time of the introduction. The treating physician should obtain permission for the study team to contact the patient and state to the patient that he or she (the treating physician) will provide the patient's name and contact information to the study team. The treating physician should document in the medical record that permission was obtained.
- Patient obtains recruitment material from treating physician's office (e.g., waiting room) or from a public area (e.g., bulletin board) and contacts researcher directly if interested in participating or learning more about the study.

"Treating physician" refers to a clinician with whom the prospective subject has a relationship that predates introduction of the research. The key to the above, or other, acceptable recruitment methods is that when a researcher contacts a patient for recruitment in a research study, the treating physician (or the medical director of the ED, ICU, or resident-based clinic) is aware of the specific patients who are being contacted, and has approved the contact, prior to the contact occurring, and that the initial contact with the patient is made by his or her treating physician (or the medical director of the ED, ICU, or resident-based clinic).

When the treating physician is also the researcher, the IRB must assess whether the consent process, beginning with recruitment, may be conducted without undue influence or elements of coercion, whether due to inherent aspects of the physician-patient relationship or intentional. This is particularly important in research that presents significant risk to the prospective participant. The IRB process, beginning with the preliminary review, may include requests to the researcher about how elements of coercion and undue influence may be avoided in the consent process, i.e., how the

researcher will manage his/her dual roles and associated responsibilities of the fiduciary relationship vs. objective scientific inquiry. Use of a witness to the consent process, assessment by a subject advocate of the patient's understanding of procedures, risks and benefits of study participation, employment of an impartial individual to conduct the consent process, and referral of the patient to an impartial physician are among the options that the IRB and researcher may consider to address concerns of undue influence or coercion.

Prior to initial approval of a protocol, and at each continuing review, the IRB will determine that plans for subject recruitment that involve advertising or other direct contact with potential subjects outside the doctor-patient relationship are consistent with the protocol, the consent form, and FDA Guidelines found in the FDA Information Sheets (the latter for those protocols to which the FDA regulations apply).

The Board, or an expedited reviewer, may review a recruitment recording (audio or video) submitted without an approvable script. If the tape follows the Board advertising review guidelines appropriately, it may be approved. However, if there is anything in the tape that an expedited reviewer finds unacceptable, review of the tape may be referred to additional reviewers or to the full Board. At any time during the review process, the research team may be asked to submit a script so that the full Board may indicate, in writing, the modifications that the Board requires for approval.

Audio scripts that are intended to serve as "ON HOLD" communications for phone systems or public service announcements will be reviewed by the Board or an expedited reviewer. These scripts may be approved if acceptable to the reviewer and must be used verbatim.

### 9. Additional Protections are in Place for Vulnerable Subjects (applies the principle of beneficence)

Prior to initial approval of a protocol, and at each continuing review, the IRB will determine that there are appropriate additional safeguards included in the study to protect the rights and welfare of subjects who are likely to be vulnerable to coercion or undue influence, e.g., children, prisoners, pregnant women, handicapped or mentally disabled persons, persons with acute or severe physical or mental illness, persons who are economically or educationally disadvantaged, or persons who are vulnerable because they are institutionalized (45 CFR 46.111(b); 21 CFR 56.111(b)).

When the capacity of the prospective subject to provide legally effective consent is in question, the IRB may require that an advocate be provided, or that a Legally Authorized Representative (LAR) or agent named in a Health Care Proxy (HCP), the latter under appropriate circumstances, provide permission for enrollment, in addition to consent or assent from the subject. Procedures for determining capacity must be described by the investigators when individuals who may lack capacity to consent will be considered for enrollment. If the study population involves individuals who are likely to lose full capacity to provide consent during the course of their participation, procedures for

periodically assessing capacity, and implementing measures to provide appropriate protection measures throughout the study should also be included. These may include execution of a Health Care Proxy at the time of enrollment, procedures for ending participation when the individual can no longer make competent decisions, or involvement of a study partner who is authorized to provide information about the subject. The Surrogate Consent section of the IRB Informed Consent Policy provides additional guidance for these situations.

In any situation, but particularly when a prospective subject is subordinate to or has a fiduciary relationship with a researcher (e.g., patient, student, employee), the IRB may observe the consent process, or require changes in recruitment procedures to eliminate or reduce elements of coercion or undue influence.

When children will be enrolled, the requirements of Subpart D of 45 CFR 46 and 21 CFR 50 will be considered. Assent will be obtained when deemed appropriate by the Board, and parental permission will be sought, unless waiver criteria stipulated in the federal regulations are met. Permission of one parent is generally sufficient, however, the permission of both parents will be required (with the qualifiers identified in Subpart D) for research that is greater than minimal risk but does not offer the prospect of direct benefit for individual subjects. If wards will be enrolled in such research, an independent advocate will be identified for each subject; it may be acceptable for one advocate to represent more than one child. The IRB Research Involving Children policy provides additional guidance for these situations.

The requirements of Subparts B and C of 45 CFR 46 will be considered for all research that involves pregnant women or prisoners, respectively, and the reviewing IRB will make all necessary determinations.

Additional information about the review of research involving vulnerable subjects may be found in Section VI.D., Review of Specific Types of Research.

**10. Potential Conflict of Interest of Investigators is Eliminated, Mitigated or Managed**

Annual and protocol-specific COI forms are reviewed through a process that involves individual evaluation of positive responses (“anomalies”) by RCT staff.

Protocol-specific COI disclosures for all key personnel of the research team named on IRB protocols are submitted electronically in Rascal and reviewed by RCT. If there is a positive response on a protocol-specific disclosure, then the electronic submission system flags the study as positive for COI; submissions are generally not approved until the flag is cleared administratively by RCT. The majority of COI reviews are conducted through this process.

- Notification of the outcome of this review for anomalies that do not meet the University threshold to be considered a significant financial interest is provided to the IRB for consideration during its review.
- Procedures are in place to refer conflicts that meet or exceed the University threshold for significant financial interests to the institutional COI Committee. The Committee is comprised of faculty and representatives from administrative units within the University that have responsibility for research functions, and serves to eliminate, mitigate, or manage significant financial conflicts of interest. Notification of Committee action for conflicts that required full Committee review and involve human subjects research is provided to the IRB for consideration during its review of the research.

The University threshold for a significant financial interest is defined in the 'University Policy on Financial Conflicts of Interest in Research'. The Policy is posted on the website of the Executive Vice President for Research.

The IRB is notified of the outcome of the administrative or Committee review, as applicable, by attachment within Rascal of the disclosure form and accompanying notes to the relevant protocol. The documentation includes the responses from the disclosure form, indicates whether the financial interest was considered significant or nonsignificant in relation to the University COI policy, and describes any actions taken to eliminate or mitigate the COI. Such actions may include reduction of a significant interest to a nonsignificant level, change in roles for the individual(s) with the conflict, or departure from the research team of the individual(s) with the conflict. The IRB has the authority to impose any additional requirements it deems appropriate, regardless of the outcome of the review by the RCT, and COI Committee (if applicable), although the IRB may not overturn decisions made by either entity. If it is necessary to review the protocol at a convened meeting prior to final resolution of the COI by RCT and/or the COI Committee, and RCT provides details of the COI, the IRB may consider the COI and make decisions contingent upon potential resolution options. Final IRB approval may not be issued until the COI has been resolved; if the resolution differs from that upon which the IRB decisions were based, re-review by the convened IRB will be necessary.

Additionally, the IRB may forward COI concerns to RCT or the COI Committee, beyond those that may be received by RCT through the electronic submission system. If, during its review, the IRB identifies a financial interest that was not disclosed on the Protocol-specific disclosure form, and therefore did not undergo review by RCT, the issue will be referred to that office for review as a result. The referral will be documented in the relevant IRB meeting minutes if the IRB review was at a convened meeting. If the IRB review was an expedited process, or the protocol qualified for exemption, the referral will be documented in the Rascal Notes for the specific protocol. The usual process for review of anomalies would then commence, with review by the COI Committee, if warranted, and attachment of a summary resolution form in Rascal. Final approval by the IRB will not be granted until the COI Committee review(s) are complete, the IRB has had an opportunity to review the outcome, and the IRB is either satisfied with the COI

Committee requirements or implements additional requirements (e.g., consent form disclosure).

Annual disclosures of financial interests that are not protocol-specific are also required, for all individuals listed on IRB submissions. Instructions for the annual disclosure forms state that a new disclosure form must be filed whenever changes to the individual's or his/her family's financial portfolio change such that a response on the disclosure form must be modified.

# VI. IRB Review of Specific Events, Types of Research, and Types of Documents

## A. IRB Review of Specific Events

### 1. Initial Review (Review of a New Protocol)

The term "initial review" as used in this section refers to the review of a new protocol until such time as it is approved, i.e., if several reviews by the convened Board or expedited reviewer were necessary prior to approval, all would be considered part of the initial review. Rascal labels these Events at Y1M0 (Year 1 Modification 0).

The Boards follow DHHS and FDA regulations concerning institutional review boards and the requirements of these procedures for conducting their initial review of research and for reporting their findings and actions to the investigator, and when applicable, to the institution (45 CFR 46.108; 46.103(b)(4); 46.103(b)(5); 21 CFR 56.108 (a)(1)).

Each Board will determine that the requirements identified in Section V.B, IRB Criteria for Review, are satisfied before they approve research.

In addition, the Boards will ensure that all applicable approvals, confirmations or review, as applicable, from internal and external committees have been or will be obtained. These include, but are not limited to, the HICCC PRMC, the IBC, the JRSC, the RDRC (all internal), and the RAC (external).

If a protocol is in any way cancer-related, review by the IRB generally does not occur until approval from the PRMC is obtained (Reference Documents #6 and 7). IRB review may proceed while other approvals or confirmations are in progress, insofar as the information that will be obtained from the respective approval or confirmation is not needed to conduct the IRB review.

Compliance with institutional policies or requirements such as qualifications of PIs (Reference Document #13), submission to Medicare for approval to bill for allowable items relative to Category A or B devices (see Reference Document #162), and training requirements for research staff (see Section X.D of these procedures) will also be verified during the initial review.

The expiration date of IRB approval is the last date on which the study can be conducted under the respective IRB approval. The expiration date for new protocols and renewals is calculated electronically in Rascal as follows:

a. for full Board reviews, by adding one year to the date of the last convened meeting at which the submission was discussed and subtracting one day;
b. for expedited reviews, by adding one year to the date on which the submission was approved and subtracting one day; and
c. for exempt reviews, by adding two years to the date on which the submission was approved and subtracting one day.

It is noted that the calculation of expiration date, when an approval occurs during a leap year on February 29, results in an expiration date of February 27 either one year (for full Board and expedited reviews) or two years (for exemption determinations) after the approval.

IRB staff may revise the expiration date when preparing minutes. Such action would be necessary when:

a. The IRB specifies an approval period of less than one year;
b. A submission is approved by a facilitated review process when CU is not the IRB of Record and the official expiration date is the one determined by the IRB of Record; or
c. A modification is approved for a protocol that was formerly determined to be exempt, but no longer meets the exemption criteria due to the nature of the modification.

When a modification is approved, the expiration date of IRB approval for the protocol, which was calculated at the most recent review of the entire protocol (e.g., initial review or continuing review), is retained.

**2. Review of Modifications**

Regulations require, and Columbia policy reiterates, that any change to an approved non-exempt protocol must be submitted to the IRB for prospective review prior to implementation, except when a change is necessary to eliminate an immediate hazard to subjects and there is not sufficient time for IRB review before the change must be implemented. A change may relate to any aspect of the study, e.g., personnel, study procedures, consent documents, recruitment material, sponsor's protocol, study instruments. Changes are commonly referred to as modifications at Columbia, although technically they may be additions, revisions, or deletions.

When a change is proposed for a study that requires full Board review, the modification must also be reviewed by the convened Board if the change is substantive. The regulations do not define what is meant by a substantive change; therefore, a guidance document has been prepared for use by Columbia investigators that identifies types of changes that are likely to be considered substantive (see Reference Document #112). Substantive changes are those that affect one or more of the regulatory criteria for approval. The approval date for modifications that require full Board review will be either: a) the date of the meeting at which the convened IRB reviewed and approved the modification, if the IRB did not require any revisions; or b) the date that the IRB Chair or other experienced IRB member approved the modification after the revisions stipulated by the IRB at the convened meeting were reviewed and found to be adequate. Non-substantive changes (to a study that, in its entirety, requires full Board review) may be reviewed by expedited review, in accordance with the expedited review categories defined by FDA and DHHS (63 FR 60364-60367, November 9, 1998).

Changes proposed for studies that are eligible for expedited review may also be reviewed by expedited review, unless the change causes the protocol to be ineligible for expedited review (e.g., increases risk level to greater than minimal, adds procedures that do not fall into any of the expedited review categories).

The Chair has the prerogative to route any modification to the full Board for review, regardless of whether it is eligible for expedited review per the federal regulations.

The Boards must ensure that the IRB review criteria articulated in 45 CFR 46.111 and 21 CFR 56.111, as applicable, are met for the protocol prior to approving a modification to an existing protocol. Local requirements such as review by the Cancer Center PRMC, IBC signoff, JRSC or RDRC review, and training requirements must also be satisfied.

When a modification includes new information related to risks, additional or modified procedures, or other factors that may affect subjects' willingness to continue participation, the IRB must consider options for providing this information to participants. These may include obtaining signatures on a revised consent form, providing an information sheet to participants, or verbally informing subjects by telephone or in person. Regardless of the method selected, content of the documents or scripts that will be used should be provided to the IRB for review, and the plans for documenting notification to the subjects should be specified.

Changes in approved research initiated without IRB approval, whether to eliminate an immediate hazard to subjects when there was not sufficient time for IRB review before the change had to be implemented, or that have been discovered to have occurred for other reasons (i.e., protocol violation), have to be:

- Promptly reported to the IRB; and
- Reviewed by the IRB to determine whether the change is consistent with ensuring the subjects' continued welfare, and for a determination of whether a corrective action plan is required to reduce the possibility of future occurrences.

### 3. Review of Reports of Unanticipated Problems Involving Risks to Subjects or Others

Submission of reports of unanticipated problems including adverse events will be in accordance with the CU Reporting to the IRB of Unanticipated Problems Policy (Reference Document #02).

Reports of unanticipated problems that meet the criteria for individual submission at the time of occurrence will be presented for discussion at a convened meeting of the IRB after review by a primary reviewer. The Board will determine whether the report is complete or additional information is required. In addition, a determination will be made whether the protocol and/or consent document(s) should be revised, if this is necessary as a result of the UP and has not already been initiated by the study team. Finally, the Board

may impose restrictions on the research (e.g., more frequent reporting, suspension of enrollment, suspension of the study, termination, etc.) if review of unanticipated problem reports results in a determination that the risk/benefit ratio has become less favorable, or require notification of current subjects when such information may relate to subjects' willingness to continue to take part in the research.

Particular attention will be focused on reports of unanticipated problems that occur at a Columbia site in an investigator–initiated protocol for which there is no other monitoring outside of the research team.

The Board may take action appropriate for the circumstances to protect the safety, welfare and rights of research subjects. Investigators are encouraged to report any trends to the Board.

Whenever a CU-designated IRB or the CU investigator determines that the protocol or consent form should be modified as a result of new information in a UP report, the UP should be reported to the IRB COT, which should subsequently report it to the appropriate regulatory agency.

**4. Review of Reports of Protocol Deviations or Violations**

Definitions of "deviation" and "violation" may be found in Section III.D.6 of these procedures.

Both protocol deviations and violations occur when there is a discrepancy between the protocol and the activities being performed within the study. Deviations are identified and approved by the IRB in advance, while violations are identified and reported after they have occurred. While either one may increase risk to subjects, it is particularly important that the IRB be notified immediately when the deviation or violation could potentially cause increased risk to subjects or the study as a whole.

Protocol violations can be categorized as either minor or major, and may or may not affect individual subjects. Major deviations or violations should be reported immediately to provide an opportunity for the IRB to assess whether the study should continue, and whether changes to study procedures are required.

a. Examples of major protocol violations:

    1) The violation posed a significant risk of substantive harm to the individual research subject;

    2) The violation has compromised the scientific integrity of the data collected for the study;

    3) There is evidence of willful or knowing misconduct on the part of the investigator(s) and/or study staff; or

4) There is serious or continuing noncompliance with federal, state or local research regulations.

b. Examples of minor protocol violations:

1) The violation has no substantive effect on the risks or benefits to the individual research subject(s);

2) The violation has no substantive effect on the data collected;

3) The violation was not the product of willful or knowing misconduct on the part of the investigator(s) or study staff; or

4) There is no serious or continuing noncompliance with federal, state or local research regulations.

Major protocol violations should be submitted through the Unanticipated Problems Report module in Rascal if the violation resulted in a potential increase in the risk or harm to subjects, or involves a misadministration of drug or therapy. Likewise, misadministration of drug or therapy that the investigator determines has potentially increased harm to subjects (whether an increase or decrease in prescribed dose) should also be reported to the IRB COT to ensure reporting to federal regulatory agencies, as appropriate. These should also be discussed with the patient, in accordance with the underlying philosophy of NYP's Disclosure Policy (E145) (Reference Document #315). All other protocol deviations/violations should be submitted through the Modification module in Rascal.

The IRB will review protocol deviations and modifications to determine whether the risk/benefit ratio of the protocol has increased as a result of the deviation. Potential or real harm, or risk of harm, to the subject will be assessed. A corrective plan should be submitted by the researcher with the violation and will be reviewed by the IRB to ensure that adequate steps are being taken to avoid recurrence. If a protocol violation is determined to be minor noncompliance, IRB staff will report the Event in the Minor Non-Compliance Database (MNCD) with the applicable information and provide the Event ID# in the Rascal Notes. If the situation meets the reporting criteria for serious or continuing noncompliance, referral to the COT for initiation of a noncompliance inquiry is required.

## 5. Review of Emergency Use Requests

Emergency use is defined by the FDA as the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval (21 CFR 56.102(d)). This does not include the "off-label" uses of approved medical products in the practice of medicine (i.e., not in a research context). Such uses are not considered research, but rather the practice of medicine for the treatment of patients with non-FDA-approved products. The data from such uses may not be used for research purposes.

Emergency use requests are processed by IRB staff (the ED, AD, or ADO, or a Manager of an IRB) as review by appointed IRB members or the convened Board is not required. When staff are asked to provide documentation that the IRB office is aware of an emergency use request so that the investigational product may be shipped, they do not review the procedures for use of the product. Rather, they ensure that the regulatory criteria for emergency use are met, including provisions for obtaining informed consent, or waiver under appropriate circumstances, and the need for all required information to be provided to the IRB within 5 days of use of the test article, as described in Section III.D.7 above.

In general, emergency use of an investigational agent may only be authorized once. If future need for use of the test article under similar circumstances is anticipated, a full protocol should be submitted to the IRB for review.

Section VI.B.10includes a description of provisions regarding emergency research.

**a. Initial Notification to the IRB**

Emergency use of a test article under the conditions specified in 21 CFR 56.102(d), 21 CFR 56.104, and 21 CFR 312.36 does not require prospective IRB review. However, written IRB acknowledgment of notification by a clinician of the proposed emergency use of a test article, and receipt of a consent document, if available, may be required by the manufacturer of the product to permit shipment of the investigational product to the institution.

When the IRB office is notified of the proposed emergency use of an investigational agent, a letter will be provided to the investigator from the IRB acknowledging the proposed use and advising the clinician of the need for a follow-up report to the IRB within 5 days, if all required information was not provided in the emergency use request. See Reference Document #99 for a sample letter of acknowledgment. Notification to the IRB also provides the mechanism for the institution to monitor such emergency use situations.

Consent for emergency use of an investigational agent should be prospectively obtained when possible. In these cases, the consent process, plans for obtaining assent, where applicable, and consent documents should be included in the materials submitted to the IRB with the request for emergency use. Waiver of informed consent in conjunction with emergency use is discussed in the next section.

**b. Consent Requirements for Emergency Use of a Test Article**

If the use involves the individual emergency administration of an FDA-regulated article under 21 CFR Parts 50 and 56, the requirement for prior consent may appropriately be waived, as provided for in 21 CFR 50.23 (a)-(c), 56.104(c),

56.102(d), and these procedures. The IRB will acknowledge rather than approve the waiver.

Obtaining informed consent shall be deemed feasible unless, before use of the test article (except as provided below), both the treating physician and another physician who is not otherwise involved in the use of the investigational product certify in writing all of the following:

1) the patient is confronted by a life-threatening situation necessitating the use of the test article;
2) informed consent cannot be obtained from the patient because of an inability to communicate with, or obtain legally effective consent from, the patient;
3) time is not sufficient to obtain consent from the patient's LAR; and
4) there is no available alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the patient.

If immediate use of the test article is, in the investigator's opinion, required to preserve the life of the patient, and time is not sufficient to obtain the independent determination required in the above paragraph of this section in advance of using the test article, the determinations of the clinician shall be made and, within 5 working days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the care of the patient.

The documentation described in this section and required per FDA regulation is required to be submitted to the IRB within 5 working days of the use of the test article, if it was not provided with the emergency use request.

**c. Documentation Required**

Within 5 working days of the emergency use of an investigational product, the physician responsible for the use must provide the following information to the IRB, if it was not already provided:

1) an explanation of the life-threatening situation necessitating the use of the test article and the patient's initials;
2) a description of the investigational product, including name or other unique identifier, and IND, BB-IND, or IDE number, as applicable;
3) a copy of the consent document that will be/was used or an explanation of why it will not be or was not possible to obtain informed consent (i.e., details in Section b above); also, if the patient was a child, whether assent of the child will be/was obtained;

4) concurrence from another physician who is not otherwise involved in the use of the investigational product that the situation is/was life-threatening and that no alternative standard treatment is/was available; and

5) an indication of whether additional uses are anticipated, in which case a protocol and consent form must be submitted for Board approval.

The documentation, whether received with the request for emergency use or within 5 days of use of the test article, will be reviewed by the IRB ED, AD, ADO, or one of the IRB Managers to assess compliance with the regulations and CU policy for emergency use and, when applicable, the consent form waiver. Consultation from a physician who is a member of the IRB will be sought as needed to make the required determinations.

If a protocol for additional uses is submitted, the Board will prospectively review, at a convened Board meeting, proposals for the treatment (FDA 21 CFR 312.34 and 312.35) or compassionate use of the test article under applicable FDA regulations and in accordance with the review of protocols involving investigational products as described in these procedures. Data collected from these activities, when the proposed activities have been reviewed by the convened Board, may be used for research purposes.

### 6. Facilitative Review

Facilitative review will occur when CU is relying upon the review of another IRB, in accordance with the terms of an IAA. The type of reviewer and extent of review required is dependent upon the specific Agreement, as described in Reference Document #05.

IAAs to which Columbia is a party and which apply to multiple projects are updated as necessary and are kept on file in the IRB office. Periodic meetings are held between representatives of the CU IRB Office and the IRB of each institution with which an Agreement exists. The purpose of these meetings is three-fold: a) to ensure that procedures remain appropriate; b) to discuss whether the respective Agreement requires updating or should be dissolved; and c) to keep abreast of the IRB processes and institutional research perspectives of each institution.

### 7. Continuing Review (Renewal)

All non-exempt human subjects research for which there are plans to continue beyond the expiration of the current IRB approval must be re-reviewed and approved by the IRB for an additional period of up to one year. Continuing review should optimally occur within 60 days prior to the study's expiration date. Renewals are not required only when the research is permanently closed to the enrollment of new subjects, all subjects have completed all research-related interventions, and collection and analysis of research-related data at Columbia has been completed.

The Board will determine whether all regulatory and institutional criteria have been met during the conduct of the research to date. While the focus of the initial review is to determine whether the risk/benefit ratio of the proposed research is acceptable, plans have been developed to minimize risk, and informed consent procedures are appropriate, the focus of the continuing review is to provide oversight and to evaluate, to the extent possible, whether the actual risk/benefit ratio is still considered to be acceptable, and to assess the conduct of the research activities to date.

Review of a change in the study does not routinely alter the date by which continuing review must occur.

Each Board has the authority to determine, at its discretion during the continuing review process, which research activities need verification from sources other than the investigator that no material changes in the research have occurred since the previous IRB review. To determine which projects need verification, the Board will consider such things as an unexplained or sudden increase in risk to subjects, FDA audits, site visits conducted by authorized personnel, reports from "whistleblowers," etc (45 CFR 46.103(b)(4); (FDA 21 CFR 56.108(a)(2)). Verification may be obtained through contact with the sponsor, FDA, or cooperative group, as applicable, (e.g., to verify protocol version dates), by audit of the investigator's files, and via requests for information from a coordinating center or monitoring board.

When initial review was conducted by an expedited review procedure, continuing review will usually be conducted via an expedited process, provided that all study procedures continue to fall within one or more of the federal categories of expedited review. For protocols reviewed via expedited review, the approval period is usually one year, because protocols that are eligible for expedited review do not generally present the safety concerns that would warrant review more frequently.

For studies approved under expedited procedures, continuing review must occur within one year of the date of expedited approval by the IRB Chair or designee.

When the initial review was conducted by a convened meeting of the IRB, and the procedures have not substantively changed, continuing review will also be conducted at a convened meeting (45 CFR 46.108(b); 46.109(e)), with the exception of the limited circumstances described by expedited review categories (8) and (9). (See List of Expedited Review categories, Appendix IX.) If study procedures have evolved, whether through modifications or completion of active intervention, such that all remaining procedures meet the criteria for one or more of the expedited review categories, continuing review may be conducted via an expedited review process.

For full Board reviews, the maximum approval interval is one year minus one day from the date of the convened meeting at which the study was approved, either unconditionally (i.e., "approved") or with specific conditions which the IRB Chair or his/her designee can verify, i.e., "deferred to Chair" status.

There are times when a renewal can be approved for already enrolled subjects (or another subset of the study population), but not for new enrollment, or perhaps excluding a particular subset, until specific IRB requirements are satisfied. In these situations, the Board (for full Board reviews), or the Chair or other reviewer (for those submissions eligible for expedited review), may approve the protocol to avoid a lapse in approval. If the IRB determines that it is important to add the excluded procedures or subject group, the approval may include a requirement that the remaining elements be added and the entire project reviewed by a specific time within the coming year, i.e., designate an approval period of less than one year.

Each Board has the authority to suspend or terminate the approval of research that is not being conducted in accordance with federal regulations or in accordance with stipulations imposed on the research activity by the IRB. This may occur at the time of continuing review, or at any other time after initial approval of the research.

IRB review criteria as articulated in 45 CFR 46.111 and 21 CFR 56.111 must be satisfied before any non-exempt Event that is submitted for review and approval may be approved. If a Board, during a full Board review, determines that the review criteria are no longer met, study activities may be suspended or the study may be terminated, with an explanation for the reason by which the review criteria cannot be met. Similar situations encountered during an expedited review of a modification will be brought to the Board for discussion although the Chair may suspend study activities prior to the Board review, if warranted to ensure subject safety or the integrity of the research.

Any suspension or IRB-initiated for-cause terminations that occur during continuing review will be reported promptly to the investigator, and to the ED, AD, and COT, who will inform the appropriate IO. The ED will notify the FDA, if applicable, and OHRP of the suspension or termination (45 CFR 46.108(a); 21 CFR 56.113). If suspension or termination occurs at the time of continuing review, the IRB, in consultation with the researcher or other appropriate individuals, will determine the appropriate procedures for discontinuing study procedures with enrolled subjects. Safety of subjects will be the primary concern.

Modifications to approved research may be considered by the IRB during continuing review and must be approved prior to implementation. When a modification is submitted in conjunction with a renewal request, the Board may approve both or approve the renewal without the modification.

When a modification includes new information related to risks, additional or modified procedures, or other factors that may affect subjects' willingness to continue participation, the IRB must consider options for providing this information to participants. These may include obtaining signatures on a revised consent form, providing an information sheet to participants, or verbally informing subjects by telephone or in person. Regardless of the method selected, content of the documents or scripts that will be used should be provided to the IRB for review, and plans for documenting notification to the subjects should be specified.

Further explanation of how continuing review serves an important function in oversight monitoring is provided in Section IX.A.

**a. Continuation Past Expiration of IRB Approval**

Applicable regulations require that each non-exempt protocol be reviewed at least annually. The IRB may not extend a study's approval beyond the expiration date without conducting a review, but must consider various factors when addressing active studies for which there may be a lapse in IRB approval:

1) Where the IRB does not re-approve a research study by the specified IRB expiration date, subject accrual may not occur and all study-related procedures must cease pending re-approval of the research by the IRB. Study-related procedures include recruitment, advertisement, screening, enrollment, consent, interventions, interactions, collection of private identifiable information, and data analysis.
2) Where failure to continue study procedures would seriously and adversely affect the safety or well-being of enrolled subjects, the IRB Chair may review these studies on an individual basis prior to substantive review of the protocol by the convened Board or designated reviewer (as applicable to the level of review required). The purpose of the Chair review is to assess whether he/she concurs with the PI that there exists the potential for harm to subject(s) as a result of interruption of study procedures.

Continuation of research activities for currently enrolled subjects may be permitted when the IRB Chair finds that it is in the best interest of the individual subjects to do so and the PI is actively pursuing renewal of the study protocol. When an IRB Chair elects this option, the approval to allow currently enrolled subjects to continue study treatment must be documented in writing and effective for a finite period that allows opportunity to complete the IRB review.

3) When continuing review of a research protocol does not occur prior to the end of the IRB approval period, IRB approval expires automatically. This expiration will not be reported to OHRP as a suspension of IRB approval under DHHS regulations, in accordance with DHHS guidance.

**b. Procedures for Determining Which Projects Require Review More Often Than Annually**

For each approval, the IRB will determine the interval for which approval should be granted, appropriate to the vulnerability of subjects, experience of the investigator, degree of risk to which subjects are exposed and other information provided for the initial or continuing review of study. In no case will the IRB grant approval for a non-exempt study for a period that is greater than one calendar year.

These considerations for the length of approval time will be made at the time of motion for approval of a study during the IRB meeting, for projects that require full Board review. For expedited reviews, the IRB Chair may make the determination. When any of the following (non-inclusive) situations exist, the Board will consider an approval period of less than one year:

1) the need for increased monitoring to evaluate anticipated risks;
2) scant safety data due to early introduction of a test article in clinical studies (e.g., early Phase I studies); or
3) the need for increased monitoring to evaluate potential noncompliance or for projects conducted by investigators who have previously failed to satisfy IRB requirements.

## 8. Review of Termination (Closure) Requests

Requests by researchers for closure of an approved project are reviewed by a primary reviewer prior to presentation at a convened meeting. The Board reviewer will have access to the staff reviewer's notes and will evaluate information provided about the number of subjects enrolled, unanticipated problems, and study results to determine whether closure is appropriate and to ensure that all outstanding issues have been adequately addressed.

If follow-up of participants for safety reasons is permitted or required by the IRB, participants should be so informed, and any unanticipated problems or adverse outcomes should be reported to the IRB. In these cases, IRB approval should remain current.

In situations where it becomes known that a PI is no longer at CU, and IRB approval has expired, the IRB may initiate closure. Attempts to have a co-investigator create the closure submission and efforts to determine the status of the study since the last approval period will generally precede the IRB-initiated closure. In some cases, it may be appropriate for another member of the study team to continue the research.

## 9. Suspension and IRB-initiated For-cause Termination of Research

Each Board has authority to suspend or terminate the approval of research that is not being conducted in accordance with federal regulations, state law, or institutional policy, has been associated with unexpected serious harm to subjects, has an unfavorable risk/benefit ratio, or is not being conducted in accordance with stipulations previously imposed on the research activity by the IRB Board.

A suspension is a directive of the convened IRB or other authorized individual to temporarily stop some or all previously approved research activities short of permanently stopping all previously approved research activities. Suspended protocols remain open and require continuing review.

A termination of IRB approval is a directive of the convened IRB to permanently stop all activities in a previously approved research protocol. Terminated protocols are considered closed and no longer require routine continuing review. Depending on the cause of the termination and status of subjects at the time, monitoring by the IRB may be required for a specified period.

The ED, AD (in the absence of the ED), or an IRB Chair may unilaterally suspend a study if he/she receives information that requires the immediate action for the protection of human subjects or to address a concern regarding potential noncompliance with federal, state, or institutional regulations/policies. The IRB Executive Committee may also suspend or terminate activities that affect more than one Board. Such actions should occur when, in the judgment of the ED, AD (in the absence of the ED), or IRB Chair, it would be inappropriate to wait until the next meeting of the IRB or Executive Committee of the IRB.

When study approval is suspended or terminated, the convened IRB, or the individuals making the determination, consider the following:

- Actions to protect the rights and welfare of currently enrolled subjects.
- Whether any adverse Events or outcomes have been reported to the IRB.
- Whether current subjects must be informed of the termination or suspension, and if so, in what manner.
- Whether procedures for withdrawal of enrolled subjects take into account their rights and welfare (e.g., making arrangements for medical care outside of a research study, transfer to another investigator, or continuation in the research under independent monitoring).

Any suspension or for-cause termination of IRB approval will be reported promptly to the investigator and, if the action was initiated by the Chair, the ED, AD, and COT, which will notify the appropriate IOs, the FDA (Director, Division of Biomedical Monitoring, Office of Compliance, Center for Devices and Radiological Health, for device research; Branch Chief, Division of Scientific Investigations, Office of Compliance, Center for Drug Evaluation and Research, for drug research), if applicable, and OHRP (Division of Compliance Oversight) of the suspension or termination (45 CFR 46.108(a);(21 CFR 56.113). If the action was initiated by the ED or AD, the Chair of the reviewing IRB will also be notified of the action.

Although there is no regulatory authority for appeal of Board decisions in suspending or terminating approval of research, the PI may reply in writing to suspension or determination decisions and have the response considered by the applicable Board.

## B. Review of Specific Types of Research

### 1. Review of Research involving Investigational Drugs

For studies involving investigational drugs, or approved drugs used off-label, IRB staff will perform the following functions during the pre-review process:

a. Determine whether the regulatory status of the drug as used in the proposed research is clearly indicated in the materials submitted for Board review, with appropriate documentation of FDA status if necessary.

b. If the regulatory status is not clear, staff will request one of the following from the investigator or sponsor:

1) A letter from FDA that documents the status, and if an IND is required, a letter from FDA that documents the approval of the IND;
2) A copy of the sponsor's protocol or Investigator's Brochure that reflects the IND number (for drugs that are not approved by the FDA) or a copy of the package insert (for drugs that are FDA-approved);
3) A current Form 1572 if one has not been provided;
4) Other appropriate documentation of the status, the need for an IND, or an exemption therefrom.

During its review of the proposed research, the IRB will consider, in addition to the review criteria previously described that applies to all reviews:

a. Whether an IND is required, if one has not been obtained;
b. Whether the investigational drug is being dispensed in accordance with the NYP Investigational Drug Policy (Reference Document #18) and Research Pharmacy policies (Reference Document #172), as applicable;
c. Whether specific information regarding birth control measures must be provided to subjects with reproductive capacity; and
d. Whether special handling is required by research staff, subjects, or others.

### 2. Review of Research involving Medical Devices

For studies involving medical devices, IRB staff will perform the following functions:

a. Determine whether the regulatory status of the device is clearly indicated in the materials submitted for Board review and, if an IDE is required, documentation of the FDA status.
b. If the regulatory status of the device is not clear, staff will request one of the following from the investigator or sponsor:

1) A letter from the sponsor stating and explaining why the device is non-significant risk (NSR); or

2) If the device is a Significant Risk (SR) Device, a letter from the FDA approving the IDE and providing the IDE Number or IDE Supplement Number, a letter from the sponsor providing the IDE number, or a revised protocol from the sponsor that includes the IDE number; or

3) Other written documentation that sufficiently establishes the regulatory status of the device, which may include a statement by the sponsor that the device is not of a regulatory status for which individual written FDA documentation exists, or a letter from the FDA declining to issue an IDE number, stating it was not necessary; for device studies that meet the exempt criteria in 21 CFR 812.2, and which may not have been submitted to FDA, the investigator should justify how the exemption criteria are met.

c. Ensure that a trial involving a device which has been identified as requiring authorization for billing to Medicare receives such authorization before subjects are enrolled. Procedures described in Reference Document #162, which addresses notification to the Office for Billing Compliance and CTO of a device study for which such procedures apply, will be followed.

d. Ensure that plans are in place for appropriate handling, storage, and disposition of the devices.

If the protocol is being conducted by an individual who is a S-I, IRB consultation with the IAP staff to confirm that they are aware of the study is necessary. The IRB and CTO work together, under the provisions of the CUMC Compliance Program for FDA-regulated research, to ensure that regulatory requirements are met (Reference Document #311).

The Board acts in accordance with the following reference information regarding medical device approval when reviewing a protocol that involves an investigational device.

a. Research involving a medical device for human use that qualifies as an NSR Device (unless the device is banned), may begin upon approval by an IRB and does not require the issuance of an IDE by the FDA (21 CFR 812.2 (b)(1)).

b. Research involving a medical device for human use that does not qualify as an NSR device and is not exempt is classified as a SR Device. Research involving SR devices cannot begin until the FDA issues an IDE and approval is granted by an IRB (21 CFR 812.30 (a)).

A SR device is an investigational device that meets any of the following criteria (21 CFR 812.3(m)):

a. is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;

b. is purported or represented to be for use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;

c. is for a use of substantial importance in diagnosis, curing, mitigating, or treating disease, or otherwise preventing impairment of human health, and presents a potential for serious risk to the health, safety, or welfare of a subject; or

d. otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

Before approving research involving a medical device for human use, the IRB will determine if the device is a SR Device, a NSR Device, or whether the research use of the device is exempt from the IDE regulations.

a. If the FDA has issued an IDE for the proposed use of the device, then it is, in most cases, considered to be an SR device.

b. If the FDA has not issued an IDE for the proposed use of the device, the Board considers the following elements in determining whether the device is SR or NSR:

   1) An explanation provided by the sponsor of why the device is not a significant risk device; and

   2) Whether the use of the device might cause harm to any of the subjects, and the nature of the harm that may result from use of the device.

   Note: If the subject must undergo a medical procedure as a part of the study, and that medical procedure is not one which the subject would otherwise undergo as part of standard medical care, the Board must consider the risks associated with the procedure as well as the use of the device. If potential harm to subjects could be life-threatening, could result in permanent impairment of body function, or permanent damage to body structure, the device should be considered SR.

c. If the IRB determines that the device is NSR, the Board may proceed to review the research activities and investigator under its normal procedures for reviewing research projects.

d. If the Board determines the device is SR, and there is no IDE assigned, it will provide the investigator and, if appropriate, the sponsor, with its finding. The sponsor is responsible for notifying the FDA of the Board's SR determination.

   The Board will not review the research until the sponsor provides documentation that the FDA has granted an IDE to the sponsor. If the FDA has not responded to the IDE application, as described in 21 CFR 812.30, this documentation may consist of a letter showing that an IDE application was submitted at least 30 days

prior to the date on which the Board reviews the research and the FDA has not issued a hold on use of the device.

e. If the Board determines that the investigation meets one of the IDE exemptions listed at 21 CFR 812.2(c), this finding will be noted in the minutes, and the Board will not make a SR/NSR determination. Also, if the investigation involves a device that is cleared for marketing through the Premarket Approval (PMA) process, and the device is being studied for the purpose(s) for which the device is labeled, the Board will consider the investigation exempt from the IDE regulations. This finding will be noted in the minutes, and the Board will not make a SR/NSR determination.

In those infrequent instances when a medical device study is approved under expedited review procedures (category 1.b.), documentation of the required findings by the Board reviewer are entered in Notes section of Rascal.

### 3. Review of Humanitarian Use Devices

Humanitarian Use Devices (HUDs) are intended to benefit subjects in the treatment or diagnosis of diseases or conditions that affect or manifest in fewer than 4,000 individuals in the United States per year. HUDs are considered by the FDA to be approved for marketing. FDA regulations permit marketing of these devices under a Humanitarian Device Exemption (HDE).

The degree of safety and efficacy testing required for FDA approval of a HUD is less than that required for other medical devices, because more rigorous testing prior to marketing is not feasible for devices that affect a relatively small subset of the population. Therefore, IRB review is required for these approved devices because safety and efficacy data will be collected while it is marketed.

Two general situations exist for which a protocol that utilizes an HUD is submitted to the IRB:

- Where the HUD will be used as described and for the indication approved in the HDE;

- Where the HUD will be used in a manner, for an indication, or in a population other than that approved in the HDE.

The former does not constitute research, while the latter does.

All protocols involving HUDs will be reviewed at a convened meeting of the full Board for the initial review. The continuing review of any protocol involving a HUD can be reviewed by expedited review if: 1) the use of the device is consistent with the approved indication (e.g., not done for research purposes or for a new indication); and 2) there is no new substantive information that may affect the risk/benefit analysis. When proposing a motion for approval of any protocol involving a HUD, the convened IRB should include

consideration as to whether the continuing review should be done by full Board or expedited review and the basis for such a determination (e.g., HUD used within the approved indication and the continuing review period is approved for one year). If the minutes of a full Board review of a protocol involving a HUD do not specify whether the IRB approved that the next continuing review can be done by expedited review, then the next continuing review should be reviewed by the full Board.

a. Use in Accordance with the HDE

IRB review of HUDs is required under federal regulation (21 CFR 814). During review of the proposed use of the HUD, the Board must determine that:

1) the FDA has granted a HDE to the sponsor; and

2) the investigator intends to use the HUD according to its FDA-approved use.

After the Board has determined that the FDA has granted a HDE, the Board may proceed to review the proposed activities in consideration of the IRB review criteria described in 45 CFR 46.111, with the exception of the requirement for informed consent. Informed consent is not required for use of a HUD in accordance with its FDA-approved indication. However, the Board may require consent in such instances at its discretion.

b. Use Not in Accordance with the HDE

When use of a HUD for research is proposed, the IRB should consider all factors relevant to use of an investigational device, as well as the IRB review criteria defined in 45 CFR 46.111.The Board will require informed consent for any research use of the HUD (i.e., uses outside of the FDA-approved indications).

**4. Review of Research involving Pregnant Women, Neonates, and Fetuses (45 CFR 46, Subpart B)**

Pregnant women, fetuses, and neonates are a vulnerable population and, as such, require additional protections when they are research subjects. It is recognized, however, that pregnant women, fetuses, and neonates should not be denied the benefits of participating in research. Distinction must be made between studies for which the reproductive status of the pregnant woman or the unique characteristics of fetuses and neonates are criteria for inclusion in the research, and studies for which the pregnancy status of the woman is incidental. In regards to the latter, Subpart B requirements need not be met although in all cases, risks specific to pregnant women, neonates, or fetuses should be addressed during the consent process.

When the Boards consider research that requires the involvement of pregnant women, neonates, or fetuses, they will ensure that all requirements of 45 CFR 46 Subpart B are met prior to approval of the research.

In addition to applying the criteria for IRB review identified in 45 CFR 46.111, they will ensure that:

a. there is adequate expertise on the Board to evaluate the risks and benefits relating to the inclusion of pregnant women, fetuses and neonates, engaging consultants where necessary;

b. the determinations required by Subpart B are documented appropriately in the IRB record;

c. the proposed involvement of pregnant women or fetuses meets all requirements for inclusion as stated in 45 CFR 46.204;

d. the proposed involvement of neonates meets all requirements for inclusion as stated in 45 CFR 46.205;

e. proposals for which the inclusion of pregnant women, neonates, or fetuses is not approvable per Subpart B will be referred to the HHS Secretary for review;

f. informed consent is obtained per Subpart B for pregnant women who have reached the age of majority or are legally emancipated;

g. informed consent is obtained per Subparts B and D for pregnant minors (where research is related to prenatal care, consent of the pregnant minor may be acceptable);

h. consent documents contain information regarding risks of breastfeeding, when risks to the pregnant woman or neonate is determined to be greater than minimal; and

i. consideration is given to excluding pregnant women when the woman's reproductive status is not relevant to the research and risks to the pregnant woman or fetus is determined to be greater than minimal.

CU has developed guidance (Reference Document # 103) for obtaining consent from women during labor, in acknowledgement of the fact that some research can only be done during this period, it may not be possible in some circumstances to obtain consent before labor begins, and women who are capable of providing consent during labor and wish to participate in research should be able to do so.

Proposed informed consent procedures for pregnant women who are not in labor will be reviewed in consideration of the general requirements for informed consent, with special attention to the explanation of potential risks and benefits to both the woman and fetus.

## 5. Review of Research involving Prisoners (45 CFR 46, Subpart C)

The purpose of this section is to provide guidelines for review that will ensure additional safeguards for the protection of prisoners involved in research. Prisoners may be under constraints because of their incarceration, which could affect their ability to make a truly voluntary and non-coerced decision whether or not to participate as subjects in research.

Prisoner means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other 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.

An IRB Chair may elect to review protocols that include populations with an increased risk of incarceration as prisoner protocols, even if the protocol is not designed to recruit prisoners. Such proactive reviews address the possibility of subjects becoming prisoners, and may avert the need to either terminate the involvement of subjects who become prisoners or re-review the protocol as a prisoner protocol. Although all required determinations per Subpart C cannot be made in these situations, because the details of the penal facility are not known, the IRB may make the determination that the proposed research is permissible for prisoners. Some of the subpart requirements relate to recruitment within the prison which would not be applicable for these situations; others such as effect of participation on parole decisions would have to be made after a subject becomes a prisoner. In cases where the IRB reviews a protocol in this manner, the approval letter should include a statement that the IRB should be advised via the modification module that such a situation has occurred. The Board can then consider the other items.

If a subject becomes incarcerated while enrolled in a study that was not reviewed in light of the Subpart C requirements, the subject should be removed from the study unless the study is re-reviewed under Subpart C. Unless required to avert immediate risk of harm to the individual, his/her participation should not continue until the study has been re-reviewed.

Each Board that reviews research involving prisoners will have at least one prisoner representative, i.e., a member or alternate who is or was a prisoner, or who has the appropriate background and experience to represent the rights and welfare of the prisoners. All protocols that will recruit prisoners as subjects will be reviewed by a prisoner representative. When a convened Board reviews research involving prisoners, if the prisoner representative is present at the meeting, he/she will count toward quorum for these protocols. The reviewer form for prisoner research (Reference Document #94), or equivalent, will be completed for each review by the prisoner representative.

In addition to its other responsibilities prescribed in these Written Procedures, the Board may approve research involving prisoners only if it finds that all requirements described in 45 CFR 46.300 (Subpart C) are met.

Human subjects research may involve prisoners as subjects only if the Board has approved the research, considering the above requirements, and the proposed research involves solely research permitted per the federal regulations.

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 following definition of minimal risk will be applied to research involving prisoners:

> 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.

The Board will determine that the research under review represents one of the categories of the research permissible under 45 CFR 46.306(a)(2).

Details of the IRB review for any research project involving prisoners that is federally-supported or conducted will be given to the ED or AD promptly after review, with a draft certification letter for submission to OHRP. The ED, AD, or designee, will prepare a report for submission to OHRP to satisfy the certification requirements described in 45 CFR 46.305(c). Research with prisoners may not begin in these situations until OHRP approves the certification.

Prisoner research is not eligible for an exempt determination.

### 6. Review of Research involving Children (45 CFR 46, Subpart D)

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

Federal regulations require that:

a. children be included in certain research activities unless there is a justification for excluding them; and

b. additional precautions be taken when children are research subjects, depending on the degree of risk involved in the research.

NIH policy, which guides the conduct of much human research due to funding relationships, has similar requirements.

The regulations also set forth requirements for obtaining parental permission and, where appropriate, assent by the children themselves. The CU IRBs review research that involves children following Subpart D of the applicable DHHS and FDA regulations, New York state law, and institutional policy. When appropriate, requirements for involvement of minors in research postulated by the NYC Administration for Children's Services (ACS), and/or the DOE, are also considered. Reference Document #107, Research involving Children, provides additional information.

Information provided by the investigator regarding level of risk, prospect of direct benefit (when applicable), assent and parental permission, and inclusion of wards/foster children is evaluated by the IRB, which may concur with the investigator's determinations, make alternative determinations, or impose additional requirements.

Use of the Subpart D Reviewer Form (Reference Document #100) helps to ensure that all necessary elements are considered by the IRB reviewer.

**a. Determination of Risk/Benefit Category**

When a Board (or qualified reviewer for research that is eligible for expedited review) reviews research involving children, it will be determined which of the risk/benefit categories described in 45 CFR 46 (Subpart D) and 21 CFR 56 (Subpart D) the research fits into, whether assent will be required, the manner in which assent will be obtained, if required, the requirements for parental permission or approval of waiver thereof, and the appropriateness of the inclusion of wards/foster children if their involvement is proposed for research that involves greater than minimal risk with no prospect of direct benefit. The IRB will consider information provided by the research team in the Child Involvement section of the Rascal submission. The Board's (or reviewer's, for research that is eligible for expedited review) determinations will be entered into the minutes for the meeting at which the research was reviewed, if full Board review is indicated, or in the IRB record, in the case of expedited reviews. Concurrence or disagreement with the information provided by the researchers, and basis for the latter, should be included in the documentation of Subpart D findings.

The four possible categories of research involving children are:

1) 45 CFR 46.404; 21 CFR 50.51: Research not involving greater than minimal risk.

"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.

The IRB, or designated expedited reviewer, will provide the basis for the determination of minimal risk; if there is concurrence with the PI's assessments as entered in the Child Involvement section, a notation to this effect will be sufficient.

The IRB, or designated expedited reviewer, may determine that the permission of one or both parents is required for research in this category, and will determine whether assent for some or all minors is required.

2) 45 CFR 46.405; 21 CFR 50.52: 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.

The IRB, at a convened meeting, will provide the basis for the determinations of greater than minimal risk and prospect of direct benefit; if there is concurrence with the PI's assessments as entered in the Child Involvement section, a notation to this effect in the minutes will be sufficient.

The IRB may determine that the permission of one or both parents is required for research in this category, and will determine whether assent for some or all minors is required.

3) 45 CFR 46.406; 21 CFR 50.53: 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 45 CFR 46.406 and 21 CFR 50.53, 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; and

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. (45 CFR 46.407 and 408).

The IRB, at a convened meeting, will provide the basis for the determinations of greater than minimal risk and no prospect of direct benefit; if there is concurrence with the PI's assessments as entered in the Child Involvement section, a notation to this effect in the minutes will be sufficient.

The permission of both parents is required for research in this category, unless one parent cannot reasonably provide permission, as allowed per Subpart D. The assent of the minors involved is required unless the Board determines that some or all are not capable of providing assent.

4) 45 CFR 46.407; 21 CFR 50.54: Research not fitting into the aforementioned categories which presents a reasonable opportunity to understand, prEvent, or alleviate a serious problem affecting the health or welfare of children.

The IRB, at a convened meeting, will provide the basis for its determinations regarding risk level and potential for direct benefit; if there is concurrence with the PI's assessments as entered in the Child Involvement section, a notation to this effect in the minutes will be sufficient.

If the research is supported by DHHS jurisdiction, and falls in this category, it cannot be performed without review by the Secretary of the HHS as outlined in 45 CFR 46.407.

Research under FDA jurisdiction that falls in this category cannot be performed without review by the Commissioner of Food and Drugs as outlined in 21 CFR 50.54.

The respective IRB staff will prepare a request for panel review promptly after the IRB review, and will provide such to the ED or AD. The ED, AD, or designee will prepare a report for submission to OHRP and/or request a panel review as described in 45 CFR 46.407 or 21 CFR 50.54, as applicable.

Research in this category that is not federally funded and does not involve FDA-regulated products will be reviewed by a special panel convened by the IRB office to make the determinations that would be considered by DHHS or FDA when evaluating research in this category.

The permission of both parents is required for research in this category, unless one parent cannot reasonably provide permission, as allowed per Subpart D. The assent of the minors involved is required unless the Board determines that some or all are not capable of providing assent.

### b. Assent Determination

After the Board makes the risk/benefit determination, they must consider the issue of child assent, as described in 45 CFR 46.408(a) and 21 CFR 50.55 (Subpart D). The Board must decide whether assent is necessary, and also whether and how it will be documented if it is necessary.

Among the formats the Board may consider are the following:

1) waiver of assent;

2) determination that the children lack the ability to provide assent;

3) verbal assent, without documentation;

4) verbal assent, with documentation by the investigator and/or the legally authorized representative(s);

5) written assent form, with subject signature; or

6) subject signature block on consent form (for older children only).

The federal regulations do not require that assent be sought from children starting at a specific age, but that their assent should be sought when, in the judgment of the IRB, the children are capable of providing their assent. IRBs are to take into account the ages, maturity, and psychological state of the children involved (see 45 CFR 46.408(a) and 21 CFR 50.55(b)).

When the research offers the child the possibility of a direct benefit that is important to the health or well-being of the child and is available only in the context of the research, the IRB may determine that the assent of the child is not necessary (45 CFR 46.408(a) and 21 CFR 50.55(c)).

### c. Inclusion of Wards in Research

Special protections must be considered whenever children who are wards of the state or any other institution, agency, or entity are considered for inclusion in research that is greater than minimal risk with no prospect of direct benefit. Of primary concern are consent issues, i.e., who has authority to enroll a child who is a ward in research. Responsibility for ensuring that appropriate individuals provide permission rests with the PI, and must be in compliance with applicable statutes and the process described in the protocol that was approved by the IRB.

Federal regulations do not require special provisions for wards enrolled in research that is either minimal risk or greater than minimal risk with the prospect of direct benefit. However, the Board may impose additional requirements if the research and/or status of the child(ren) warrant additional safeguards. New York state laws

and NYC ACS policies will be considered during review of research that involves wards.

Wards may only be included in research that is greater than minimal risk and does not offer the prospect of direct benefit (45 CFR 46.406 or 45 CFR 46.407) when such research is either related to their status as wards, or conducted in a facility at which most of the children are not wards.

If it is proposed that wards will be enrolled in research that is greater than minimal risk and does not offer the prospect of direct benefit, an advocate or advocates who will serve to ensure the best interests of each child are being upheld must be appointed, in addition to obtaining permission from any other individual acting on behalf of the child, e.g., as guardian or in loco parentis. One individual may serve as an advocate for more than one child. Whether the investigator, the IRB, or ACS provides suggestions for appropriate advocates, the selection requires approval by the IRB after consultation with or approval from ACS.

The CU policy, "Research Involving Children" (Reference Document #107), provides detailed information regarding the protections required when children are subjects in research.

**7. Review of Research involving Other Vulnerable Adults**

When all or some of the subjects in proposed research are vulnerable adults, and their vulnerability stems from factors other than pregnancy or incarceration, the Boards will ensure that additional protections are included where necessary to uphold the principles of respect for persons, justice, and beneficence. Specific requirements for the inclusion of pregnant women and prisoners are described elsewhere in these procedures.

Adults may be considered to be vulnerable for a variety of reasons, including but not limited to:

a. impaired cognitive capacity, either temporary or permanent;
b. economic or educational disadvantage;
c. inability to speak or understand English;
d. medical condition; or
e. relationship to researcher.

When the Boards find that the subjects in a research protocol are vulnerable, the Boards will consider additional safeguards on a case-by-case basis (21 CFR 56.111(b); 45 CFR 46.111(b)).

For studies involving the possibility of consent by legally authorized representatives for adult subjects, the Boards must consider how it should be determined that a subject is capable of providing his/her own consent, who may legally provide consent if the subject

is not capable, and the issue of subject assent. The Boards must determine whether assent is necessary, and how it will be documented if it is necessary.

The IRB must first consider whether the research must be done with the particular group of vulnerable subjects identified in the protocol. If yes, appropriate justification needs to be made for the inclusion of these subjects in any research that will not directly benefit these subjects; this is especially important for those studies that present greater than minimal risk of harm. Even with such justification, additional safeguards should be included to minimize the vulnerability of such individuals. These may include assignment of a research partner or the involvement of a consent form monitor.

## 8. Review of Research involving Non-English Speaking Subjects

The Belmont Report identifies "justice" and "respect for persons" as two fundamental ethical principles that must underlie the conduct of all human subjects research. The principle of justice requires that the burdens and benefits of research are equitably distributed. The principle of respect for persons requires that "adequate standards for informed consent are satisfied" so that subjects are provided with sufficient meaningful information to decide whether they want to enroll in a research study.

In the review of a protocol the IRB will evaluate the "special populations" information entered in Rascal by the research team and determine the number or percentage of non-English speaking subjects that are expected to be enrolled. Determinations will be made regarding the need for translation of study instruments and consent documents, in accordance with federal regulations and the CU IRB policy, "Enrollment of Non-English Speaking Subjects" (Reference Document #101). This policy also defines acceptable translators and describes the short form consent process, which utilizes verbal consent when a non-English speaking subject is unexpectedly encountered.

It is important that means of effective communication with non-English speaking subjects throughout the course of their participation be considered by both the researchers and the IRB.

## 9. Review of Research involving International Sites

As noted previously in these documents, IRB review of international research raises additional considerations related to obtaining local knowledge of applicable laws, institutional commitments and regulations, standards of professional conduct and practice, cultural norms, and local community attitudes (relative to the study site). Physical, social and psychological risks may vary from those in the NYC communities within which the Columbia campuses reside, i.e., the area "local to" the CUMC and CU-MS IRBs. Assessing the risks and benefits of research conducted internationally may raise challenges if there is not adequate knowledge of the local setting or population to be included. Care must be taken to ensure that the cultural norms of the host country are respected and that the participants will not suffer adverse consequences from

participation, such as being subjected to retaliation from local authorities or the local community.

Research projects that take place outside the United States require compliance with Columbia policies and the relevant laws of the host country. International research must also comply with 45 CFR 46 or equivalent standards, such as the 1993 Council of International Organization of Medical Sciences (CIOMS) International Ethical Guidelines for Biomedical Research Involving Human Subjects, the ICH standards, or the 1998 Medical Research Council of Canada Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans.

It is important for researchers to provide information to address these considerations and for the IRB to gain sufficient knowledge of the research locale to accurately assess the risks and benefits of participation and to provide appropriate protections to subjects. Use of consultants is both acceptable and encouraged.

The IRB must consider the following in addition to the review requirements described in Section VI, and in other relevant sections of this document:

a. The research protocol should generally be designed to address an issue characteristic of the local setting, or conditions that affect the local setting, particularly in developing countries. If the research is greater than minimal risk, then the research should be designed to provide potential benefit to the subjects and/or to the local community. If a research study is not designed accordingly, the investigator should provide satisfactory justification as to why the study is proposed to be conducted in the given setting(s).

b. In an effort to gain knowledge of the local setting, the IRB should consider the most appropriate means of obtaining this information. The type of research, level of risk, study population, location of the research and whether collaborative efforts are involved are all factors that will affect the means of obtaining the knowledge of the local setting.

For all international research studies, researchers should provide details of the local context within the protocol to provide a basis for the IRB review.

The IRB may obtain local knowledge from literature, documentation, or available written information, or by inclusion of a consultant knowledgeable of the local setting, in accordance with OHRP guidance (IRB Knowledge of Local Research Setting, August 1998). For review of minimal risk studies, this level of knowledge may be adequate for the IRB to make the necessary risk-related determinations.

For greater than minimal risk studies, efforts should be made to obtain review and approval from an ethical review committee that is local to the study site or has particular knowledge of the proposed setting. One source for identification of

potential international ethical review committees or IRBs is the list of IRBs registered with OHRP.

IRBs should recognize that international ethical review committees which are affiliated with an institution may not be willing to review research conducted by investigators outside their institution. Access to local ethical review committees may be facilitated when CU researchers collaborate with researchers at the local institution.

The local ethical review committee or IRB should comply with the IRB composition requirements of 45 CFR 46.107 or 21 CFR 56.107, as applicable. In order to increase efficiency, review and approval by the local ethics committee or IRB should usually be obtained after review by the CU IRB.

If review by a local human research ethics committee cannot be obtained for greater than minimal risk research, the IRB review must include consultation by an expert who is independent of the research team and is familiar with the local site's culture and norms. The research team may refer such an individual to participate in the review by the convened CU IRB.

c. Obtaining informed consent in accordance with 45 CFR 46 and 21 CFR 50 in certain international settings may raise challenges due to a difference in the norms of the host country. The process for obtaining and documenting informed consent must comply with U.S. regulations and with Columbia policy. Where local practices are inconsistent with U.S. requirements an equivalent process may be considered, e.g., in countries with spoken but no written language, appropriate alterations to the consent process may be necessary.

If the legal age of an adult differs in another country from New York State (NYS) Law (e.g., 18 years of age), the IRB should accept the local age of majority when considering who may provide their own consent.

d. When consent and recruitment documents have already been translated into a language other than English, the researcher should provide a copy of the document in English, a copy in the language to be used in the foreign location, and certification from an appropriate individual that the translated version of the document is complete and does not contain information that is not presented within the context of the approved English version of the document.

When the CU IRB-approved informed consent document in the local language is reviewed by an international IRB or ethics committee, the local approved consent document should be back-translated into English by an appropriate individual who will certify that the resulting English version and the local consent document are consistent in content, style, and level of readability. Back translation is required for greater than minimal risk studies; the approval of the local review committee is adequate verification for minimal risk studies.

e. When the research will be conducted in an institution or organization such as a school, business, or hospital that is not otherwise involved in the research, a letter(s) of agreement should be submitted from the appropriate official(s) (e.g., government officials, school officials, community officials, chief executive officers, etc.) indicating that the research protocol, and any and all instruments to be used, have been reviewed and that the study is acceptable to be conducted in the institution or organization. The letter of agreement must be on letterhead stationery and carry an original signature, or otherwise meet acceptable professional standards for a signed document.

f. The research study should provide a plan for oversight of the research that will be conducted in an international setting, particularly when the CU research staff will not be present at the foreign site.

g. The research study should provide a plan for data collection, protecting the confidentiality of the data, and transport of the data back to CU, or elsewhere in the U.S. or another region.

1) If data will be collected by an individual(s) other than those on the Columbia research team, that(those) individual(s) must be identified and letters of agreement to protect confidentiality should be presented to the IRB. An IIA may be required if the individual is engaged and is not affiliated with an institution that has an IRB. If the non-Columbia researcher(s) will have access to the data for research purposes, the extent of the access should be specified.
2) Methods for assuring anonymity and/or confidentiality of all data must be specified, particularly if the analysis will occur away from CU.
3) Processes for transporting data from the international location to CU, with particular reference to protecting the confidentiality of the data while in transit, must be addressed.
4) If personal health information with identifiers will be transmitted to the U.S., HIPAA requirements must be addressed.

h. If the research study will collect tissues or any other biological samples, the study should provide a plan for the storage and use of the samples, and a plan to protect confidentiality of the samples. If the samples will be transported back to CU or the U.S., the protocol must provide a plan for shipment of the samples that is in accordance with both the local country and U.S. regulations and policies.

Unsterilized specimens of human and animal tissues (such as blood, body discharges, fluids, excretions or similar material) containing an infectious or etiologic agent require a permit in order to be imported (USPHS 42 CFR 71) to the U.S. Details on the regulatory requirements, process for obtaining a permit, and shipping and

handling of such tissues can be found on the Centers for Disease Control and Prevention (CDC) website.

If the material being imported has been rendered sterile (e.g., radiation or chemical treatment) and is known not to contain infectious agents for humans, a permit is not required for importation.

The IRB recognizes that there are instances for which parts of the guidance cited above for international studies would be inappropriate, such as with ethnographic research, both domestic and international, where researchers observe, interact and may live with subjects in their native environment, often for long periods of time. Research that presents concerns that are unique to a population and its culture would, by necessity, require careful consideration by the IRB and the researcher as to how best to protect the rights and welfare of the subjects.

**10. Review of Planned Emergency Research**

Emergency research refers to the study of acute, life-threatening clinical situations. Often, informed consent from the subjects is not feasible because the subject lacks the capacity to provide their own consent (e.g., unconscious) and/or there is insufficient time because treatment must be promptly administered. The conduct of planned research in life-threatening emergent situations requires special consideration by the IRB, including consideration of whether consent may be waived. The specific conditions under which prospective consent of the subject may be waived for planned emergency research are provided by 21 CFR 50.24; the FDA-DHHS Harmonized Rule on Waiver of Consent for Emergency Research permits application of the FDA regulations to planned emergency research situations that do not involve an FDA-regulated drug, medical device, or biologic.

If waiver of consent is proposed for those subjects who are not capable of providing consent, and will not have a legally authorized srepresentative present, the research plan must include not only public disclosure of the study to the community in which the research will be conducted, but also community consultation. The purpose of the community consultation is to assess whether members of the local population at large would approve of the conduct of the emergency research, i.e., whether they are in favor of such procedures being performed on them if they were in a particular emergency situation. The community consultation should include individuals who represent the targeted subject population that will be enrolled in the study, and must be completed before IRB approval to enroll subjects is provided. It is recommended that the research team meet with the IRB staff to discuss the plan for community consultation prior to its initiation.

The plan for the emergency research study, including the plan for community consultation and public disclosure, must also be approved in advance by FDA if the research involves an investigational or FDA-approved product. The plan must be submitted to the FDA under an emergency IND/IDE by the sponsor or PI responsible for

the IND/IDE. The community consultation and the public disclosures, however, generally do not have to be completed prior to submission for FDA approval.

The IRB may approve the study prior to FDA approval of the IND/IDE. When this occurs, the IRB approval will specifically restrict enrollment of subjects as appropriate until the IRB receives notice of FDA approval of the IND, and all outstanding concerns have been adequately addressed.

If the emergency research study is federally-supported or conducted and does not involve an investigational or FDA-approved product, approval must be obtained from OHRP (on behalf of the DHHS Secretary).

**a. Emergency Research Consent Waiver**

The Boards may waive the requirement for informed consent for research involving emergency medical situations if it finds and documents that the requirements of 21 CFR 50.24, which include review and approval of the proposed waiver by FDA, are met. FDA review addresses the requirement in NYS law that consent may only be waived, for activities that meet the NYS definition of medical research, if the activity is subject to federal oversight.

In order to approve an emergency research consent waiver, the Boards shall find and document, with the concurrence of a licensed physician who is a member of, or consultant to, the IRB and is not otherwise participating in the clinical investigation, that:

1) The human subjects who will meet eligibility criteria will be in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

2) Obtaining informed consent is not feasible because:

    a) Subjects will not be able to give informed consent because of their medical condition;

    b) The intervention under investigation must be administered before consent from the subject's LAR is feasible unless the LAR is with the subject or arrives within a defined period; and

    c) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

3) Participation in the research holds out the prospect of direct benefit to the subjects because:

a) Subjects are facing a life-threatening situation that necessitates intervention;

b) Appropriate animal and other pre-clinical studies have been conducted, and the information derived from those studies and related evidence supports the potential for the intervention to provide a direct benefit to the individual subjects; and

c) Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

4) The clinical investigation could not practicably be carried out without the waiver.

5) The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a LAR for each subject within that window of time and, if feasible, to asking the LAR for consent within that window rather than proceeding without consent. The investigator will summarize the efforts made to contact LARs and make this information available to the Board at the time of continuing review.

6) The Board has reviewed and approved informed consent procedures and a consent document consistent with 45 CFR 46.116 and 21 CFR 50.25. These procedures and the consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible.

7) Protection of the rights and welfare of the subjects will be provided, including, at least:

a) Consultation (including, where appropriate, consultation carried out by the Board) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn.

b) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits.

c) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results.

d) Establishment of an independent data-monitoring committee to exercise oversight of the clinical investigation.

e) If obtaining informed consent is not feasible and a LAR is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window, a surrogate for the subject who is a legally authorized representative (in accordance with the IRB Informed Consent Policy), and obtaining permission for the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact surrogates and make this information available to the Boards at the time of continuing review.

8) The application to the IRB clearly identified the procedures and environment in which subjects would not be able to provide informed consent.

The Board will ensure that there are procedures in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a LAR of the subject, or if such a representative is not reasonably available, a family member:

1) of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document;

2) that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

If a legally authorized representative or family member is informed about the clinical investigation, and the subject's condition improves such that he/she is capable of providing informed consent, the subject is also to be informed as soon as possible.

If a subject is entered into a clinical investigation for which consent is waived and the subject dies before a LAR or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible. The IRB should also be notified of such situations and provided with a summary of the subject's enrollment, the procedures conducted for research purposes, and information relating to notification of the legally authorized representative.

All study related documents are to be retained by the IRB for at least three (3) years after termination of the clinical investigation, and the records shall be accessible for inspection and copying by the FDA.

The Board will require that a separate IND or IDE will be obtained by the sponsor or the investigator, even for marketed products.

The Board will promptly notify in writing the investigator and sponsor when it determines that it cannot approve an emergency consent exception study. The notice shall include the reasons for the disapproval.

The Board may require additional protections for subjects in an emergency research consent waiver study as appropriate.

### 11. Review of Research that involves Human Embryonic Stem Cells

Research that involves stem cells must be reviewed by the University Human Embryo and Human Embryonic Stem Cell Committee prior to review by the IRB. In cases where this Committee determines that the research does not meet the criteria in 45 CFR 46 to be considered "human subjects research", additional review by the IRB is not required. Review by the IRB of research that involves stem cells will be conducted in accordance with the IRB Review Criteria described in 45 CFR 46, the Columbia University Policy on the Conduct of Research with Human Embryos and Human Embryonic Stem Cells, and additional criteria identified in Section IV.B., "IRB Criteria for Review", items 8 through 10, of these procedures.

### 12. Review of Research Conducted by Students

Many submissions for studies that will be conducted by students are received by the Columbia IRBs each year. This is anticipated due to the nature of the institution and encouraged in order to foster experience with research methodology and application of ethical principles in research. Nonetheless, special consideration is required for these projects due to the relative inexperience of student researchers.

All student projects are required to have an individual who meets the criteria to serve as PI and assume overall responsibility for conduct of the study in accordance with the IRB-approved protocol. In addition, some projects that may not technically meet the criteria to be considered "research" per the federal regulations, but involve a significant level of risk may be required to be submitted for IRB approval. These and other criteria for student research projects are explained in detail in the IRB Student Research policy and in the accompanying guidance document (Reference Document #304). Both may be accessed on the IRB website. These documents should be reviewed early in the development of student research activities, to avoid delays that may compromise the ability of the student to complete the project in time to meet course or degree deadlines.

## C. Review of Specific Types of Documents

### 1. Review of Recruitment Material

Any item that is intended to be used to encourage a potential subject to consider volunteering for a research study must be reviewed and approved by the IRB before being used**.** The FDA Guidelines indicate that advertising is considered to be an

extension of the informed consent process, and thus subject to Board review. Refer to the FDA Information Sheet, "Recruiting Study Subjects", for additional information.

The IRB defines advertising as any research-related information that will be seen or heard by a potential subject before he or she has read and signed a consent form for the study. This means that advertising may include:

- Printed items in newspapers, magazines, flyers, posters, etc.
- Radio announcements
- TV productions or commercials
- Video presentations
- Internet postings
- Web pages
- Informational brochures
- Letters to potential subjects
- Imprinted items (notebooks, bags, etc.)

The IRB will review:

- The information contained in advertisements.
- The mode of their communication.
- The final copy of printed advertisements.
- The final audio- or video recorded advertisements (or script thereof).

Advertising materials for new protocols that are submitted with the study materials will generally be included in the initial full Board or expedited review.

Advertising material submitted after initial approval of research will generally be reviewed by expedited review. The Board member who is conducting the expedited review may approve the material, require modifications before approval, or refer the proposed materials to the full Board for consideration.

The IRB will ensure that advertisements and recruitment materials:

- Do not state or imply a certainty of favorable outcome or other benefits beyond what was outlined in the consent document and the protocol.
- Do not include exculpatory language.
- Do not emphasize the payment or the amount to be paid, by such means as larger or bold type.
- Do not promise "free treatment" when the intent is only to say subjects will not be charged for taking part in the investigation.
- Are limited to the information prospective subjects need to determine their eligibility and interest, such as:
    - The name and address of the investigator or research facility.
    - The purpose of the research or the condition under study.

- In summary form, the criteria that would be used to determine eligibility for the study.
- A brief list of participation benefits, if any.
- The time or other commitment required of the subjects.
- The location of the research and the person or office to contact for further information.

For FDA-regulated research, the IRB will ensure that advertisements and recruitment materials:

- Do not make claims, either explicitly or implicitly, about the drug, biologic or device under investigation that were inconsistent with FDA labeling.
- Do not use terms, such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational.
- Do not include compensation for participation in a trial offered by a sponsor to involve a coupon good for a discount on the purchase price of the product once it had been approved for marketing.

Approved recruitment material will be stamped with the IRB approval stamp. In some instances, when recruitment materials will be commercially produced or for other reasons, it may be difficult to stamp. In those situations, the IRB may stamp one copy for documentation, and accept a process whereby the stamped copy is retained by the researcher for documentation of IRB approval, but the actual documents may be produced and distributed without the stamp on each copy. This exception to stamping of each copy is subject to the requirements of the facility in which copies will be posted, e.g., NYP requires that each copy be stamped.

The approval stamp for non-exempt research will indicate the IRB number, the date of approval and expiration, and the initials of the person stamping the document. Approval stamps on documents related to exempt research will include the date of the exempt determination date rather than approval and expiration dates.

Board review of advertising that will be presented as audio or video advertising will involve both scripts and copies of the recording prepared according to the script, when appropriate. Actual recordings must be submitted for approval following approvable review of the scripts. No deviation from the approved script is permitted without prior IRB review and approval.

Miscellaneous points to keep in mind relative to recruitment:

- Obtain permission and/or abide by local policy, as applicable, when posting recruitment flyers in both public and private spaces, e.g., NYC has restrictions and guidelines for posting documents in public places, and NYP restricts posting in some areas;
- Review by Columbia's Communications & Public Affairs office, CUMC's Newsroom office, and/or NYP's Office of External Relations is recommended, and may be required, for recruitment outside of Columbia, including but not limited to

public service announcements or press releases; (Reference Document #312 provides a list of these contacts and general scope of authority).

**2. Review of Funding Documentation**

In accordance with the requirements of 45 CFR 46.103(f), documentation of funded procedures will be reviewed and required for all federally funded projects. This material will be reviewed by the IRB to (at a minimum) ensure that all funded procedures are included in the research protocol, evaluate relationships among collaborators to determine necessary approvals, and confirm key personnel.

Verification of IRB approval will be obtained by pre-award departments of the University prior to creation of an account for award funds.

**3. Review of Investigational Drug Brochure**

The IDB supplied by corporate sponsors will be reviewed by the primary reviewer, to facilitate evaluation of risks and benefits through an understanding of the mechanism by which the investigational product acts, preclinical and animal data, and the intricacies of the study design. Review of the IDB occurs during both initial and continuing reviews, and when a modification includes revision of the document (Reference Document #8).

**4. Review of Payments to Participants**

The reasons for which individuals decide to volunteer for research participation vary widely. In no case, however, should an individual be induced to accept significant risk for research purposes because of the monetary payment they may receive. The IRB, in its review of payment schedules, must ensure that any monetary payment or other form of compensation is fair, and that elements of coercion or undue influence are not present.

When developed with consideration for the burden or expense that participation may involve, compensation may be justifiable. It may be appropriate, for example, to compensate individuals who participate in research studies for their time and effort, or for transportation expenses. Token acknowledgment of the participants' contribution to science may also occur in the form of payment, provided it is reasonable. For studies that do not offer the prospect of direct benefit, it may also be appropriate to provide reasonable compensation to induce enrollment. In general, such inducement would only be appropriate for minimal risk protocols.

It is important to distinguish "reimbursement" for costs of participation (e.g., transportation or child care expense) from compensation for time, effort, or inconvenience of participation. The former is not considered income whereas the latter is considered income. Compensation of greater than $600 in a calendar year must be reported to the IRS by the University therefore there are potential tax implications for the participant. This must be described in the consent form.

Compensation should generally be pro-rated, i.e., distributed evenly among visits, when more than one study visit is involved. If particular visits are significantly longer than others, an uneven distribution may be acceptable if justification is provided. Individuals who withdraw prior to completing all study visits should receive the compensation allotted for all visits that were completed.

Completion "bonuses" may be acceptable if reasonable, i.e., not so large that average participants are compelled to continue study procedures simply to obtain the bonus.

Monetary compensation for children requires special consideration. In general, small age-appropriate books or toys are preferred for young children; cash or a gift certificate of a reasonable amount may be appropriate for older adolescents. The IRB will consider the age of the children and types of study procedures when compensation to minors is proposed. Payments to parents for their child's participation will require special consideration by the IRB.

The IRB will determine that:

• The amount of payment and the proposed method and timing of disbursement is neither coercive nor presents undue influence.
• Credit for payment accrues as the study progresses and is not contingent upon the subject completing the entire study.
• Any amount paid as a bonus for completion is reasonable and not so large as to unduly induce subjects to stay in the study when they would otherwise have withdrawn.

The following are prohibited:

• Payments to professionals in exchange for referrals of potential subjects ("finder's fees").
• Payments designed to accelerate recruitment that are tied to the rate or timing of enrollment ("bonus payments") unless they are judged not to interfere with providing prospective subjects with sufficient opportunity to consider whether to participate and do not increase the possibility of coercion or undue influence on investigators or subjects.

Terms of all payments to participants, whether for reimbursement or compensation, should be explained during the consent process, and clearly stated in consent documents. Per NIH guidelines for writing consent documents, monetary compensation should not be described as a benefit in the consent form. If Social Security numbers will be collected to process payments, subjects should be so informed.

# VII. IRB Convened Meetings: Organization and Management

## A. Schedule of Meetings

Each Board has regularly scheduled meetings, with additional meetings scheduled as necessary. The schedule of meetings is available on Columbia's IRB websites.

## B. Agenda Preparation

Members of the Board to which a protocol is assigned have electronic access to all submitted materials for any given Event via Rascal. Approximately one week prior to the meeting, the agenda is closed and members are notified. Although members have access to the agenda within Rascal, they are provided by email or through other means with a copy of the Rascal short agenda, which lists new protocols, modifications, renewals, UPs, and Other Topics along with reviewer assignments, as a reference. Board members are also advised to review the approved minutes from the prior meeting.

Within Rascal, members have access to all information and documents submitted by the investigator, as well as pre-review notes from staff. Documents may include, but are not limited to, the sponsor's protocol, package inserts or investigational drug brochures for drugs, device manuals, study instruments, consent documents (including recruitment material), approvals from other IRBs, authorizations from study sites, and grant applications. In the case of renewals, modifications, and UPs, members also have access to all prior submissions for the protocol, with documentation of the IRB action that was taken.

## C. Primary Reviewer Assignments

Events that require review by the convened IRB or are eligible for expedited review will be assigned to a primary reviewer. The Chair may elect to serve as the primary reviewer or designate this responsibility to another qualified Board member.

Details of the primary reviewer process may be found in the Process section (Section IV.C.) of these procedures.

## D. Voting Requirements

No official action may be taken at a convened meeting unless a quorum is present either in person or via teleconference, and at least one non-scientist is present. Quorum is defined as more than one half of all voting members listed on the IRB roster. The IRB will ensure and document that a quorum is present for review of each Event that requires full Board review.

A motion that is seconded, then carried or denied by a majority of the voting members present is required for acting on approvals, deferrals to Chair (referred to as "pending" in Rascal), deferrals to Board (referred to as "returned" in Rascal), suspension, and acknowledgement (where applicable). The Chair is a member of the IRB, and therefore, he/she counts towards the quorum and his/her vote is counted.

The Board does not have to vote to "defer", as an action in Rascal (i.e., table review until a meeting in the future), an item that is on an agenda but is not reviewed due to time constraints, absence of the primary reviewer, loss of quorum or other administrative causes.

A member who has a conflict of interest with respect to the research under consideration (e.g., member of the research team, or has a financial conflict of interest related to sponsorship of the study) may not vote on any action related to that research project. The member will also not count towards the quorum for that study. When necessary to ensure adequate expertise and/or understanding of the research question, a member with a conflict of interest, such as a member who is a PI or holds other status on a research project, may present the study to the Board and answer the Board's questions prior to recusing him/herself and leaving the meeting room for the rest of the discussion and vote for that study.

## E. Minutes

### 1. Recording of Minutes at the Convened Meeting

The minutes for a convened Board meeting must contain sufficient information to comply with regulatory requirements and to serve as the documentation of attendance and actions taken at the meeting.

Assigned IRB staff will be responsible for preparation of the minutes, and will follow the standard Board guidelines, described in Reference Document #102. The minutes will, at a minimum, clearly show the following:

a. Date and time of the meeting;
b. Identification of the individual who served as Chair, attendance and voting status of members/alternate members (and for whom each alternate served), attendance of staff and guests, and for guests, the purpose of their attendance;
c. Any changes in attendance (people called away, coming in late, etc.) and voting status; this should include the names of IRB members who leave the meeting because of a conflict of interest along with a statement that a conflicting interest is the reason for the absence;
d. Agenda categories brought before the Board, and clear identification of each item and/or investigator the Board considers;
e. For each item reviewed:
    1) Title and PI;
    2) Name of primary reviewer(s);
    3) A summary of discussion of controverted issues, with resolution;
    4) The basis for requiring changes in or disapproving research;
    5) Any additional conditions required by the Board that may be satisfied after approval of the project, but must be adequately addressed before approval of the withheld item is provided (e.g., receipt of approved Certificate of Confidentiality

before a consent form may be released, or completion of educational requirements before an individual may participate in the research);

6) A clear indication of the Board action taken for each item with a statement of the vote, the number voting for, against, and abstaining, and total number voting;
7) Statement that IRB review criteria articulated in 45 CFR 46.111 and 21 CFR 56.111, if applicable, have been met (if action is "approved", or "pending");
8) Determination of risk level for new protocols, and those events for which the risk level has changed since the last review (if action is "approved", or "pending");
9) For initial and continuing review, the approval period; and
10) Waivers (e.g., some or all elements of informed consent, documentation of informed consent, parental permission) that are approved, and the basis for the waiver.

f. For items that are returning to the Board after having been deferred back to the Board, a statement of the area(s) that required significant revision and/or the area(s) of primary concern;

g. For research involving minors, the applicable category of research per HHS and FDA regulations, as applicable, the basis for the determination, requirements for parental permission and assent, requirements for documentation of assent, determination of number of parents who must provide permission, and when applicable, conditions for enrolling wards in research that is greater than minimal risk with no prospect of direct benefit;

h. For research involving pregnant women and fetuses, a statement that the research meets the criteria for allowable research involving pregnant women, the basis for the findings, and consent requirements;

i. For research involving prisoners, a statement that the research meets the criteria for allowable research for prisoners, the basis for the findings, and documentation of review by a prisoner representative;

j. For research involving other vulnerable adults, additional protections as determined by the Board;

k. For research involving devices that are not approved by the FDA, a statement that the IRB has determined whether the test product is a significant risk device or a nonsignificant risk device; if the determination is significant risk, an IDE will usually be required;

l. For planned emergency research when informed consent will not be obtained, reference to 21 CFR 50.24 (exception to informed consent requirement), the basis for determination that the requirements of 21 CFR 50.24(a)(1-7) are satisfied, and a summary of the IRB review of plans for community consultation per 21 CFR 50.24(b); and

m. A summary of the discussion of noncompliance incidents and other new or old business items.

## 2. Board Approval of Minutes

Board members are notified by email that the minutes have been approved, with instructions for reviewing the minutes in Rascal and/or an attached copy of the minutes. Minutes are ratified, or revisions requested, as applicable, by the full Board at a subsequent meeting of the Board.

## 3. Notification of IRB Action

Investigators are notified in writing of IRB actions in approving, disapproving, suspending, or requiring changes to (in order to approve) research. IOs are provided with copies of minutes that reflect all actions taken at convened meetings as well as all approvals and exempt determinations.

Investigators are notified electronically via Rascal correspondence of reasons for return as well as approvals. Upon approval or return of a submission, the study team receives an automated "action taken" email that advises them that details of the action will be forthcoming via Rascal correspondence. Automated approval emails state that although the submission has been approved, procedures should not commence until the correspondence has been received; this helps to ensure that the study team is aware of the conditions of IRB approval.

LOAs (Reference Document #93) and LODs (Reference Document #96) are also generated and provided in Rascal. Letters may be signed by a Manager, ADO, AD, or ED.

A disapproval notice must include the basis for the disapproval and provide an opportunity, generally within a 30-day timeframe, for the investigator to respond to the Board in person or in writing regarding its action. The Board will consider the response prior to finalizing the disapproval.

A summary of the number of items reviewed, compliance matters, and controverted issues is included in the cover memo (Reference Document #104) that accompanies the minutes when forwarded to the IOs.

## 4. Appeal of IRB Decision

If the Board decides to disapprove a research activity, it must include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in writing. In general, a 30-day timeframe in which to respond will be imposed.

There is no regulatory authority for appeal of Board decisions in suspending or terminating approval of research.

## VIII. Record Retention and Documentation

### A. Records Maintained

All required records and reports specified by applicable federal regulations and these written procedures (45 CFR 46.115; 21 CFR 56.115) are retained in Rascal and/or in IRB files (a paper and/or electronic file may serve as retention of records as a back-up or for some records that were not uploaded in the Rascal system).

Documentation of the following IRB activities and regulatory requirements is maintained:

1. Copies of all research protocols reviewed;
2. Scientific evaluations, if any, which accompany the protocols;
3. Approved consent documents;
4. Statements of significant new findings provided to subjects as required by 45 CFR 116(b)(5), 21 CFR 50.25(b)(5);
5. Copies of all modifications or amendments to protocols;
6. Reports of unanticipated problems;
7. Records of continuing review (i.e., renewal) activities;
8. Progress reports submitted by research investigators;
9. Minutes of IRB meetings (see Section IV.D and VII.E: Meeting Preparation and Follow Up);
10. IRB review (e.g., in Notes, correspondence, IRB reviewer form), including actions taken by a reviewer or Board, approval and expiration dates, determinations (e.g., waiver of informed consent, waiver of documentation of informed consent, Subpart-specific determinations), restrictions (e.g., suspensions, contingencies), and reviewers;
11. Correspondence between the IRB and the research investigators;
12. List of Board members and their alternates identified by:
    a. Name;
    b. Earned degrees;
    c. Representative capacity;
    d. Indications of experiences such as board certifications, licenses, etc.;
    e. Information sufficient to describe each member's chief anticipated contributions to the IRB deliberations; and
    f. Any employment or other relationship between the member and the institution;
10. Board member curriculum vitae, appointment letters, and other relevant correspondence involving member service;
11. Emergency use reports;

12. Reports submitted to the IRB regarding any subject complaints or injuries to subjects;
13. Exemption determinations, including category of exemption;
14. Reviews conducted under an expedited review process, including category, actions taken by the reviewer such as returns or approval, and required determinations;
15. NHSR determinations, if submitted to the IRB via Rascal or to an IRB staff member via email;
16. Investigations related to allegations of noncompliance;
17. Not-for-cause audits; and
18. Interactions with federal regulatory agencies regarding compliance matters.

## B. IRB Files

Each protocol is assigned a unique number and is maintained in an individual file within Rascal. The Rascal electronic record is considered to be the official IRB file. Copies of some submissions or documents relating to submissions may also exist in paper form in file cabinets located in the IRB office area or in electronic form on office servers. Original hard copy IRB records may not be removed from the IRB Office without the written approval of the ED or AD.

IRB records are confidential and access is limited. Individual protocol files are accessible to members of the study team and approvers listed on the submissions, IRB administrative staff, Columbia personnel and business associates who need to access the files to fulfill their institutional or contractual responsibilities (e.g., CTO/SPA/RCT/OFBC staff, OGC, outside counsel), representatives of regulatory and accrediting agencies (e.g., OHRP, FDA, AAHRPP), and others for whom the ED and/or AD have authorized access. Access to IRB minutes and other office files is likewise restricted to individuals with a legitimate need to review the material.

## C. Record Retention Term

1. Research Records

In general, records relating to a specific research activity, including research records collected by investigators, must be maintained for at least three years after completion of the research (45 CFR 46.115(b); 21 CFR 56.115(b); 21 CFR 312.62). This minimum retention period applies whether or not any subjects were enrolled in the study.

a. If the research is FDA regulated, records should be retained for at least two years after approval of the investigational agent by FDA; if it is not approved, records should be retained at least two years after the study is terminated and FDA is notified (note the additional requirement below for clinical research studies);

b. If the research involves clinical intervention or clinical diagnostic procedures at CUMC and/or NYP, the clinical records, including consent forms that document

these research-related procedures, must be retained in medical records by the institution for at least seven years, per CUMC and NYP policy which is based on state law.

2. IRB Records

Protocol-specific IRB records, and IRB records that are not protocol specific (e.g., minutes, rosters, or communications not related to a specific study), in Rascal will be maintained within the system and on backup media so long as Rascal is used as Columbia's protocol submission and tracking system. If Rascal is superseded by another electronic system, and all data are not transferred to that system, the Rascal data will be retained electronically for a period thereafter of at least three years.

Protocol-specific hard copy IRB records that are not in Rascal will be maintained on-site for a minimum of 6 months after termination or withdrawal of the protocol. They may then be transferred to long-term storage off-site.

Hard-copy IRB records that are not protocol specific (e.g., minutes, rosters, or correspondence not related to a specific study) will be maintained on-site for at least 6 months after the period in which they are current. They may then be transferred to long-term storage off-site.

Documents transferred to off-site storage will be retained for at least 3 years.

## D. Procedures if PI Leaves Columbia

If a PI will be moving to another institution, the procedures related to retention of research records will vary depending upon such factors as type of trial, status of the study, and funding. Consultation with the IRB, and if the project is funded, with SPA and/or CTO, should commence as soon as a move is confirmed. Related information related to transfer of funded projects can be found in the Sponsored Projects Handbook.

Subject to approval of the department or school of the faculty member and the terms of funding awards, contracts, or other agreements, the PI may take research records because he/she is responsible for the data. The department or school of the faculty member must retain complete copies of not only the research records that a faculty member may take with him/her upon leaving Columbia, but also complete copies of the research records that were obtained during the study for the above-mentioned retention periods.

Clinical records are the property of the institution and must be retained at CU or NYP, as applicable. If permitted by the relevant institutional policy(ies) related to clinical records, copies that relate to research participation may be made.

If PHI or other sensitive, identifiable data will be removed, an agreement that describes acceptable use and storage of the data may be required if such requirements are not otherwise covered in the terms of a contract or grant.

## E. Confidentiality of Records

IRB records, including records relating to specific research protocols, are kept confidential to the extent possible and allowed by law. However, authorized representatives of sponsors, federal regulatory agencies, University officials, IRB staff, University staff with legitimate access, and IRB Board members may review, inspect, and/or copy records.

## F. Inspection of Records

IRB records are accessible for inspection and copying by authorized representatives of the FDA, OHRP, and other agencies, when appropriate jurisdiction exists, at reasonable times and in a reasonable manner (45 CFR 46.115(b); 21 CFR 56.115(c)). Requests for photocopying and release of any IRB records must be received in writing and approved by the ED or AD.

## G. Off-site Storage of IRB Files

Hard copy study files may be stored off-site if they meet the following qualifications:

- The study has been terminated and no submissions for the file are pending a review;
- The study was disapproved; or
- The study was never approved due to failure to respond satisfactorily to IRB requests.

Off-site storage location: Morgan Manhattan
1405 Jerome Ave.
Bronx, NY 10452
Telephone: 718-538-3976
Fax: 718-538-3978

The storage space is alarm-protected and fireproof. Retrieval of a file is generally completed within 1-2 business days after a request.

Shipment or retrieval of any item to or from off-site storage may occur only after approval is provided by the ED, AD, or ADO. A log is kept in the IRB office of all files transferred to off-site storage.

## IX. Oversight Monitoring

The Columbia HRPP assures oversight monitoring of human subjects research by various means, such as:

1) continuing review of the research by the IRB and inquiries with investigators and/or into research records following concerns raised by IRB review;
2) IRB review of UPs;
3) requiring data and safety monitoring by either an internal or external committee, when applicable;
4) compliance oversight initiatives by the COT, including for-cause and not-for-cause investigations, and oversight monitoring of studies that had prior compliance concerns;
5) additional reviews, investigations or monitoring by the RP, JRSC, RDRC, or IBC;
6) oversight monitoring activities conducted by the Cancer Center Research Management Office (CRMO);
7) COT's review of any audit conducted by a federal agency (e.g., FDA, NCI) or external organization (e.g., audits performed by cooperative oncology groups); these reports are forwarded to the COT; and
6) additional reviews conducted by either the CTO or RCT.

Furthermore, quality improvement efforts provided by the IRB office, as described in Section XI, serve as additional mechanisms to provide oversight monitoring of human subjects research.

### A. Renewal (Continuing Review)

As described in Sections III.D.3, V.A.2, and VI.A.7, continuing review serves a key role in monitoring of all human subjects research that is not exempt. By requiring submission of a report of the progress of the study during the past approval period, the IRB receives information about and insights into the risks associated with the study and the quality of study management. Through these insights, the IRB may make determinations that additional oversight monitoring may be necessary and, in such cases, consider what additional measures may be needed. The IRB may require the study team to provide additional reports, or may refer a given study to the COT for further investigation or audit.

IRB staff and members are mindful of the expiration dates of IRB approval during the review process, particularly when subjects are actively participating and an interruption in the conduct of study procedures may pose an increase in risk to those subjects. While the IRB may not extend the IRB approval period without additional review, consideration by the IRB Chair may be given to allowing the continued participation of enrolled subjects to prevent harm or an increase in risk of harm. Investigators are advised to submit renewal requests sufficiently in advance of the expiration date to ensure sufficient time for review.

## B. Review of Unanticipated Problems Involving Risks to Subjects or Others (including Adverse Events)

The review of UPs (e.g., adverse events, risks, or problems that were not expected at the onset of the research or at the time of the most recent IRB review, related to the research and suggest an increase in risk of harm) provides an important role in the oversight of human subjects in research. The process for IRB review of UPs is described in Sections V.A.4 and VI.A.3. Timing of and action subsequent to IRB review of UPs depends on the severity, relationship to the test article, and whether the event occurred under the auspices of Columbia or at another site that relies on a non-Columbia IRB for review of the event(s). Depending on how these criteria apply to the situation, the CU IRBs review reports of UPs promptly, with a summary required at the time of continuing review.

## C. Data and Safety Monitoring

The IRB will review a data and safety monitoring plan for certain research studies as described in Section V.B.6. During the course of studies conducted by Columbia (either at Columbia or elsewhere), the IRB will review and/or solicit information from the applicable data and safety monitoring board or committee to address any relevant IRB concerns. The IRB will also rely on the data and safety monitoring boards and/or the sponsor to provide assessments of the adverse events and other UPs that may occur during the study.

## D. Reviews or Monitoring by the Research Pharmacy, Radiation Safety Committees, or Institutional Biosafety Committee

For monitoring of human subjects research providing specific risks from radiation, hazardous materials (including research with human organs, tissues, or fluids), or investigational drugs and devices, the IRB may also rely on oversight provided by the RP, JRSC, RDRC, RSO (which provides administrative support to both radiation committees) or the IBC. The Columbia HRPP provides for effective partnering and communication between each of these committees or offices and the IRB as appropriate. The IRB may rely upon either the COT or oversight monitoring by these other groups in lieu of, or as an adjunct to, the oversight monitoring provided by the IRB.

To enhance the oversight of human subjects research/clinical investigations involving ionizing radiation, communication between the IRB and radiation safety committees (i.e., JRSC and RDRC) includes:

1) For any study involving human subjects and an investigational radiopharmaceutical that requires RDRC review, the IRB will forward a copy of the IRB approval to the RDRC.

2) For any study involving human subjects and a radiographic procedure that is not standard practice (or the frequency of the procedure is greater than standard practice), the IRB will forward a copy of the IRB approval to the JRSC.

3) For continuing review of any study covered in items 1 or 2 above, the IRB will forward a copy of continuing review (i.e., renewal) IRB approval to the RDRC or JRSC, as appropriate.

4) For any UP related to an investigational radiopharmaceutical, radiation therapy or a radiographic procedure, the IRB will forward the UP report along with the IRB review of the event to the RDRC or JRSC, as appropriate.

5) Any IRB approval of a modification or amendment to a protocol that involves or affects procedures involving ionizing radiation will be forwarded to the RDRC or JRSC, as appropriate.

When ionizing radiation exposure beyond that required for clinical care is proposed for research purposes, IRB approval to commence the research, at least for the component of research involving radiation, is not granted until RDRC or JRSC approval, as appropriate, has been issued.

## E. Reviews by Research Administration Offices

The CTO (including the IAP), RCT, and SPA each provide additional oversight of human subjects research during their routine review of contracts or grants. Each of these offices will communicate with the IRB office to resolve issues regarding IRB review of human subjects research. Issues commonly addressed include assurance of IRB review of grants, review of subcontracts by the appropriately designated IRB, resolution of conflict of interest issues, terms of payment for research related injuries, and miscellaneous issues that could be identified during the routine review of contracts or grants.

## F. Compliance Oversight

Compliance oversight procedures address two types of Noncompliance: Research Noncompliance and IRB Noncompliance.

"Research Noncompliance" means Noncompliance by anyone other than the ED or any member of the IRB staff or the IRB (in his/her/their capacity as such).

"IRB Noncompliance" means Noncompliance by the ED of the IRB or any member of the IRB staff or the IRB (in his/her/their capacity as such).

For purposes of IRB policy, "Noncompliance" means a failure to comply with University policy or applicable federal and state laws, regulations and policies governing the protection of human subjects in research.

The COT is responsible for the management of all investigations of potential non-compliance. The COT determines, with the direction of the ED, which incidents of potential noncompliance require investigation. If an IRB staff member finds and determines that noncompliance is minor based on established criteria in Appendix 1 of the IRB Noncompliance with Human Subject Regulations" policy (Reference Document #89), the

findings are entered by the appropriate IRB staff into a central IRB database for tracking purposes and aggregate review by the COT. The COT relies on this information to evaluate patterns or behaviors that may suggest poor management or regulatory oversight of a study by the research team.

All other incidents of potential noncompliance are reported to the COT. Based on the seriousness of the allegations, the COT will determine whether an onsite investigation is required and whether a full or targeted audit is appropriate.

The response to an allegation of noncompliance consists of one to three phases, each of which is explained in more detail in the CU "Noncompliance with Human Subject Regulations" policy (Reference Document #89).

**Phase 1 - Inquiry:** the gathering of preliminary information and fact-finding to assess whether an allegation has substance and, if so, whether an Investigation is warranted (an "Inquiry"); this phase is brief and does not involve a substantive analysis of any information, but determines whether the PI is actually conducting, or has conducted, the study, whether the information presented in the allegation appears to be potentially relevant, affiliation of the source of the allegation with the University, and whether any documents should be sequestered.

**Phase 2 - Investigation:** following an Inquiry, the further investigation of facts with respect to whether Noncompliance has occurred (an "Investigation"). This phase may involve an audit/review conducted by the COT. Upon completion of all COT investigations of potential serious noncompliance, a report is released to the PI, and copied to the ED, AD, applicable IRB, applicable department chair and departments, appropriate IO(s), EVPR and, when appropriate, the relevant regulatory agency and sponsor. Determinations that allegations are unfounded are also reported to all relevant parties.

**Phase 3 - Outcome:** following an Investigation, the determination as to whether Noncompliance has occurred and what corrective actions, if any, are required (an "Outcome").

If, at any point in the three phases, serious noncompliance is discovered, the noncompliance is reported to the appropriate regulatory agencies. When an investigation is complete, a follow-up or final letter is sent to the applicable regulatory agencies.

Not-for-cause audits are also conducted by the COT to randomly review IRB-approved research or records and activities for compliance with federal regulations as well as institutional policies. Not-for-cause audits focus primarily on investigator-initiated studies and studies that have little, if any, external oversight.

Additional oversight may consist of ongoing monitoring visits conducted by the COT in cases where a follow-up audit/review may be necessary to confirm that certain necessary corrective actions have been initiated/completed or appropriate follow-up to COT reports has

occurred. Regular ongoing monitoring visits by the COT may be conducted in cases where serious noncompliance was identified.

Related concepts of appeal, reconsideration, and notification to regulatory agencies are also addressed in the CU "Noncompliance with Human Subject Regulations" policy (Reference Document #89), as are guidelines for safeguards for the complainant and respondent, and measures to ensure confidentiality, preserve evidence, and sequester documents.

## X. Education and Training

The CU IRB considers ongoing education of IRB staff, Board members, and research personnel to be of utmost importance in maintaining effective protection of human subjects research conducted under the auspices of the institution.

To the extent possible, documentation of educational activities supported by the IRB and/or attended by staff and IRB members is maintained. See Reference Document #105 for a list of educational events.

### A. Research Community

The following media and initiatives are used to keep the research community at Columbia up to date on matters related to human subjects research:

1. Web sites;

2. Email list servs;

3. Group meetings with research personnel and other individuals involved in the Human Research Protection Program., e.g., Monthly IRB-investigator Meetings, IRB 101 sessions, focus groups with research personnel, Rascal submission and consent form training, and departmental meetings;

4. Clinical Research Handbook;

5. Annual IRB Educational Conference.

The CUMC and CU-MS IRB offices also hold weekly Consultation Hours during which research personnel may obtain consultation from an IRB officer within 15 minutes of arrival, without having to make an appointment. This initiative supplements the service that IRB staff regularly provide through email and phone responses to inquiries, and to consultative meetings scheduled with individual officers.

To facilitate communication between the IRB administrative office and the research community, the IRB maintains one or more email accounts for receipt of inquiries related to the protection of human subjects. The account(s) are monitored, and responses are generated, by IRB staff. Analysis of the inquiries that are received may identify areas in which additional education is needed.

### B. Board Members and Chairs

All incoming Board Members must attend an IRB orientation upon being appointed to the IRB. This session includes exposure to the Belmont Report, relevant federal regulations, IRB policies, and the RASCAL reviewer functions.

The following material is distributed or made available to all newly appointed Board Members:

1. Columbia IRB SOPs; and
2. "Protecting Study Volunteers in Research" (Dunn & Chadwick).

All Board Members are required to have the following training:

1. Appropriate HSP course as required by Columbia policy for research personnel;
2. Columbia University HIPAA course.

Perusal of the OHRP Assurance Training modules is also recommended for IRB Chairs and Members.

All Members are exposed to ongoing educational opportunities such as regional or local IRB conferences and CU IRB sponsored events. An educational event (e.g., conference or educational retreat) is held periodically for all Board Members and staff. Continuing education information is distributed to the Board Members on an ongoing basis, and is posted on the IRB web site for future reference.

All Board Members and Chairs will have access to publications related to the protection of human subjects in research, such as:

1. Newsletters;
2. Relevant articles; and
3. Literature.

**C. Administrative Staff**

The IRB Office holds regular education sessions for IRB staff. These sessions address all facets of human subjects protections.

The following material is distributed or made available to all IRB Staff:

1. Columbia IRB SOPs;
2. "Protecting Study Volunteers in Research" (Dunn & Chadwick).

All IRB Staff are required to have the following training:

1. Appropriate Human Subjects Protection course, as required by Columbia policy for research personnel;
2. Columbia University HIPAA course.

All staff have access to other educational opportunities, as resources allow. These include:

1. Attending local and national IRB conferences;
2. Access to the CITI online training program; and

3. Access to publications related to the protection of human subjects in research, such as:
    a. Newsletters;
    b. Relevant articles;
    c. Literature.

All eligible staff are encouraged to pursue the CIP status, which is obtained through successful completion of a comprehensive exam administered by the Council for Certification of IRB Professionals (CCIP). Details regarding eligibility, the content of the exam, and registration may be obtained from the CCIP website: <http://www.ptcny.com/clients/CCIP>.

IRB staff at the officer level are evaluated formally at least once per year as per the recommendations of the Human Resource department at Columbia. The job descriptions for all IRB officers includes a requirement to stay abreast of both changes to existing relevant regulations and statutes, and those that are newly implemented.

Support staff are regularly provided with feedback from their supervisors regarding performance. All staff members are encouraged to attend informational sessions relative to the protection of human subjects, whether such events are presented by the IRB Office or by another entity.

**D. Researchers**

Before a protocol will be approved by a CU IRB, the PI must complete the HSP course offered by Columbia and receive a passing score of 80 or greater. The course is accessed from the Rascal Training Center but is part of the CITI program administered by the University of Miami. Research personnel other than the PI who have contact with subjects, contact with confidential study data, or are otherwise engaged in the research (i.e., key personnel) must also complete training in the protection of human subjects prior to participation in the research.

Online modules are accessible via the Rascal Training Center and documentation of training is maintained electronically within the Rascal system. Some courses are managed through the CITI system although for proper accounting all users must access the CITI courses through Rascal. In 2011, a requirement for all CU researchers to update their existing Good Clinical Practice (GCP)-Biomedical, GCP-Epidemiological, or CU-MS Human Subjects Training by completing the HSP training course (TC0087) was implemented. In 2012, a requirement for continuing education three years after completion of TC0087 was implemented. The Rascal system sends automated reminders of the need for continuing education at specified intervals prior to the 3-year anniversary of completion of TC0087.

Key personnel on the CUMC campus must also complete the CUMC online HIPAA training course prior to participation in the research. If a protocol submitted by faculty from the CU-

MS campus involves the creation, use, or disclosure of PHI, completion of the HIPAA training course is also required for research personnel named in the submission.

Key personnel involved in human subjects research are required to have the following training:

1. Columbia University HSP training;
2. For all key personnel at CUMC and for key personnel who collect or access PHI at CU-MS, Columbia University HIPAA training;
3. If children will be involved as subjects, the CITI Biomedical Research with Children online module, within the CITI HSP course.
4. If drug(s) or device(s) will be the focus of a study, or clinical research will be conducted, the CITI FDA-regulated Research online module, with "FDA-regulated" research considered to be a) that which is subject to FDA regulation; or b) that which involves clinical procedures (e.g., biomedical testing, collection or handling of biomedical specimens);
5. At CUMC, if an individual's role is Study Coordinator, Regulatory Coordinator, Research Nurse, Data Manager, Research Assistant, or other coordinator role, the Clinical Research Coordinator online module; and
6. If the PI is also the sponsor of the project, meeting the criteria of "sponsor" per FDA regulations, the online S-I module.

The IRB Office holds regular educational sessions for all researchers. Educational opportunities are also available through departmental and divisional meetings, and by request.

Investigators are apprised of new or revised policies, procedures, and regulations by email notification via the IRB listservs and posting on the IRB website.

Explanation for required changes via return correspondence (i.e., in correspondence transmitted when submitted materials are returned to the investigators) provides another avenue for education on a protocol-specific basis.

## XI. Quality Assurance and Improvement

The CU IRB is committed to the improvement of the quality, performance and efficiency of its reviews and internal processes, in addition to those of University research teams with respect to the conduct of research with human subjects. The IRB Office has implemented various processes to monitor performance of the staff and Boards, as well as the effect of their efforts on both quality of submissions and the conduct of approved research. The focus of these activities is on enhancing the ethical conduct of research while also providing optimal customer service. Customers are defined as Investigators, research staff, human subjects, and any other individuals or entities involved with the Columbia HRPP.

Quality assurance and improvement activities are administered primarily through the ED, AD, and ADO who oversee the collection and processing of data that enables the IRB Office to quantify and assess the performance and efficiency of the IRB and the University researchers (relative to quality and timeliness of submissions and responsiveness to IRB requests). In addition to data collected manually for assessment, Rascal reports are generated as necessary by, or under the direction of, the ADO, AD, or ED.

### A. Assessment and Improvement Initiatives of Internal Processes

Reports may be prepared on a regular schedule, such as the retinue of weekly reports described below, or on an ad hoc basis. Reports to be prepared will be determined based on institutional and office needs. Reports are forwarded to the ED, AD, and/or ADO for review. Managers are copied on weekly reports, which function as one tool by which they manage their team's work.

The ADO or designee is responsible for the primary analysis of data and other information that is collected on the quality and performance of the overall IRB operation. Recommendations made by the ED, AD, ADO and Managers for specific types of reviews or events, based on these data analyses, are forwarded to the relevant individuals within the operation. Recommendations and comprehensive reports prepared under the direction of the ED, AD, or ADO are forwarded, as appropriate, to the IRB Executive Committee.

Knowledge gained from the measures described provides input for educational efforts and provides an opportunity to improve a process or policy.

Weekly reports include the following, all of which are distributed to Managers, and the ED, AD, and ADO:

1. Administrator Correspondence Queue report: Measures the number and timeliness of responses to the researchers in the Rascal system with respect to individual IRB review.
2. Log In Queue report: Measures the number and timeliness of reviews of submissions and responses from researchers to previous IRB correspondence or actions.

3. Delayed IRB Reviews by Team report: Identifies individual reviews by IRB members that are pending for longer than two weeks but less than one month, and longer than one month.

Monthly and quarterly reports of pre-reviews of new protocols, approval of IRB meeting minutes, and IRB turnaround time are also provided.

**B. Assessment and Improvement of External Processes**

Various procedures will be conducted to assess the impact of IRB performance on researchers, to identify areas for which education or training efforts should be implemented, to ensure that study procedures are conducted in accordance with the protocol that was approved by the IRB, and to gain an understanding of the services the IRB may provide that may facilitate the ethical conduct of research.

These procedures may include, but are not limited to:

1. Researchers and research subjects will be surveyed periodically to determine levels of satisfaction and to identify areas in need of improvement.
2. Informed consent processes will be randomly monitored.
3. Unanticipated Problem reporting will be monitored for timeliness of the reporting and compliance with the Columbia Reporting to the IRB of Unanticipated Problems Policy.

Processes, whether newly instituted, recently improved, or ongoing, will be monitored continuously for their effectiveness.

## XII. Subject Outreach

### A. Information for Potential Subjects

Information regarding the rights of research participants, and issues that an individual should consider prior to enrolling in a research study, are distributed throughout clinical areas at CUMC and are posted on the IRB website.

The IRB Office maintains a relationship with Community Board #12, which represents the Washington Heights area surrounding CUMC, and is developing a relationship with the community board(s) surrounding Morningside Heights. The primary objective for these interactions is to inform the community about the role of the IRB and its efforts to ensure the ethical conduct of research, and to address any concerns that the community may have regarding research. Additionally, the IRB offers opportunities to inform the community about the differences between standard practice and research, the consent process for research, and what information one should obtain to make an informed decision whether or not to participate in a study.

On the CU-MS campus, outreach efforts are focused on students, who are the most frequent subjects in research that is conducted on campus. Much of the research originating from CU-MS faculty is conducted at non-Columbia sites both in the U.S. and abroad.

The IRB also endeavors to be present at local health fairs and other community events where information about the rights of participants in research may be disseminated.

Posted on the CUMC and CU-MS IRB home pages is a link entitled “For Research Subjects.” This link provides information that will inform potential subjects of what they should know when considering participation in a research study. This information is also provided in pamphlets that are distributed at local health fairs and community events. The CUMC IRB website also provides a link to the ClinicalTrials.gov website that provides basic information about open clinical trials under the purview of the FDA.

ResearchMatch is an online recruitment tool through which individuals may enter their interest in research participation, and researchers may obtain this information along with the individuals’ contact information. A link to the ResearchMatch portal is provided on the CUMC IRB website.

### B. Information from Research Subjects and the Community

The IRB Office receives information from investigators relating to community attitudes and preference about research participation, particularly in regards to recruitment, privacy, and confidentiality. This information is obtained by the investigators through surveys, interviews, and focus groups that are administered under IRB-approved protocols, and is informative to the IRB review process.

## C. Compliance Hotline

The University maintains a confidential hotline through which concerns, about research conducted by Columbia personnel, may be reported by individuals who believe that they have observed unethical, illegal or suspicious behavior. Reports are confidential and allegations may be submitted anonymously. The phone number for the Hotline and a link to the website are posted on the CUMC IRB and CU-MS IRB websites.

Appendix I: Abbreviations and Terms Used in Columbia University IRB Standard Operating Procedures 2012

A: Alphabetical Order

| Abbreviation or Term* | Explanation | First Use |
|---|---|---|
| AAHRPP | Association for the Accreditation of Human Research Protection Programs | Intro |
| ACS | Administration for Children's Services | VI |
| AD | Associate Director, IRB | Intro |
| ADO | Assistant Director for IRB Operations | I |
| ARC | Administrative Review Committee | Intro |
| BB-IND | Biologic IND | III |
| CBE | Center for Bioethics | I |
| CC-DSMP | Cancer Center Data and Safety Monitoring Program | V |
| CCIP | Council for the Certification of IRB Professionals | X |
| CDC | Center for Disease Control and Prevention | VI |
| CFR | Code of Federal Regulations | Intro |
| CIOMS | Council of International Organization of Medical Sciences | VI |
| CIP | Certified IRB Professional | I |
| CIRB | Central Review Board | II |
| CITI | Collaborative IRB Training Initiative | III |
| COC | Certificate of Confidentiality | III |
| COI | Conflict of Interest | I |
| Columbia | Columbia University | Intro |
| COT | Compliance Oversight Team | I |
| CRC | Clinical Research Center | I |
| CRCT | Clinical Research Coordinator Training | I |
| CRMO | Cancer Center Regulatory Management Office | III |
| CTMAP | Clinical Trials Monitoring Assistance Program for FDA Regulated Human Subjects Research | I |
| CTO | Clinical Trials Office | Intro |
| CTSA | Clinical and Translational Service Award | I |
| CU | Columbia University | Intro |
| CUMC | Columbia University Medical Center | Intro |
| CU-MS | Columbia University – Morningside campus | Intro |
| DHHS or HHS | United States Department of Health and Human Services | Intro |
| DNA | Deoxyribonucleic acid | III |
| DoOD | U.S. Department of Defense | II |
| DOE | Department of Education | III |
| DSMB | Data and Safety Monitoring | III |
| DSMC | Data and Safety Monitoring Committee | V |
| ED | Executive Director, HRPP | Intro |
| EU | Emergency Use | III |

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| Events * | RASCAL term for submissions to the IRB for review (e.g., new protocol, modification, renewal) | III |
| EVPHBS | Executive Vice President for Health and Biomedical Sciences and Dean of the Faculties of Health Sciences and Medicine | Intro |
| EVPR | Executive Vice President for Research | Intro |
| FDA | United States Food and Drug Administration | Intro |
| FERPA | Family Education Rights and Privacy Act | II |
| FWA | Federal-wide Assurance | Intro |
| GCP | Good Clinical Practices | X |
| HCP | Healthcare Proxy | V |
| HDE | Humanitarian Device Exemption | VI |
| HHS | United States Department of Health and Human Services | Intro |
| HICCC | Herbert Irving Comprehensive Cancer Center | I |
| HIPAA | Health Information Portability and Accountability Act | I |
| HRPP | Human Research Protection Program | Intro |
| HSP | Human Subjects Protection | V |
| HUD | Humanitarian Use Device | VI |
| HVTN | HIV Vaccine Trials Network | II |
| IAA | IRB Authorization Agreement | II |
| IAP | IND/IDE Assistance Program | I |
| IBC | Institutional Biosafety Committee | I |
| ICH | International Conference on Harmonization | Intro |
| IDB | Investigational Drug Brochure | III |
| IDE | Investigational Device Exemptions | I |
| IEC | IRB Executive Committee | I |
| IIA | Individual Investigator Agreement | II |
| IICTR | Irving Institute for Clinical and Translational Research | I |
| IND | Investigational New Drug | I |
| IO | Institutional Official | Intro |
| IRB | Institutional Review Board | Intro |
| IRB Exp | CUMC IRB for all research that initially qualifies for expedited review | II |
| IT | Information Technology | Intro |
| JRSC | Joint Radiation Safety Committee y | I |
| LAR | Legally Authorized Representative | V |
| LOA | Letter of Approval | IV |
| LOD | Letter of Disapproval | IV |
| MNCD | Minor Noncompliance Database | VI |
| MSCHONY | Morgan Stanley Children's Hospital of New York | Intro |
| NCI | National Cancer Institute | II |
| NGS | National Government Services | III |
| NHSR | Not Human Subjects Research | IV |
| NHSR per 45 CFR 46 | Not Human Subjects Research per 45 CFR 46 | IV |

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|---|---|---|
| NIH | National Institutes of Health | I |
| NSF | National Science Foundation | III |
| NSR | Non-sSignificant Risk designation for medical device | VI |
| NYC | New York City | I |
| NYP | New York Presbyterian Hospital | Intro |
| NYS | New York State | VI |
| NYSPI | New York State Psychiatric Institute | I |
| OFBC | Office for Billing Compliance | I |
| OGC | Office for General Counsel | Intro |
| OHRP | United States Office for Human Research Protection | II |
| PHI | Protected Health Information | V |
| PHS | Public Health Service | III |
| PI | Principal Investigator | I |
| PMA | Premarket Approval | VI |
| PO | Privacy Officer | I |
| PRMC | Protocol Review and Monitoring Committee | I |
| PSA | Patient Services Administration | I |
| RAC | Recombinant DNA Advisory Committee at NIH | III |
| RCT | Office for Research Compliance and Training | Intro |
| RDRC | Radioactive Drug Research Committee | I |
| RP | Research Pharmacy | I |
| RSO | Radiation Safety Office | I |
| S-I | Sponsor-Investigator | I |
| SOP | Standard Operating Procedures | Intro |
| SPA | Sponsored Projects Administration | Intro |
| SR | Significant Risk designation for medical device | VI |
| SSA | SEIU United Healthcare Workers East, Supporting Staff Association Area | I |
| SSNs | Social Security Numbers | III |
| STC | Spanish Translation Center | I |
| The University | Columbia University | Intro |
| U.S. | United States | Intro |
| UAW | Local 2110 International Union, UAW/AFL-CIO Technical, Office and Professional Workers | I |
| UP | Unanticipated Problem involving Risks to Subjects or Others | III |
| VPRO | Vice President for Research Operations | Intro |

Appendix I: Abbreviations and Terms Used in Columbia University IRB Standard Operating Procedures 2012
B: In Order of Appearance

| Abbreviation or Term* | Explanation | First Use |
|---|---|---|
| Columbia | Columbia University | Intro |
| CU | Columbia University | Intro |
| The University | Columbia University | Intro |
| HRPP | Human Research Protection Program | Intro |
| AAHRPP | Association for the Accreditation of Human Research Protection Programs | Intro |
| NYP | New York Presbyterian Hospital | Intro |
| FWA | Federal-wide Assurance | Intro |
| CUMC | Columbia University Medical Center | Intro |
| CU-MS | Columbia University – Morningside campus | Intro |
| MSCHONY | Morgan Stanley Children's Hospital of New York | Intro |
| EVPR | Executive Vice President for Research | Intro |
| ED | Executive Director, HRPP | Intro |
| IRB | Institutional Review Board | Intro |
| VPRO | Vice President for Research Operations | Intro |
| IO | Institutional Official | Intro |
| EVPHBS | Executive Vice President for Health and Biomedical Sciences and Dean of the Faculties of Health Sciences and Medicine | Intro |
| SOP | Standard Operating Procedures | Intro |
| U.S. | United States | Intro |
| DHHS | United States Department of Health and Human Services | Intro |
| HHS | United States Department of Health and Human Services | Intro |
| FDA | United States Food and Drug Administration | Intro |
| ICH | International Conference on Harmonization | Intro |
| AD | Associate Director, IRB | Intro |
| ADO | Assistant Director for IRB Operations | I |
| OGC | Office for General Counsel | Intro |
| CTO | Clinical Trials Office | Intro |
| SPA | Sponsored Projects Administration | Intro |
| RCT | Office for Research Compliance and Training | Intro |
| IT | Information Technology | Intro |
| ARC | Administrative Review Committee | Intro |
| CFR | Code of Federal Regulations | Intro |
| IEC | IRB Executive Committee | I |
| COT | Compliance Oversight Team | I |
| HIPAA | Health Information Portability and Accountability Act | I |
| SSA | SEIU United Healthcare Workers East, Supporting Staff Association Area | I |

| | | |
|---|---|---|
| UAW | Local 2110 International Union, UAW/AFL-CIO Technical, Office and Professional Workers | I |
| CIP | Certified IRB Professional | I |
| PO | Privacy Officer | I |
| OFBC | Office for Billing Compliance | I |
| RP | Research Pharmacy | I |
| IND | Investigational New Drug | I |
| IDE | Investigational Device Exemptions | I |
| IAP | IND/IDE Assistance Program | I |
| CTMAP | Clinical Trials Monitoring Assistance Program for FDA Regulated Human Subjects Research | I |
| CRCT | Clinical Research Coordinator Training | I |
| STC | Spanish Translation Center | I |
| S-I | Sponsor-Investigator | I |
| COI | Conflict of Interest | I |
| JRSC | Joint Radiation Safety Committee y | I |
| NYSPI | New York State Psychiatric Institute | I |
| NYC | New York City | I |
| RDRC | Radioactive Drug Research Committee | I |
| RSO | Radiation Safety Office | I |
| IBC | Institutional Biosafety Committee | I |
| PRMC | Protocol Review and Monitoring Committee | I |
| HICCC | Herbert Irving Comprehensive Cancer Center | I |
| IICTR | Irving Institute for Clinical and Translational Research | I |
| NIH | National Institutes of Health | I |
| CTSA | Clinical and Translational Service Award | I |
| CRC | Clinical Research Center | I |
| PSA | Patient Services Administration | I |
| CBE | Center for Bioethics | I |
| PI | Principal Investigator | I |
| DoE | U.S. Department of Education | |
| FERPA | Family Education Rights and Privacy Act | II |
| DOD | U.S. Department of Defense | II |
| OHRP | United States Office for Human Research Protection | II |
| IRB Exp | CUMC IRB for all research that initially qualifies for expedited review | II |
| IAA | IRB Authorization Agreement | II |
| NCI | National Cancer Institute | II |
| CIRB | Central Review Board | II |
| HVTN | HIV Vaccine Trials Network | II |
| IIA | Individual Investigator Agreement | II |
| Events * | RASCAL term for submissions to the IRB for review (e.g., new protocol, modification, renewal) | III |
| CITI | Collaborative IRB Training Initiative | III |
| PHS | Public Health Service | III |

| | | |
|---|---|---|
| NSF | National Science Foundation | III |
| CRMO | Cancer Center Regulatory Management Office | III |
| COC | Certificate of Confidentiality | III |
| SSNs | Social Security Numbers | III |
| DSMB | Data and Safety Monitoring | III |
| UP | Unanticipated Problem involving Risks to Subjects or Others | III |
| EU | Emergency Use | III |
| IDB | Investigational Drug Brochure | III |
| DNA | Deoxyribonucleic acid | III |
| RAC | Recombinant DNA Advisory Committee at NIH | III |
| BB-IND | Biologic IND | III |
| NGS | National Government Services | III |
| NHSR | Not Human Subjects Research | IV |
| NHSR per 45 CFR 46 | Not Human Subjects Research per 45 CFR 46 | IV |
| LOA | Letter of Approval | IV |
| LOD | Letter of Disapproval | IV |
| HSP | Human Subjects Protection | V |
| PHI | Protected Health Information | V |
| HCP | Healthcare Proxy | V |
| LAR | Legally Authorized Representative | V |
| DSMC | Data and Safety Monitoring Committee | V |
| CC-DSMP | Cancer Center Data and Safety Monitoring Program | V |
| MNCD | Minor Noncompliance Database | VI |
| NSR | Non-Significant Risk designation for medical device | VI |
| SR | Significant Risk designation for medical device | VI |
| PMA | Premarket Approval | VI |
| HUD | Humanitarian Use Device | VI |
| HDE | Humanitarian Device Exemption | VI |
| ACS | Administration for Children's Services | VI |
| CIOMS | Council of International Organization of Medical Sciences | VI |
| NYS | New York State | VI |
| CDC | Center for Disease Control and Prevention | VI |
| CCIP | Council for the Certification of IRB Professionals | X |
| GCP | Good Clinical Practices | X |

## Appendix II
## Referenced Regulations, Laws, Standards

The Belmont Report; Ethical Principles and Guidelines for the Protection of Human Subjects of Research

Department of Health and Human Services (HHS) Regulations for the Protection of Human Subjects

United States Food and Drug Administration (FDA) **r**egulations for the Protection of Human Subjects

HHS/FDA List of Expedited Review categories

Department of Education FERPA (Family Educational Rights and Privacy Act) regulations

Department of Defense regulations

Health Insurance Portability and Accountability Act (HIPAA) Privacy Standard

New York State Laws 2440/441

New York State Law Article 7, Section 79-1 Confidentiality of Genetic Tests

New York State Family Health Care Decisions Act

International Conference on Harmonization (ICH) "Guidance for Industry- E6 Good Clinical Practice: Consolidated Guideline"

AAHRPP Accreditation Standards