

**COLUMBIA UNIVERSITY**  
**IN THE CITY OF NEW YORK**



**Institutional Review Board**  
**Standard Operating Procedures**

Version 5.1: Effective April 12, 2018

Version 5.0: Effective December 21, 2017

# Columbia University Institutional Review Board

## Standard Operating Procedures

Version 5.1 April 12, 2018  
Version 5.0 December 21, 2017

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## I. Introduction to the Columbia Human Research Protection Program

Columbia University (CU or Columbia or the University)<sup>1</sup> 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 program 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, conduct and oversight of human research by Columbia faculty, staff, students and others acting as agents of Columbia, whether conducted at a Columbia campus or elsewhere. CU has two Federalwide Assurances (FWAs): one for the Columbia University Medical Center (CUMC) and one for the Morningside and Lamont campuses (CU-MS). Research activities at Columbia's Manhattanville campus are conducted by researchers who are affiliated with a department or school at one of the other campuses; hence, the research is covered under the respective FWA. Columbia provides IRB review services for the NewYork-Presbyterian Hospital (NYP) on the CUMC campus and for other designated affiliates of NYP. NYP is a separate legal entity from CU and the NYP facilities for which Columbia provides IRB review each have their own FWA. 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<sup>2</sup>, NYP-Hudson Valley Hospital and NYP-Lawrence Hospital. The Columbia HRPP maintains five FWAs and is responsible for all human subjects research conducted at CUMC, CU-MS, and the afore-mentioned components of NYP, or by any affiliated faculty, students, or staff of CU and NYP, as applicable, regardless of location of the research. Please see Section II.A.5 for the criteria used to determine whether specific 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

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<sup>1</sup> Please see Appendix I for a list of all abbreviations.

<sup>2</sup> NewYork-Presbyterian Hospital has facilities that are affiliated with either Columbia University or Cornell University. At Columbia, the primary facilities are Allen Hospital, Milstein Hospital, Herbert Irving Pavilion and the Morgan Stanley Children's Hospital of New York (MSCHONY) (collectively, "NYP at Columbia"). The Columbia IRBs also provide IRB review for human subjects research at Lawrence Hospital and for certain such research at Hudson Valley Hospital; both are NYP affiliates. For simplicity, all of these affiliates of NYP will be referenced as "NYP".



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, researchers also actively conduct research at other sites both domestic and international. Furthermore, many Columbia researchers collaborate on projects with investigators at other institutions. The Columbia HRPP processed approximately 2,200 new human research studies in 2016, and manages approximately 6,000 studies that have been approved or determined to be exempt.

## **A. Institutional Leadership**

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 Office](#) (ED), who is also responsible for the management of all Institutional Review Board (IRB) operations at CU. Section I of these written procedures outline and summarize the Columbia HRPP.

The ED reports to the EVPR, through the Chief Operating Officer of the Office of the Executive Vice President for Research and Vice President for Research Operations and Policy (VPRO), and ensures that the Institutional Officials (IOs) designated on the FWAs of CUMC, CU-MS, and NYP are kept apprised of all pertinent information. 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 and Dean of the Faculties of Health Sciences and Medicine, and Chief Executive, Columbia University Medical Center (Dean, CUMC), 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. Neither the EVPR, nor other Columbia or NYP officials, may approve research involving human subjects that has not been approved by a Columbia IRB or an IRB upon which Columbia is relying. 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.

Evaluation of resources needed for the HRPP is conducted at least annually and includes consideration of the needs of all components of the HRPP that are under the purview of the EVPR. In conjunction with the VPRO, leadership within each research administrative office considers the requirements of their respective unit in terms of personnel, space, equipment, and any other factor relevant to attainment of unit goals. In addition, resources required to maintain regulatory review committees, including IRBs, radiation safety committees, and the institutional biosafety committee, are evaluated at least annually. Financial and other resources needed to ensure adequate education and training activities for members of the research community and administrative personnel, production of handbooks and other university-wide research tools, quality assurance and improvement activities for the entirety of the research program, and maintenance of the Office of the EVPR are also routinely evaluated. The EVPR and VPRO assess the support received from University and external legal counsel, and other offices that provide research-related services throughout the University, in terms of availability, expertise, and adequacy to meet the needs of research-related offices and functions.

## **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. These procedures describe the means by which research with human subjects will be reviewed, approved, and monitored.

The IRB SOPs comply, where applicable, 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 humans. The written procedures also comply with the International Conference on Harmonization (ICH) "[Guidance for Industry- E6 Good Clinical Practice: Consolidated Guideline](#)," to the extent that they are consistent with federal law and regulations,

Review of protocols supported or conducted by other federal agencies, such as the Department of Defense (DoD), Environmental Protection Agency (EPA), U.S. Department of Education (DOE), U.S. Department of Energy (DOEn), and the National Institutes of Justice (NIJ), includes consideration of compliance with the agency's regulations for the protection of human subjects. Similar considerations are made for research that is subject to additional federal policies, e.g., conducted within facilities under the purview of the Bureau of Prisons, subject to the [Family Educational Rights and Privacy Act](#) (FERPA), or subject to the [Protection of Pupil Rights Amendment](#) (PPRA).

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, or otherwise as necessary, under the direction of the ED.

The IRB SOPs will be reviewed regularly. 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 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, and the relevant Director(s), Assistant Director, Senior Manager(s) and, when appropriate, to all IRB Chairs, the VPRO 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 signoff by the ED.
  - 2) If substantive changes are made during the review period, a revised version is again circulated as described above. 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, the need to release a new or revised policy is time-sensitive or the process is not moving forward.

- 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, Office of Research Administration, which includes the 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 CU HRPO/IRB listserv, at a minimum, and posted on the CU HRPO website. Appropriate individuals (e.g., research personnel, HRPO 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 relevant Director, any change to the SOPs may be implemented immediately without following this process if a determination is made by the ED or the relevant Director 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 administration and compliance Information Technology (IT) system. Non-exempt projects must be prospectively approved by the appropriately designated IRB under one of Columbia's FWAs or by an IRB to which Columbia has ceded IRB review through the terms of a reliance agreement. 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. It is a Columbia policy that investigators may not make the final determination of exemption, i.e., protocols that appear to meet federal criteria for exemption must be submitted in Rascal 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.)

*Systematic Investigation*: an activity that involves a prospective study plan that incorporates data collection and analysis, either quantitative or qualitative, to answer a study question. Investigations designed to develop or contribute to **generalizable knowledge** are those designed to draw general conclusions (i.e., knowledge gained from a study may be applied to populations outside of the specific study population or situation).

*Human subject*: a living individual about whom an investigator (whether professional or student) conducting research obtains

- (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*" and "*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 under section 505(i) or 520(g) of the Food, Drug and Cosmetic Act, or is not subject to requirements for prior submission to the FDA under these sections of the act, but 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\(c\)](#)). The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical laboratory studies.

When the FDA Investigational New Drug (IND) regulations ([21 CFR 312](#)) apply, “clinical investigation” is defined as any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice ([21 CFR 312.3\(b\)](#)).

When the FDA Investigational Device Exemption (IDE) regulations ([21 CFR 812](#)) apply, an “investigation” is defined as a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device ([21 CFR 812.3\(h\)](#)).

Emergency use of a test article, other than a medical device, is considered a clinical investigation, and FDA may require data from emergency uses for a marketing application [21 CFR 56.104(c)]. See FDA Guidance, “[Emergency Use of an Investigational Drug or Biologic - Information Sheet](#)” for additional information.

*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 act or under sections 351 and 354-360F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n); ([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\(e\)](#)).

When the FDA IDE regulations ([21 CFR 812](#)) apply, a “subject” is defined as a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease ([21 CFR 812.3\(p\)](#)).

Patients who are recipients of test articles in emergency use situations are considered human subjects, about whom FDA may require data for a marketing application. When medical device research involves *in vitro* diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human subjects.

## **F. Rascal**

Rascal was developed at Columbia to facilitate the management, review, and oversight of Columbia research, and facilitate 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, regardless of whether a Columbia IRB is the Reviewing IRB. When a non-Columbia IRB serves as the Reviewing IRB, the protocol must be submitted in Rascal for tracking purposes and to confirm satisfaction of local requirements. The Rascal 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 (HRPP)**

A brief overview of the Columbia HRPP is provided below.

### **A. Institutional Review Boards and Human Research Protection Office (HRPO)**

The mission of the CU IRBs and the CU HRPO, 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, and other Columbia and NYP researchers, regardless of location of the research. The CU IRBs perform this mission through their review of human subjects research, and are supported in this endeavor by the HRPO 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 Dean of CUMC, the President of NYP, and the EVPR, each of whom 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 HRPO 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 HRPO is responsible for the management and oversight of all IRBs at CU-MS and CUMC. In addition, the HRPO 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 HRPO is a team that consists of the ED, the Directors in the areas of Operations, IRB Management and Compliance Oversight and the Assistant Director for IRB Management (collectively, D/ADs) that works closely with the managers of the teams that directly support the IRBs. The HRPO has two locations: a) on the CUMC campus, and b) on the Manhattanville campus, (see Reference Document #160, IRB Contact Information, for current addresses).

The HRPO convenes ad-hoc meetings that involve the heads of other HRPP units as necessary to address any incidents or issues that may require consideration from or action by one or more of those units. As warranted, the ED or other director 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 ED also leads twice monthly 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 D/ADs. 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. Managers and Assistant Managers are encouraged to attend IEC meetings. When agenda items warrant, all IRB officers are also encouraged to 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. HRPO Administrative Staff**

The ED maintains overall responsibility for the management of all CU IRBs and the HRPO staff. Oversight of the performance and management of specific areas have been delegated to the D/ADs:

- IRB Operations to the Director for Operations (DO), who reports to the ED
- Day to day activities of all CU IRBs to the Director for IRB Management (DIM), who reports to the ED and to whom the Assistant Director for IRB Management (ADIM) reports. Each IRB Chair and IRB Manager are responsible for the daily management of their respective Board;
- Compliance Oversight to the Director for Compliance Oversight (DCO), who reports to the ED.

The HRPO 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 HRPO is evaluated internally on an ongoing basis by the ED and D/ADs, with input from the IRB Managers, as applicable, and additional support is provided as needed. Through regular meetings with the VPRO and CUMC IO, the ED communicates office-wide requests for additional support as warranted.

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



## **a. Organization**

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

Each IRB is administered by a team of staff comprised of a senior HRPO staff member, who will generally be a Manager or Senior Manager, and at least one other officer. A Senior Manager may oversee more than one IRB or review committee, or have defined office-wide responsibilities in addition to managing a team that supports a specific IRB. 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 teams whose submissions have been reviewed.

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 or review template based on the type of submission. The pre-review process is designed to help ensure that each submission is complete and can proceed for review by an IRB member or, in the case of CUMC exempt research, an HRPO officer, and that each study will receive all relevant regulatory considerations. Once a study has undergone 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 DCO and auditors. The COT is responsible for investigating, managing and tracking 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 tracking all other allegations and incidents of noncompliance. Allegations of noncompliance, concerns, or complaints may be received from anyone, e.g., the IRBs, HRPO 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, concerns and complaints, as well as any event that must be reported to federal regulatory agencies (e.g., serious and/or continuing noncompliance, certain unanticipated problems, and suspension of IRB approval) are logged by the COT into a database for tracking and reporting purposes. The DCO keeps the ED informed of all cases through regular meetings and reports. The COT also works with the Office for HIPAA Compliance (OHC) regarding any concern or finding of research noncompliance with the Health Insurance Portability and Accountability Act (HIPAA).

Alleged incidents of noncompliance are handled in accordance with the CU Noncompliance with Human Subjects Regulations Policy (Reference Document #89). When a determination of noncompliance has been made by an IRB, an appropriate corrective and preventive action plan is developed, as applicable, and documentation of the determination is provided through IRB meeting minutes, Notes in Rascal and/or a COT report. When a COT investigation is involved, and under certain other circumstances, a report is filed with the respective IRB, the appropriate IO(s), the EVPR, and when appropriate, with the relevant regulatory agency(ies) and sponsor. The COT monitors studies where it is deemed necessary to perform follow up reviews of corrective and preventive action plans.

The COT also conducts routine or “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, and for individual professional development, periodic performance evaluations, minimally once per year, are conducted for officer-level staff, and regular feedback is provided to support level staff. Collective Bargaining Agreements with the University guide the supervision and employment of support staff.

#### **c. Education and Training**

HRPO 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. In addition, all officers and supervisory staff are required to complete certain training courses required by Human Resources. HRPO staff are provided ongoing and continuing educational opportunities (e.g., professional development and regulatory seminars, conferences and workshops; HRPO informational sessions; distribution of continuing education information; and access to the HRPO website and document library). 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 and supported.

Details of education and training initiatives are provided in Section X.C of these SOPs.

#### **d. Confidentiality and Conflict of Interest**

All HRPO 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 HRPO, holds regular educational sessions for HRPO staff, members of the CU research community, and IRB members. The Committee is chaired by an experienced officer on the HRPO staff. Committee membership is comprised of HRPO staff, each of whom contributes to an active, year-round schedule of events that includes monthly IRB-investigator meetings, IRB conferences, “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.

#### **b. Policy Committee**

The Policy Committee, also established in 2003 within the HRPO, 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 HRPO staff. Committee membership is comprised of HRPO staff, but may include individuals from outside of the IRB.

#### **c. Accreditation Committee**

The Accreditation Committee, which was established in 2004 within the HRPO, is chaired by an experienced HRPO officer, 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 by AAHRPP, originally granted in 2010, can be maintained.

#### **d. Rascal Committee**

The Rascal Committee was established in 2004 within the HRPO 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 HRPO staff, and is comprised of HRPO staff. An executive subcommittee consisting of the ED and DO 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 HIPAA Privacy Rule. The implementation of policies and processes to ensure such compliance is the responsibility of the Chief Privacy Officer (CPO), who directs the [Office of HIPAA Compliance](#) and reports to the Billing Compliance Officer within the Office for Billing Compliance (OFBC). The CPO coordinates such efforts with the ED and/or D/ADs of the HRPO, 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, is responsible for the administration of all sponsored research conducted by Columbia. SPA works closely with the HRPO staff to ensure that all such human subjects research has obtained appropriate IRB approval prior to creation of an account for research funding and prior to execution of any data sharing or material transfer agreements. Any potential noncompliance with the regulations for human subjects protection that is identified by a SPA staff member is promptly reported to the ED and/or the DCO.

## **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 and/or the DCO. The CTO also administers the Research Pharmacy (RP), the Investigational New Drug (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). The CTO also manages the Departmental Quarterly Monitoring Program.

### **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 may serve on one or more of the CUMC IRBs. The close working relationship between the RP and the IRB not only provides pharmacy input to the IRBs, but also helps to 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 and/or the DCO.

### **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 services 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 HRPO 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 and/or the DCO.

### **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 (Reference Document #101). Any document that will be translated by the STC or other acceptable translation options must first be approved in English by the IRB. Final approval by the

IRB of translated document(s) is granted after review and approval of the translated document certified by the STC or accompanied by a certification of accuracy by another translator. Any potential noncompliance with the regulations for human subjects protection that is identified by the STC is promptly reported to the ED and/or DCO. 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.

## **5. Departmental Quarterly Monitoring Program**

On a quarterly basis, departments are required to provide a report of the monitoring of clinical research that has been conducted during the preceding quarter. Each department or, in the case of smaller departments, a group of departments, has a designated monitor who conducts the reviews and generates a report that is provided to the research team, department and the CTO. Summaries of the reports are generated by the CTO and distributed to designated institutional representatives including the Senior Vice Dean, the General Counsel, the VRPO, the Vice President for Research Administration, and the ED.

### **E. Office of Research Compliance and Training**

RCT develops and provides certain educational training initiatives for Research Administration Offices that do not have their own education training program, or to supplement other training. RCT works with the Columbia HRPO on an ad hoc basis to complement the educational training initiatives of the HRPO.

RCT also provides certain compliance oversight efforts. One such effort is to manage 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 officers 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 with the IRB in both protocol review and compliance matters. Any study that includes research-only ionizing radiation procedures with 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 and/or the DCO.

#### **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. The ED is a member of the IBC and the DO serves as an alternate. Any potential noncompliance with the regulations for human subjects protection that is identified by the IBC is promptly reported to the ED and/or the DCO.

#### **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 through Rascal 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 and/or the DCO.

## **I. Irving Institute for Clinical and Translational Research**

The Columbia Irving Institute for Clinical and Translational Research (ICTR) has been awarded a 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 Resource](#) (CRR) that allows investigators to conduct both inpatient and outpatient studies involving adults and children. All research conducted at the CRR is first reviewed by a scientific review committee called the CRR Advisory Committee. The ED serves as an ex-officio member of the CRR Advisory Committee. Any problems or concerns with a proposed study involving human subjects that is raised during the CRR scientific review are forwarded to the HRPO for consideration by the IRB, as appropriate. Likewise, any potential noncompliance with the regulations for human subjects protection that is identified by the CRR is promptly reported to the ED and/or the DCO.

## **J. NYP Pharmacy**

The NYP Pharmacy works with the CUMC Research Pharmacy and the HRPO 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 HRPO 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 and/or the DCO.

## **K. NYP and Columbia Doctors Patient Services Administration/Office**

The NYP Patient Services Administration (PSA) and the Columbia Doctors Patient Services Office are 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, these offices serve as a possible repository of concerns expressed by research subjects. They have established a close working relationship with the HRPO to ensure that any concerns from research subjects who participate in human research conducted at NYP on the CUMC campus are addressed satisfactorily. The HRPO and patient services offices will inform each 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 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. In 2018 the Center's role will be taken on and expanded by the new Department of Humanities and Medical Ethics at CUMC currently under development.

### **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 human subject research 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 and/or the DCO.

## 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](#), [D](#) and [E](#);
- b. the U.S. FDA regulations, 21 CFR Parts [50](#), [56](#), [312](#), [600](#), and [812](#);
- c. the Department of Education (DOE) regulations [34 CFR 97](#) including the Family Education Rights and Privacy Act (FERPA), [34 CFR 99](#), the Protection of Pupil Rights Amendment, [34 CFR 98](#), and the National Institute for Disability and Rehabilitation Research, [34 CFR 350](#);
- d. the U.S. Department of Defense (DoD) regulations and [DoD Directive \(DoDD\) 3216.02](#);
- e. the U.S. Environmental Protection Agency (EPA) regulations, [40 CFR 26, Subpart A](#);
- f. the U.S. National Institute of Justice regulations, [28 CFR 46](#);
- g. the U.S. Department of Justice, Bureau of Prisons regulations, [28 CFR 512](#);
- h. the U.S. Department of Energy (DoEn) regulations, [10 CFR 745](#);
- i. New York State Public Health Law [Article 24-A](#) (Protection of Human Subjects) and [Civil Rights Law Article 7, Section 79-1](#) (Confidentiality of Genetic Tests);
- j. the HIPAA Privacy Rule of 1996, [45 CFR 160](#) and [164](#);
- k. Columbia institutional policies; and
- l. the AAHRPP Accreditation Standards.

The IRBs 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 seven review panels in the Columbia HRPP. Six 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 six CUMC IRBs, one is designated to review cancer-related research that initially requires review at a convened meeting (also referred to as a “Full Board” review) (IRB 4), one is designated to review research for which next generation sequencing is the primary aim and that initially requires review at a convened meeting, as well as limited cancer-related research (IRB 5), 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 HRPO staff with sufficient expertise or by IRB Chairs; collectively they comprise the IRB ARC. Additional IRBs or specialized review committees 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 non-exempt studies at least annually 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 the 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. Individuals who are responsible for business development at Columbia or NYP are not permitted to serve as IRB members or ex-officio members or carry out day-to-day operations of the review process.

IRB members and staff who experience or become aware of efforts to influence IRB decisions are expected to report such situations to the ED, who will in turn notify the EVPR and VPRO. If attempts to unduly influence the IRB originate with the ED, notification should instead be provided directly to the EVPR or VPRO. Efforts to unduly influence IRB outcomes will be addressed directly by the EVPR or designee. Consultation with appropriate institutional parties, e.g., OGC or RCT, will be included in the process when necessary.

Copies of meeting minutes that document IRB actions are routinely forwarded to the IOs who represent CUMC, CU, and NYP for informational purposes and 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 research scientist/scholar appointed as an officer of research or instruction, 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 state law or institutional policy. These activities include student projects as described in the [IRB Students as Researchers Policy](#) (Reference Document #304), and genetic testing on anonymous samples as described in the [IRB Policy on Research Involving Genetic Testing Under Section 79-1 of the New York State Civil Rights Law](#).

Reliance by Columbia on the review by 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. Approval in Rascal denoting satisfaction of local requirements is required when Columbia is relying on a non-Columbia IRB.

## **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, or outsourcing to independent IRBs, 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 (i.e., continuing review, review of modifications, and unanticipated problem considerations) will, whenever feasible, be performed by that same Board. The Board may delegate compliance oversight activities for alleged serious or continuing noncompliance situations to the COT for purposes of conducting an inquiry, in accordance with the [Noncompliance with Human Subjects Regulations Policy](#) (Reference Document #89), 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. The ED and/or DIM will provide guidance in such situations.

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 Dean of CUMC for discussion of IRB issues.

The EVPR is responsible for providing adequate support and resources for the overall operation of the HRPO and all IRBs. Coordination of inter-Board activity is achieved by the IEC.

a. Membership

Each Board is constituted to meet the regulatory requirements mandated by DHHS and the FDA, and institutional needs, i.e., membership includes individuals with the necessary expertise to evaluate the type and volume of protocols submitted for review. Alternate IRB members and consultants may serve these roles in addition to regular IRB members. Among all CUMC IRBs, consistent membership and involvement as a voting member by at least one nurse is supported.

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 to provide awareness of considerations of the local community. Examples include: a) cardiologists are involved in the review of innovative cardiac surgery and device protocols; b) psychology faculty are assigned as reviewers or asked to consult on research procedures that may result in participant stress requiring intervention; and c) investigators who are experienced in the design and conduct of community-based participatory research are available to provide consultation during IRB review of such research protocols.

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. One member may fulfill more than one requirement. 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 who is a physician present at meetings.

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. When reviewing prisoner research, a majority of the IRB members have no association with the prison involved, apart from their membership on the IRB.

Experienced IRB officers may serve as alternate members of the IRB but may not generally conduct expedited reviews, other than for those submissions that have been determined to qualify for administrative review. For example, Columbia policy for administrative approval of translated documents permits an IRB staff member to verify that the appropriate English version of a document is the basis for the translated documents, confirm that there is an attestation of accuracy, and review the qualifications of the translator. When such requests are submitted in Rascal as a modification, an experienced IRB officer who has been appointed as an alternate IRB member may review and approve the submission via the expedited review process.

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. Consultants may provide their assessment and recommendation to the Board in written format, participate by tele- or videoconference, or attend the convened meeting. If participating in the meeting, these individuals may not vote with the Boards, unless they are appointed as an alternate to the respective Board and are serving in that capacity for a regular Board member.

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. If present at the meeting or participating by tele- or videoconference, the Board may ask consultants questions related to the protocol prior to completion of the discussion, after which the consultant will disconnect the call/connection or 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 the respective Chair or HRPO 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 HRPO.

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

### **a. Chair/Vice Chair**

#### **1) Selection and Appointment**

The IO listed on the CUMC or CU-MS FWA, as applicable, appoints the Board Chairs and Vice Chairs, after consultation with the ED, DIM and/or DO, 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 HRPO staff for approval and signature of the appropriate IO. Copies of the signed memo are sent to appropriate individuals, including the IO, ED, DIM, DO, ADIM when relevant, 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, DIM, DO, ADIM when relevant, 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 generally 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, unless delegated to a HRPO senior officer. 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.

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 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, Vice Chair, or other experienced IRB member as explained in the next section, 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 HPRO 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 DO, DIM 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, DIM, DO, ADIM if relevant, 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. 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 real or perceived 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 or Vice Chair may remain to answer relevant questions asked by the Board, but must leave the room during relevant Board deliberations related to decision, including the vote; the Chair will not count towards quorum for that review. HRPO staff, during preparation of the agenda for full Board meetings, will identify those submissions for which a Chair or Vice 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. If the conflicted Chair or Vice Chair is presiding over the meeting, this role would be covered, as previously described, during the discussion and vote.
- 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. HRPO 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 and Alternates

### 1) Selection and Appointment

The Chairs and/or IO, in consultation with the DIM, DO and, when relevant, the DIM (or ED when necessary), recommend candidates for appointment as IRB

members and alternates, and the IO named on the FWA makes the appointment to the Board via signature on an appointment memo. Members and alternates 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 prior to appointment, and a request for an updated version will be made periodically by the IRB.

A letter of appointment is prepared by HRPO 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, DIM, DO, ADIM when relevant, and Manager of the relevant IRB. A copy is retained in the IRB member file.

## 2) Length of Term/Service

Members and alternates are generally 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 or an alternate 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 and alternates may be granted an extended leave due to medical, personal or professional reasons, then return to complete their term.

IRB members and alternates are compensated for their service. In accordance with the “Recognition of Service by IRB Members” memo (Reference Document #127), IRB members and alternates 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 and alternates (when serving as a voting member) 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) protocol deviations; and e) closure requests.

Members and alternates (when serving as a voting member) also review and vote on other pertinent business, including compliance oversight activities, which is included on the agenda.

Experienced members or alternates may be assigned by the Chair or Vice Chair to review research activities that qualify for expedited review. An “experienced IRB member” means a voting member or alternate voting member who has received training relative to the expedited review categories and institutional policies governing human subjects research, and possesses the expertise needed to review the proposed research.

#### 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. Regular attendance for the unaffiliated member represents at least 75% of all convened board meetings. 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 or alternates must notify the Board Chair and/or the ED, or designee of their intentions in writing. The DO (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, DIM, and ADIM when relevant, 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 or alternates 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, DIM, DO, ADIM when relevant and Manager of the relevant IRB. A copy is retained in the IRB member file.

## 6) Liability Coverage for IRB Members and Alternates

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

## 7) Education and Training

Members and alternates 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 and alternates 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 and alternates 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 or alternates who have a real or perceived 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 or alternate may remain to answer questions asked by the Board, but must leave the room during relevant Board deliberations related to decisions, including the vote; the conflicted member will not count towards quorum for that review. IRB staff, during preparation of the agenda for full Board meetings, will identify those submissions for which a Board member or alternate 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 or alternate 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, HRPO 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 or alternate 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 Agreement (IAA) with other 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;
- description of a funding agency’s determination of a reviewing IRB for all sites; and/or
- consultation with IOs and/or the OGC.

The agreement through which the reliance agreement is documented will describe the division of responsibilities between Columbia and the other institution.

**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 and/or D/ADs 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, CTSA status, 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 HRPO 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 HRPO staff member and an IRB member.

CUMC and NYP, collectively, have multiple-project IAAs with numerous institutions, including NYSPI, 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.

The CU HRPO leadership (ED and DO) meets on an ad-hoc basis with representatives from external IRBs 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.

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 issued), or may require facilitative 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. Note that the terms Single IRB, Central IRB and Reviewing IRB all refer to an IRB that has been designated to review a study or group of studies for more than one study site, and may appropriately be used interchangeably in many situations.

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 Columbia 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 (reviewing IRB). 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 processes that the HRPO will follow to ensure appropriate review for each protocol are provided in Section VI. The HRPO may develop additional procedures/processes that will be applied to specific studies or research programs that rely on IRB review by a non-Columbia IRB. The IRB will establish a QA process for internal protocols reviewed by these processes, 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 certain low risk research. The ED or DO 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.

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. All clinical research conducted at CUMC must be covered by a Columbia IRB protocol with a Columbia PI. Therefore, the protocol and supporting documents for the proposed research should be submitted to the ED or DIM 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.

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 DIM 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 DIM 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 DIM 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., background, drugs/biologics, and subjects pages) should be reviewed and the relevant materials included in the submission.

#### **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 module 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, 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,” via the Consent Forms module in Rascal.

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 for edit only to study personnel listed on the protocol who have edit privileges and only while the Event status is “creating”, i.e., prior to initial submission of the respective Event to the IRB or when the Event has been returned to the study team by the HRPO/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. HRPO staff and IRB members may view all entries and attachments for a given Event once the Event has been submitted, and at any time thereafter, and may attach documents to the submission, but may not otherwise modify the submitted material, i.e., cannot revise text that has been entered into fields on Rascal screens or change options on Rascal screens that were selected by the researcher. Staff and members can attach updated or additional documents, and these are clearly labeled with the name of the individual who attached the document, and the date they were attached. If the HRPO modifies an attached document (e.g., to decrease returns by making changes that involve standard text), the document attached by the researcher will be designated as inactive but will remain attached, the revised document will be given a new filename and, when the revised document is attached, Rascal will document that the HRPO staff member attached it and the date on which it was attached. In such

instances, HRPO staff will contact a member of the study team to 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 of convened meetings), and correspondence transmitted between HRPO staff and/or between IRB members and HRPO staff. The submission is locked against changes by the research team at any time that it has been submitted and is in an 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. Completion of required training modules via the online Collaborative IRB Training Initiative (CITI) program is documented in Rascal and appears on the Data Sheet, when appropriately accessed via the Rascal system. Designated HRPO staff have the ability to manually upload training results if automated upload from CITI to Rascal does not occur. 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, regulatory coordinators and any other engaged personnel as part of the submission approval process.

## **B. IRB Abbreviated Submission Process**

The IRB supports an abbreviated submission process for studies that have a stand-alone protocol. The process requires completion of all Rascal fields that provide information regarding local implementation of the study, for multicenter studies, or information that is not covered in the stand-alone protocol. However, entering study information into the relevant Rascal fields is not required, as the Columbia IRBs will rely on the attached stand-alone (e.g., sponsor's) protocol for review of the overall objectives.

The abbreviated process eliminates the need to summarize the complete protocol on various pages in Rascal. If a researcher selects the Abbreviated Submission checkbox in Rascal, and a section is not covered by the submitted stand-alone protocol, the researcher must go back and provide this information on the appropriate page(s) in Rascal.

## **C. Personnel**

The Rascal Personnel page solicits information about the individuals who will be involved in with the conduct of 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 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.

Rascal will permit only one individual to be named as PI. CUMC requires that oncology studies managed through the Clinical Protocol & Data Management Office name an individual (Investigator) who will provide clinical coverage for when the PI is traveling or otherwise unavailable. The role of the Investigator who will ensure this coverage should be explained in the respective Role & Experience field of the Personnel section in Rascal. The IRB may determine that for other, e.g., higher risk studies, the study team also designate a covering Investigator 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 research involving human subjects may be conducted without IRB approval or determination of exempt status, the latter in accordance with [45 CFR 46](#), and by designated HRPO staff or IRB Chairs. Exempt research is human subjects research that falls into designated categories that are exempt from the requirements of the federal regulations. Although a PI may make a determination of "Not Human Subjects Research" (i.e., the regulatory definitions of "research" and/or "human subject" are not met) on his/her own without submission to the IRB, the PI will be responsible for any noncompliance that results, if that decision is later found to be incorrect. 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**

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, rests with the PI, who may delegate tasks but retains responsibility for them. IRB correspondence that provides the outcome of IRB reviews or decisions, e.g., approval letters and notifications of suspensions, whether sent through the Rascal correspondence queue or in hard copy, is addressed to the PI. Rascal correspondence requesting clarification or changes to submitted Events is sent to the PI as well as to those members of the research team designated per Rascal procedures (Reference Document #95).

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 an individual who is Non-Engaged Personnel), and duties for the study change such that he/she will be performing duties beyond that role (e.g., moving from Non-Engaged Personnel to Other Engaged-Personnel, Coordinator, etc.), 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 generally be appointed as an Officer of Research or Instruction and are constrained by the parameters for the position as described in the Columbia University Faculty Handbook. Individuals who will be observing research procedures for 3 months or less, usually for training purposes, must adhere to the requirements of the University’s Guidelines for Short-Term Visitors in Research-Related and Clinical Activities (Document #306).

## **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.

- Most required training modules must be accessed via the Rascal Training Center; for these courses, evidence of completion is maintained electronically within Rascal.
- Security Essentials training that is required annually for the CUMC workforce and anyone named on a CUMC protocol is managed outside of the Rascal system. HRPO staff do not monitor completion, but access to Rascal and certain other electronic systems will be restricted if this training is not completed within the specified timeframe. This training, while not targeted specifically to research

personnel, provides information about data security requirements that helps to reduce the risk of breaches of confidentiality of research data.

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

### **1. Submission Materials: New Protocol**

When a new protocol is being created, Rascal screens solicit core information about the study, including Attributes, Background, Exempt/Expedited; Funding, Locations, Personnel, Privacy and Data Security, Procedures, Recruitment and Consent, Research Aims and Abstracts, Risks, Benefits and Monitoring, and Subjects, Responses to questions on these screens may initiate a requirement to complete additional screens, e.g., Drugs/Biologics, Devices or Analysis of Existing Data.

The following information or documentation should be included or attached for new protocols and will be accessible for review by at least one IRB member, whether for convened IRB review or for expedited review:

- a. list of personnel (members of the Columbia research team) involved in the research;
- b. request for exemption, if applicable (this is optional);
- 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, or other documentation of the supported research (e.g., the complete DHHS-approved protocol (when one exists), sponsor's protocol, investigator's brochure, the DHHS-approved sample consent document (when one exists));
- 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 Analysis of Existing Data and/or Prospective Record Review page if existing data and/or prospective data collected for non-research purposes will be utilized;



- k. completion of the Biological Specimens page if any tissue or fluid will be obtained from subjects or stored specimens will be used;
- l. completion of the Drugs/Biologics or Devices page, if a drug, device, or biologic is under investigation as part of the research;<sup>1</sup> ;
- m. recruitment material, if applicable (e.g., recruitment flyer or letter, letter to clinicians to notify their patients about the study, text for Internet advertisement);
- n. the location where study procedures under the purview of Columbia researchers will take place;
- o. study instruments, if applicable (e.g., survey, focus group guide, interview script, questionnaire);
- p. approvals from other institutions, if applicable and available;
- q. Data Use Agreements, Material Transfer Agreements and other ancillary agreements (collectively, “Ancillary Agreements”) if applicable and available; and
- r. documentation of the investigational product regulatory status.

The IRB needs requires information that allows the IRB to conduct an analysis of the risks and potential benefits of research procedures proposed, including a detailed description of all study procedures (inclusive of those being performed already for diagnostic or treatment purposes) 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), the researcher must provide this information on the appropriate page(s) in Rascal.

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, the “[ ] Abbreviated Submission” designation should be selected on each applicable page, and the stand-alone protocol must be attached. All other pages that do not allow for the abbreviated submission option must be completed. In addition, if any of the information required in these pages are not included in the attached document, or differ from the stand-alone protocol, each page will need to include this missing information. The abbreviated process described above eliminates the need to summarize many elements of a stand-alone protocol within the Rascal application. Additional information related to the Abbreviated Submission Process is posted throughout the IRB application in Rascal.

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.

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<sup>1</sup> 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.

## 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 during the course of a study that there is the potential for imminent harm to subjects, and changes must be made to eliminate or mitigate the risks, but there is no time to obtain IRB approval, the investigator should implement any change(s) necessary 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. This modification must be submitted to the IRB at the earliest possible opportunity after the change is made. Submission of an Unanticipated Problem report in Rascal may also be necessary if the criteria, as described in Section III.D.4., are met.

Any change in the protocol that is necessary for the enrollment of a specific subject (e.g., deviation from the approved inclusion/exclusion criteria) or to address a temporary situation (e.g., a temporary drug shortage) 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, and IRB approval was issued, before enrollment) or violation (if the study team did not [both] identify the change and obtain IRB approval for it, before enrollment) by the IRB. Protocol deviations and major 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 event module. Minor violations may be submitted at the time of renewal. See Section III.D.6 for additional information regarding submission of reports of deviations and violations.

The Modification Information page (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 violation, and if so, how many of each are included;
- c. checklist to designate the pages that are being revised as part of the modification submission;
- d. designation of the modification as an administrative change, if applicable;
- e. study enrollment status (e.g., enrollment ongoing, study closed to enrollment) and a summary of information needed to explain the study status; and
- f. if the consent form has been revised as a result of the protocol change.

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 page in Rascal, if personnel change is involved;
- d. updated Subjects page in Rascal to reflect the current number of enrolled subjects;
- e. updated pages in Rascal as appropriate, e.g. if a change in recruitment is suggested, revision to the Recruitment and Consent page is required to reflect the change;
- f. updated Procedures page in Rascal to reflect procedure change (e.g. biological specimens, imaging); and
- g. 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. In addition, Rascal will send notification of an “expired” status on the day that the IRB approval expires, if a renewal has not yet been submitted and approved, and will send reminders every 30 days until a current IRB approval status has been obtained. Investigators are required to submit renewal requests in Rascal and are strongly encouraged to submit appropriate reports for ongoing research activities no fewer than 60 days prior to the expiration date of the IRB approval for the study. Expiration date reminders are sent as a courtesy to researchers. It is the responsibility of the study team to ensure that renewals are submitted in time to allow for appropriate review by the IRB prior to expiration. Researchers relying on an external (non-CU) IRB must comply with the specific timeframe for that IRB.

The Renewal Information Page (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) and summary of information needed to explain the study status;
- b. list of relevant literature, interim findings, and publications;
- c. report of subjects who were enrolled utilizing the Short Form consent process;
- d. inquiry regarding recent Data Safety and Monitoring Committee (DSMC) or Board (DSMB) or other relevant multi-center trial reports, if applicable;
- e. request for recent Progress Report, if applicable and available;
- f. if the renewal includes a modification, a summary of the proposed change(s), checklist to designate the pages that are being revised as part of the included modification and if the consent form has been revised as a result of the protocol change; and
- g. if the submission includes a protocol violation, and if so, how many are included.

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

- a. original number of participants anticipated;
- b. number of participants enrolled/accrued to date at CU site;
- c. number of participants enrolled/accrued last year at CU site;
- d. number of participants who completed the study at CU site;
- e. number of participants expected to enroll/accrue next year;
- f. number of participants who remain on study and number who are off study;
- g. number of, and explanation for participant complaints at CU site;
- h. number of, and explanation for participants removed by the PI;
- i. number of, and explanation for participants who withdrew from the study;
- j. number of participants who died while on study;
- k. demographic information for subjects enrolled at CU site;
- l. subject population justification;
- m. subject compensation and justification, if applicable;
- n. consent waiver or alteration requests, if applicable; and
- o. 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. reporting of 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 Certificate of Confidentiality (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.

When preparing a renewal submission, obsolete or superseded study-related documents should be detached (if they are Rascal-generated consent forms), or deleted (all other forms). Exceptions are HIPAA forms that were appropriate for the protocol at any phase of the research, which should be removed from the HIPAA page in Rascal and attached through the “Attach Documents” page, whether or not they are still being used.

#### **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. evaluation of whether the UP was unanticipated, related to participation in the study, and suggests an increase in risk to subjects or others;
- b. if the incident/experience/outcome occurred at an external site;

- c. if the monitoring entity determined that the event was unanticipated, at least possibly related, and places subjects or others as a greater risk of harm than was previously known or recognized;
- d. subject identifier and UP keyword;
- e. date, location, and description of the UP;
- f. relationship of the UP event to the study;
- g. date and means by which the PI became aware of the UP;
- h. entities to which the UP has been/will be reported;
- i. if the submission includes a protocol violation, and if so, how many are included; and
- j. 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. A modification can be submitted concurrently with the UP Event.

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

The report of a change that was implemented without prospective IRB review, to eliminate an immediate hazard to subjects, should be submitted to the IRB as a UP (to report the UP), and also as a modification (if changes to the consent form and/or protocol are required as a result of the UP).

Reports of UPs 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: Closure**

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

The Closure Report form requests 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. why the study is being closed, including documentation to support premature closure, when applicable and if available;
- c. if any research-related activities were conducted after the date of expiration, if the study is expired;
- d. confirmation that all requests and/or requirements as requested by the IRB have been addressed;
- e. number of participants enrolled to date at CU site;
- f. number of participants enrolled last year at CU site;
- g. number of participants expected to enroll next year;
- h. number of participants who remain on study
- i. number of participants who completed the study at CU site;
- j. number of participants expected to enroll next year;
- k. number of, and explanation for participant complaints at CU site;
- l. number of, and explanation for participants removed by physician;
- m. number of, and explanation for, participants who withdrew from the study;
- n. number of, and explanation for participants removed by the PI;
- o. number of, and explanation for participants lost to follow-up;
- p. number of, and explanation for participants who have died while on study;
- q. number of, and explanation for participant complaints at CU site;
- r. number of participants enrolled to date at other sites; and
- s. demographic information for subjects enrolled at CU site.

## **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 divergence from the approved protocol, IRB determinations or IRB policies for one subject or to address a temporary situation that is identified by the research team and approved by the IRB before implementation. A protocol violation is defined as a divergence from the approved protocol, IRB determinations or IRB policies that was implemented without prospective approval by the IRB and was not implemented to avoid or minimize imminent harm. Protocol violations may be considered as non-compliance with the federal regulations for the protection of human subjects. Information on submission materials required for Deviations or

Violations when Columbia University is the Reviewing IRB and when a non-Columbia IRB is the Reviewing IRB is detailed in Columbia University IRB Guidance for Protocol Deviations and Violations (Reference Document #364).

The IRB recognizes that some deviations (e.g., 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 a Protocol Violation is unexpected, at least possibly related to the research, and involves risks to subjects or others, it is considered an UP and must be reported to the IRB within one week (5 business days) using the UP functionality in Rascal. The description of the circumstances surrounding the deviation/modification should be clearly stated in the Unanticipated Problem Report (Reference Document #188). If the UP results in a modification to the protocol, consent form or other study related documents, those changes should be submitted as a Modification. 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 Violations that are not UPs are categorized as Minor or Major Violations. Major Violations are those that violate the rights or welfare of subjects, negatively affect the integrity of the study or result in the need for a change to the protocol or consent document(s). In most cases, they will be reported to the IRB as a Modification and should be clearly stated in the summary section of the Modification Information form (Reference Document #69). However, when reporting of the major violation coincides with submission of a Renewal, the violation may be reported within the Renewal application (Reference Document #61). Modification submissions to report Major Violations should include the PI's assessment that the event does not meet the UP criteria and must be reported to the IRB promptly, generally within one week (5 business days) of occurrence or, if it is not known to the PI at that time, of discovery by the PI, to provide an opportunity for the IRB to assess, within a reasonable timeframe relative to protection of subjects, whether the study should continue, and whether changes to study procedures are required.

Minor violations are violations that are not UPs and do not meet the criteria to be considered major violations. These should be reported to the IRB at the time of continuing review, in a list or log that includes all UPs, deviations, and violations. The log should reflect when individual submissions of each UP, deviation, or major violation were made.

The following information should be included for deviations and violations:

- 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: Expanded Access, Including Emergency Use**

Expanded access, including emergency use, is the use outside of a clinical trial of an investigational medical product (i.e., a drug/biologic or device that has not been approved by FDA).

Information related to submission materials for each category of expanded access are discussed below:

### **a. Emergency Use**

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 FDA must be notified of all emergency use situations by the manufacturer or sponsor.

When possible, the HRPO should be notified in advance of the proposed emergency use. For some emergency use situations, notification to the HRPO may be necessary because the manufacturer of the product may not agree to ship the product until a letter confirming the IRB is aware of the impending use of the investigational product is received. The CTO (IAP) should also be notified when emergency use of an investigational product occurs.

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:

- 1) 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) notification;

- 2) 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
- 3) 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 by email to [irboffice@columbia.edu](mailto:irboffice@columbia.edu) 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:

- 1) product name and type (i.e., drug, device, biologic);
- 2) if a device, product model/version number, if applicable;
- 3) IND or IDE number, if one has been obtained for this use;
- 4) description of product;
- 5) name, affiliation of non-participating physician, and date of affirmation;
- 6) number and submission date of protocol submitted for IRB review of this article, if applicable; and
- 7) date of notification to FDA.

The ED, DIM and/or DO may be copied on the email that is sent to the [irboffice@columbia.edu](mailto:irboffice@columbia.edu) inbox. FDA authorization is required before emergency use of drugs/biologics may proceed. Emergency use of an investigational medical device may proceed without FDA approval.

FDA regulations ([21 CFR 56.104\(c\)](#)) allow for *one* emergency use of a test article per institution. Any subsequent use of the investigational product at the institution is subject to **prospective IRB review and approval**. However, when prior IRB review and approval is not feasible for a subsequent expanded access emergency use at a particular institution, the FDA will not deny the subsequent request for emergency use based on lack of time to obtain prospective IRB review, as long as that use will be reported to the IRB within five working days of initiation of treatment ([21 CFR 56.104\(c\)](#)).

#### **b. Non-Emergency Expanded Access (Drugs/Biologics)**

For drug products, “expanded access refers to the use of an investigational drug when the primary purpose is to diagnose, monitor or treat a patient rather than to obtain the kind of information about the drug that is generally derived from clinical trials.”<sup>2</sup>

1) Requirements for Expanded Access to Investigational Drugs for Treatment Use:

According to [21 CFR 312.305\(a\)](#), FDA must determine and the IRB must concur that:

- a) the patient or patients to be treated have a serious or immediately life-threatening disease or condition\*, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;
- b) the potential patient benefit justifies the potential risks of the treatment use and those potential risks are not unreasonable in the context of the disease or condition to be treated; and
- c) providing the investigational drug for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use.

\* For the purpose of expanded access to investigational drugs for treatment use, immediately life-threatening disease or condition means a stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment. Serious disease or condition means a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one ([21 CFR 312.300\(b\)](#)). (See also the FDA’s [Expanded Access to Investigational Drugs for Treatment Use - Questions and Answers](#).)

Under FDA’s current regulations for investigational drugs and biologics, there are three categories of expanded access:

- For individual patients ([21 CFR 312.310](#))
- For intermediate-size patient populations (generally smaller than those typical of a treatment IND or treatment protocol — a treatment protocol is submitted as a protocol to an existing IND by the sponsor of the existing IND) ([21 CFR 312.315](#))
- For widespread treatment use through a treatment IND or treatment protocol (designed for use in larger patient populations) ([21 CFR 312.320](#))

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<sup>2</sup> <https://www.fda.gov/downloads/drugs/guidances/ucm351261.pdf>

- Note that [Subpart D](#) of 21 CFR 312 (Responsibility of Sponsors and Investigators) is applicable to expanded access use of investigational drugs/biologics.

**c. IRB Submission Process for Non-Emergency Expanded Access Use of Investigational Drugs or Biologics**

Prior IRB review and approval is required for all non-emergency expanded access use. Emergency use procedures are discussed separately in this document.

For individual-patient expanded access, submit the following:

- 1) documentation confirming criteria under [21 CFR 312.305\(a\)](#) noted above are met;
- 2) investigator's determination that the probable risk to the person from the investigational drug is not greater than the probable risk from the disease or condition;
- 3) confirmation of IND submission to the FDA or FDA-issued IND if available;
- 4) confirmation that informed consent will be obtained via an acceptable consent process;
- 5) for individual-patient expanded access INDs only, notification that the investigator has requested a waiver under [21 CFR 56.105](#) of the requirements noted in [21 CFR 56.108\(c\)](#) requiring full committee review as indicated on FDA Form 3926; *and*
- 6) documentation evidencing FDA determination that the patient cannot obtain the drug under another IND or protocol, e.g. FDA approval for Single-Patient expanded access to proceed.

If a waiver under [21 CFR 56.105](#) is selected on FDA Form 3926, concurrence by the IRB Chairperson or another IRB member can serve as prospective IRB review.

For intermediate-size patient populations (IND or Protocol), submit the following:

- 1) documentation confirming criteria under [21 CFR 312.305\(a\)](#) are met;
- 2) statement of whether the drug is being developed or is not being developed and description of the patient population to be treated. If the drug is not being actively developed, an explanation why the drug cannot currently be developed for the expanded access use and under what circumstances the drug could be developed;
- 3) if the drug is being studied in a clinical trial, clarify why patients to be treated cannot be enrolled in the clinical trial and under what circumstances the sponsor would conduct a clinical trial in these patients;
- 4) confirmation of IND submission to the FDA or FDA-issued IND if available; *and*

- 5) confirmation that informed consent will be obtained via an acceptable consent process.

Convened IRB review is required for intermediate-size patient populations (IND or Protocol), as per [21 CFR 56.108\(c\)](#).

For treatment IND or treatment protocol, submit the following:

- 1) documentation confirming criteria under [21 CFR 312.305\(a\)](#) are met;
- 2) confirmation of IND/Protocol submission to the FDA or FDA-issued IND if available; and
- 3) confirmation that informed consent will be obtained via an acceptable consent process.

Convened IRB review is required for treatment INDs or treatment protocols, as per [21 CFR 56.108\(c\)](#).

Important Notes on timing of Expanded Access Use:

- A non-emergency expanded access IND (individual-patient, intermediate or treatment) goes into effect 30 days after the FDA receives the IND, or after an earlier notification is provided by the FDA that the expanded access use may begin.
- There is no 30-day waiting period for expanded access use of a drug or biologic under an individual patient protocol or intermediate-sized patient population protocol, however the protocol must be submitted to the FDA and receive IRB approval before treatment may begin.
- There is a 30-day waiting period from the date the FDA receives a treatment protocol, before expanded access use of a drug or biologic under a Treatment protocol may begin, unless the FDA notifies the sponsor that treatment may begin earlier.

#### **d. Non-Emergency Expanded Access (Devices)**

An unapproved medical device may normally only be used on human subjects through an approved clinical study in which the subjects meet certain criteria and the device is used in accordance with the approved protocol by a clinical investigator participating in the clinical trial. However, there may be circumstances under which a physician may wish to use an unapproved device to save the life of a patient or to help a patient suffering from a serious disease or condition for which no other alternative therapy exists.

If enrollment in an existing clinical trial protocol is not possible (e.g., a patient is not eligible for any ongoing clinical trials, or there are no ongoing clinical trials to address

the patient's condition), patients/physicians may request expanded access to investigational devices under one of three alternative mechanisms:

- Emergency Use
- Individual-Patient/Small Group (commonly referred to as “Compassionate Use”)
- Treatment Use

IRB Submission Process for Non-Emergency Expanded Access Use of Investigational (i.e., non-FDA approved) Medical Devices

FDA approval is required for all non-emergency expanded access use. Emergency use procedures are discussed separately in this document.

For Individual-patient/small group (“compassionate use”):

Ensure the following criteria are met:

- 1) the patient has a life-threatening or serious disease or condition; and
- 2) no generally acceptable alternative treatment for the condition exists.

If an IDE exists or there is no IDE for the device, submit the following:

- 1) confirmation that the IDE sponsor (can be device manufacturer or a physician who has submitted the IDE to conduct the clinical study for the device) has submitted an IDE supplement requesting approval for a compassionate use under section [21CFR812.35\(a\)](#), which includes:
  - a) a description of the patient's condition and the circumstances necessitating treatment;
  - b) a discussion of why alternative therapies are unsatisfactory and why the probable risk of using the investigational device is no greater than the probable risk from the disease or condition;
  - c) an identification of any deviations in the approved clinical protocol (if any) that may be needed in order to treat the patient, and;
  - d) the patient protection measures that will be followed which includes:
    - i. obtaining informed consent from the patient or a legal representative;
    - ii. an independent assessment from an uninvolved physician;
    - iii. clearance from the institution as specified by their policies\*;
    - iv. concurrence of the IRB chairperson\*; and
    - v. authorization from the IDE sponsor, if an approved IDE exists for the device.
- 2) Confirmation of IDE submission to the FDA or FDA-issued IDE if available;

- 3) an appropriate schedule for monitoring the patient, taking into consideration the investigational nature of the device and the specific needs of the patient; and
- 4) if no IDE exists (only): Include a description of the device provided by the manufacturer.

\*FDA regulation nor guidance clarifies circumstances under which Chair concurrence may be acceptable for individual-patient/small group expanded access. Note that expanded access request for individual-patient/small group use may be routed to the convened IRB on the recommendation of the Chair and/or other reviewer.

Important Note: Follow up information on the use of the device should be submitted to FDA in an IDE Report after compassionate use has ended.

For more information see [FDA Information Sheet Guidance for IRBs, Clinical Investigators and Sponsors: Frequently Asked Questions about Medical Devices](#) (January 2006).

For Treatment Use:

Ensure the following criteria are met and submit documentation confirming:

- 1) the device is intended to treat or diagnose a serious or immediately life-threatening disease or condition;
- 2) there is no comparable or satisfactory alternative device available to treat or diagnose the disease or condition in the intended patient population;
- 3) the device is under investigation in a controlled clinical trial for the same use under an approved IDE, or all clinical trials have been completed; and
- 4) the sponsor of the controlled clinical trial is pursuing marketing approval/clearance of the investigational device with due diligence.

Convened IRB is required for Treatment Uses of medical devices.

Important Notes on timing of Treatment Use: According to [21 CFR 812.36\(d\)](#), expanded access use under a treatment IDE may not begin until 30 days after FDA receives the application, unless FDA notifies the sponsor earlier than 30 days that the treatment use may or may not begin.

## **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 Drugs/Biologics page to list the investigational product<sup>3</sup> (Reference Document #92) for each agent involved;
- f. data and safety monitoring plan;
- g. FDA Form 1572; and
- h. FDA Form 1571 when a CU Faculty member is IND holder.

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(Reference Document #18), [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 (Reference Document #311) outlines the institutional oversight of S-I research. An IAP (Reference Document #314) has been

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<sup>3</sup> 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 on the Drugs/Biologics pages.



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 Form of Notice by CU Faculty IND/IDE Holder letter (Reference Document #367) 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.

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 Drugs/Biologics page to list the investigational product<sup>4</sup> (Reference Document #92) for each agent involved; and
- f. data and safety monitoring plan.

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<sup>4</sup> 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 on the Drugs/Biologics page.

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.

### **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 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 Device Page to list the investigational product<sup>5</sup> (Reference Document #92) for each device involved;
- d. data and safety monitoring plan;
- e. device management plan;
- f. Clinical Investigator Agreement; and

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<sup>5</sup> 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 on the respective page.

- g. Confirmation of Medicare contractor, National Government Services (NGS) or Centers for Medicare and Medicaid Services (CMS) coverage decision, if the study meets the requirements for device studies that must be submitted for a determination of NGS billing clearance.
  - 1) If the IDE study was approved before 1/1/2015: the study must be submitted to the Medicare contractor, National Government Services (NGS); the PI of the study submits request to the Medicare Administrative Contractor provider/local NGS representative and receives a determination letter.
  - 2) If the IDE study was approved on or after 1/1/2015: the Sponsor must submit request for coverage to CMS. Approval will be posted on the CMS website and all sites must be listed on the [www.clinicaltrials.gov](http://www.clinicaltrials.gov) record for the study.

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. IDE regulations at [21 CFR 812.110](#) require that the investigator manage the device supply such that they are used only with subjects under the investigator's supervision. In addition, the investigator may not supply an investigational device to any person not authorized to receive it. Upon completion or termination of the clinical investigation or the investigator's part of the investigation, or at the sponsor's request, the investigator must return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs. Device use must be tracked and records retained of each device and its disposition; this is particularly important for implantable devices. When devices are labeled with a serial number, the number must be recorded within or connected to the research records of the individual who received the device.

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);
- 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)); and
  - 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/IDE, 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.B.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 (LAR), 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](#) (i.e., Exception from Informed Consent Requirements for Emergency Research).

#### **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 (See Reference Document #357 for additional detail); 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 #103) 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.

(See Reference Document #356, and search for “prisoner” within the document, for additional information that may be relevant if the research is subject to the requirements of federal agencies other than DHHS or FDA).

## **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 page 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 CU HRPO website.

(See Reference Document #356, and search for "children" within the document, for additional information that may be relevant if the research is subject to the requirements of federal agencies other than DHHS or FDA).

## **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 (HCP), 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.

Additional details on obtaining Surrogate Consent can be found in the CU Informed Consent Policy.

## **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 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 IRB 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 targeting students enrolled in the CU College of Physicians & Surgeons, the IRB must seek clearance of this targeted population by the P&S Advisory Group. 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 policies related to international activities. The Office of Research Compliance and Training website provides additional information on International Research.

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.

Researchers conducting international research are advised to review the OHRP International Compilation of Human Research Standards for information about local regulations and laws in international sites.

The RCT must be advised of any research proposed to be conducted in a sanctioned country. All research conducted within such countries must abide by the restrictions outlined by the U.S. Department of the Treasury.

## **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. Rascal includes questions to capture whether the study includes one or more components that apply to a subset of the overall study population, as well as the target enrollment for each substudy.

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, if any;
  - 4) identification of the individual who will serve as the overall PI for the project;
  - 5) a clear description of what 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;
  - 8) appropriate agreement for the transfer of data or material.
- 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) if applicable, 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 (IAA)**

Federal regulations permit an IRB at one entity to rely on the review of an IRB at another entity or an independent IRB in certain situations, and the terms of the relationship are typically described in an agreement that may be called a reliance agreement or an 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 DO.

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. 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, are specific to the relevant IAA. All instances of collaborative research that is conducted under an IAA should be appropriately reflected in the Rascal IRB submission.

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, including studies that rely on a designated single IRB of record (sIRB), generally need to be submitted to the Columbia IRB via Rascal for tracking purposes and for confirmation that all local and institutional requirements (e.g., training and COI disclosure) are met. The process and list of

documents needed for submission in Rascal for when Columbia relies on a sIRB, included what fields need to be completed, can be found in Reference Document #365.

When Columbia serves as the IRB for other sites, including instances where Columbia is designated as the sIRB, there may be a need for separate submissions to facilitate the sIRB for all sites and for the IRB review of Columbia as a research site. The process and list of documents needed for each submission in Rascal for when Columbia serves as a sIRB, included what fields need to be completed, can be found in Reference Document #366.

### **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:

- a. contact information for each site;

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

Additional guidance:

- a. If the external sites are international, please refer to Section III.E.11 of these procedures for additional guidance.
- b. If there will be collaboration with investigators from other institutions, please refer to Section III.E.13 and/or III.E.14 of these procedures for relevant guidance.
- c. 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, e.g., modification, renewal or closure, 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:

- a. 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;
- b. 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;
- c. 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; and



- d. an appropriate agreement must be executed prior to any data or material that was originally collected at Columbia is transferred to an external site.

For research that has not yet started or for which all activities have concluded, but the study remains open while awaiting publication, a closure submission should be submitted to the IRB.

### **18. Submission Materials: Federally-Supported or Conducted Research**

Per the requirements of [45 CFR 46.103\(f\)](#), the IRB must review the entire grant application for research that is funded by a federal agency. A complete copy of each application, from face page to the end, excluding appendices, should be attached to the IRB submission. Where necessary to safeguard confidentiality, salaries and similar information may be redacted. 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.

During its review of research that is supported or conducted by specific federal agencies, and/or is subject to the requirements of those agencies, or is subject to specific federal policies, the IRB will consider the requirements of the respective agencies and policies as they relate to the protection of human subjects, and make specific determinations regarding them (e.g., related to informed consent, reporting, monitoring, etc.). These requirements are in addition to the requirements for approval of research that the IRB considers for all research involving human subjects.

Awareness by researchers of these regulations, policies, and affiliated required determinations will facilitate inclusion, in the submission to the IRB, of the information that must be considered before these determinations can be made. Reference Document #356, Additional Requirements for Protocols Funded by Specific Federal Agencies or Subject to Specific Federal Policies, provides guidance to facilitate a complete submission that addresses the additional regulatory concerns of these agencies and policies.

Particular attention should be paid when preparing protocols that are subject to Department of Defense regulations. Requirements vary depending upon the DoD component. Detailed guidance is provided in Reference Document #356, Additional Requirements for Protocols Funded by Specific Federal Agencies or Subject to Specific Federal Policies.

## **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 HRPO staff 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; details will vary based on the type of Event.

The outcome of the pre-review is that the submission is either logged in to the Chair’s queue or returned 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 preliminarily assess the appropriate 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 an IRB based upon the level of review required and, where applicable, the type of research: CUMC IRBs 1-3 for full board non-oncology and non-genomic studies; CUMC IRB 4 for full board oncology studies; CUMC IRB 5 for full board genetic/genomic and oncology studies; CUMC IRB Exp for protocols eligible for expedited review; the CUMC ARC for determination of exemption for Not Human Subjects Research (NHSR), i.e., definition of research is not met, or [NHSR per 45 CFR 46](#), i.e., research, but the definition of human subject is not met; or MS IRB for protocols originating from CU-MS researchers.

A reviewer form is also completed by staff during pre-review of renewal (continuing review) submissions (Reference Document #110, “Renewal Pre-review Form”), and the review of closure reports is guided by specific criteria (Reference Document #111, “Closure Return Criteria”), followed by a summary entry in the Notes field. A template for notes for modification submissions is used to guide, in a consistent manner, the administrative review of modifications to approved protocols. The outcome of staff pre-review of other Events such as review of unanticipated problems is also entered in the Notes field.

At the conclusion of the pre-review for new protocols, renewals, modifications, closures, and unanticipated problem reports, the reviewer facilitates the Event being logged in (i.e., accepted for review) or returned to the researcher for revision or additional documentation/information. Correspondence in Rascal to the study team follows each return. As previously indicated, if the submission is returned, the action will undergo another staff review upon resubmission. 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 to the Chair’s queue after being logged in by HRPO staff. Individuals designated as Chair or Vice Chair (either, for purposes of these review sections, 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 view the level of review recommended by the staff reviewer. Depending upon the level of review required, the Chair will review the Event him/herself or distribute it to an experienced IRB or Committee

member for review. A Chair may delegate to an IRB Manager the responsibility for distributing certain Events. 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 pre-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 or “[NHSR per 45 CFR 46.](#)”

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 senior HRPO staff, for completion of the review and documentation of the determination. At CU-MS, the Chair makes the NHSR determination. Although an IRB Chair or HRPO staff member must review the protocol in order to make a NHSR determination, if the protocol is submitted, 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.

The Rascal system includes a process by which investigators can assess through their responses whether a proposed project is NHSR. At the conclusion of this assessment, investigators can elect to have the IRB confirm the accuracy of this assessment or can elect to forego IRB review once this assessment is made. Justification that the project does not meet the criteria to be considered human subjects research should be provided, if the PI is seeking such a determination from the IRB.

For all protocol submissions, regardless of whether the investigator made a preliminary assessment of NHSR, 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](#), 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.

In general, researchers are strongly encouraged to submit protocols via Rascal in order to proceed through the NHSR decision pathway. However in rare circumstances, an investigator may request administrative review of a proposal outside of the Rascal system to determine whether review by the IRB is required. Prior to submission of a new protocol, if it is unclear whether research with human subjects is involved, an investigator may request an administrative review of a proposal outside of the Rascal system to determine whether review by the IRB is required. In those rare cases, an HRPO staff member 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. The HRPO reserves the right to require submission in Rascal for a formal determination rather than reviewing outside of the system.

HRPO 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\(b\)](#) and [21 CFR 56.104\(a-d\)](#)) may be determined to be exempt from the requirements of [45 CFR 46](#) and/or [21 CFR 56](#). Protocols that the investigator has indicated may be eligible for exemption are reviewed by a designated reviewer (i.e., Chair at CU-MS, and staff at CUMC), to determine whether the research fulfills the organization's ethical standards for exempt research, which include but are not limited to:

- a. The research holds out no more than minimal risk to subjects;
- b. The selection of subjects is equitable;
- c. If there is recording of identifiable information, there are adequate provisions to maintain the confidentiality of the data; and
- d. There are adequate provisions to maintain the privacy interests of subjects.

After review, the designated reviewer may approve the project as exempt, designate the protocol as eligible for expedited review (if more appropriate than exemption), recommend full board review or return the protocol to the investigator. The protocol will be returned if revisions, additions, or deletions are required. The designated reviewer has the authority to either remove an exempt selection that was entered by the PI, or designate a protocol as exempt even if the PI has not entered an exempt selection.

The staff reviewer on the ARC or the CU-MS Chair, can revise or remove an Exempt selection, or make an initial exempt selection, as appropriate.

The Rascal system does not permit a Chair or ARC member to electronically distribute Events that include an Exempt selection. 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 IRB reviewer or staff member may initiate this contact. Communication via Rascal correspondence is recommended. If e-mail communication is used, the messages should be summarized in the Notes section and attached as an internal document 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. In addition, 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., activities that are subject to FDA regulations).

As noted in the CU IRB 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 approvals are communicated to the research team via electronic Letter of Approval (LOA) (Reference Document #93) by HRPO staff.

Exempt determinations are valid for a period of five years. At the end of the five-year period, a 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 five year period (Reference Document #9).

A list of exempt determinations by the ARC is generated via the Rascal IRB minutes function to document the reviews, and the resultant document is approved by HRPO staff. Copies of approved minutes, including the ARC 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 that are FDA-regulated:

- a. any investigation which commenced before July 27, 1981 if specific conditions are met ([21 CFR 56.104\(a\)](#));
- b. any investigation which commenced before July 27, 1981 and IRB review was not required ([21 CFR 56.104\(b\)](#));
- c. emergency use of an investigational article ([21 CFR 56.104\(c\)](#)); and
- d. taste and food quality evaluations and consumer acceptance studies if specific conditions are met ([21 CFR 56.104\(d\)](#)).

### **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](#).

As stated above, 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 Chair or designated reviewer conducts expedited reviews of protocols originating from CU-MS researchers except in cases where the protocol is assigned for review by a CUMC IRB, either because certain expertise is required that is not available on the CU-MS IRB, or the proposed research is FDA-regulated.

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, if the researcher did not select the category(ies). The Chair may also revise, add or remove category selections. 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 must ensure 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. 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 for review by the convened IRB.

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.

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 hard copy documents such as handwritten or typed comments available to the HRPO 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.

Approvals made by expedited review are communicated to the research team 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 IAAs when CU is not the IRB of Record (additional detail in following section), the second was implemented to permit processing of submissions for sponsored projects for which human research exists only in the individual studies that involve research with human subjects, and each receive their own 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 or personnel need to be hired and trained before human subject involvement commences but IRB approval is required by the funding agency.

##### **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 or other reliance agreement. 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 review of joint and cooperative projects involving multiple sites and/or investigators. The ED or DO may agree to permit another IRB with whom an IAA has been executed 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.

Details of the level of, and criteria for, review of protocols that are subject to an IAA can be found in Section VI. A. Approvals under these categories are reported to members of the IRB that conducted the facilitative review and to IOs 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 if conducted by Columbia personnel; for other projects, the PI of the award must maintain documentation of

appropriate IRB review. For each individual submission at Columbia, IRB review will be conducted and all necessary IRB determinations made.

CU pre-award research administrative offices require a Columbia 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 federally 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 in which the study design involving human subjects has yet to be developed, and studies for which personnel need to be hired and trained before human subject involvement commences. The Rascal system allows for researchers to select an option suggesting that their projects eligibility for a “118” determination, which allows for submission of an abbreviated Rascal submission.

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 IRB review. The involvement of human subjects may not commence until the modification is reviewed and all IRB criteria for approval are satisfied. The level of review will change as warranted by the level of risk and type of procedure.

### **5. Level of Review: Convened IRB Review (aka “Full Board” Review)**

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.

Each protocol that requires full Board review will be assigned to a primary reviewer; the primary reviewer system is described in detail below. Review criteria are explained in more detail in the Review section (Section VI) of these procedures. All regular and alternate 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 HRPO staff and the IRB Chair or other members, and Internal Documents attached by HRPO staff or the IRB Chair or other members.

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

Board members are also notified by email of the items 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, i.e., each submitted Event is assigned to a primary reviewer, based on related expertise. Primary reviewers are responsible for conducting an in-depth review of all available documentation and presenting the study to the Board. Although a primary reviewer system is used, all members who will be participating in the review are expected to review all agenda items.

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 and will not participate in the vote on the protocol 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 HRPO staff and IRB members, Internal Documents, or reviewer assignment.

When making reviewer assignments, the Chair or designee considers the type of research and any recommendations from HRPO 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). A Chair may authorize a senior HRPO staff member to make assignments for certain Events.

Protocols are distributed electronically within Rascal. When necessary to ensure a substantive review of a submitted Event, more than one reviewer may be assigned. An individual Board may elect to assign more than one 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. Consultants who do not have Rascal access will receive material by other means.

If vulnerable populations are involved in the research, and considering the risk level of the study, the Chair will endeavor to assign the protocol to an IRB member with the requisite experience to make appropriate determinations for the target population; it is preferable 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 protocol that involves prisoners, to avoid disruption of participation or the need for re-review should a subject become a prisoner. The PI's perspective as to whether continued participation of a subject who becomes incarcerated during participation would be desirable should be obtained to inform this decision. The reviewer is guided by the Prisoner Research review form (Reference Document #94).

## **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 generally 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

A prisoner representative is assigned to review each renewal that involves prisoners as subjects. 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 review the 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 generally 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 or HRPO staff.

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) and/or protocol is deemed necessary, the Board determines whether currently enrolled subjects also need to be informed, how this should be documented and, in the case of revised consent forms, whether their consent should be re-obtained. 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: 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 requires that all closure requests be assigned to a Board meeting regardless of the level of review that the study had previously received. 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, the agenda listing the closures is converted into minutes and approved by the Exp Chair on rotation. 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 (See Reference Document #95 for an explanation of the members of the research team to whom correspondence is sent within Rascal). Minutes of full Board meetings, which include the outcome of an event reviewed at the meeting, will usually be approved in their entirety prior to transmittal to researchers of the outcome of individual events via Rascal. 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 will be included.

Minutes for the entire meeting need not be approved before correspondence requesting revision(s) or an electronic LOA (Reference Document #93) documenting approval 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).

Each Board 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 \(a\)\(1\)](#)). Electronic copies of minutes are provided to IOs with a cover memo highlighting items that may require additional institutional consideration or to note compliance or other matters of concern that were discussions by the Board.

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

All requests and concerns of the IRB, whether from 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.

Approval of a human subjects research activity, whether exempt or non-exempt, will 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 through approval of minutes or of previously pending items, or by an authorized expedited reviewer, and must be signed by a designee with signing authority.

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 and outcome;
- e. approval and expiration dates;
- f. consent and HIPAA requirements (if any);
- g. study status;
- h. conditions to the approval, e.g., requirement to translate consent documents;
- i. information regarding Researcher Responsibilities including continuing review requirements, reporting of UPs, the need to submit modifications for approval prior to implementation, and request to submit a closure report once the study has been completed; and
- j. electronic signature of the individual with signing authority.

The LOA for changes to an approved research project, or for a continuing review request that includes changes to the research project, will include, in addition to the items noted above, a description of the modification.

When a CU IRB serves as the IRB of Record for a non-Columbia institution, the Columbia research team is responsible for providing a copy of the LOA to each institution, as appropriate.

### **2. Notification: Disapproval**

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 an electronic Letter of Disapproval (LOD) (Reference Document #96) that 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.

The LOD must include the reason that the research, or proposed modification, was disapproved. This document will also include:

- a. the title of the research project;
- b. the name of PI;
- c. that the investigator may appeal the decision, in person or in writing, within 30 days from the release of the LOD;
- d. contact information for the IRB.

When a CU IRB serves as the IRB of Record for a non-Columbia institution, the Columbia research team is responsible for providing a copy of the LOD to each institution, as appropriate.

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

### **3. Notification: Suspension and/or Termination**

Correspondence relating to suspensions and terminations that occur outside of a convened IRB meeting will initially be sent to the PI either by email or hard-copy letter, and may follow via Rascal correspondence, whereas such actions occurring at a convened meeting may be communicated solely via Rascal correspondence. When a CU IRB serves as the IRB of Record for one or more non-Columbia institution(s), notification related to suspension and/or termination of the protocol at all sites, or suspension and/or termination of the research at a single relying site, will be communicated by the ED and/or DCO to the PI(s) and Institutional Official(s), as previously identified by the affected relying site(s), according to the terms of the IAA between CU and the non-Columbia institution(s).

Documentation of the non-Rascal notification will be entered in the Notes section of the protocol or as an attached document in Rascal.

When a hard copy letter is issued, the PI's Department Chair and/or Division Chief, as appropriate, the relevant IO(s) and other need-to-know individuals 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 CFR 56.111](#)) 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 or will be satisfied when dictated revisions to the protocol/consent form(s) have been made.

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 IRB, and shows the expiration date. The stamp is only used on finalized documents that will be provided to the research subject(s), and will appear on each page of the consent form, recruitment material and study instruments. The electronic stamp will also include the IRB number and the approval and expiration dates.

The approval stamp will be applied to the document only when the IRB 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., background, drugs/biologics, and subjects pages) 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 new protocol or other Event. 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, TC0087, Human Subjects Protection (HSP), that is available through the Rascal Training Center. Individuals must complete both the HSP and research-related HIPAA (TC0019) 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 HRPO staff, then reviewed by the IRB Chair at CU-MS, or by a member of the Administrative Review Committee at CUMC. Chairs of the CUMC IRBs also have the authority to make exemption or “Not Human Subjects Research” determinations, i.e., that the definition of *research* or *human subject* is not met.

Research involving procedures that fall within one or more of the allowable categories for expedited review will initially be pre-reviewed by HRPO 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 constitute *research* with *human subjects* and do not meet the criteria for exemption or expedited review will initially be pre-reviewed by HRPO staff, and then reviewed at a convened meeting of the IRB. This process is described more fully in Sections VI and VII.

At each step of the review process, the Event under review is assigned a specific status (e.g., submitted, logged in, distributed, 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 HRPO 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 (i.e., “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, HRPO 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 to enable the IRB to meet criteria for approval or for tracking or reporting purposes, 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, PI is not in the CU Directory, or the PI’s privileges have been suspended by the IRB;
- b. the PI has not completed the required human subjects/S-I/FDA/HIPAA/Minors/ Good Clinical Practice (GCP) training specific to the proposed study procedures;



- c. the Attributes section of the submission does not appropriately identify the IRB of Record and all Relying Institutions, as applicable;
- d. the study is cancer-related research but the procedures page indicates “no” to cancer-related research or, if it indicates “yes”, an appropriate selection (e.g. “Involves an intervention designed to diagnose, treat, prevent, or provide supportive care to subjects with or at risk of developing a form of cancer; Uses specimens or patient information to assess cancer risk, clinical outcomes or response to therapies, Utilizes observation or surveillance [no intervention or alteration of patient status],” etc.) has not been designated;
- e. the sponsor’s protocol, investigator’s brochure, device manual or other component of the formal description of the research is missing and efforts to obtain document(s) outside of Rascal have not been successful;
- f. the grant application or other documentation of funded procedures is not included, if the study is externally funded and efforts to obtain document(s) outside of Rascal have not been successful;
- g. consent/parental permission/assent documents are not included, a waiver of consent may be appropriate, and a waiver of informed consent/parental permission/assent is not requested;
- h. consent/parental permission/assent documents are not included, a waiver of consent would not be appropriate, and efforts to obtain document(s) outside of Rascal have not been successful;
- i. consent/parental permission/assent documents do not include all of the required elements of consent/assent;
- j. study instruments (e.g., surveys, questionnaires, interview or focus group guides, etc.), if a specific number of instruments, or a specific instrument, are referred to but multiple instruments are not provided;
- k. plans for recruitment are not provided;
- l. there is no data and safety monitoring plan, if the study is greater than minimal risk;
- m. the study will enroll children but the subjects page (vulnerable subjects section) does not reflect this population;
- n. the study involves the use of an investigational product but the Drugs/Biologics or Devices page(s), as applicable, has not been completed;
- o. Appendix A (for recombinant DNA, including gene transfer), B (for infectious agents), D (for lasers), H (for certain research procedures involving ionizing radiation exposure) or I (for controlled substances) is required but is not attached;
- p. the study involves administration of unapproved radiopharmaceuticals intended to solely obtain information about the human physiology, pathophysiology, biochemistry or metabolism of the drug but there is no confirmation of RDRC review or final outcome;

- q. there is not enough information to conduct an adequate review; or
- r. the Event is eligible for expedited review or exemption, and is either in “approvable condition” except for minor items that need to be revised or added, or more significant changes are required.

When information is missing for any event (e.g. new protocol, continuing review, modification, etc.), HRPO staff will use their professional judgment to evaluate if the submission should be returned to the researcher in order to obtain the missing information. Where appropriate, every effort will be made to obtain missing information without returning the submission. In either case, whenever missing information cannot be obtained, and such information is not required in order to meet IRB criteria for approval, the HRPO staff will note the missing information and the IRB review will proceed.

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 for non-exempt studies 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 provided appears to be incorrect, and/or information regarding enrolled subjects is not included;
- b. enrollment is ongoing, consent/parental permission/assent forms are not attached, and a waiver of informed consent/assent/parental permission is not requested;
- c. the PI is not qualified, the PI is not in the CU Directory, or the PI’s research privileges have been suspended;
- d. the PI has not completed the required human subjects/S-I/FDA/HIPAA/Minors/GCP training specific to the proposed study procedures;
- e. the Attributes section of the submission does not appropriately identify the IRB of Record and all Relying Institutions, as applicable;
- f. the sponsor’s protocol, investigator’s brochure, device manual, grant, or other component of the formal description of the research is missing and efforts to obtain documentation outside of Rascal have not been successful;

- g. a summary of UPs, recent reports from a data and safety monitoring body, or Progress Report, is not included, where applicable and efforts to obtain documentation outside of Rascal have not been successful;
- h. the Oversight Monitoring/Unanticipated Problems section applies but was not completed;
- i. the study will enroll members of a vulnerable population but the subjects page (vulnerable subjects section) does not reflect this population;
- j. the study is cancer-related research but the procedures page indicates “no” to cancer-related research or, if it indicates “yes”, appropriate selections (e.g. “Involves an intervention designed to diagnose, treat, prevent, or provide supportive care to subjects with or at risk of developing a form of cancer; Uses specimens or patient information to assess cancer risk, clinical outcomes or response to therapies, Utilizes observation or surveillance (no intervention or alteration of patient status),” etc.) have not been designated;
- k. Appendix A (for recombinant DNA, including gene transfer), B (for infectious agents), D (for lasers), H (for certain research procedures involving ionizing radiation) or I (for controlled substances) is required but is not attached;
- l. the study involves administration of unapproved radiopharmaceuticals intended to solely obtain information about the human physiology, pathophysiology, biochemistry or metabolism of the drug but there is no confirmation of RDRC review or final outcome;
- m. the study involves the use of an investigational product but the Drugs/Biologics or Devices page(s), as applicable, has not been completed; or
- n. other information that is necessary to adequately address IRB review criteria is missing.

HRPO 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 HRPO 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 and such information is not required in order to meet IRB criteria for approval, the HRPO staff will note the missing information and the IRB review will proceed, at a minimum to allow continued participation for subjects who are currently enrolled, if the submission assures participant safety and particularly if participants could be harmed by a disruption in study procedures.

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 HRPO 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, recommends 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 if efforts to obtain information and/or documentation outside of Rascal have not been successful.

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 conducted by HRPO staff 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 as an UP by the IRB.

The IRB does not review Adverse Event (AE) reports unless the AE(s) meet the criteria to be an UP. UP Reports that meet the criteria or require committee discussion to determine if criteria are met will be logged in. The HRPO staff reviewer may also review the current consent document and/or protocol 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. The staff reviewer will also make a preliminary assessment as to whether the UP Report can be reviewed by expedited review (for studies that initially were eligible for expedited review and if the UP does not raise the risk level to greater than minimal) or requires full Board review.

Board members have access to UP Reports as well as all material previously submitted for the protocol, in addition to the pre-review comments. For UP Reports reviewed 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: Closure Requests**

Closure Requests are pre-reviewed by HRPO staff to verify that all information requested in the Rascal Closure 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 cessation of IRB oversight of the study. 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 that 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 Closure Return Criteria (Reference Document #111) to guide the pre-review, and will enter 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 Approval of Research**

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, individuals with impaired decision-making ability, 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](#) and [21 CFR 50.25](#).
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:

1. Recruitment methods and advertising material are appropriate.
2. Additional protections are in place for vulnerable subjects.
3. 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 identifying 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;
- f. allocating adequate time to conduct and complete the research;
- g. ensuring that adequate facilities are available;
- h. when indicated, consideration of whether an adequate number of qualified staff are included;
- i. having access to a population that will allow recruitment of the necessary number of subjects;
- j. ensuring the availability of medical or psychosocial resources that subjects may need as a consequence of the research.

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 have been enrolled, 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 study 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, e.g.:

- 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 who may be subject to undue influence or coercion, such as children, prisoners, and individuals with impaired decision-making ability, so that their enrollment and participation in the study is not adversely affected, or risk of procedures increased, by their vulnerability. Recruitment of women who are in labor also requires special consideration. 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 CU's HRPO [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, parental permission 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. If the IRB determines that written consent is required, the subject or the subject's legally authorized representative will sign and date the consent document.

- a. Documentation of the consent process includes:
  - i. The written consent document should be signed and personally dated by the subject or by the subject's legally acceptable representative.
  - ii. The written consent document should be signed and personally dated by the person who conducted the informed consent discussion.
  - iii. If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion.
    1. After the written consent document and any other written information to be provided to the subject is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial and, if capable of doing so, has signed and personally dated the consent document, the witness should sign and personally date the consent document.
    2. By signing the consent document, the witness attests that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that consent was freely given by the subject or the subject's legally acceptable representative.
  - iv. The subject or the subject's legally acceptable representative should receive a copy of the signed and dated written consent document and any other written information provided to the subjects.

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 and/or provide the necessary information; securing a consultant with expertise about surrogate consent, the proposed study population 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 LAR. 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 Notes, as appropriate to the level of review. If revision is necessary after the Board’s or designated expedited reviewer’s review, HRPO staff members will notify the investigator via Rascal correspondence of the changes that should be made to the consent form. The investigator will make the required changes to the consent form(s), and return the corrected consent document(s) to the IRB for confirmation. For changes requested at a convened meeting, 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 requested by the IRB are substantive, whether they are limited to the consent document(s) or involve other changes as well, 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 (Section VI.8) and in the “Enrollment of Non-English Speaking Subjects in Research Policy,” which is available on the CU HRPO [website](#).

It is noted that when a professional interpreter (e.g., an interpreter hired by the study team) 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 video-recording, 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 Audio- and Videotaping Policy and Sample Audio-/Videotaping Addendum (Reference Document #16) which is available on the CU HRPO [website](#).

**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 has been 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 recommends not seeking consent for research on the same day as elective procedures when possible, and providing 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 CU HRPO [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 available on the CU HRPO [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, 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, video-recording 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. Researchers are advised to incorporate options only after careful consideration of how use of the samples may be restricted if subjects opt out, and to carefully document and track subject choices to ensure that any future use of the samples is consistent with those choices. If agreement to storage and potential future use of specimens is a requirement of participation, this should be clearly stated in the consent form and should not include yes/no options.

If future genetic testing on stored specimens is anticipated, the requirements of the [IRB Policy on Research Involving Genetic Testing](#) 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. Careful tracking of subject selections is the responsibility of the PI to ensure that no efforts are made to contact individuals who indicated that they did not want to be contacted.

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.

### **10) Electronic Informed Consent**

When it is anticipated that electronic systems or media (e.g., text, graphics, audio, video, podcasts, websites, etc.) will be employed to obtain informed consent of subjects who wish to participate in a study, a request to use either In-Person or Remote e-Consenting, each as defined in the IRB “Guidance on Electronic Consent” (Reference Document #369), must be submitted and approved by the IRB prior to its implementation.

The e-Consenting information must be submitted to the IRB in a format that facilitates review and includes a description of the e-Consenting process, the applicable eConsenting system or software and all ancillary information that will be provided to a subject through links or branching options and if an Electronic Signature (“e-Signature”) would be used. When a research study will involve a vulnerable population, the manner in which the e-Consenting process will address the specific characteristics of such population should be described. More information on e-Consent is provided in the IRB “Guidance on Electronic Consent” that is available on the CU HRPO [website](#).

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

The HHS regulations at [45 CFR 46.116\(d\)](#) allow the Board or an expedited reviewer to waive the requirement for informed consent, 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\(c\)](#)).

In July, 2017, the FDA issued guidance for immediate implementation allowing the Board or an expedited reviewer to approve a consent procedure, for certain FDA-regulated minimal risk clinical investigations, that does not include, or that alters, some or all of the elements of informed consent set forth in [21 CFR 50.25](#), or that waives the requirement to obtain informed consent when the IRB finds and documents that:

1. The clinical investigation involves no more than minimal risk (as defined in [21 CFR 50.3\(k\)](#) or [56.102\(i\)](#)) to the subjects;
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. The clinical investigation 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.

FDA intends to revise its informed consent regulations to add this waiver or alteration, and does not intend to object to an IRB approving such consent procedures prior to revision of the regulations.

The FDA allows an exception to informed consent in planned emergency research situations involving investigational (non-approved) FDA-regulated products. . The regulatory citation for the exception in these situations, is [21 CFR 50.24](#) (exception from informed consent regulation for emergency research). 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 LARs of the subjects, no legally effective informed consent can be obtained. Consultation with the community is a requirement; researchers who propose planned emergency research should consult with the IRB prior to submission of the protocol to ensure that appropriate procedures are planned, to avoid a delay in approval. 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 section of Rascal, and in the final IRB approval letter. 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, becomes a record of the subject's consent for both the research team and the subject. Procedures usually include plans 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](#).

When e-Signature is proposed, the submission should include information about the electronic media that will be used to capture the e-Signature of a subject (e.g. computer-readable ID cards, biometrics, digital signatures and user name and password combinations). In general, clicking an "I Agree" icon, hyperlink or other similar method to document consent to participate in a study, when an identifier is not linked to that action, is not considered to be an acceptable e-Signature. For such mechanisms, waiver of written documentation of informed consent by the IRB may be appropriate. If a research study involves a FDA-regulated product and is subject to FDA regulations (a "FDA Study"), compliance with the requirements of [21 CFR 11](#), including verification of the identity of the signing individual, is required prior to the e-Consent being signed. The date that the e-Consent was signed should be recorded in the applicable system for FDA Studies.

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, or otherwise document informed consent by electronic signature, 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\(d\)\(2\)](#)), the content of which would be reviewed by the IRB. This decision will be documented in IRB records.

For research under HHS jurisdiction that does not involve a 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 and if the IRB requires the investigator to provide subjects with a written statement regarding the research, the content of which would be reviewed by the IRB. 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 section of Rascal, 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 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 Plan (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	<ul style="list-style-type: none"> <li>• Study population is small</li> <li>• Narrow range of factors that could have a significant impact on risks and benefits</li> <li>• Continuous, close monitoring by the study team is possible</li> <li>• Phase I and some Phase II trials</li> </ul>
Data Monitoring Committee or equivalent (More than Individual Investigator but less formal than a Data and Safety Monitoring Board as described by the NCI in 1999)	<ul style="list-style-type: none"> <li>• Death or severe disability is not a likely consequence of participation</li> <li>• Low to moderate risk research</li> <li>• Many industry-sponsored multicenter trials</li> </ul>
Data and Safety Monitoring Board	<ul style="list-style-type: none"> <li>• Moderate to high risk research</li> <li>• Multiple sites or large numbers of subjects</li> <li>• Double-Blind study design</li> <li>• Inclusion of vulnerable populations</li> <li>• Definitive Phase III trials</li> </ul>

\*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 confidentiality 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, how electronic data will be protected from unauthorized access, and where data may be transmitted are required in the submission. In addition, consideration will be given to whom has access to the data. Awareness of CU IT and IRB policies for 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 TRAC Committee. This approval should be requested after IRB approval is issued. The purpose of the TRAC 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 identifiable 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. All biomedical, behavioral, clinical or other research funded wholly or in part by the NIH, whether supported through grants, cooperative agreements, contracts or other transaction awards that collects or uses identifiable, sensitive information is deemed to be issued a Certificate of Confidentiality, if the research was ongoing as of, or commenced after, December 16, 2016.

When Social Security Numbers (SSNs) will be collected, adherence to University policies for 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 for a research purpose 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 HRPO [website](#).

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 OHC, when applicable. HRPO staff review and approve all HIPAA forms that are attached to a protocol, other than waiver requests, which must be approved by an IRB or IRB Member. For protocols that include a covered HIPAA transaction, HIPAA authorization language may be included in the consent form for the respective study, or provided in a separate Authorization Form. Combined consent/authorization forms are encouraged, to reduce the number of forms that need to be signed, and may be utilized if requested by a sponsor or in other situations where a single form is preferable.

The CU policy, “CU Policy on the Privacy Rule and the Use of Health Information in Research,” clarifies when individually identifiable, health-related research data are PHI and when they are Research Health Information (RHI). It describes requirements for the use and disclosure of PHI, including specific forms to be used and data security requirements. The policy is available on the CU HPRO [website](#).

Additional information may be obtained via Rascal or from the CU HRPO website.

## **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:

- Introduction of the study to the patient, verbally or in writing, depending on the specific circumstances of the study.
  - If it is proposed that information in medical records will be used to identify and contact patients in writing for possible participation in research, the contact should be made by the treating physician, e.g., a letter signed by the physician, or co-signed by the physician and researcher.
    - It is not appropriate in most situations for the researcher to contact a patient directly, using information obtained from medical records. However, it is recognized that, although every patient is assigned a Physician of Record when receiving medical care, in some situations, the patient and treating physician have only a transient relationship and involving the physician in recruitment efforts does not add to patient protection, i.e., the patient will not be reassured that the privacy of his/her information is being safeguarded by someone he/she trusts. Therefore, if recruitment will occur in a setting, such as the Emergency Department, where such transient relationships are the norm, the medical director of the unit should be aware of the potential recruitment and can co-sign the recruitment letter.
    - 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 contact information for the study team, and must take action within a specified interval, 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 is given contact information for the study team and initiates contact if he or she wishes to learn more about the study. The former approach is recommended; both the former and latter require IRB approval.

- The treating physician may verbally inform his/her patients about research. In such cases, the patient should be provided with a written brochure or description of the study (e.g., recruitment material) 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/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.
- If in-patients will be identified through review of unit/departmental logs or other records, the treating physician should be notified of the intent to approach his/her patient about study participation and should be provided the opportunity to discuss the proposed approach with the researcher. Ultimately, it is the patient's decision whether to participate but the treating physician should be aware of the potential participation, to discuss options with the patient and, if the patient enrolls and remains under the treating physician's care, appropriately monitor and, if necessary, revise the patient's treatment.
- 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 the opportunity to communicate disagreement with enrollment procedures or enrollment of the specific patient(s), if that is the case.

When the treating physician is also the researcher, the IRB must assess whether the consent process, beginning with recruitment, can 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 pre 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 assess whether 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 recording follows the Board advertising review guidelines appropriately, it may be approved. However, if there is anything in the recording that an expedited reviewer finds unacceptable, review of the recording 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 protocol to protect the rights and welfare of subjects who are likely to be vulnerable to coercion or undue influence, e.g., children, prisoners, or individuals with impaired decision-making capacity, 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 LAR or agent named in a HCP, the latter under appropriate circumstances, provide permission for enrollment, in addition to consent or assent from the subject, when appropriate. 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 HCP 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), or when a

protocol involves significant risk, the IRB may observe the consent process, or require changes in recruitment procedures to eliminate or reduce elements of coercion or undue influence. The College of Physicians and Surgeons has an advisory committee that reviews all research targeting their students to ensure that issues of coercion or undue influence are prevented. For studies that target these students, approval by this advisory committee must be obtained prior to IRB approval.

When children will be enrolled, the requirements of Subpart D of [45 CFR 46](#) and, as applicable, [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 and the Institution is Eliminated, Mitigated or Managed**

All Columbia faculty must complete an on-line COI disclosure form in the Rascal system upon hire and must update this form at least annually, and whenever circumstances change. In addition, all PIs, 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. RCT works closely with the Columbia IRB office to foster the ethical conduct of research at Columbia.

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

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.

- 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 of the research.
- Cases that meet or exceed the University threshold for significant financial interests are referred to the University’s Committee on Financial Conflicts of

Interest and Research (FCOI Committee). The FCOI Committee is comprised of faculty and representatives from administrative units within the University that have responsibility for research functions, and serves to determine whether a particular significant financial interest constitutes a conflict and, if so, whether it can be managed. Notification of Committee determinations involving 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's [Policy on Financial Conflicts of Interest in Research](#) (FCOI Policy). The FCOI Policy is posted on the [RCT website](#).

Once RCT clears a protocol-specific disclosure form (either after administrative or FCOI Committee review, as needed), Rascal automatically provides access to the form and RCT clearance notes to IRB staff reviewing 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 FCOI 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 FCOI Committee (if applicable). If it is necessary to review the protocol at a convened meeting prior to final resolution of the COI by RCT and/or the FCOI 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 FCOI 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 RCT 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 FCOI Committee, if warranted, and communication back to the IRB of the result in Rascal. Final approval by the IRB will not be granted until the FCOI Committee review(s) are complete, the IRB has had an opportunity to review the outcome, and the IRB is either satisfied with the FCOI Committee requirements or implements additional requirements (e.g., consent form disclosure).

In addition to the policy covering disclosure, review and management of individual conflicts of interest, the University has implemented a Policy on Institutional Conflicts of Interest and Research (ICOI Policy), which is also posted on the RCT website. The ICOI Policy was adopted by the University Senate in 2014. As defined in the ICOI Policy, an ICOI relating to research may occur whenever the significant financial interests of the

institution, or of an institutional official who has authority to act on behalf of the institution (“Covered Official”), might affect, or reasonably appear to affect, institutional processes for the design, conduct, reporting, review, or oversight of research.

Significant financial interests held by Columbia or Covered Officials (collectively, “ISFI”) are disclosed primarily on “intake forms” submitted through a new ICOI system in Rascal. ISFI include those gifts, equity, royalty payments, and Covered Official financial interests that exceed thresholds set by the ICOI Policy. The intake forms are prepared and submitted to Rascal by offices best positioned to be aware of ISFI, including Columbia Technology Ventures, Alumni and Development, and RCT. Covered Official financial interests are also sometimes detected through RCT’s review of individual COI disclosure forms. RCT screens these institutional financial interests, and where a disclosed ISFI is flagged as relating to current University research, refers the case to the ICOI Committee.

The ICOI Committee includes at least one senior officer representative of the University from the following schools: Columbia University Medical Center, Arts & Sciences, and one from the School of Engineering and Applied Sciences and is staffed by RCT. Non-voting participants include representatives from the Office of the General Counsel; Columbia Technology Ventures; Alumni and Development; and other research administration offices as appropriate.

The ICOI Committee assesses the potential risks to research integrity and human subjects presented by ISFI to determine whether the ISFI constitutes an ICOI. The ICOI Committee and the University make every attempt to resolve institutional conflicts in a manner that enables research to proceed at the University. However, if the ICOI Committee finds that an ICOI cannot be managed, and divestment is not feasible, then the affected research should not proceed at the University.

Where the ICOI Committee reviews an ICOI that relates to IRB research, RCT communicates relevant information regarding the existence and management of the ICOI to the IRB. At present, ICOI-related communications between RCT and the IRB are not fully integrated into Rascal, but additional electronic integration between the two offices is being planned.

## 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 as 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 \(a\)\(1\)](#)). The Boards also follow applicable regulations for research that is supported by other federal agencies. See Reference Document #356 for additional information. When designated through a reliance agreement as the IRB of Record for non-Columbia study sites, the Boards will also follow these regulations in the review of research for those sites,

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

In addition, for Columbia research, the Boards will ensure that all required 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). The extent to which the Boards are responsible for monitoring equivalent requirements at non-Columbia sites, when serving as the IRB of record for those sites, will be determined by the terms of the applicable agreement.

If a protocol is cancer-related, and review by the PRMC is necessary, IRB review may proceed while PRMC 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. Final IRB approval may not be granted until approval from the PRMC is obtained.

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 five 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 for five 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, CU is not the IRB of Record and the official expiration date is the one determined by the IRB of Record. Rascal allows an IRB reviewer to manually change the expiration date for an Event under facilitated review so that the expiration date in Rascal can match the expiration date that has been set by the reviewing IRB; or
- c. a modification is approved for a protocol that was formerly determined to be exempt (and thus approved for five years), but no longer meets the exemption criteria due to the nature of the modification. In this instance, manual revision is required because 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 normally retained by Rascal.

When a Columbia IRB serves as the IRB of Record for another institution, including when serving as a sIRB, the IRB is responsible for the review of the protocol, consent form, and all study related documents, and review will be conducted in light of local context provided by each external site when this is requested. As referenced in Section III.E.14 and in Reference Document #366, when Columbia is both the IRB of Record for multiple sites and Columbia is a site, two protocol submissions are required. One will be a “Master Protocol” (MP) for review of the protocol, consent form template, and other study documents for all sites, and one will be for the Columbia study site. See Reference Documents #365 for detailed information about review when the CU IRB serves as the IRB of Record for other institutions.

When CU relies on a non-Columbia IRB, a protocol submission in Rascal is required in order for tracking purposes and to facilitate compliance with all institutional policies for the protection of human subjects (e.g., conflict of interest, radiation safety, institutional biosafety committee, etc.), as well as to provide local context in the manner requested by

the non-Columbia IRB. These protocol submissions should generally be made after the IRB of Record approves the MP. When appropriate, an IRB Chair or designated IRB member will confirm the local context issues raised, which will be provided to the IRB of Record. The protocol should be resubmitted in Rascal after the IRB of Record has approved CU as a research site, and all specific final IRB approved study material should be attached in Rascal. After it is confirmed that all CU and local requirements have been satisfactorily addressed, the submission will be logged in for approval via facilitated review by an IRB Chair or designated IRB member.

## **2. Review of Modifications**

Regulations require 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. Columbia policy reiterates this regulatory requirement and extends oversight to require submission of protocol modifications to exempt research. 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, amendments, 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 ([Conditions for IRB Use of Expedited Review, Nov. 9, 1998](#)). Changes proposed for studies that will expire within 60 days should be included in a renewal submission in place of submission of a modification, when feasible.

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 that are 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, if a major violation, otherwise, reported at the time of continuing review; 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.

Refer to Section III.D.4 on how to submit the report of changes made without prospective IRB approval to address imminent harm to subjects and for required supporting documentation/information for each type of event.

When CU serves as the IRB of Record for other institutions, the terms of the IAA will dictate the types of modifications that need to be submitted to the IRB for review. If the IAA does not specify terms, then the CU IRB will review all modifications for a given study.

When CU relies on a non-Columbia IRB as the IRB of Record, the terms of the IAA will dictate the types of modification submissions that need to be submitted to the IRB of Record for review (e.g., a change to the protocol, consent form, or any substantive change) versus submissions that may only need review by the Columbia IRB (e.g., changes in study personnel other than the PI). When a modification needs to be submitted to a non-Columbia IRB for review, it will follow the same process as outlined above in Section VI.A.1 for the review of new protocols. When a modification only needs to be reviewed by the CU IRB, the process will follow that of all other



modifications that are submitted for CU IRB review when a CU IRB is the IRB of Record.

### **3. Review of Reports of Unanticipated Problems Involving Risks to Subjects or Others**

Submission of reports of unanticipated problems, including adverse events that meet the criteria to be unanticipated problems, 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 either be assigned to an agenda for review by the IRB Chair or be presented for discussion at a convened meeting of the IRB after review by a primary reviewer. The IRB 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 IRB may impose restrictions on the research (e.g., more frequent reporting, suspension of enrollment, suspension of the study, termination, etc.) if review of one or more 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 IRB 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 IRB.

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 will subsequently report it to the appropriate regulatory agency within 30 days of the final UP determination. When research is federally supported or conducted by federal agencies other than DHHS or FDA, there may be additional reporting requirements for the IRB and/or investigator. See Reference Document #356 for additional information.

When CU serves as the IRB of Record for other institutions, all UPs that meet the definitions outlined in CU's UP Policy and occur at any relying site must be submitted to the CU IRB for review in accordance with the CU UP Policy.

When CU relies on a non-Columbia IRB as the IRB of Record, the terms of the IAA will dictate if UPs will be reported to the IRB of Record. Regardless of whether an UP is reported to the IRB of Record or not, all UPs must also be submitted in Rascal.

#### **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. Additional guidance can also be found in [CU IRB Guidance for Protocol Deviations and Violations](#) available on the CU HRPO website (Reference Document #364).

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. All requests for deviations from, and reports of violations of IRB policies or IRB determinations, including departures from the requirement for adherence to the approved protocol, must be reported to the IRB. It is particularly important that the IRB be notified promptly when a deviation or violation could potentially cause increased risk to subjects or the study as a whole, as explained in more detail below.

When approval for a deviation is being required, and the study is externally sponsored, approval from the sponsor should be provided with the request in Rascal. When a non-Columbia IRB is the Reviewing IRB, requests for protocol deviations should be submitted to the reviewing IRB in accordance with procedures established by the Reviewing IRB. Documentation of the request and the Reviewing IRB’s decision should be submitted in Rascal once available.

Protocol violations can be categorized as either minor or major, and may or may not affect individual subjects. Major violations should be reported promptly, generally within one week (5 business days), to provide an opportunity for the IRB to assess whether the study should continue, and whether changes to study procedures are required.

The IRB will review protocol violations to determine whether the risk/benefit ratio of the protocol has increased as a result of the violation(s). Potential or real harm, or risk of harm, to the subject will be assessed.

If the PI’s assessment is that the violation meets the criteria of an UP, it should be submitted using the UP report Event. Otherwise, the PI must assess whether it is a major or a minor violation, and submit accordingly. The IRB, upon review of the submission, may disagree with the PI’s categorization of the violation and require a different type of submission. A corrective action 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 found to be nonsignificant noncompliance based on the definition in the IRB “[Noncompliance in Human Subjects Research](#)” policy (Reference Document #89), the findings are entered by the HRPO staff member into the notes for review by the Chair or his/her designee and documented in the minutes, as appropriate, for events that require convened review.

If the situation appears to meet the reporting criteria for serious or continuing noncompliance, referral to the COT for initiation of a noncompliance inquiry or other appropriate action is required.

When CU serves as the IRB of Record for other institutions, all protocol violations that occur at any site that is relying on CU as the IRB Review should be submitted in Rascal for review by the CU IRB.

When CU relies on a non-Columbia IRB as the IRB of Record, the terms of the IAA will dictate which protocol violations must be reported to the IRB of Record. Regardless of whether a protocol violation is reported to the IRB of Record or not, all protocol violations must also be submitted in Rascal.

## **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). Emergency uses are not considered research, but rather the practice of medicine for the treatment of patients with non-FDA-approved products.

The data from emergency use of a test article, other than a medical device, may not be used for research purposes under DHHS regulations but may be required by FDA for use in a marketing application. Based on FDA definitions, the emergency use is a clinical investigation, and the patient is a subject. DHHS regulations do not permit procedures related to or data obtained from patients who received the test article in an emergency use situation to be classified as human subjects research, nor permit the outcome of such care to be included in any report of a research activity that is subject to DHHS regulations.

Emergency use requests are processed by HRPO staff (the ED, DIM, DO, ADIM 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 HRPO or IRB is aware of an emergency use request so that the investigational product may be shipped, as discussed in more detail below, they do not review the procedures for use of the product. Rather, they ensure that the regulatory criteria for emergency use are met, confirm appropriate patient protection procedures will be followed, including obtaining informed consent from the patient or legal representative when possible, and in the case of emergency use of unapproved medical devices, confirm that an independent assessment from an uninvolved physician and authorization from the device manufacturer are provided. HRPO staff also ensure that all required information is provided to the IRB within 5 days of use of the test article, as described in Section III.D.7 above.

FDA regulations ([21 CFR 56.104\(c\)](#)) allow for one emergency use of a test article per institution. Any subsequent use of the investigational product at the institution is subject to prospective IRB review and approval. However, when prior IRB review and approval

is not feasible for a subsequent expanded access emergency use at a particular institution, the FDA will not deny the subsequent request for emergency use based on lack of time to obtain prospective IRB review; reporting such use to the IRB within five working days of initiation of treatment ([21 CFR 56.104\(c\)](#)) is required.

Section VI.B.10 includes 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](#) does not require prospective IRB review or notification. However, when possible, the HRPO should be notified in advance of the proposed emergency use. For some emergency use situations, notification to the HRPO may be necessary because the manufacturer or Sponsor of the test article will not ship the product until a letter from the IRB, stating that the IRB is aware of the impending use of the product, is provided.

Notification to the HRPO is also required when concurrence of the IRB Chair will be one of the subject protection measures to be used. If the proposed emergency use is associated with an existing IRB protocol, the HRPO will request that the Chair or Vice Chair of the reviewing Board provide concurrence that the emergency use meets the emergency use criteria. If that Chair or Vice Chair is not available, or the proposed emergency use is not associated with an existing IRB protocol, the HRPO will request that one of the other IRB Chairs or Vice Chairs conduct the review.

When the IRB office is notified of the proposed emergency use of an investigational agent, a letter or other communication 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 HRPO 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 FDA requires informed consent of the subject, or the subject's legally authorized representative, be obtained unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all the criteria of [21 CFR 50.23 \(a-c\)](#).

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 HRPO via email ([irboffice@columbia.edu](mailto:irboffice@columbia.edu)) 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 test article, 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 HRPO ED, DIM, DO, ADIM 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 ([21 CFR 312](#)) 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 a reliance agreement. Specific instructions related to the review of each different type of Event is explained in the respective section (e.g., new protocols, modifications, UPs).

## **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. 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, a closure report rather than a renewal should be submitted.

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 and approval 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 and reports from “whistleblowers” ([45 CFR 46.103\(b\)\(4\)](#); [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 minus one day from the date of the approval, 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). 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, DIM, and DCO, who will inform the appropriate IO. The ED or DCO 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 submission at the time of continuing review 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.

When the CU IRB serves as the IRB of Record for other institutions, the IRB will review the renewal information on behalf of all sites that are relying on the CU IRB as the IRB of Record as designated in a reliance agreement.

When a non-Columbia IRB is the IRB of Record, a renewal submission in Rascal is required following approval by the IRB of Record. HRPO staff will review the submission and assess whether any changes made to the protocol impact the previously determined local context considerations and will confirm that documentation of IRB



approval from the IRB of Record for continuation of the research has been provided. The renewal will be approved via facilitated review by an IRB Chair or designated IRB member.

**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 Closure Requests**

Requests by researchers for closure of an approved project are reviewed by a primary reviewer prior to being added to an agenda for approval by an IRB Chair or presentation at a convened meeting. The Board reviewer will have access to the staff reviewer's notes and will evaluate information provided 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 as the PI.

## **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.

A suspension is a directive of the convened IRB, IRB Chair, IRB Executive Committee, ED or DIM (in the absence of the ED only) 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 or IRB Executive Committee or ED 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, DIM (in the absence of the ED and IRB Chair), 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, DIM (in the absence of the ED and IRB Chair), or IRB Chair, it would be inappropriate to wait until the next meeting of the IRB or Executive Committee of the IRB. Suspensions and terminations by someone other than the convened IRB must be reported to and reviewed by the convened 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 the COT, which will notify within 30 days the appropriate IOs; the compliance office of the applicable FDA center, if the research is FDA-regulated; and OHRP (Division of Compliance Oversight) of the suspension or termination ([45 CFR 46.108\(a\)](#));([21 CFR 56.113](#)). Regardless of by whom the action was initiated, the ED, DIM and Chair of the reviewing IRB must also be notified of the action. Rascal clearly reflects the status of any study for which IRB approval has been suspended as “SUSPENDED” or “SUSPENDED TO NEW ENROLLMENT”, as applicable, on the Protocol Overview page in Rascal.

When research is federally supported or conducted by federal agencies other than DHHS or FDA, the IRBs will promptly (within 30 days) report the suspension or termination to the appropriate individual at the funding agency. See Reference Document #356 for additional information.

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 and Biologics**

For all clinical investigations of biologics, drugs, or approved drugs used off-label, HRPO 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 (via the investigator):
  - 1) a letter from FDA that documents the status, such as approval of the IND, or since the IND goes into effect 30 days after the FDA receives the IND (unless the sponsor receives earlier notice from the FDA), an IND acknowledgment letter which documents the FDA's receipt of the application. If an IND acknowledgement letter is submitted to document the status, the applicant should provide confirmation that no additional comments or questions have been communicated by the FDA since issuing the letter;
  - 2) a copy of the sponsor's protocol 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.

The IRB will restrict use of the investigational product until an active IND is in place. The researcher must not begin recruiting, obtaining consent, and/or screening participants for the study until the IND is active and in effect.

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 specific information regarding birth control measures must be provided to subjects with reproductive capacity; and
- c. whether special handling is required by research staff, subjects, or others.

The IRB will also confirm that the drug/biologic will be dispensed by the Research Pharmacy in accordance with the NYP Investigational Drug Policy (Reference Document #18) and Research Pharmacy policies (Reference Document #172), as applicable, or that a waiver from the Research Pharmacy of such requirement has been granted.

## **2. Review of Research Involving Medical Devices**

For clinical investigations of devices to determine safety and effectiveness, HRPO 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 coverage from the Centers for Medicare and Medicaid Services (CMS) 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. Information related to CMS authorization may be found on the [CTO website](#).
- 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 an S-I, HRPO consultation with the IAP staff to confirm that they are aware of the study is necessary. The HRPO, 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 \(b\)\(1\)](#)). FDA considers an NSR device study to have an approved IDE after IRB approval and when sponsors meet the abbreviated requirements as noted in this paragraph.
- 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 IRB 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 not more than 8,000 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. Informed consent is required if data are collected under a clinical investigation, even if the device is used according to its approved labeling.

b. Use Not in Accordance with the HDE

Clinical investigations of a HUD for an indication other than the one(s) approved by FDA must be conducted in compliance with IDE regulations at [21 CFR Part 812](#). 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](#) and [21 CFR 56.111](#). 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. See Reference Document #357 for additional details.

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](#), including requirements for appropriate number of consent signatures depending on the research's prospect of direct benefit, if any, and to whom;
- 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 (Research Involving Pregnant Women, 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.

Common examples, as explained in OHRP's Prisoner Research FAQs, of the application of the regulatory definition of prisoner are as follows:

- Individuals who are detained in a residential facility for court-ordered substance abuse treatment as a form of sentencing or alternative to incarceration are prisoners; however, individuals who are receiving non-residential court-ordered substance abuse treatment and are residing in the community are not prisoners.
- Individuals with psychiatric illnesses who have been committed involuntarily to an institution as an alternative to a criminal prosecution or incarceration are prisoners; however, individuals who have been voluntarily admitted to an institution for treatment of a psychiatric illness, or who have been civilly committed to non-penal institutions for treatment because their illness makes them a danger to themselves or others, are not prisoners.

- Parolees who are detained in a treatment center as a condition of parole are prisoners; however, persons living in the community and sentenced to community-supervised monitoring, including parolees, are not prisoners.
- Probationers and individuals wearing monitoring devices are generally not considered to be prisoners; however, situations of this kind frequently require an analysis of the particular circumstances of the planned subject population. Institutions may consult with OHRP when questions arise about research involving these populations.

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 IRB can then consider the other items.

If a subject becomes temporarily incarcerated while enrolled in a study that was not reviewed in light of the Subpart C requirements, and the temporary incarceration has no effect on the study, he/she may remain enrolled as a study participant. However, the subject should be removed from the study if he/she becomes permanently detained or involuntarily confined in a penal institution, 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.

For research involving prisoners reviewed by the convened IRB:

- 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 IRB reviews research involving prisoners, the prisoner representative present at the meeting will count toward quorum for these protocols. A majority of IRB members will have no association with the prison involved, apart from their membership on the IRB. The reviewer form for prisoner research

(Reference Document #94), or equivalent, will be completed for each review by the prisoner representative.

- The prisoner representative may attend the meeting by phone, video-conference, or webinar, as long as the representative is able to participate in the meeting as if he/she was present in person at the meeting.
- The prisoner representative must present his/her review either orally or in writing at the convened meeting of the IRB at which the research involving prisoners is reviewed.
- Modifications involving more than a minor change and reviewed by the convened IRB must use the same procedures as for initial review including the responsibility of the prisoner representative to review the modification and participate in the meeting.

For research involving prisoners reviewed by an expedited review procedure:

- Research involving interaction with prisoners may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied.
  - The prisoner representative must concur with the determination that the research involves no greater than minimal risk.
  - The prisoner representative must review the research as a reviewer, designated by the chair, or consultant. This may be as the sole reviewer or in addition to another reviewer, as appropriate.
  - Review of modifications and continuing review must use the same procedures for initial review using this expedited procedure including the responsibility of the prisoner representative.
- Research that does not involve interaction with prisoners may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied.
  - Review by a prisoner representative is not required.
  - The prisoner representative may review the research as a reviewer or consultant if designated by the IRB chair.
  - Review of modifications and continuing review must use the same procedures as initial review.

In addition to its other responsibilities prescribed in these Written Procedures, the IRB may approve research involving prisoners only if it finds that all requirements described in [45 CFR 46.300](#) (Subpart C) are met. See Reference Document #356, and search for “prisoners”, for additional information, if the protocol is federally funded.

Human subjects research may involve prisoners as subjects only if the IRB 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 IRB will determine that the research under review represents one of the categories of the research permissible under [45 CFR 46.306\(a\)\(2\)](#). In accordance with [Subpart C](#) of the DHHS regulations, when research involves prisoners as subjects, the consent process approved by the IRB will include a determination that:

- the information will be presented in language that is understandable to prisoners;
- each prisoner will be informed in advance that participation in the research will have no effect on his or her parole.

Details of the IRB review for any research project involving prisoners that is federally-supported or conducted will be given to the ED or DIM promptly after review, with a draft certification letter for submission to OHRP. The ED, DIM, 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 be denied 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. See Reference Document #356, and search for “children”, for additional information, if the protocol is federally funded.

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 convened 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 on the Child Involvement page 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 on the Child Involvement page, a notation to this effect in Rascal for protocols edible for review under an expedited pathway, or documentation in the minutes for protocols reviewed at a convened meeting, 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 on the Child Involvement page, 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 on the Child Involvement page, 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 DIM. The ED, DIM, 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 HRPO 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.

IRB reviewers may employ the use of component analysis to assess the potential benefits and risks of individual research interventions or procedures. If component analysis is used, different procedures in a single protocol may be approved under different [Subpart D](#) standards as noted above.

If the IRB, or designated expedited reviewer, does not agree with the PI's assessments regarding risk level and potential for direct benefit, as entered in the Child Involvement section, the IRB determinations, which are documented in review Notes or in meeting minutes, as applicable to the level of review, will prevail.

#### **b. Assent Determination**

After the IRB, or designated expedited reviewer, 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 IRB must decide whether assent is necessary for all children, some children or none of the children, and also whether and how assent will be documented if it is necessary.

Among the formats the IRB, or designated expedited reviewer, 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. When the IRB determines that assent is not a requirement for some or all children, the IRB determines and will document (either in Rascal Notes or in the expedited review approval comments, for research that qualifies for review via an expedited pathway, or in the meeting minutes, if convened review is required) which children are not required to provide 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\(b\)](#)).

Documentation will indicate one or more of the following:

- i. The children are not capable of providing assent based on the age, maturity, or psychological state;
- ii. The capability of the children is so limited that they cannot reasonably be consulted;
- iii. The intervention(s) or procedure(s) involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the child and is available only in the context of the research.
- iv. Assent can be waived using the criteria for waiver of the consent process.

### **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 IRB 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, 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. incarceration;
- b. impaired cognitive capacity, either temporary or permanent;
- c. economic or educational disadvantage;
- d. inability to speak or understand English;
- e. medical condition; or
- f. relationship to researcher.

When the IRB, or designated expedited reviewer, finds that the subjects in a research protocol are vulnerable, additional safeguards will be considered on a protocol-by-protocol 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 IRB 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 IRB 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 information on the Subjects page entered in Rascal by the research team and determine the number or percentage, if any, of

non-English speaking subjects that are expected to be enrolled. In addition, the research team can self-declare their intent to target non-English speaking subjects within the Recruitment & Consent page in Rascal. If the enrollment of non-English speaking subjects is anticipated, 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. 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/ethics committee composition requirements of applicable regulations. If a foreign site for which Columbia has responsibility will be obtaining local IRB/ethics committee approval, and the research is funded by a U.S. federal agency and/or is FDA-regulated, the composition of a reviewing IRB may need to comply with [45 CFR 46.107](#) and/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 consent differs in another country from New York State (NYS) Law (i.e., 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. This plan should include, but not be limited to, procedures for notifying the CU PI of events such as reports of noncompliance (e.g. major protocol violations), significant participant complaints and unanticipated problems involving risk to subjects or others, to ensure that these

events are reported to the IRB within the appropriate time frame. The plan should also outline the procedures for notification to the local ethics committee, as applicable.

- g. The research study should provide a plan for IRB consideration that describes data collection, protection for the confidentiality of the data, and transport of the data back to CU, or elsewhere in the U.S. or another region.
  - 1) If identifiable subject data will be collected by an individual(s) other than those on the Columbia research team, or that (those) individual(s) will have access to identifiable subject data, they 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.
- 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 HRPO 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

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 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 considerations for exception from informed consent requirements. FDA regulations at [21 CFR 50.24](#) and the conforming amendments in [21 CFR Parts 56, 312, 314, 601, 812, and 814](#) provide a narrow exception for such research to the requirement that the investigator obtain informed consent from each subject, or the subject's legally authorized representative, prior to enrollment. The FDA-DHHS Harmonized Rule on Waiver of Consent for Emergency Research permits application of [21 CFR 50.24](#) to planned emergency research situations that do not involve an FDA-regulated drug, medical device, or biologic.

If exception from informed consent is proposed for those subjects who are not capable of providing consent, and will not have a legally authorized representative 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.

In order to approve an exception to informed consent for planned emergency research, the IRB must find and document that the research involves subjects who may be unable to provide consent for themselves; if the research is a clinical investigation involving an FDA-regulated article, it will be carried out under FDA IND or IDE regulation, as applicable; and the requirements for exception from informed consent for emergency research detailed in [21 CFR 50.24](#) have been met, as discussed in more detail below. 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/IDE, 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. Exception from Informed Consent**

The IRB responsible for the review, approval and continuing review of the clinical investigation may approve the investigation without requiring that informed consent be obtained from research subjects if the IRB finds and documents that the requirements of [21 CFR 50.24](#), which include review and approval of the proposed exception 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 exception, the IRB 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) The protocol is performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that might include subjects who are unable to consent.
- 3) 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.
- 4) 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.
- 5) The clinical investigation could not practicably be carried out without the waiver.
- 6) 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.
- 7) 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.
- 8) 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 Board at the time of continuing review.
- 9) The application to the IRB clearly identified the procedures and environment in which subjects would not be able to provide informed consent.

If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception or because of other relevant ethical concerns, the IRB will document its findings and provide these findings promptly (no longer than 30 days) in writing to the clinical investigator, who in turn will notify the sponsor of the clinical investigation. 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 an LAR 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 an 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 a clinical investigation for which an exception to informed consent was proposed because the investigation does not meet the criteria articulated in [21 CFR 50.24](#) for exception to informed consent, or because of other relevant ethical concerns. 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 human embryonic 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 human embryonic stem cells will be conducted in accordance with the IRB Review Criteria described in [45 CFR 46](#), the [CU 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.

### **13. Review of Research that is Federally-supported or -conducted, or is Otherwise Subject to Federal Policy**

Many submissions for research that is subject to federal policy or regulation are received by the IRB each year. Every attempt is made by the IRB to identify applicable policies and/or regulations, and to ensure that the respective requirements are met.

To facilitate a comprehensive and efficient review that addresses all applicable regulatory requirements, investigators are encouraged to provide relevant regulatory material (e.g., instructions from their program official) with their application to the IRB, particularly when: a) the funding source is a federal agency that may not frequently provide support or become involved in the conduct of human subjects research at Columbia (i.e., a department other than DHHS); b) when a federal policy is applicable to a non-routine situation; and c) when an applicable federal regulation has recently been revised.

To enhance the inclusion in IRB submissions of information that is required for compliance with federal regulations that are unique to various agencies, the IRB has prepared a guidance document (Reference Document 356, Additional Requirements for Protocols Funded by Specific Federal Agencies or Subject to Specific Federal Policies) which is posted on the IRB websites.

## **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 IRB review. Refer to the FDA Information Sheet, “Recruiting Study Subjects”, for additional information.

The HRPO 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 convened 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 convened IRB 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. Exceptions to NYP requirements for posted advertisements may be considered on a case-by-case basis by the IO of NYP or designee, which is facilitated by the ED or designee.

The approval stamp for non-exempt research will indicate the IRB number, and the dates of approval and expiration. Approval stamps on documents related to exempt research will include the date of the exempt determination date rather than approval and expiration dates.

IRB review of advertising that will be presented as audio or video advertising may 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 Communications and Public Affairs 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 to 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 \$600 or more 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 other than IRB Exp has regularly scheduled meetings, with additional meetings scheduled as necessary. The schedule of meetings is available on Columbia's HRPO [website](#).

### **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. HRPO staff strive to complete all administrative reviews in order to finalize the meeting agenda and distribute it to members at least five calendar days in advance of the meeting. 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 pre-review notes from staff as well as all documents and information submitted by the investigator which 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.

More than one reviewer may be assigned to a protocol. 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 or videoconference. Quorum is defined as more than one half of all voting members listed on the IRB roster and a non-scientist is present. If members leave the room and quorum is lost, votes cannot be taken until the quorum is restored. The IRB will ensure and document in the minutes that a quorum is present for review of each event that requires full Board review. HRPO Staff (Senior IRB Specialist and/or IRB Specialist) are responsible for monitoring the members present at a convened IRB meeting to ensure that the meeting is appropriately convened at the beginning of the meeting and for each subsequent vote.

It is preferable to have at least one member who represents the general perspective of subjects present at convened meetings. This requirement is usually met through the attendance of a non-scientific member, who may also be an individual not affiliated with the institution. The participation of alternate members who are substituting for regular non-scientific or non-affiliated members will also satisfy this requirement.

The IRBs will defer to another meeting or obtain consultation if there is not at least one person on the IRB roster with appropriate scientific or scholarly expertise, or other expertise or knowledge, to conduct an in-depth review of the protocol or, at a minimum, be involved in the review.

A motion that is seconded, then carried or denied by a majority of the voting members present is required for acting on approvals, confirming determinations to defer subsequent review to the Chair or primary reviewer (“pending”) or to the convened IRB (“return”), confirming decisions by the convened IRB to suspend or terminate IRB approval, 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, determinations, summaries of controverted issues 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, i.e., listing of members who attended any part of the meeting, 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. Agenda categories brought before the Board, and clear identification of each item and/or investigator the Board considers;
- d. 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) Statement that IRB review criteria articulated in [45 CFR 46.111](#) and, if applicable, [21 CFR 56.111](#) or other regulations, have been met (if action is “approved”) or will be met after the clarifications/revisions requested by the Board are addressed (if action is “pending”);
  - 6) Determination of risk level for new protocols, ongoing studies at the time of continuing review, and events for which the risk level has changed since the last review (if action is “approved”, or “pending”);
  - 7) For initial and continuing review, the approval period;
  - 8) 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;
  - 9) 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;
  - 10) 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); and
  - 11) Any changes in attendance from the aforementioned list 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.
- 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, as applicable, FDA or other regulations, 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, if any.

## **2. Approval of Minutes**

The minutes of agenda items reviewed by a convened Board are administratively processed after the convened meeting by HRPO staff, reviewed by Senior HRPO staff and, once complete, sent for review by the Chair and, as appropriate, other Board member(s). Once the minutes for each event are reviewed by the Chair, the minutes are entered into the minutes module in Rascal and finalized, after which they are electronically approved by the Chair or designee. Once the minutes are approved by the Chair or designee, the protocol status for each Event changes according to the Board's determination (approved or pending, returned or deferred for items not approved). Rascal will automatically return protocol events that are marked as pending or returned and automatically generates any follow up correspondence entered in the minutes module by HRPO staff. LOAs or correspondence to request clarification or revisions, as necessary, are then released by HRPO staff with designated authority.

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. Board members are reminded to pay particular attention to the minutes for items for which they served as the primary reviewer. The presiding Chair will accept the minutes at a subsequent meeting of the Board if no objections or requests for revisions are made.

### **3. Notification of IRB Action**

Investigators are notified in writing of IRB actions to approve, disapprove, suspend, terminate or require changes to (in order to approve) research.

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 or, in the case of approvals, by an electronic approval letter. Automated approval emails state that although the submission has been approved, procedures should not commence until the approval letter has been released; this helps to ensure that the study team is aware of the conditions of IRB approval. Investigators are notified electronically via Rascal correspondence of reasons for returns.

Letters of Approval (LOAs) (Reference Document #93) and Letters of Disapproval (LODs) (Reference Document #96) are electronically generated and provided in Rascal. LOAs for items approved at a convened meeting may be released by senior HRPO officers. Release of LOAs may be delegated to IRB Specialists (Board Coordinators) as appropriate. LODs must include the basis for the disapproval and may only be released by a senior HRPO officer.

IOs are provided with copies of minutes that reflect all actions taken at convened meetings as well as all approvals and exempt determinations processed outside of meetings. A summary of the number of items reviewed, and identification of compliance matters, reports of unanticipated problems requiring reporting to federal agencies, and identification of 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**

LODs will include notification to the investigator that s/he may appeal the disapproval decision, in person or in writing to the ED, within 30 days from release of the LOD.

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 IRB activities and adherence to regulatory requirements is maintained:

1. Documents considered during IRB review, including but not limited to:
  - a. all versions of research protocols submitted;
  - b. Investigator Drug Brochures, device manuals, package inserts for drugs, and other similar supporting documentation;
  - c. recruitment materials; scientific evaluations, if any, which accompany the protocols;
  - d. all modifications or amendments to protocols;
  - e. progress reports submitted by research investigators;
  - f. statements of significant new findings provided to subjects as required by [45 CFR 116\(b\)\(5\)](#), [21 CFR 50.25\(b\)\(5\)](#);
  - g. approved consent documents;
  - h. reports of unanticipated problems;
  - i. continuing review (i.e., renewal) submissions; and
  - j. data and safety monitoring reports, if any.
2. Documentation of HRPO administrative reviews and IRB determinations and decisions required by laws, regulations, codes and guidance, including but not limited to:
  - a. notes, correspondence, IRB reviewer form and other documents reflecting actions taken by a staff or IRB reviewer or Board;
  - b. approval and expiration dates;
  - c. determinations (e.g., waiver of informed consent, waiver of documentation of informed consent, Subpart-specific determinations), restrictions (e.g., suspensions, contingencies), and names of reviewers;
  - d. minutes of IRB meetings (see Section IV.D and VII.E: Meeting Preparation and Follow Up) which include documentation that criteria for approval are met and other determinations such as, but not limited to findings of noncompliance, including whether noncompliance is serious or continuing, and whether a reported event is an unanticipated problem involving risks to subjects or other, and associated follow-up procedures;
  - e. correspondence between the IRB and the research investigators;

- f. exemption determinations, including category of exemption, whether made by an IRB Chair or ARC member;
  - g. reviews conducted under an expedited review process, including category, actions taken by the reviewer such as returns or approval, and required determinations; and
  - h. NHSR determinations, if submitted to the IRB via Rascal or to an IRB staff member via email.
3. Membership, including but not limited to:
    - a. list of Board members and their alternates identified by:
      - 1) name;
      - 2) earned degrees;
      - 3) representative capacity;
      - 4) indications of experiences such as board certifications, licenses, etc.;
      - 5) signed Confidentiality/Conflict of Interest Statement (Reference Document #76);
      - 6) information sufficient to describe each member's chief anticipated contributions to the IRB deliberations;
      - 7) any employment or other relationship between the member and the institution; and
    - b. Board member curriculum vitae, appointment letters, and other relevant correspondence involving member service.
  4. Emergency use reports.
  5. Activities of the Compliance Oversight Team, including but not limited to:
    - a. reports submitted to the IRB or HRPO regarding any subject complaints or injuries to subjects;
    - b. reports of investigations related to allegations of noncompliance; and
    - c. reports of not-for-cause audits.
  6. Interactions with federal regulatory agencies regarding compliance and other reportable matters.
  7. Documentation of reliance relationships and activities, whether Columbia is a relying institution or the reviewing IRB.

## **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; in secured, long-term, off-site storage; 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, DIM or DO.



IRB records, including records relating to research protocols, are confidential to the extent possible and allowed by law, and access is limited. Individual protocol files are accessible to members of the study team and approvers listed on the submissions, HRPO administrative staff, IRB members, 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), authorized representatives of sponsors with appropriate controls, and others for whom the ED and/or DO have authorized access. Access to IRB minutes and other files is likewise restricted to individuals with a legitimate need to review the material. Copying of material is acceptable only in certain circumstances.

### **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 policies that are 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. 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 certain IRB records must be received in writing and approved by the ED, DIM or DO.

#### **F. 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, DO, or DIM. 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 non-exempt research by the IRB at least annually 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 routine (i.e., “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, as necessary;
- 6) oversight monitoring activities conducted by the Herbert Irving Comprehensive Cancer Center Clinical Protocol and Data Management Office (CPDM);
- 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 HRPO, as described in Section XI, serve to provide additional 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 non-exempt human subjects research. 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, for example, the study team to provide additional reports, or may refer a given study to the COT for further investigation or audit.

HRPO staff and IRB 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, if the continuing review cannot be completed by

the expiration date of the current IRB approval. 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 (i.e., 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, at least possibly related to the research and suggest an increase in risk of harm) serves 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 of the event, relationship of the event to the test article and/or research activity, 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). The CU IRBs review reports of UPs promptly, with priority depending on how these criteria apply to the situation. A summary of UPs is 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 board 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) Documentation in the IRB module of the JRSC or RDRC, as applicable, review and approval of Appendix H (JRSC/RDRC application) that is appended to the IRB

protocol. The RSO, which administers the JRSC and RDRC, has access to the IRB protocol, including documentation of review and status, and the Appendix.

- 2) For any UP related to an investigational radiopharmaceutical, radiation therapy or a radiographic procedure, the IRB will forward the UP report along with documentation of the IRB review of the event 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, grants and COI disclosures. Each of these offices will communicate with the HRPO 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 HRPO staff or the IRB (in his/her/their capacity as such).

“IRB Noncompliance” means Noncompliance by the ED of the HRPO or any member of the HRPO staff or the IRB (in his/her/their capacity as such).

For purposes of IRB policy, “Noncompliance” means a failure to comply with (a) federal, state or local laws or regulations or institutional policies governing the protection of human subjects in research or (b) the requirements or determinations of the IRB.

The COT is responsible for the management of investigations of potential non-compliance. The COT determines, with the input of the ED, which allegations of potential noncompliance require investigation. If a HRPO staff member finds and determines that noncompliance is nonsignificant based on the definition in the IRB “Noncompliance in Human Subjects Research” policy (Reference Document #89), the findings are entered by the HRPO staff member into the notes for review by the Chair or his/her designee and documented in the minutes, as appropriate, for events that require convened review.

If the IRB has all necessary information and can appropriately make a noncompliance determination, referral to the COT is not required. The IRB noncompliance determination

will be reported to the COT, with a statement about whether any additional action by the COT is necessary. All other incidents of potential noncompliance are reported to the COT, which will determine whether an investigation is required and, if an audit is necessary, 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 IRB “Noncompliance in Human Subjects Research” 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, the 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 noncompliance, a report is released to the PI, and copied to the ED, DIM, applicable IRB, applicable department chair and departments, appropriate IO(s), EVPR and, when appropriate, the relevant regulatory agency and sponsor.

**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, a determination of serious or continuing noncompliance is made, the noncompliance is reported promptly (within 30 days) to the appropriate regulatory agencies. When an investigation is complete, a follow-up or final letter is sent to the applicable regulatory agencies. For protocols that are funded by specific federal agencies, there may be different or additional reporting requirements. Reference Document #356 provides information on the requirements of specific federal agencies.

The COT conducts routine audits of IRB-approved research for compliance with applicable regulations as well as institutional policies. Research protocols are selected for routine audits based on criteria that are periodically reviewed and revised according to the needs identified by HRPO.

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 required 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 and/or continuing noncompliance was identified.

Related concepts of appeal, reconsideration, and notification to regulatory agencies are also addressed in the IRB “Noncompliance in Human Subjects Research” 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 HRPO considers ongoing education of IRB staff, Board members, and research personnel to be of utmost importance in maintaining effective protection of human subjects in research conducted under the auspices of the institution.

To the extent possible, documentation of educational activities supported by the HRPO and/or attended by staff and IRB members is maintained.

### **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. website;
2. CUMC and CU-MS email listservs;
3. group meetings with research personnel and other individuals involved in the Human Research Protection Program., e.g., Monthly IRB-investigator Meetings, quarterly IRB 101 sessions, focus groups with research personnel, Rascal submission and consent form training, and departmental meetings/presentations;
4. Research Compliance Foundations Course;
5. Research Administration Forums
6. Clinical Research Newsletters;
7. Clinical Research Handbook; and
8. IRB Educational Conferences.

When the HRPO develops policy or guidance on a particular topic, the research community is made aware of the material through the following process: a) dissemination of a broadcast email message; b) posting on the CU HRPO website; and c) discussion at an educational session scheduled by the HRPO, e.g., Monthly IRB-Investigator Meeting. Additional measures may also be taken to disseminate the new information, e.g., direct email to department Chairs, or meeting with faculty in one or more department(s) that are uniquely affected by the information.

The CUMC and CU-MS HRPO offices host weekly Consultation Hours during which research personnel may obtain consultation from a HRPO staff member 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 by research personnel with individual officers.

To facilitate communication between the HRPO and the research community, the HRPO 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 HRPO staff.

Analysis of the inquiries that are received may identify areas in which additional education is needed.

The [IRB Liaison Service](#), which is jointly supported by the HRPO and the Irving Institute, is a free service available to CUMC researchers seeking assistance with understanding and addressing IRB requirements and requests. The IRB Liaison serves as a link between the IRB and CUMC investigators who have submitted or will submit a protocol for review by one of the CUMC IRBs. The primary objective for this service is to improve the quality and efficiency of human subject research protocol submissions and responses to IRB requests.

The IRB Liaison provides consultation in preparing protocols to be compliant with IRB requirements. In addition, the IRB Liaison provides support to investigators for responding to IRB reviews of research protocols, explanation of IRB requests and assistance in providing appropriate responses and/or implementing requested changes. Consultations from the IRB Liaison are in addition to existing consultation services provided by HRPO staff.

## **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;
2. CU IRB Member Handbook (Reference Document #368).

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.

### **Continuing Education:**

Education and training initiatives for IRB Members are continuous and ongoing to ensure all regulatory determinations made by IRB Members remain consistent with current regulatory and policy application.

IRB Members satisfy continuing education requirements on an annual basis and throughout their term, when specific training is required on a less frequent than annual basis. The following continuing education initiatives are offered to CU IRB Members:

1. All Members are exposed to ongoing educational opportunities such as regional or local IRB conferences and CU HRPO sponsored events. Funds are made available for IRB members to attend conferences that present pertinent and/or emerging ethical and scientific issues.

2. An educational event (e.g., conference or educational retreat) is held periodically for all Board Members and staff.
3. Board Members are required to complete CU Human Subjects Training (TC0087), including the refresher course every three years, throughout their appointment
4. CUMC Board Members are required to complete the Columbia University HIPAA in Research course (TC0019).
5. Perusal of the OHRP Assurance Training modules (<https://www.hhs.gov/ohrp/education-and-outreach/human-research-protection-program-fundamentals/index.html/assurance-training>) is recommended for IRB Members.
6. Board Members will receive, on an ongoing basis, continuing education information related to changes to institutional policy, relevant legal statutes and the Rascal system, and evolving interpretation of regulations, policies, and laws:
  - a. When the HRPO develops policy or guidance on a particular topic, notification to IRB Chairs and Members is through a group email to all Chairs and Members and/or presentation of the information at IRB meetings. The policy or guidance is also discussed at an IRB Executive Committee meeting. The information is posted on the HRPO website for easy reference.
  - b. Ongoing, protocol-specific training may be provided for interesting case studies, or topics pertinent to human subjects protection, on a case by case basis.
7. CUMC Board Members must complete Security Essentials (data security) training annually. Failure to complete the training by the deadline that is established will result in loss of access to email, Rascal and certain University resources.

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.

IRB Member participation and attendance in continuing education initiatives deemed mandatory by the ED, DIM, or other University entity are tracked. An assessment of each IRB Member's ability to satisfy the responsibilities of the position will be conducted periodically. At a minimum, such an assessment will be conducted at the time of reappointment. If a concern about a Member's ability to fulfill the role arises, an assessment will also be conducted at that time. In consultation with the IRB Chair, IRB Members who have not fulfilled their continuing education requirements are not assigned as primary reviewer until attendance or participation in the initiative is documented. Failure to complete training, if it is determined to be on a continual basis, may result in termination of the IRB Member's appointment or lack of renewal of the appointment. Evaluation of Continuing Education requirements is included as part of the evaluation of the performance of IRB Members.

### **C. Administrative Staff**

All new HRPO staff will be oriented to relevant federal regulations, IRB policies and procedures, the Belmont Report and Rascal.

The following material is distributed or made available to all HRPO staff:

1. Columbia IRB SOPs;
2. Relevant CU and all CU IRB policies;
3. Reviewer forms and checklists; and
4. CU IRB guidance documents.

All HRPO Staff are required to have the following training:

1. Appropriate Human Subjects Protection course (TC0087), as required by Columbia policy for research personnel, including completion of refresher course every 3 years;
2. Columbia University HIPAA in Research course (TC0019);
3. On an annual basis, Security Essentials (data security) training.

#### **Continuing Education:**

As with IRB members, education and training initiatives for HRPO staff are continuous and ongoing to ensure all regulatory and institution-specific determinations identified during administrative review remain consistent with current regulatory and policy application.

HRPO staff are required to attend multiple monthly continuing education sessions, and education events for the research community that are sponsored by the HRPO. Attendance at education sessions/events is tracked. In order to ensure consistent information is disseminated to all staff, even those not in attendance during the presentation or discussion, all material presented during HRPO education sessions are made available for review on an office shared drive.

The following continuing education initiatives are made available to HRPO staff:

1. The HRPO holds regular staff education sessions to present protocol- or topic-specific unique case studies. These sessions address both simple and complex regulatory and policy application for specific cases.
2. The HRPO holds regular regulatory refresher training (“brown bag refresher training”) for HRPO staff as part of the HPRO’s commitment to continuing education and professional development of staff. These sessions address all facets of human subjects protections.

3. When the HRPO releases policy or guidance on a particular topic, HRPO staff are notified via group email. In addition, the information is posted on the CU HRPO website and within the office's shared electronic space for easy reference. Development of most policies and guidance is a collaborative effort within the HRPO which facilitates an advanced understanding of the issues involved and the ability to apply the tenets immediately upon release.
4. All eligible staff are encouraged to pursue the Certified IRB Professional (CIP) status, which is obtained through successful completion of a comprehensive exam administered by Public Responsibility in Medicine & Research (PRIM&R). PRIM&R is a membership organization for IRB professionals and others involved in human subjects research. It disseminates educational information via its Research Ethics Digest Self-Study Program, which allows PRIM&R members to earn continuing education credits that can be applied toward renewal of their CIP credential. Details regarding eligibility for the exam, the content of the exam, and registration may be obtained from PRIM&R's [CIP website](#). The HRPO sponsors PRIM&R membership for staff.
5. HRPO staff who meet internal eligibility criteria, e.g., seniority and performance requirements, are offered attendance at the PRIM&R Advancing Ethical Research annual conference.

All staff have access to other educational opportunities, as resources allow. These include:

1. Attending local and national IRB conferences;
2. Access to the Collaborative Institutional Training Initiative (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; and
  - c. literature.

HRPO staff at the officer level are evaluated formally at least once per year as per the recommendations of the Human Resource department at Columbia and required by the EVPR. The job descriptions for all HRPO Officers includes a requirement to stay abreast of both changes to existing relevant regulations and statutes, and those that are newly implemented. Evaluation of Continuing Education requirements, including attendance at HRPO sponsored education events, is included as part of the evaluation of the performance of HRPO staff.

#### **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 through the Biomedical Research Alliance of New York. 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. Since 2012, continuing HSP education every three years after completion of TC0087 has been required. The Rascal system sends automated reminders of the need for continuing education at specified intervals prior to the 3-year anniversary of completion of CU Human Subjects Training (TC0087).

Key personnel, i.e., personnel who are engaged in human subjects research, on the CUMC campus must also complete the CUMC online HIPAA training course prior to participation in research. If a protocol submitted from the CU-MS campus involves the use or disclosure of protected health information as per the CU IRB Policy on the Privacy Rule and the Use of Health Information in Research, 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. Columbia University HIPAA training for all key personnel at CUMC, and any other personnel who will use, disclose or access PHI;
3. the CITI Biomedical Research with Children online module, within the CITI HSP course, if children will be involved as subjects;
4. the CITI FDA-regulated Research online module, within the CITI HSP course, 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), if FDA-regulated drug(s) or medical device(s) will be the focus of a study, or clinical research will be conducted;
5. the CITI Good Clinical Practice (GCP) in CITI, or documentation provided of a previously completed GCP training by an accredited third-party provider, for all NIH-funded investigators and staff who are involved in the conduct, oversight or management of a clinical trial;
6. the Informed Consent in Genetic Research course in Rascal, for all CRCs who are involved in obtaining informed consent from research subjects who will undergo Genetic Testing as defined by NYS Civil Rights Law Article 7 Section 79-1, when the results of such Genetic Testing will be returned to the subjects;
7. at CUMC, the Clinical Research Coordinator module in Rascal, if an individual’s role in greater than minimal risk research is equivalent to a clinical research

- coordinator (examples are Study Coordinator, Regulatory Coordinator, Research Nurse, Data Manager, Research Assistant, or other coordinator role); and
8. the S-I module in Rascal, if the PI is also the sponsor of the project, meeting the criteria of “sponsor” per FDA regulations.

The HRPO 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 CU HRPO 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 goals of the Columbia IRB Quality Improvement (QI) Program are to improve the quality, performance, and efficiency of IRB review, the IRB compliance oversight process, and other internal processes. An additional goal is to enhance compliance activities within the Columbia HRPO. The HRPO conducts various processes to monitor performance of the staff and Boards, as well as to assess 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 HRPO.

Quality assurance and improvement activities are administered primarily under the direction of the DO, who oversees the collection and processing of data that enables the HRPO 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 DO, DIM, or ED. Additional details are provided in Reference Document #355: Columbia Quality Improvement Program.

### **A. Assessment and Improvement Initiatives of Internal Processes**

Reports may be prepared on a regular schedule, such as the routine of regular 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, DO, and/or DIM for review, as applicable to areas of responsibility and shared with staff as applicable to their work.

The DO 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, DO and/or DIM based on these analyses are forwarded to the relevant individuals within the operation. Recommendations and comprehensive reports 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.

Regular reports include but are not limited to the following:

1. Log In Queue report: Measures the number and timeliness of reviews of submissions and responses from researchers to previous IRB correspondence or actions.
2. 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.

Reports on the processing of pre-reviews of new protocols, IRB turnaround time and IRB processes are also generated on a regular basis and disseminated as appropriate.



In addition to regular reports, HRPO staff conduct continuous quality improvement initiatives to assess routine functions, e.g., minutes of IRB meetings to ensure regulatory determinations, as applicable, are appropriately documented. Individuals with designated authority to release LOA also conduct quality assurance review of protocols when LOA are released.

## **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 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 in known subject recruitment areas throughout CU, and are posted on the [HRPO website](#).

The HRPO maintains a relationship with Community Board #12 (CB12), which represents the Washington Heights area surrounding CUMC. The primary objectives for interactions with CB12 and other community organizations is to inform the community about the role of the IRBs and the HRPO, and their efforts to ensure the ethical conduct of research, and to address any concerns that the community may have regarding research. The HRPO also offers opportunities to inform the community about the differences between standard practice and research, the consent process for research, and 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. Other research originating from CU-MS faculty is conducted at non-Columbia sites both in the U.S. and abroad.

The HRPO endeavors to be present at local health fairs and other community events where information about the rights of participants in research may be disseminated. At CUMC, the HRPO is advised of such events by various means, e.g., directly from CB12, through investigators who conduct community-based research, by the [Community Engagement Core Resource](#) (CECR) that is supported by the Clinical and Translational Science Award (CTSA) or through the [CUMC Office of Governmental Relations](#).

Posted on the HPRO website is a link to information “[For Research Participants](#)”, the objective of which is to inform potential subjects of what they should consider before enrolling in a research study and provide links to studies in which they may consider participating. The “information to consider” is also provided in pamphlets that are distributed at local health fairs and community events. With respect to providing information about open studies, links are provided to the [ClinicalTrials.gov](#) website that provides basic information about open clinical trials under the purview of the FDA, and to the [RecruitMe](#) and [ResearchMatch](#) websites. RecruitMe is a CU initiative that both allows users to search open studies at CU and to register to receive information about current or current studies. 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.

### **B. Information from Research Subjects and the Community**

The HRPO 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.

Representatives from the HRPO, including senior leadership, meet periodically with investigators who lead efforts to identify and address issues from the community that are related to research. The purpose of these meetings is to create more interaction between Columbia and the community, through enhanced communication among all parties and increased awareness of barriers to participation in research, particularly in projects that offer the prospect of direct benefit to participants.

CECR, which is facilitated by the Irving Institute for Clinical and Translational Research, promotes health research that contributes to the health and well-being of the Upper Manhattan communities. CECR fosters community partnerships and participation in health research through educational training, funding, and outreach opportunities.

CECR collaborates with several other Irving Institute Resources including the Biomedical Informatics Resource, the Clinical Research Resource, and the Regulatory Knowledge and Ethics Resource, as well as other CUMC centers and multi-sector stakeholders in Northern Manhattan, and fosters community-engaged research between CUMC researchers, multi-sector stakeholders, and the community at-large by:

1. providing educational, training, and funding opportunities;
2. developing health-literate resources and services to facilitate recruitment and retention of research participants;
3. providing informatics tools to promote community outreach, social networking, and research dissemination to community stakeholders;
4. providing off-campus space for health research, education, and promotion activities; and
5. linking community residents to health research, information, and services.

One of the main components of CECR is the [Columbia Community Partnership for Health \(CCPH\)](#). CCPH provides free space for health related activities to Columbia University investigators and community groups and is designed to facilitate the health information and research needs of our community residents, social service and community-based organizations, and CUMC researchers. CECR supports community-engaged research between CUMC researchers, multi-sector stakeholders, and the community at-large through the Community Based Participatory Research Scholars and Awards program, the Health Literacy Review Service, health lectures, and the [Get Healthy Heights](#) and [Get Healthy Harlem](#) websites.

### **C. Compliance Hotline**

The University maintains a confidential hotline through which concerns about Columbia research may be reported by individuals who believe that they have observed or been subject

to (for example) 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 HRPO website.

#### **D. IRB Education and Review**

HRPO staff and IRB members receive information about, and guidance for how to address, matters that influence the participation of community members in research that is conducted or supported by Columbia. These include but are not limited to privacy and confidentiality concerns, principles and methodologies involved in [Community Based Participatory Research](#) (CBPR), local recruitment challenges, return of research results, and informed consent.

Investigators who are experienced in the design and conduct of community participatory research are available to provide consultation during IRB review of such research protocols, and one or more will serve as alternate or regular IRB members.

#### **E. Evaluation of Outreach Efforts**

At least annually, the HRPO will evaluate the status of outreach efforts that are directed towards identifying and addressing research-related issues of importance to individuals who are local to Columbia campuses and/or likely to be exposed to recruitment materials for Columbia research projects. For the CUMC campus, these would be residents in the Washington Heights and Inwood communities, and for the CU-MS campus, these would be Columbia students.

The Subject Outreach Subcommittee of the HRPO Education and Training Committee, under the guidance of the ED or DIM, will lead and document these efforts.

Evaluation procedures may include one or more of the following:

- meetings with investigators who conduct research in the Washington Heights and Inwood communities and on the CU-MS campus;
- review of progress reports for grants that are related to community outreach activities;
- analysis of HRPO and IRB participation in research-related community events;
- consideration of the extent to which English and Spanish language brochures that were produced through HRPO efforts and provide information for individuals to consider prior to participating in research, have been distributed;
- discussions with representatives of the CTSA Community Engagement core to consider current efforts and how HRPO-CTSA interaction related to community engagement may be enhanced;

- discussions with representatives of the CTSA recruitment core to consider current efforts and how HRPO-CTSA interaction related to recruitment matters may be enhanced;
- review of and revision to consent templates to ensure that information is presented at the appropriate health literacy level;
- attendance at local Community Board meetings;
- meetings with representatives of Columbia schools through which research participation is either required or is offered as a means to obtain credit towards degree- or coursework;
- interaction with student representatives or organizations to discuss issues related to research participation; and
- analysis of subject-related calls to the University Compliance Hotline and/or subject complaints received by the HRPO.

Results of the evaluation efforts will be utilized to enhance outreach efforts. This may be done through an increase in HRPO efforts to interact with prospective subjects, revision to IRB guidance related to recruitment and consent documents, updating of the subject information brochures that are produced by the HRPO, enhanced interaction with investigators or entities at Columbia who regularly conduct or facilitate community participation in research, or other to-be-developed activities.

Formalization of an advisory committee to identify and address community research-related matters, particularly those that are discovered through Columbia research projects, is under discussion. The manner in which representatives of the HRPO would participate in such a committee is also being considered.

## Appendix I:

### Abbreviations and Terms Used in Columbia University HRPO Standard Operating Procedures 2017

#### A: Alphabetical Order

<b>Abbreviation or Term*</b>	<b>Explanation</b>	<b>First Use</b>
AAHRPP	Association for the Accreditation of Human Research Protection Programs	Intro
ACS	Administration for Children's Services	VI
ADIM	Assistant Director for IRB Management, HPRO	I
AE	Adverse Event	V
ARC	Administrative Review Committee	Intro
BB-IND	Biologic IND	III
CB12	NYC Community Board 12	XII
CBPR	Community Based Participatory Research	XII
CC-DSMP	Cancer Center Data and Safety Monitoring Program	V
CCPH	Columbia Community Partnership for Health	XII
CDC	Centers for Disease Control and Prevention	VI
CECR	Community Engagement Core Resource of the IITCR	XII
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
CPDM	The Herbert Irving Comprehensive Cancer Center Clinical Protocol and Data Management Office	IX
CPO	Chief Privacy Officer	I
CRCT	Clinical Research Coordinator Training	I
CRR	Clinical Research Resource	I
CTMAP	Clinical Trials Monitoring Assistance Program for FDA Regulated Human Subjects Research	I
SCTO	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
D/Ads	Directors/Assistant Directors, HRPO	I
DCO	Director for Compliance Oversight, HPRO	I
Dean of CUMC	Dean of the Faculties of Health Sciences and Medicine/ Chief Executive, Columbia University Medical Center	Intro
DHHS or HHS	U.S. Department of Health and Human Services	Intro
DIM	Director for IRB Management, HPRO	I
DNA	Deoxyribonucleic acid	III
DO	Director of Operations, HPRO	I
DoD	U.S. Department of Defense	Intro
DOE	U S. Department of Education	Intro
DOEn	U.S. Department of Energy	Intro
DSMB	Data and Safety Monitoring Board	III
DSMC	Data and Safety Monitoring Committee	III
ED	Executive Director, HRPO	Intro
EPA	Environmental Protection Agency	Intro
EU	Emergency Use	III
Event*	RASCAL term for submissions to the IRB for review (e.g., new protocol, modification, renewal)	III
EVPR	Executive Vice President for Research	Intro
FCOI	Financial Conflict of Interest	V
FDA	U.S. Food and Drug Administration	Intro
FERPA	Family Education Rights and Privacy Act	Intro
Full Board, convened Board./review/meeting*	Full Board, convened Board, convened review, and convened meeting all refer to an IRB review where a quorum of board members is present	II
FWA	Federalwide Assurance	Intro
GCP	Good Clinical Practice	V
HCP	Health Care Proxy	III
HDE	Humanitarian Device Exemption	VI
HHS or DHHS	U.S. Department of Health and Human Services	Intro
HICCC	Herbert Irving Comprehensive Cancer Center	I
HIPAA	Health Insurance Portability and Accountability Act	I
HRPP	Human Research Protection Program	Intro
HSP	Human Subjects Protection	V
HSR	Human Subjects Research	Intro
HUD	Humanitarian Use Device	VI
IAA	IRB Authorization Agreement	II
IAP	IND/IDE Assistance Program	I
IBC	Institutional Biosafety Committee	I

ICH	International Conference on Harmonization	Intro
ICOI	Institutional Conflict of Interest	V
IDB	Investigator's Drug Brochure	III
IDE	Investigational Device Exemption	Intro
IEC	IRB Executive Committee	I
IIA	Individual Investigator Agreement	II
IICTR	Irving Institute for Clinical and Translational Research	I
IND	Investigational New Drug	Intro
IO	Institutional Official	Intro
IRB	Institutional Review Board (also referred to as "Board")	Intro
IRB Exp	CUMC IRB for all research that initially qualifies for expedited review	II
ISFI	Institutional Significant Financial Interests	V
IT	Information Technology	Intro
JRSC	Joint Radiation Safety Committee	I
LAR	Legally Authorized Representative	III
LOA	Letter of Approval	IV
LOD	Letter of Disapproval	IV
MP	Master Protocol	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
NIH	National Institutes of Health	I
NIJ	National Institutes of Justice	Intro
NSR	Non-significant 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
OHC	Office of HIPAA Compliance	I
OHRP	U.S. Office for Human Research Protection	II
PHI	Protected Health Information	V
PI	Principal Investigator	III
PMA	Premarket Approval	VI
PPRA	Protection of Pupil Rights Amendment	Intro
PRMC	Protocol Review and Monitoring Committee	I



PSA	NYP Patient Services Administration	I
QI	Columbia IRB Quality Improvement Program	XI
RAC	NIH Recombinant DNA Advisory Council	III
RCT	Office for Research Compliance and Training	Intro
RDRC	Radioactive Drug Research Committee	I
RHI	Research Health Information	V
RP	Research Pharmacy	I
RSO	Radiation Safety Office	I
S-I	Sponsor-Investigator	I
sIRB	single IRB of record for a multi-site review	III
SOP	Standard Operating Procedures	Intro
SPA	Sponsored Projects Administration	Intro
SR	Significant Risk designation for medical device	VI
SSNs	Social Security Numbers	V
STC	Spanish Translation Center	I
The University	Columbia University	Intro
U.S.	United States	Intro
UP	Unanticipated Problem involving Risks to Subjects or Others	III
VPRO	Vice President for Research Operations	Intro

Abbreviations and Terms Used in Columbia University HRPO  
Standard Operating Procedures 2017

**B: In Order of Appearance**

<b>Abbreviation or Term*</b>	<b>Explanation</b>	<b>First Use</b>
AAHRPP	Association for the Accreditation of Human Research Protection Programs	Intro
ARC	Administrative Review Committee	Intro
CFR	Code of Federal Regulations	Intro
Columbia	Columbia University	Intro
CTO	Clinical Trials Office	Intro
CU	Columbia University	Intro
CUMC	Columbia University Medical Center	Intro
CU-MS	Columbia University – Morningside campus	Intro
Dean of CUMC	Dean of the Faculties of Health Sciences and Medicine/ Chief Executive, Columbia University Medical Center	Intro
DHHS or HHS	U.S. Department of Health and Human Services	Intro

DoD	U.S. Department of Defense	Intro
DOE	U.S. Department of Education	Intro
DOEn	U.S. Department of Energy	Intro
ED	Executive Director, HRPO	Intro
EPA	Environmental Protection Agency	Intro
EVPR	Executive Vice President for Research	Intro
FDA	U.S. Food and Drug Administration	Intro
FERPA	Family Education Rights and Privacy Act	Intro
FWA	Federalwide Assurance	Intro
HHS or DHHS	U.S. Department of Health and Human Services	Intro
HRPP	Human Research Protection Program	Intro
HSR	Human Subjects Research	Intro
ICH	International Conference on Harmonization	Intro
IDE	Investigational Device Exemption	Intro
IND	Investigational New Drug	Intro
IO	Institutional Official	Intro
IRB	Institutional Review Board (also referred to as "Board")	Intro
IT	Information Technology	Intro
MSCHONY	Morgan Stanley Children's Hospital of New York	Intro
NIJ	National Institutes of Justice	Intro
NYP	New York Presbyterian Hospital	Intro
OGC	Office for General Counsel	Intro
PPRA	Protection of Pupil Rights Amendment	Intro
RCT	Office for Research Compliance and Training	Intro
SOP	Standard Operating Procedures	Intro
SPA	Sponsored Projects Administration	Intro
The University	Columbia University	Intro
U.S.	United States	Intro
VPRO	Vice President for Research Operations	Intro
ADIM	Assistant Director for IRB Management, HPRO	I
CIP	Certified IRB Professional	I
COI	Conflict of Interest	I
COT	Compliance Oversight Team	I
CPO	Chief Privacy Officer	I
CRCT	Clinical Research Coordinator Training	I
CRR	Clinical Research Resource	I
CTMAP	Clinical Trials Monitoring Assistance Program for FDA Regulated Human Subjects Research	I
CTSA	Clinical and Translational Service Award	I
D/Ads	Directors/Assistant Directors, HRPO	I
DCO	Director for Compliance Oversight, HPRO	I

DIM	Director for IRB Management, HPRO	I
DO	Director of Operations, HPRO	I
HICCC	Herbert Irving Comprehensive Cancer Center	I
HIPAA	Health Insurance Portability and Accountability Act	I
IAP	IND/IDE Assistance Program	I
IBC	Institutional Biosafety Committee	I
IEC	IRB Executive Committee	I
IICTR	Irving Institute for Clinical and Translational Research	I
JRSC	Joint Radiation Safety Committee	I
NIH	National Institutes of Health	I
NYC	New York City	I
NYSPI	New York State Psychiatric Institute	I
OFBC	Office for Billing Compliance	I
OHC	Office of HIPAA Compliance	I
PRMC	Protocol Review and Monitoring Committee	I
PSA	NYP Patient Services Administration	I
RDRC	Radioactive Drug Research Committee	I
RP	Research Pharmacy	I
RSO	Radiation Safety Office	I
S-I	Sponsor-Investigator	I
STC	Spanish Translation Center	I
CIRB	Central Review Board	II
Full Board, convened Board./review/meeting*	Full Board, convened Board, convened review, and convened meeting all refer to an IRB review where a quorum of board members is present	II
IAA	IRB Authorization Agreement	II
IIA	Individual Investigator Agreement	II
IRB Exp	CUMC IRB for all research that initially qualifies for expedited review	II
NCI	National Cancer Institute	II
OHRP	U.S. Office for Human Research Protection	II
BB-IND	Biologic IND	III
CITI	Collaborative IRB Training Initiative	III
COC	Certificate of Confidentiality	III
DNA	Deoxyribonucleic acid	III
DSMB	Data and Safety Monitoring Board	III
DSMC	Data and Safety Monitoring Committee	III
EU	Emergency Use	III
Event*	RASCAL term for submissions to the IRB for review (e.g., new protocol, modification, renewal)	III

HCP	Health Care Proxy	III
IDB	Investigator's Drug Brochure	III
LAR	Legally Authorized Representative	III
NGS	National Government Services	III
PI	Principal Investigator	III
RAC	NIH Recombinant DNA Advisory Council	III
sIRB	single IRB of record for a multi-site review	III
UP	Unanticipated Problem involving Risks to Subjects or Others	III
LOA	Letter of Approval	IV
LOD	Letter of Disapproval	IV
NHSR	Not Human Subjects Research	IV
NHSR per 45 CFR 46	Not Human Subjects Research per 45 CFR 46	IV
AE	Adverse Event	V
CC-DSMP	Cancer Center Data and Safety Monitoring Program	V
FCOI	Financial Conflict of Interest	V
GCP	Good Clinical Practice	V
HSP	Human Subjects Protection	V
ICOI	Institutional Conflict of Interest	V
ISFI	Institutional Significant Financial Interests	V
PHI	Protected Health Information	V
RHI	Research Health Information	V
SSNs	Social Security Numbers	V
ACS	Administration for Children's Services	VI
CDC	Centers for Disease Control and Prevention	VI
CIOMS	Council of International Organization of Medical Sciences	VI
HDE	Humanitarian Device Exemption	VI
HUD	Humanitarian Use Device	VI
MP	Master Protocol	VI
NSR	Non-significant Risk designation for Medical Device	VI
NYS	New York State	VI
PMA	Premarket Approval	VI
SR	Significant Risk designation for medical device	VI
CPDM	The Herbert Irving Comprehensive Cancer Center Clinical Protocol and Data Management Office	IX
QI	Columbia IRB Quality Improvement Program	XI
CB12	NYC Community Board 12	XII
CBPR	Community Based Participatory Research	XII
CCPH	Columbia Community Partnership for Health	XII
CECR	Community Engagement Core Resource of the IITCR	XII

## **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, [45 CFR Part 46](#), Subparts A (Common Rule), B, C, D and E

United States Food and Drug Administration (FDA) regulations for the Protection of Human Subjects, [21 CFR Parts 50](#), [56](#), [312](#), [600](#), and [812](#)

HHS/FDA List of Expedited Review categories

Department of Education (DOE) regulations [34 CFR 97](#) including the Family Education Rights and Privacy Act (FERPA), [34 CFR 99](#), the Protection of Pupil Rights Amendment, [34 CFR 98](#), and the National Institute for Disability and Rehabilitation Research, [34 CFR 350](#)

Department of Defense (DoD) regulations and [DoD Directive \(DoDD\) 3216.02](#)

Environmental Protection Agency (EPA) regulations, [40 CFR 26.121, Subpart A](#)

National Institute of Justice regulations, [28 CFR 46](#)

Department of Justice, Bureau of Prisons regulations, [28 CFR 512](#)

[Department of Energy regulations, 10 CFR 745](#)

[Health Insurance Portability and Accountability Act \(HIPAA\) Privacy Standard, 2006](#)

New York State [ARTICLE 24-A](#), PROTECTION OF HUMAN SUBJECTS





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](#)

**Appendix III  
Standard Operating Procedures Version 5  
Chronology**

Version	Effective Date	Scope	Signoff
4.0	June 12, 2012	All (Introduction, Sections I – XII, Appendices I and II)	
4.1	July 9, 2012	Revision of Section IX; Addition of Appendix III	
4.2	Nov. 2, 2012	Revision of Sections Introduction, II, III, V, VII, VIII, IX, X, XI, XII, Appendices II, III	
5.0	December 21, 2017	All (Introduction, Sections I- XII, Appendix I)	
5.1	April 12, 2018	Revisions of Sections Introduction, II, III, IV, V, VI, VII, VIII, IX, X, Appendix III	