Columbia University

Institutional Review Board (IRB)

Policies and Procedures

June 9, 2006
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Introduction

Columbia University (CU or Columbia) 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 staff is conducted ethically and in a manner that promotes the protection of human subjects in research. All such research must not only be in compliance with state and federal regulations, but must also meet or exceed the standards of accreditation as set forth by the Association for Accreditation of Human Research Protection Programs (AAHRPP).

The Columbia HRPP covers all entities, offices, and individuals engaged in and/or responsible for the review and conduct of human research at Columbia and New York Presbyterian Hospital (NYPH). CU has two Federal-wide Assurances (FWAs): one for Columbia University Medical Center (CUMC) and one for the main campus at Morningside Heights (CU-MH). NYPH has its own FWA and is a separate legal entity from CU. Although there are three FWAs, the Columbia HRPP is responsible for all human research conducted at CUMC, CU-MH, and NYPH, or by any affiliated faculty, employees, or staff of CU and NYPH regardless of location. The Columbia HRPP is managed by the Executive Director, Human Research Protection Program (EDHRPP), who is also responsible for the management of all Institutional Review Boards (IRBs) at CU. Sections I and II of these written procedures outline and summarize the Columbia HRPP.

The Columbia research enterprise is extensive in its size and broad in its scope and nature of activities, including biomedical, behavioral, and epidemiological research, as well as studies in the area of health services. Although much of the research is conducted in the New York City area and on Columbia campuses, faculty members also actively conduct research at other sites both domestic and international. Furthermore, many Columbia faculty members collaborate on projects with investigators at other institutions. The Columbia HRPP accounts for approximately 1,400 new human research studies each year.

To facilitate management, review, and oversight of its research enterprise, Columbia has developed an electronic submission system called RASCAL. The RASCAL system requires that all research proposals be submitted in the system for review by the IRB and other administrative offices. This system provides a high level of accountability for all research protocols, as it allows for tracking of research, systematic administration of reviews by the IRBs and other committees, processing and accounting of human research educational training, and management of conflicts of interest.
I. Institutional Leadership

The Columbia HRPP reports to the Executive Vice President for Research (EVPR) and the Institutional Officials designated on the FWAs of CUMC, CU-MH, and NYPH. The EVPR is responsible for central oversight of the entire Columbia HRPP and also serves as the Institutional Official (IO) on the FWA for CU-MH. Each IO is responsible for ensuring that all research under his/her FWA is conducted ethically and in compliance with all regulatory standards. The EVPR, together with the IOs of CUMC and NYPH, the Vice President of Research Operations (VPRO), and the EDHRPP provide a team approach for oversight of the protection of human subjects in research.

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 NYPH recognize that the ethical conduct of research is not only vital for the success of the research enterprise and the public trust of surrounding communities 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 NYPH 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.

II. IRB Office

The IRB Office is the central administrative office for the Columbia HRPP. This office serves as the central repository of all information affecting the protection of human subjects in research. The IRB Office is responsible for the management and oversight of all IRBs at CU-MH and CUMC, as well as the reporting of all safety and noncompliance issues regarding research involving human subjects. In addition, the IRB Office is responsible for ensuring that all relevant information affecting the safety and welfare of human subjects in research is reported to the IRBs, and as appropriate to the IOs, federal regulatory agencies, sponsors, and AAHRPP. The IRB Office has two locations: a) on the CUMC campus, on the fourth floor of the Mailman School of Public Health building, and b) on the CU-MH campus, in Room 522 of the Interchurch Building on Riverside Drive and 120th Street.

The IRB Office leads quarterly meetings with the heads of all Columbia HRPP units involved in the administration and conduct of human research. The purpose of these meetings is to ensure coordination and communication of policies and issues relevant to the protection of human subjects in research. In addition, the IRB Office convenes ad hoc meetings as necessary to address any incidents or issues that may require additional consideration or more immediate action. As necessary for prompt notification, the IRB Office sends electronic 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 IRB Office also leads semi-monthly meetings with the Executive Committee of the IRB. This Committee is comprised of the Chairs and Vice Chairs of all four IRBs, the VPRO, the Associate Director, IRB (AD), and the EDHRPP. The purpose of these meetings is to improve the quality and consistency of the work performed by the four IRBs and to address overarching issues and challenges that may face all IRBs. Once a month, all IRB officers also attend this meeting.

Five other committees support initiatives to improve the ethical conduct and review of research: 1) Education and Training Committee, 2) Policy Committee, 3) Accreditation Committee, 4) Quality Improvement Committee, and 5) RASCAL Committee. The purpose of each committee is discussed in more detail below. Additional committees may be constituted as necessary to support office initiatives.

A. Institutional Review Boards

There are four IRBs (commonly referred to as “Boards”) in the Columbia HRPP. Three IRBs are responsible for review of human subjects research conducted by faculty, employees, staff, and students at CUMC and NYPH and one IRB is responsible for human research conducted by faculty, employees, staff, and students at CU-MH. All four IRBs are governed by the principles of the Belmont Report and the federal regulations for the protection of human subjects in research as codified by:

1. the U.S. Department of Health and Human Services (HHS) regulations, 45 CFR Part 46, Subparts A (Common Rule), B, C, and D (Appendix VI);

2. the U.S. Food and Drug Administration (FDA) Regulations, 21 CFR Parts 50, 56, 312, 600, and 812 (Appendix VII);

3. the Department of Education Family Education Rights and Privacy Act (FERPA);

4. New York State Laws 2440/441 and Article 7, Section 79-1 (Confidentiality of Genetic Tests);

5. Columbia institutional policies; and

6. the AAHRPP Accreditation Standards.

All four 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 IRBs are not solely responsible for the integrity and conduct of such research, nor 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’s Office for CUMC, the Chief Medical Officer for NYPH, and the EVPR.

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

There are four teams of staff that provide administrative support for the IRBs. Each IRB has its own dedicated team. In addition, the Compliance Oversight Team and the Central Review Team provide administrative support to each of the four IRBs, as described below.

B. External IRBs

CUMC and NYPH, collectively, have IRB Authorization Agreements with the Western IRB (WIRB), the New York State Psychiatric Institute’s (NYSPI), the Weill Medical Center of Cornell University, the National Cancer Institute Central IRB (CIRB), and the Biomedical Research Alliance of New York (BRANY) to rely on reviews by their IRBs for certain types of research projects. Details regarding each agreement are provided later in this manual. The CU IRB management meets on an ad-hoc basis with representatives from each external IRB to consider issues relevant to the review of human subjects research at Columbia.

C. IRB Staff Teams

Each IRB is administered by a team of staff composed of a Team Manager, Assistant Team Manager or Board Coordinator, and one or two administrative support staff. Each team is responsible for ensuring that all research reviewed by its IRB is in compliance with all above-referenced standards and that all reviews are handled efficiently and at a high level of quality. Each team is responsible for preparing its IRB with the necessary information to conduct its reviews and to process all communication to the research team.

D. Central Review Team

The Central Review Team (CRT) handles the initial receipt of research studies for IRB review and triages these studies for an initial pre-review by IRB staff, followed by a review by one of the three CUMC IRBs, or CU-MH, as appropriate. Each incoming new study receives a thorough pre-review by IRB staff utilizing a detailed pre-review form. The pre-review process is designed to help ensure that each study is submitted with the necessary information to proceed for IRB review and that each study will receive all relevant regulatory considerations. Once a study has received a pre-review it is assigned to an IRB for review.

The CRT is responsible for conducting pre-reviews of all continuing review requests, and all modifications or amendments submitted to the CUMC IRBs for approved research studies. The
pre-review of continuing review submissions also utilizes a pre-review form to ensure that the necessary information is submitted. This pre-review includes a quality assurance assessment of the study for the most recent 12-month period to ensure that all prior actions were appropriately handled and that any outstanding items will be addressed at the upcoming IRB review. Pre-review of modifications or amendments is also done, in order to prepare the IRB for its review of these submissions.

The CRT conducts a pre-review of all reports of adverse events and unanticipated problems that are submitted to the CUMC IRBs. The pre-review ensures that these reports meet the CU Adverse Event Reporting policy and cases are identified that require immediate attention. For such reports that satisfy Columbia’s individual event reporting policy, the CR staff conducts the preliminary review to determine if the informed consent document and/or protocol require revision. Reports of events that do not meet the criteria for individual submission are returned without review with instructions to include the event in a summary of adverse events at the time of continuing review.

E. Quality Improvement Program

The Columbia IRBs are committed to the improvement of quality, performance and efficiency of their reviews and internal processes. Towards these ends, the CU IRB Quality Improvement Program (QIP) is charged with the responsibility of conducting quality assurance, quality improvement, and continuous quality improvement assessments of IRB reviews and processes to ensure excellence. The QIP is administered by the CRT. The CRT is responsible for the collection and processing of data and other information on the quality and performance of the IRB operation. The CRT then prepares and forwards reports to the Quality Improvement Committee for review.

A program to assess and improve the performance and compliance of research teams is in development.

Knowledge gained from these efforts provides input for educational training efforts and/or the opportunity to improve a process or policy.

F. Compliance Oversight Team

The Compliance Oversight Team (COT) is responsible for investigating and handling all allegations of noncompliance, concerns about research conduct, and complaints with respect to the protection of human subjects in research. Allegations of noncompliance, concerns, or complaints may be received from IRBs, faculty, research staff, IOs, departmental administrators, research subjects, federal and state regulatory agencies, the media, or the general public. All allegations of noncompliance, concerns, or complaints are logged into a tracking system by the COT, which promptly notifies the EDHRPP of such reports.
Alleged incidents of noncompliance are handled in accordance with the Columbia Noncompliance with Human Subjects Regulations Policy. When a determination of noncompliance has been made an appropriate corrective action plan is developed. A follow-up report of serious or continuing noncompliance is then filed with the appropriate IO(s), the EVPR, and when appropriate, with the relevant regulatory agency.

G. Education and Training Committee

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

Efforts by staff to expand their knowledge of the ethical and regulatory bases for human subject protection by completing online tutorials, attending local and national conferences, and obtaining Certified IRB Professional status are strongly encouraged. Educational training activities for staff include both mandatory and voluntary initiatives.

H. Policy Committee

The Policy Committee, also established in 2003 within the IRB Office, is responsible for the formulation and drafting of policies related 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 officer on the IRB staff. Committee membership is comprised of IRB staff and the Policy Advisor to the IRB, who also serves as the Director, Center for Bioethics. The VPRO serves as an ad-hoc member.

I. Accreditation Committee

The Accreditation Committee was established in 2004 within the IRB Office 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 investigators). The Committee is charged with the added responsibility and authority for the monitoring and oversight of internal IRB processes so that accreditation can be obtained and maintained.
J. Quality Improvement Committee

The Quality Improvement Committee (QIC) is responsible for the assessment of data and other information that is collected on the quality and performance of the IRB operation. The QIC is composed of members of the CRT, the Team Manager or designee of each IRB, the AD and the EDHRPP.

Assessments and recommendations made by the QIC for specific reviews or events are forwarded to the relevant IRB Team Manager and IRB Chair, if appropriate. More general recommendations and comprehensive reports made by the QIC are forwarded to the EDHRPP, AD, IRB Team Managers, IRB Chairs, and, as appropriate, the Executive Committee of the IRB.

K. RASCAL Committee

The RASCAL Committee was established in 2004 within the IRB Office and is charged with working with the RASCAL Information Technology (IT) Team for further development and enhancement of the RASCAL system as it relates to the IRB module. The RASCAL Committee is the central repository of all suggestions for improvement of the system. The Committee is responsible for prioritizing all requests for RASCAL improvements with the input of the four CU IRB Chairs and staff.
III. IRB Policies and Procedures

A. Development

Columbia University has adopted these IRB written procedures to ensure the ethical conduct of research and protection of the rights and welfare of human subjects participating in research conducted under the authority of the University. This document describes the means by which research with human subjects will be reviewed, approved, and monitored.

The Boards have adopted these written procedures to comply with the U.S. HHS Regulations on research with human beings (Appendix VI), and the U.S. FDA regulations on research with human beings (Appendices VII). To the extent consistent with federal law & regulations, the written procedures comply with the International Conference on Harmonization (ICH) “Guidance for Industry- E6 Good Clinical Practice: Consolidated Guideline” (Appendix VIII).

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

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

B. Process for Revising Policies and Procedures

1. The proposed revision must be submitted to either the Policy or Accreditation Committee for consideration.

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

   b. Minor or less significant changes should be handled by the Accreditation Committee.

2. If necessary, the Chairs of each Committee will discuss jurisdiction of any proposed revision and make a decision as to which Committee will consider the revision. The EDHRPP will have the authority to make the final decision.

3. Once a proposed revision is considered by either Committee, a draft will be forwarded to the EDHRPP, the AD, all IRB Chairs, the VPRO, and staff for review and consideration. After a one week review, all comments will be considered by the Committee that drafted the proposed revision.

4. If no substantive change has been made during the one week review period, the final draft version will be forwarded to the EDHRPP for approval. Approval of revised policies will be indicated with the date and signature of the EDHRPP.
5. If substantive changes have been made during the one week review period, a revised version will again be circulated to the IRB Chairs and staff for a one week period. This process may continue until the final revised policy is approved. The EDHRPP has the authority to revise and approve the policy at a point when all remaining concerns are editorial or grammatical.

Revisions to the policies may be made on a section or item basis. This process will allow more timely updates to the policy rather than requiring re-approval of the entire set of IRB Policies and Procedures with each revision.

Proposed revisions may be forwarded to any of the IOs or the Columbia Office of General Counsel for consultation and input.

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

The Boards have the responsibility and the authority to:

- review all human subjects research described in Section IV.A, for prospective IRB approval;
- review progress of studies at least yearly and more often when deemed necessary;
- observe or have a third party whom the Boards determine is qualified and appropriate observe the consent process or any aspect of the research;
- suspend or terminate approval of any study that has an unanticipated problem involving risks to human subjects or others, serious or continuing noncompliance with any federal regulation, or serious or continuing noncompliance with the requirements or determinations of the IRB. Such actions will generally be determined at a convened meeting of the full Board with a quorum present and will be incorporated into the minutes of the meeting. However, an IRB Chair or the EDHRPP may suspend any study outside of an IRB meeting if new information regarding risks becomes available or it is otherwise determined to be in the best interest of the subjects;
- restrict any study it determines to warrant such action. If one aspect of a study fails to comply with federal regulations or Board requirements or determinations, the Boards may restrict the study.

CU IRB approval is required before implementation of any research involving human subjects, including review of records, tissues, or other derived materials.

A. Research Conducted by Investigators Affiliated with Columbia

Under the terms of the FWAs, CU has given the Boards the authority to protect all human subjects involved in research at CU, 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 this institution (CU);
2. the research is conducted by or under the direction of any employee or agent of this institution, in connection with his or her institutional responsibilities;
3. the research is conducted by or under the direction of any employee or agent of this institution using any property or facility of this institution; or
4. the research involves the use of this institution’s nonpublic information, e.g., to identify or contact human research subjects or prospective subjects, for review/analysis.
Columbia University may enter into an IRB Authorization Agreement (IAA) with other FWA entities to delegate IRB review to another designated IRB.

B. 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. In addition, investigators at other institutions may propose a study to be conducted, all or in part, on a CU campus.

The need for review by the CU IRB will depend upon the nature of the involvement of the individual who is affiliated with CU in the former situation, and the proposed use of CU facilities, resources, and/or non-public data in the latter circumstance. Therefore, a description of the research that is proposed should be submitted to the EDHRPP or AD for administrative review and a determination as to whether CU IRB review is also needed.

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:

1. Intervene or interact with living individuals for research purposes;
2. Obtain individually identifiable private information for research purposes; or
3. 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. 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.

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; or
3. Private, confidential information about members of the Columbia University community will be released for research.

For those protocols that require review by the CU IRB, submission in RASCAL is required.

The EDHRPP serves 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 EDHRPP can provide advice on such matters as the risks and benefits of the proposed research, informed consent, etc.).
C. Research Investigators

A Columbia University faculty Officer of Instruction, with a full-time appointment, who has the rank or instructor or higher may serve as a Principal Investigator (PI) on a protocol. Full-time Officers of Research at the rank of Associate Research Scientist (or equivalent) or higher may also serve as a PI. Exceptions will be considered by the appropriate authority on the relevant campus (Working Practice Document #13).

The PI has ultimate responsibility for his/her research project and all official IRB correspondence is addressed to the PI. No studies involving human subjects may be conducted without IRB approval.

Before a protocol will be approved by a CU IRB, the PI must review the most pertinent Good Clinical Practice (GCP) or Human Subjects Research course offered by Columbia and receive a passing score of 80 or greater on the relevant exam. 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.

Key personnel on the CUMC campus must also complete the CUMC online HIPAA (Health Insurance Portability and Accountability Act) training course prior to participation in the research.

If the study population includes children, completion of the CITI Biomedical Research with Minors module is required.

Evidence of GCP, Human Subjects Research, and HIPAA certification is maintained electronically within the RASCAL system.

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.

D. Organization and Membership of the Boards

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 make the necessary modifications, including constitution of additional Boards, to ensure adequate review.

Each IRB will ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable laws, and standards for professional conduct and practice.
Once a Board has reviewed a protocol, all additional oversight and actions will, whenever feasible, be performed by that same Board (i.e., continuing review, expedited review, and adverse event considerations). The Board will delegate compliance oversight activities to the COT for purposes of conducting investigations, but will receive and act on the COT reports as discussed in Section IX.

Each Board will be distinct and completely separate from the other Boards. 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 will address the issue separately or in a joint session, at the discretion of the Chairs, the EDHRPP, and/or the Executive Committee.

Each Board has its own chairperson. The Chairs on the CUMC campus are administratively responsible to the Vice Dean of the Faculty of Medicine/Senior Associate Dean for Clinical Affairs (DCA) at CUMC and the EVPR; the Chair on the CU-MH campus is administratively responsible to the EVPR. The Chairs have direct access to the EVPR, DCA (as applicable), and to the CU President for discussion of IRB issues.

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

1. Membership

The Columbia IRBs are comprised of three non-specialized Boards on the CUMC campus, and one on the CU-MS campus, each of which meets an average of two times per month. Each Board is constituted to meet the regulatory requirements mandated by HHS and FDA, and institutional needs, i.e., individuals with the necessary expertise to evaluate the type and volume of protocols submitted for review.

2. Qualification of Members

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

Each IRB includes among its membership at least one individual who has no affiliation with CU (and no immediate family member with an affiliation with CU) other than his/her IRB membership. There is at least one member at every meeting whose interests and background are primarily non-scientific (lay person). One IRB member may fulfill both criteria. In addition, each Board that reviews FDA-regulated products (drugs, biologics, and devices) has at least one member present who is a physician.

3. Membership Diversity

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

One or more alternate members exist for key members of each IRB. Such alternate members must be of the same category of membership, and meet the afore-mentioned guidelines.

E. Appointment and Terms of IRB Chairs and Members

The EDHRPP and the AD are responsible for the management of all CU IRBs and the IRB office staff. The IRB Chairs, together with the EDHRPP and AD, are responsible for management of the respective Boards.

1. Chair

a. Selection and Appointment

The IO listed on the FWA will appoint the Board Chairs, after consultation with the EDHRPP. 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.

A letter of appointment is prepared by IRB staff for approval by the appropriate IO. This letter can be signed by either the EDHRPP, or by the relevant IO. A copy is retained in the IRB member file.

b. Length of Term/Service

The Board Chair will be appointed to serve a three-year term, which may be renewed. The terms correspond with the fiscal year (July 1 to June 30). If a Chair is appointed mid-year, his/her term will be calculated from the following July 1st. The IO and the EDHRPP, considering input from Board members, investigators, and other administrators, will evaluate the Chairs on a regular basis and renew terms accordingly. Shorter terms may be considered in special circumstances.

In accordance with the “Recognition of Service by IRB Members” memo (Working Practice Document #109), IRB Chairs will receive a token of appreciation upon completion of their service, or as otherwise determined.

c. Duties

Each Board Chair has the responsibility to ensure the compliance of the Board with all federal regulations, and manages his/her review Board and the matters brought before it according to HHS and FDA regulations pertaining to the rights and welfare of research subjects. Each Board
Chair is responsible for conducting the Board’s meetings. The signatory responsibility for IRB correspondence is designated by the Chair, in accordance with IRB policies (see Section V.H.1).

A Vice Chair will be appointed for each Board, and will run the meeting 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 EDHRPP 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.

d. Resignation/Removal

Resignation from the Board may occur at the end of a term or mid-term. Notice should be provided to the relevant Chair and EDHRPP as far in advance as possible to facilitate identification, appointment, and training of a qualified replacement.

After consultation with the EDHRPP, the EVPR or the IO designated on the FWA may remove a Chair.

Individual termination letters are prepared and signed by either the EDHRPP, or an IO. Once signed, copies are distributed to appropriate individuals, including the IO, respective IRB Chair, EDHRPP, AD, and Team Manager of the relevant IRB. A copy is retained in the IRB member file.

e. Education and Training

Chairs are expected to participate in initial and continuing education initiatives to understand, and keep abreast of, changes to institutional policy, relevant legal statutes, the RASCAL system, and evolving interpretation of regulations, policies, and laws. Details of education and training initiatives are provided in Section X.

f. Liability Coverage for IRB Chair/Members

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

g. Confidentiality/Conflict of Interest Statement

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

Chairs who have a conflict of interest with a particular protocol, event, or issue that is reviewed by the Board are expected to recuse themselves from relevant Board deliberations and votes.
2. IRB Members

a. Selection and Appointment

The Chairs and/or IO, in consultation with the EDHRPP, recommend candidates for appointment as IRB Board Members and the IO named on the FWA makes the appointment to the Board. Members will be selected in a manner that will ensure that all requirements of these IRB procedures and federal regulations are followed. A curriculum vitae will be required upon appointment, and a request for an updated version will be made periodically by the IRB.

A letter of appointment is prepared by IRB staff for approval by the appropriate IO. This letter can be signed by either the EDHRPP, or by the relevant IO.

Once approved, copies are distributed to appropriate individuals, including the IO, respective IRB Chair and Vice Chair, EDHRPP, AD, and Team Manager of the relevant IRB. A copy is retained in the IRB member file.

b. Length of Term/Service

Members are appointed to a term of up to three years, which may be renewed. Board Members may be granted an extended leave due to medical, personal or professional reasons, then return to complete their term.

In accordance with the “Recognition of Service by IRB Members” memo (Working Practice Document #109), IRB members will receive a token of appreciation upon completion of their service, or as otherwise determined.

c. Duties

Members independently evaluate project submissions prior to the IRB meeting, participate in appropriate discussions, and vote to approve, disapprove, defer to Chair (i.e., require specific changes), defer to Board (i.e., substantive revision required), or defer (table) each submission during the IRB meeting. These actions apply to: (a) initial reviews, (b) continuing reviews, (c) modifications (amendments), (d) serious adverse events; and e) protocol deviations.

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

Experienced members may be appointed by the Chair to review research activities that qualify for expedited review or activities that may be considered exempt.

d. Attendance Requirements

Members are provided with notice of meeting dates several months in advance and are expected to regularly attend meetings of their assigned IRB. 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 whenever possible. 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, three consecutive absences by a member may result in removal from the Board.

e. Removal, Resignation

Members may be removed 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 EDHRPP, or an IO. Once signed, copies are distributed to appropriate individuals, including the IO, respective IRB Chair, EDHRPP, AD, and Team Manager of the relevant IRB. A copy is retained in the IRB member file.

Resigning members must notify the Board Chair and/or the EDHRPP of their intentions in writing. The EDHRPP will notify the appropriate IO.

f. Liability Coverage for IRB Members

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

g. Education and Training

Members are expected to participate in initial and continuing education initiatives to understand, and keep abreast of, changes to institutional policy, relevant legal statutes, the RASCAL system, and evolving interpretation of regulations, policies, and laws. Details of education and training initiatives are provided in Section X of these written procedures.

h. Confidentiality/Conflict of Interest

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

IRB members should not disclose the results of IRB reviews to investigators or others without the expressed permission of the IRB Chair, IRB Team Manager, or the EDHRPP.

Board members who have a conflict of interest with a particular protocol, event, or issue that is reviewed by the Board are expected to recuse themselves from relevant Board deliberations and votes.
Primary reviewers are assigned by the Chair based on expertise and availability. There is no selection of IRB members as primary reviewers by investigators.

i. Use of Consultants

The Boards may, at their discretion, invite individuals with competence in special areas to assist in the review of complex issues that require expertise beyond or in addition to that available on the Boards. These individuals may not vote with the Boards. Consultants will be required to sign a Confidentiality/Conflict of Interest Statement (Working Practice Document #76).

3. IRB Administrative Staff

a. Support

The IRB Administrative Office provides sufficient professional and administrative support, and adequate resources, to ensure compliance with federal and state regulations and institutional policies for the protection of human subjects in research. The commitment of staff for the IRB is evaluated on a continual basis and additional support is provided as needed.

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

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 (Working Practice Documents #91).

To improve quality, performance and efficiency, periodic performance evaluations are conducted for officer-level staff, while regular feedback is provided to support level staff. The current Supporting Staff Association (SSA) (i.e., union for support-level staff) Collective Bargaining Agreement with CUMC guides the supervision and employment of support staff.

c. Education and Training

The IRB Staff will complete the same core educational program provided to Board members. This includes training on the regulations and the Columbia IRB policies and procedures. The IRB staff will also be provided ongoing and continuing educational opportunities (IRB seminars and workshops; distribution of continuing education information; and access to the IRB website and library). Details of education and training initiatives are provided in Section X of these written procedures.
V. Procedures for Processing of Submissions to the IRB

This section describes the type of information and documentation that must be submitted to the IRB for the review of different events (e.g., new protocol, modification, adverse event report, renewal) and varying types of research (e.g., drug study, international trial, collaborative project). In addition, particular information required when vulnerable populations are involved is also explained.

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

A. Preparation of Submissions

Researchers create protocols electronically in the University’s web-based protocol tracking system, RASCAL. Various options exist for incorporation of pertinent information about the research proposal, to accommodate the various types of documentation available to the researcher. Information may be entered in fields that appear on a composite Data Sheet, existing documents may be attached electronically, and there is also a feature that permits construction of consent documents, called the “Consent Form Builder”, within RASCAL. Relevant documents that are available to the researcher only in paper form may be scanned and attached.

Step by step instructions for creating a protocol and consent document within RASCAL may be found in Working Practice Documents #64 and #71 (Creating a RASCAL Protocol, and RASCAL Consent Form How-To), respectively. In addition, a comprehensive manual for submitting events to the IRB for review, entitled “User’s Guide to the RASCAL IRB Module”, is posted on the IRB websites: http://www.cumc.columbia.edu/dept/irb/ and http://www.columbia.edu/cu/irb/.

RASCAL accommodates the various events that may occur during the active life of a protocol, i.e., initial submission, modification, adverse event, protocol deviation (submitted as modification or adverse event report, as appropriate), renewal, termination. Emergency Use follow-up reports may also be submitted and processed in RASCAL.

Information and material entered for new events is accessible only to personnel listed on the protocol while the protocol status is “creating”, i.e., prior to initial submission to the IRB.

All actions related to a specific event, including material submitted, information entered, correspondence generated, internal IRB notes and documents, history and status, are stored together electronically within an overall project. IRB staff and members may view all entries and attachments for a given event, once the event has been submitted, and may attach documents to the submission, but may not otherwise modify the submitted material. Attachments by staff and members are clearly labeled with the name of the individual who attached the document, and the date they are attached.
The researcher has access to all elements of the protocol except the internal IRB notes and documents, reviewer identification, and correspondence transmitted between IRB staff and/or between IRB members and staff.

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

Annual conflict of interest statements and evidence of satisfactory completion of training for research personnel in GCP, Human Subjects Research, Handling Biohazard Materials, HIPAA, and Research with Minors (when applicable), are documented electronically in accordance with RASCAL procedures and reflected on the Data Sheet of the submission. An electronic protocol-specific conflict of interest statement is also required for the PIs and co-investigators as part of the submission approval process.

B. Documents/Information Needed for Each Type of Event

1. Submission materials: New protocol

General Information, Personnel, Subjects, Funding, and Location screens (Working Practice Document #70) collect the data that will constitute the basic application for review.

The following information or documentation must be included or attached for basic submissions:

a. list of personnel involved in the research, with certification of any required education/training;

b. research objectives and hypothesis, as applicable;

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

d. 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;

e. funding information and, for supported projects, the grant, contract, or other documentation of the supported research, e.g., sponsor’s protocol, investigator’s brochure;

f. approvals from other institutions, if applicable and available;

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

h. recruitment material, if applicable (e.g., recruitment flyer or letter, letter to clinicians, text for Internet advertisement);

i. any other material pertinent to assessment of the potential risks and benefits of the proposed research;
j. completion of the Human Specimens section if any tissue or fluid will be obtained from subjects or stored specimens will be used;

k. justification for exemption, if applicable.

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 segment presented later in this section (Section V).

2. Submission materials: Modification

The Modification Information Form (Working Practice 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. number of subjects currently enrolled;

c. study enrollment status, e.g., enrollment ongoing, study closed to enrollment.

The following information or documentation must be attached or included:

a. clean and highlighted copies of revised documents, or a clean copy with a clear explanation of what has changed, if documents have been revised;

b. supporting documentation of modification from the sponsor, if applicable;

c. updated personnel list, if personnel change is involved;

d. updated Study Description, if previously submitted information has changed.

Protocol deviations that occur during the study should also be submitted as modifications, unless the deviation involves an unanticipated problem involving risks to subjects; the latter should be submitted using the adverse event reporting module.

3. Submission materials: Renewal (Continuing Review)

Notification that continuing review is required will be sent to investigators at least 60 days prior to the expiration date of the current IRB approval. Investigators are required to submit renewal requests in RASCAL and are encouraged to submit appropriate reports for ongoing research activities 60 days prior to the expiration date of the IRB approval for the study.
The Renewal Information Form (Working Practice Document #58) must be completed in RASCAL. This form solicits the following information:

a. study enrollment status, (e.g., enrollment ongoing, study closed to enrollment);

b. date enrollment began at CU site;

c. whether a Certificate of Confidentiality (COC) is required;

d. if a COC exists, the date it expires;

e. summary of any relevant recent literature or interim findings;

f. explanation for any change including a change to risk/benefit ratio;

g. list of papers pending or published about this study;

h. synopsis of the results to date.

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

a. original number of participants anticipated;

b. number of participants enrolled to date at CU site;

c. number of participants enrolled last year at CU site;

d. number of participants who completed the study at CU site;

e. number of participants expected to enroll next year;

f. number of, and explanation for, participant complaints at CU site;

g. number of, and explanation for, participants removed by physician;

h. number of, and explanation for, participants who withdrew from the study;

i. number of participants enrolled to date at other sites;

j. demographic information for subjects enrolled at CU site;

k. if enrollment is less than anticipated, the reasons for, and strategies to remedy, this situation;

l. subject population justification;
m. subject compensation and justification, if applicable;

n. consent waiver or alteration requests, if applicable;

o. recruitment URL, if applicable.

The following information or documentation must be attached:

a. a summary of all adverse events, any new reports of serious and unanticipated adverse events not reported previously, a description of any protocol deviations, reports of any unanticipated problems involving risks to subjects or others, and any withdrawal of subjects from the research or complaints about the research since the last IRB review;

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

c. a copy of the current informed consent document(s), and any newly proposed revisions to the consent document(s);

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

e. any 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, if applicable.

4. Submission materials: Report of adverse events/unanticipated risks to subjects or others

The Serious and Unexpected Adverse Event (AE) Report (Working Practice Document #68) in RASCAL must be completed to report serious and unanticipated adverse events in accordance with the CU AE Reporting Policy (Working Practice Document #02). This form solicits the following information:

a. date, location, and description of the event;

b. relationship of the event to the study;

c. evaluation of whether the event was serious and unanticipated;

d. date and means by which the PI became aware of the event;
e. entities to which the event was reported;

f. subject identifier and event keyword;

g. treatment location, provider and outcome;

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

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

Protocol deviations that result in unanticipated problems involving risks to subjects should be submitted via the AE Report module.

5. Submission materials: Termination

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

The Termination Report form solicits the following information:

a. changes or amendments since the most recent approval;

b. changes in personnel since the most recent approval;

c. total number of participants in the study;

d. number of participants since the most recent approval;

e. number of participants who withdrew from the study;

f. number of participants who complained about the study;

g. summary of any recent literature or findings;

h. additional information about risk associated with this study;

i. brief summary of results.

Protocol deviations are defined as events that occur during the conduct of a study that are not consistent with the approved protocol. They may or may not be considered non-compliance, depending upon the nature of the departure from the approved procedures, e.g., conducting a study visit one day late because the subject’s car broke down and they were not able to arrive at the study site on the specified day, versus enrolling a subject during a lapse in approval.

Most deviations should be reported via the Modification module in RASCAL. However, protocol deviations regarding unanticipated problems involving risks to subjects, or misadministration of drug or therapy (whether increase or decrease in prescribed dose), should be reported via the Adverse Event module.

The description of the circumstances surrounding the deviation should be clearly stated in the Adverse Event Report (Working Practice Document #68) or in the summary section of the Modification Information form (Working Practice Document #69), as applicable. Supporting documentation may be attached electronically, and should be provided whenever available.

7. Submission materials: Emergency Use Report

FDA regulations permit use of an investigational drug or device, without IRB approval, in very limited circumstances. Such use is considered to be an emergency clinical use, and FDA requirements for the research use of an investigational agent do not apply. The involvement of the IRB prior to the administration of the agent is to serve as a facilitator for shipment of the investigational product and initiation of a monitoring process. The FDA must be notified of all emergency use situations by the manufacturer or sponsor.

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) are to be considered for the emergency use exemption. None of these situations will be considered research. Physicians are encouraged to contact the IRB office immediately if such a situation arises.

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

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

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

c. If waiver of consent is requested, documentation that the criteria for waiver codified at 21 CFR 50.24 have been met must be included.
An Emergency Use (EU) Form (Working Practice Document #66), or equivalent information provided in a paper format, must be completed 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. This form solicits the following information and must be submitted to the IRB within five days:

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

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

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

d. description of product;

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

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

g. date of notification to FDA.

C. Material Needed for Review of Particular Types of Research

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 revised 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; and

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

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 (V.B.) related to the type of event (e.g., new protocol, renewal, modification), 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 Investigational New Device (IND) exemption is indicated;

e. completion of the Investigational Products section (Working Practice Document #92) for each agent involved.

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 Institutional Biosafety Committee (IBC) is required for biologics that involve recombinant DNA.

In addition to the material listed in the preceding section (V.B.) related to the type of event (e.g., new protocol, renewal, modification), the following material and/or information is required for all research involving drugs:

a. sponsor protocol, if industry-sponsored;

b. IDB, if industry-sponsored;

c. package insert, if approved drugs are administered;

d. documentation of current FDA status, if an IND for a biologic (BB-IND) is indicated;

e. completion of the Investigational Products section (Working Practice Document #92) for each agent involved.
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 revised 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 (V.B.) related to the type of event (e.g., new protocol, renewal, modification), 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, if an Investigational Device Exemption (IDE) is indicated;

c. sponsor’s determination of non-significant or significant risk;

d. completion of the Investigational Products section (Working Practice Document #92) for each agent involved.

4. **Submission materials: Emergency research**

Emergency research refers to the study of acute, life threatening clinical situations. Often, informed consent from the subjects is not feasible because the subject lacks the capacity to provide their own consent (e.g., unconscious) and/or there is insufficient time because treatment must be promptly administered. The conduct of planned research in life-threatening emergent situations requires special consideration by the IRB, including consideration of whether consent may be waived. The specific conditions under which prospective consent of the subject may be waived 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 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 FDA if the research involves an investigational or FDA-approved product. 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 plan must be submitted to the FDA under an emergency IND/IDE by the sponsor or PI responsible for the IND/IDE. The community consultation and the public disclosures, however, generally do not have to be completed prior to submission for FDA approval.

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

In addition to the material listed in the preceding section (V.B.) related to the type of event (e.g., new protocol, renewal, modification), the following material and/or information is required for all research 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.9;

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 family notification of research participation, when possible, and providing the opportunity for the family to object to participation; and plans for informing the patient of participation if/when the patient regains cognitive capacity;

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

e. description of the efforts by which the community has been advised of the planned emergency research.
Please note that 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.

5. Submission materials: Research involving pregnant woman and fetuses

In addition to the material listed in the preceding section (V.B.) related to the type of event (e.g., new protocol, renewal, modification), 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;

b. 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 (Working Practice Document #10) on when to approach women in labor should be considered when developing this information.

6. Submission materials: Research involving prisoners

In addition to the material listed in the preceding section related to the type of event (e.g., new protocol, renewal, modification), 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. rationale for including prisoners in the research, or limiting research participation to prisoners.

7. Submission materials: Research involving minors

In addition to the material listed in the preceding section (V.B.) related to the type of event (e.g., new protocol, renewal, modification), the following material is required for all research involving minors, i.e., information to support the findings required by Subpart D of 45 CFR 46:

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. 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. 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;

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

8. Submission materials: Research involving other vulnerable adults

In addition to the material listed in the preceding section (V.B.) related to the type of event (e.g., new protocol, renewal, modification), the following material is required for all research involving vulnerable populations:

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

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

c. where applicable, description of procedures that will be utilized to determine competency to provide consent;

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

e. description of procedures that will be utilized to minimize risks;

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

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

If the inclusion of non-English speaking individuals is anticipated, the consent document(s) must generally be translated by an acceptable certified translator into the prospective subjects’ first language or language of choice. 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.

See Working Practice Document #101, Enrollment of Non-English Speaking Subjects in Research, for details on translation options.

In addition to the material listed in the preceding section (V.B.) related to the type of event (e.g., new protocol, renewal, modification), the following material is required for all research involving non-English speaking subjects:

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

b. statement that consent and recruitment documents will be translated after the English version is approved;

c. 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 Board will consider whether proposed procedures to minimize such elements are adequate, and request revisions or additions if necessary.

These measures are not 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.

In addition to the material listed in the preceding section (V.B.) related to the type of event (e.g., new protocol, renewal, modification), 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;

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

When students will be recruited, the “Students as Research Subjects” policy (Working Practice Document #108) should also be reviewed for applicability.

11. Submission materials: International research

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. Physical, social and psychological risks may vary from those in the immediate New York City communities. Assessing the risks and benefits of research conducted internationally may raise challenges if there is not adequate knowledge of the local setting. 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.

In addition to the material listed in the preceding section (V.B.) related to the type of event (e.g., new protocol, renewal, modification), the following material or considerations are required prior to approval by the IRB.

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

b. local IRB/ethics committee approval or evaluation by consultant;

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;

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

Local ethics committee approval should be obtained after review by the CU IRB.
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.

In addition to the material listed in the preceding section (V.B.) related to the type of event (e.g., new protocol, renewal, modification), the following material is required for all substudies:

a. an explanation of the relationship between a previously approved 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;

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


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 (V.B.) related to the type of event (e.g., new protocol, renewal, modification), the following material/information is required for all collaborative research:

a. For all collaborative projects:

1) the name and title of 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;

3) the funding mechanisms involved;

4) identification of the individual and institution who will serve as the overall PI for the project;
5) clear description of what the CU personnel will be doing and what will be done at CU.

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:
   i) details on how local IRB approval will be obtained and maintained at each site;
   ii) 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;
   iii) assurance that unanticipated problems involving risks to subjects or others will be reported to the local and CU IRBs.

c. In addition, if the research will be federally conducted or supported:

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

2) an Unaffiliated Investigator Agreement (UIA) for any individual who is engaged in the research but is not working under the auspices of an institution or organization, including CU.

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.


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

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

When Columbia relies on another IRB to review protocols, there may or may not be a subsequent review by the Columbia IRB. When such a review is conducted by the Columbia IRB, it will often be a facilitated review, i.e., a review by an IRB Chair or an experienced member of the IRB to determine whether the protocol is appropriate for the local environment. Regardless of whether the relevant Agreement requires a facilitative review, protocols reviewed by other IRBs under IRB Authorization Agreements generally need to be submitted to the Columbia IRB via RASCAL for tracking purposes.

D. Administrative review (“pre-review”) of submitted events

This section provides an overview of the review phase of the 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 written procedures.

Upon submission, an administrative review (“pre-review”) by IRB staff is conducted. The nature of the review is contingent upon the type of event (e.g., new protocol, renewal, modification) and is described in more detail in the Review section (Section VI) of these written procedures.

As a result of the administrative review, the submission is either logged in to the Chair’s queue in RASCAL or returned electronically to the researcher. If an event is returned, it will proceed through another administrative review upon resubmission. Details of the routing process and indication of which staff member conducts each step can be found in Working Practice Document #24.

Upon completion of each administrative review of new protocols submitted for the first time, the staff reviewer completes a reviewer form (Working Practice Document #34a, “Reviewer Form: New Protocols (Biomedical)” or #34b, “Reviewer Form: New Protocols (Behavioral)”) and enters comments in the Notes field for the event.

A reviewer form is also completed by staff during pre-review of renewal submissions, followed by a summary entry in the Notes field. The outcome of staff pre-review of other events (e.g., modifications, adverse event reports, terminations) is entered in the Notes field.

At the conclusion of the pre-review, the reviewer takes appropriate action to facilitate the event being logged in (i.e., accepted for review) or returned to the researcher for revision or additional documentation/information. The format for the commentary that is entered in the Notes section can be found in Working Practice Document #20.
E. Routing of submissions to IRB per level of review required

Submissions are routed electronically to the Chairperson’s queue after being logged in by IRB staff. The Chair reviews comments entered in the Notes field relevant to each event (as a result of the administrative review) to obtain a synopsis of the event, awareness of regulatory considerations, and recommended level of review. Depending upon the level of review required, the Chair will review the event him/herself or distribute it to an experienced Board member for review. To the extent possible, reviews after the initial approval will be conducted by the Board which originally approved the study and by the primary reviewer who originally presented the study.

Per RASCAL functioning, the Chair may not electronically distribute events that include an Exempt Declaration. Therefore, the Chair reviews these events, or may request that another qualified individual review the material by retrieving it in RASCAL by the IRB number. The selected reviewer may enter comments in the IRB Reviewer Form (Working Practice Document #34) or the Notes section upon completion of their review. Only the Chair may electronically “approve” an exemption.

1. Level of Review: Not human subjects research

During the course of the Chair review of submitted new protocols, 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 Chair may label the protocol as either “not human subjects research” or “not human subjects research per 45 CFR 46”, respectively. These projects are not subject to continued oversight by the IRB.

Justification that the project does not meet the criteria to be considered human subjects research must be provided. Only the Chair may select one of the “not Human Subjects Research” options in RASCAL.

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)) may be determined to be exempt from the requirements of 45 CFR 46. Protocols for which the investigator has entered an exempt declaration and justification are reviewed by the IRB Chair, who has the capability to approve the project as exempt, or return the protocol to the investigator. The protocol will be returned if revisions, additions, or deletions are required, including removal of the exempt declaration, or if the protocol does not meet the criteria for exemption.

The exemptions apply to research with children, except for research involving survey/interview procedures that are not directly related to evaluations of standard educational practices in accepted educational settings.

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The exemptions do not apply to research that involves an investigational drug, device, or biologic, (i.e., are subject to FDA regulations).

Exempt decisions are communicated to the research team via RASCAL correspondence, and, in the case of approvals, also by hard copy Letter of Approval (LOA) (Working Practice Document #93). Exempt determinations are valid for a period of two years. At the end of the two year period, an abbreviated renewal application must be submitted for tracking purposes. Unless the research has changed in such a manner that the project is no longer exempt, approval will be provided for an additional two year period (Working Practice Document #9).

3. **Level of Review: Expedited**

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

Upon review of a submission, if it does not meet the criteria for exemption, but the criteria for expedited review appear to be met, the Chair will designate the protocol as eligible for expedited review by selecting the appropriate expedited review category in RASCAL. The Chair will then distribute the protocol for review by selecting a primary reviewer and sending the protocol electronically to the reviewer’s queue. A qualified member of the Board 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. Board action is required, however, for a decision to disapprove a study.

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

a. Minor changes in previously approved research during the period of one year or less, for which approval is authorized;

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 respective list as published by the FDA and HHS.

In reviewing the research, the reviewers may exercise all of the authorities of the Board except disapproval. If the reviewer(s) find that the protocol does not meet the criteria for expedited review, they will refer it to the full Board for action.

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

The reviewer who is conducting the expedited review may enter comments in the Notes section
of RASCAL, organize comments in a separate document, or complete the IRB Reviewer form
(Working Practice Document #34) and make non-RASCAL documents available to the IRB staff
as documentation of the review. If the reviewer does not attach the document in RASCAL, but
provides a hard copy to the IRB, the staff will attach the form.

Two functional categories exist in RASCAL in the expedited review option list: Facilitative
Review, and Administrative Review of certain types of awards to support multiple projects
involving numerous investigators. The former was developed to allow processing of protocols
subject to IRB Authorization Agreements when CU is not the IRB of Record, and the latter was
implemented to permit processing of submissions reflecting programs for which human research
exists only in individual studies that will each receive IRB approval. See Working Practice
Document #00, Email from George Gasparis to CU IRB Chairs and staff, “Addition of new
expedited review category in RASCAL”, for additional information regarding the Administrative
Review category.

A list of research that has been approved under an expedited procedure, including an explanation
of the type of research activity and the action taken, shall be provided to the full Board as soon as
practical after such expedited approval. Members participating in the expedited review shall
respond to questions, if raised, from the Board concerning the events approved in this manner.

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

Decisions made by expedited review are communicated to the research team via RASCAL
correspondence, and, in the case of approvals, also by a hard copy Letter of Approval (LOA)
(Working Practice Document #93).

4. **Level of Review: Facilitative**

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 IRB Authorization 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
approval of joint and cooperative projects involving multiple sites and/or investigators. The
EDHRPP or the Boards may agree to permit another IRB listed on a CU FWA to act as the IRB
of record for studies to be conducted by, or with the assistance of Columbia personnel, at the
facilities of another institution. In addition, a CU IRB may agree to function as the IRB of
record for another investigator and/or institution if the project involves material collaboration
from Columbia personnel.
Such Agreements will require written letters of agreement and may necessitate the completion of an FWA, a UIA, or an IAA. Specific criteria for, and procedures for implementing, each of these agreements can be found on the [OHRP website](http://www.hhs.gov/ohrp). Details of the level of, and criteria for, review of protocols that are subject to each IAA can be found in Working Practice Document #05.

5. **Level of Review: Full Board**

Full Board review is required for any protocol that involves research with human subjects and does not qualify for exemption, expedited review, or facilitative review per the terms of an IRB Authorization Agreement.

Each protocol that requires full Board review will be assigned to a primary reviewer (explained below) who will be responsible for a full review of all materials, and will lead the discussion of the protocol at the meeting. Review criteria are explained in more detail in the Review section (Section VI) of these written procedures.

Complete documentation is available electronically to all members for review.

As necessary to accommodate the needs of Board members, hard copies of review material will be distributed approximately one week in advance of the meeting to enable members to actively and constructively participate in the protocol review. Details regarding the material to be distributed, and manner of distribution can be found in the Packet Preparation section (Section VII.B.) of these written procedures.

Alternatively, Board members will be notified electronically of the protocols under consideration, to facilitate online review.

F. **Primary Reviewer system**

1. **Primary reviewer system: Initial review**

The CU IRBs use a primary reviewer system for research that requires full Board review. Each research activity is assigned to at least one primary reviewer, based on related expertise. A reviewer(s) who has a conflict of interest in regards to the protocol, (e.g., 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 the primary reviewer, but may be asked to provide information to the Board during the review.

When making reviewer assignments, the Chair considers the type of research and selects a reviewer with expertise in the relevant area. If vulnerable populations are involved in the research, the Chair attempts to assign the protocol to an IRB member with experience dealing
with the specific vulnerable population. The Chair may assign a protocol to him- or herself, another primary member, or an alternate member.

Primary reviewers are responsible for conducting an in-depth review of all available documentation and presenting the study to the Board, if the submission requires full Board review. All members have electronic access to the complete submission.

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

A prisoner representative is assigned to review each protocol that involves prisoners as subjects. The reviewer is guided by the Prisoner Research review form (Working Practice Document #94).

When additional expertise is needed that is not available among members of the Board conducting the review, consultants may be used.

2. Primary reviewer system: Continuing review (renewal)

The Chairman will select a primary reviewer (himself or herself, another primary member, a consultant, or an alternate member) and distribute the electronic renewal request to that individual. Information that is available electronically, and should be reviewed by a primary reviewer will be provided by the most appropriate means to any consultant who would not normally have access in RASCAL.

An attempt will be 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 file for the study as well as all renewal information prior to the convened IRB meeting. All members have electronic access to the complete renewal submission.

3. Primary reviewer system: Modifications, Adverse Event reports

The Chairman will select a primary reviewer (him/herself, another primary member, a consultant, or an alternate member) to receive the electronic submission. Information that is available electronically, and should be reviewed by a primary reviewer will be provided by the most appropriate means to any consultant who would not normally have access in RASCAL.

An attempt will be made to assign the event to a Board member who reviewed the initial submission or the most recent renewal request.

The reviewer has access to the complete file for the study prior to the convened IRB meeting. All members have electronic access to the complete submission.
Details of all review processes are in Section VI, IRB Review of Human Subjects Research, of these written procedures.

G. 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.

Notification to the Board 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.) section of these written procedures.

H. Notification to Researcher

Outcomes of all reviews will be communicated to researchers as expeditiously as possible after the review is complete. Minutes of full Board meetings will be approved prior to transmittal of the correspondence via RASCAL related to the outcome of an event reviewed at the meeting. Minutes for the entire meeting need not be approved before the correspondence for an individual item is sent, provided the minutes for that item are approved (through documented contact with the Chair outside of RASCAL or via use of the Immediate Action feature in RASCAL). A hard copy LOA (Working Practice Document #93) is also generated to document IRB approval.

The Boards will follow HHS 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)).

1. Notification: Approval and Outcome of Review

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

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

Approval of a research activity will also be documented and communicated by means of a hard copy LOA which will be sent to the PI. The LOA will reflect the approval provided electronically by the Chair/designee or authorized expedited reviewer, and must be signed by a designee with signing authority. This authority is limited to IRB Chairs, the EDHRPP, AD and Team Managers; letters are usually signed by the Team Manager.

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

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

a. title of the research project;

b. name of PI;

c. for funded projects, funding award number and protocol version number, if available;

d. level of IRB review;

e. approval and expiration dates;

f. consent requirements;

g. approved study-related material that will be provided to subjects;

h. conditions to the approval, e.g., requirement to translate consent documents; and

i. information regarding continuing review requirements, reporting of adverse events, and the need to submit modifications for approval prior to implementation.

The LOA for changes in an approved research project will include:

a. title of project;

b. name of PI;

c. for funded projects, funding award number and protocol version number, if available;

d. level of IRB review;

e. a description of the modification;
f. consent requirements, if revised from the originally approved procedures.

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

2. Notification: Disapproval

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

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 a hard copy Letter of Disapproval (LOD) (Working Practice Document #96) which will be sent to the PI. The LOD will reflect the disapproval issued electronically by the Chair/designee and must be signed by a designee with signing authority. This authority is limited to IRB Chairs, the EDHRPP, AD and Team Managers.

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

a. title of the research project;

b. name of PI;

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

d. contact information for the IRB.

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

All LODs will indicate to whom copies (if any) will be sent. Letters for protocols that involve cancer-related research will be copied to the Cancer Center Protocol Office. Letters for research approved under an IAA that may be copied to the respective institution’s IRB office with which the agreement was signed, depending upon the procedures applicable to the respective Agreement.
3. Notification: Suspension

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

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

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

I. Documentation of review and approval

Documentation of actions taken by the Chair or other authorized reviewer in RASCAL will be retained electronically within the RASCAL system.

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

Consent documents generated within RASCAL, using the consent form builder function, will be stamped as approved electronically when the status of the event changes to “approved”.

Consent documents, including recruitment material and study instruments that are generated outside the system but attached in RASCAL will be printed by IRB staff and stamped manually with the IRB approval stamp.

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

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

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 and is provided as guidance for use in the review process. Investigators should be familiar with the criteria for review for their particular type of research, and event submitted, to facilitate the inclusion of all necessary information in the submission. The IRB will consider all applicable factors for a given submission. For example, if a submission is for a new protocol that involves an investigational drug administered to children, the information described in each of the relevant sections (i.e., new protocol, drug study, and minors) will be evaluated.

The IRB will conduct a review of non-exempt research in accordance with 45 CFR 46, New York (NY) state law and institutional policies, and ensure that all elements of 45 CFR 46.111 are met prior to approval of the research. When the research involves FDA regulated 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].

Specific detail regarding review of each type of event (e.g., new protocol, modification, renewal) is in the event-specific section of these written procedures (Section C).

Protocols that meet the criteria for exemption will initially be pre-reviewed by IRB staff, then reviewed by the IRB Chair.

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

Protocols that do not meet the criteria for exemption or expedited review will be reviewed at a convened meeting of the IRB. This process is described more fully in Section VI, “Process”.

At each step of the review process, the event under review is assigned a specific status to reflect the action of the researcher, staff, or Board, as applicable. See Working Practice Document #04, Actions of the IRB, for specific terms and the description of each.

A. Administrative Review (“Pre-review”) of Submitted Events

Upon submission of an event (e.g., new protocol, modification, renewal) in RASCAL, an administrative review (“pre-review”) by IRB staff is conducted. Depending upon the nature of the event, the process may differ but will result in all cases with a decision to either log it in (accept the submission for review), or return it to the research team to obtain missing information and/or documentation. Details of the process for each type of event are described below.
1. Administrative Review (“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 needs to be returned for additional information, enters comments about the protocol in the Notes section of RASCAL for consideration by the Board reviewer, and recommends a level of review based on federal regulations and institutional policy.

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

a. PI is not qualified, or more than one individual is named in this role;
b. sponsor’s protocol, investigator’s brochure, device manual or other component of the formal description of the research is missing;
c. grant application or other documentation of funded procedures is not included, for funded projects;
d. consent documents are not included, and a waiver of informed consent is not requested;
e. recruitment material is mentioned but is not included.

Details of the pre-review process are included in Working Practice Document #20 and in Section V.D. of these written procedures.

2. Administrative Review (“Pre-review”): Renewals

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

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

a. enrollment status is not provided, and/or information regarding enrolled subjects is not included;
b. enrollment is ongoing, consent forms are not attached, and a waiver of informed consent is not requested;
c. PI is not qualified, or has had research privileges suspended;
d. sponsor’s protocol, investigator’s brochure, device manual or other component of the formal description of the research is missing;

e. a summary of adverse events, or recent report of a data and safety monitoring body, is not included, where applicable.

Consideration will be given as to whether there is sufficient time for the investigator to respond to avert a lapse in approval prior to returning. In such cases, the IRB will consider whatever information is available and may approve the renewal with appropriate restrictions until all of the above information is received and reviewed.

Details of the pre-review process are included in Working Practice Document #20 and in Section V.D. of these written procedures.

3. Administrative Review (“Pre-review”): Modifications

Modifications are pre-reviewed initially by staff and a brief summary of the requested modification is entered in the Notes section. The staff reviewer also indicates whether the consent form has been modified, and makes a preliminary assessment of whether the modification can be reviewed by expedited review (if changes are not substantive) or requires full Board review.

The intent of the summary is to provide the Chair with the basic information needed to process the modification request, by distributing it to a Board reviewer or him/herself. 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. Details of the process are included in Working Practice Document #97.

4. Administrative Review (“Pre-review”): Adverse Event Reports

Adverse Event Reports are pre-reviewed to ascertain whether they meet the criteria in the CU Adverse Event Reporting policy (see Working Practice Document #02) to be reported individually.

If they do not meet the criteria, they are returned with instructions to include the event in the summary of adverse events required at the time of continuing review or termination, the latter if the protocol is closed prior to the next continuing review. One important exception is for reports of research subject death that occur at a site under the purview of CU, which will be logged in for review regardless of whether death is an anticipated risk (Working Practice Document #3).

If they do meet the criteria, the Adverse Event Reports will be logged in (accepted). The staff reviewer may also review the current consent document to determine whether changes need to be made, 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. Details of the pre-review process are included in Working Practice Document #20 and in Section V.D. of these written procedures.

5. Administrative Review (“Pre-review”): Termination Reports

Termination Requests are pre-reviewed to verify that all information requested in the Termination Report has been submitted, and to make a preliminary assessment of whether there are any outstanding issues that need to be addressed prior to termination of IRB oversight. Outstanding issues may include: receipt of a final report and whether any harms to subjects occurred for which resolution has not been reached. Incomplete submissions will be returned.

The staff reviewer will enter comments in the Notes field to reflect the pre-review findings. Details of the pre-review process are included in Working Practice Document #20 and in Section V.D. of these written procedures.

B. IRB Criteria for Review

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

These criteria, as defined in 45 CFR 46.111 and 21 CFR 56.111, will be considered for each non-exempt event submitted for review prior to approval. 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 which 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. 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 (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

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

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

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

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

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

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

8. Recruitment methods and advertising material are appropriate.

9. Additional protections are in place for vulnerable subjects.

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

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

1. **Risks to Subjects are Minimized**

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

Risks to subjects may be minimized by:

a. using procedures which are consistent with sound research design;

b. using procedures which do not unnecessarily expose subjects to risk, such as reducing or eliminating an exposure; and
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;

e. adding endpoints to the study to reduce further exposure.

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 of the federally
designated expedited review categories may present no more than minimal risk to subjects.
(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 review, the Board will also consider the status of the protocol and reported
adverse events, and will carry the initial determination forward unless noted otherwise in the IRB
record.

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 increased 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**

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

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.

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-
rangle 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)).

3. Selection of Subjects is Equitable

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

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

Special consideration must be provided for the recruitment of vulnerable populations such as children, prisoners, pregnant women, and mentally disabled persons, so that their enrollment and participation in the study is not adversely affected by their vulnerability.

Renewal submissions must include demographic information for enrolled subjects, or a clear rationale for exclusion of this information.

4. Informed Consent Process is Appropriate

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(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 between the federal regulations and New York State Law in a manner that the state law more narrowly defines human research activities.

Hence, 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 HHS and FDA regulations for the protection of human subjects require that legally-effective informed consent is obtained from every subject enrolled into a study. The federal regulations require that each subject provides informed consent in a process that provides 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 (further details of the elements of consent can be found at: <http://www.cumc.columbia.edu/dept/irb/>).

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.

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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 also requires that 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 differently than the federal regulations in such a manner that it only applies to research that involves medical experimentation or research that involves medical procedures or treatment on human individuals. Therefore, research that solely involves questionnaires, surveys, or epidemiological methodology is not covered under New York State Law; hence, informed consent is not required per these statutes. (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 would be required in these situations unless appropriately waived.)

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

Informed consent will be sought from each prospective subject or the subject’s legally authorized representative, in accordance with 45 CFR 46.116, 21 CFR 50, New York State Law, and as outlined in these written procedures.

The investigator will submit a draft consent form for the Board’s review as part of the initial submission, if appropriate. The Board or designated expedited reviewer will indicate any necessary changes to the consent form at the Board meeting or will document them within RASCAL, as appropriate to level of review. If revision is necessary, IRB staff will generate correspondence to the investigator in RASCAL of the changes that need to be made to the consent form, and the correspondence will be forwarded to the Chair for transmission to the researcher. The investigator will make the required changes to the consent form, and return the corrected consent form to the Board for confirmation. The confirmation may be made by the Chair or by an assigned expedited reviewer, if the changes were specific and the event was deferred back to the Chair or primary reviewer. If the changes are complicated or substantial, 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. 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 written procedures.
b. Telephone Consent

Informed consent obtained via telephone contact without any opportunity for face-to-face contact requires additional considerations. Depending upon the method used, telephone consent may involve written documentation of informed consent, or waiver of written documentation of informed consent. Suggested methods of obtaining consent via telephone are described in Working Practice Document #53, Telephone Consent Procedures.

c. Consent for Audio- and Videotaping

To ensure informed consent, when study procedures involve audio- or videotaping, 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 Working Practice Documents #16 and #17, Audio- and Videotaping Policy and Sample Audio-/Videotaping Addendum, respectively.

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

The Board or expedited reviewer may waive the requirement for informed consent per 45 CFR 46.116 (d) (or allow an alteration of some or all of the elements of informed consent) only 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; and

2) the waiver or alteration will not adversely affect the rights and welfare of the subjects; and

3) the research could not practically 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:
i) public benefit or service programs;

ii) procedures for obtaining benefits or services under those programs;

iii) possible changes in or alternatives to those programs or procedures; or

iv) possible changes in methods or levels of payment for benefits or services under those programs; and

2) The research could not practicably be carried out without the waiver or alteration (45 CFR 46.116(c)).

Informed consent may also be waived in emergency research projects that meet the criteria described in 21 CFR 56.104 (see Section V.C.4).

Waiver of informed consent is different than waiving the requirement of documentation of informed consent, described in item 5 of this section of these written procedures.

5. Documentation of Informed Consent is Appropriate

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

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

a. Waiver of Written Documentation of Consent

The Board, or expedited reviewer, may waive the requirement that some or all subjects or the subject’s representative sign a written consent document if it is determined that:

1) the research presents no more than minimal risk of harm to subjects; and
2) the research involves no procedures for which written consent is normally required outside the research context (46 CFR 45.117(c)(2); 21 CFR 56.109(c)(1)).

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

For research under HHS jurisdiction, but not FDA jurisdiction, 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, and 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 note that the requirement to obtain written documentation of informed consent was waived.

Informed consent obtained via telephone contact without any opportunity for face-to-face contact requires additional considerations, depending on the type and risk level of the research (e.g., survey, behavioral studies). Depending upon the method used, telephone consent may involve written documentation of informed consent, or waiver of written documentation of informed consent. Suggested methods of obtaining consent via telephone are described in Working Practice Document #53, Telephone Consent Procedures.

6. Data and Safety will be Monitored

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 unanticipated problems involving risks to subjects or others, 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 Data and Safety Monitoring Board or a Data and Safety Monitoring Committee should be required.

During the course of the research, serious and unanticipated adverse events and other unanticipated problems must be reported to the IRB in accordance with the CU AE Reporting policy dated April 14, 2004 (Working Practice Document #02).
At the time of continuing review or when they are submitted as a modification, interim reports from data and safety monitoring bodies, if applicable, and a summary of adverse events to date will be reviewed by the IRB. 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**

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 produce adverse effects), and participation (e.g., by examining the extent of electronic security measures to be used to protect data).

Details of where paper records will be stored, and/or how electronic data will be protected from unauthorized access, are required. In addition, consideration will be given to who has access to the data.

At times, research may involve the collection of data that is especially sensitive due to the risk of emotional, financial, legal or other harm that may be incurred if the data were disclosed outside of the context of the research. In these cases, the Board may require that a Certificate of Confidentiality, which protects against compelled disclosure and is obtained from the federal government, be obtained.

Payments to subjects for participation or reimbursement for expenses will be processed in accordance with the CU Petty Cash policy (Working Practice 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.

When study procedures involve audio- or videotaping, additional considerations regarding confidential storage and use of the tapes is required. See Working Practice Documents #16 and #17, Audio- and Videotaping Policy and Sample Audio-/Videotaping Addendum, respectively.

NOTE: At CU, requirements of the Privacy Standard of the federal Health Insurance and Portability and Accountability Act (HIPAA) are governed by the Privacy Office, via review by
the Privacy Board, which is separate from the IRB. HIPAA language is not routinely included in
the consent form, but is provided in a separate Authorization Form.

Additional information may be obtained via RASCAL at the following URL:
<https://www.rascal.columbia.edu/comply/hipaa.html> or from the website maintained by the
Privacy Board: http://cumc.columbia.edu/hs/hipaa/policies/hipaa.html

8. Recruitment Methods and Advertising Material are Appropriate

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.

Acceptable recruitment methods, when patients are involved, include:

- Treating physician introduces the study to the patient. The patient must provide written
  consent to allow the treating physician to forward their name and contact information to the
  researcher.
- Treating physician introduces the study to the patient and provides the patient with written
  material about the study, so that the patient may contact the researcher directly if interested in
  participating or learning more about the study.
- 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.

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

The Board or an expedited reviewer may review a recruitment tape (audio or video) submitted
without an approvable script. If the tape follows the Board advertising review guidelines
appropriately, it may be approved. However, if there is anything in the tape that an expedited
reviewer finds unacceptable, review of the tape will be referred 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 which are for “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 read verbatim during the recruitment
process.

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9. Additional Protections are in Place for Vulnerable Subjects

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

To this end, the IRB may require that an advocate be provided, or that a Legally Authorized Representative (LAR) or Health Care Proxy (HCP) provide permission for enrollment, in addition to consent or assent from the subject, when the capacity of the prospective subject to provide legally effective consent is in question. Procedures for determining capacity must be described by the investigators when individuals who may lack capacity to consent will be considered for enrollment.

In any situation, but particularly when a prospective subject is subordinate to a researcher, the IRB may observe the consent process or require changes in recruitment procedures to eliminate or reduce elements of coercion or undue influence.

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

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

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

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

Annual and protocol-specific conflict of interest forms are reviewed through a process that involves individual evaluation of positive responses (“anomalies”) by staff from the Department of Research Administration. Notification of the outcome of this review of anomalies that do not meet the University threshold to be considered a significant financial interest is provided to the IRB for consideration during its review.
Procedures are in place to refer conflicts that meet or exceed the University threshold for significant financial interests to the institutional Conflict of Interest Committee. The Committee is comprised of representatives from units within the University that have responsibility for research functions, and serves to eliminate, mitigate, or manage significant financial conflicts of interest. Notification of Committee action for conflicts that require full Committee review and involve human subjects research is provided to the IRB for consideration during its review of the research.

C. Review of Specific Events

1. Initial Review

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

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

In addition, the Boards will ensure that all applicable approvals, confirmations or review, as applicable, from internal and external committees have been obtained. These include, but are not limited to, the Herbert Irving Comprehensive Cancer Center Protocol and Research Monitoring Committee (PRMC), the Institutional Biosafety Committee (IBC), the Joint Radiation Safety Committee (JRSC), the Radioactive Drug Research Committee (RDRC) (all internal), and the Recombinant DNA Advisory Committee (RAC) (external).

If a protocol is in any way cancer-related, review by the IRB may not proceed until approval from the Cancer Center Protocol Monitoring and Review Committee (PRMC) is obtained (Working Practice Documents #6 and 7). IRB review may proceed while other approvals or confirmations are in progress, insofar as the information that will be obtained from the respective approval or confirmation is not needed to conduct the IRB review.

Compliance with institutional policies such as qualifications of PIs (Working Practice Document #13), and training requirements for research staff (see Section X of these written procedures) will also be verified during the initial review.

2. Review of Reports of Adverse Events/Unanticipated Problems

Submission of reports of unanticipated problems including adverse events will be in accordance with the CU Adverse Event Reporting Policy (Working Practice Document #02).
Reports of adverse events that meet the criteria for individual submission at the time of occurrence will be presented for discussion at a convened meeting of the IRB after review by a primary reviewer. The Board will determine whether the report is complete or additional information is required. In addition, a determination will be made of whether the protocol and/or consent document(s) should be revised. 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 adverse event reports results in a determination that the risk/benefit ratio has become less favorable.

Particular attention will be focused on reports of adverse events that occur at a Columbia site in an investigator-initiated protocol for which there is no other monitoring outside of the research team.

The Board may take action appropriate for the circumstances to protect the safety, welfare and rights of research subjects. Investigators are encouraged to report any trends to the Board.

3. Review of Reports of Protocol Deviations

A protocol deviation occurs when there is a discrepancy between the protocol and the activities being performed within the study. While a protocol deviation may or may not increase risk to subjects, it is particularly important that the IRB be notified immediately when the deviation could potentially cause increased risk to subjects or the study as a whole.

Protocol deviations can be categorized as either minor or major, and may or may not affect individual subjects. Major deviations should be reported immediately to provide an opportunity for the IRB to assess whether the study should continue, and whether changes to study procedures are required.

a. Major protocol deviations:

1) The deviation posed a significant risk of substantive harm to the individual research subject;

2) The deviation has compromised the scientific integrity of the data collected for the study;

3) There is evidence of willful or knowing misconduct on the part of the investigator(s) and/or study staff;

4) There is other serious or continuing noncompliance with federal, state or local research regulations.

b. Minor protocol deviations:

1) The deviation has no substantive effect on the risks or benefits to the individual research subject(s);
2) The deviation has no substantive effect on the data collected;

3) The deviation was not the product of willful or knowing misconduct on the part of the investigator(s) or study staff.

Protocol deviations should be submitted through the Adverse Event Report Module in RASCAL if the deviation resulted in a potential increase in the risk or harm to subjects, or involves a misadministration of drug or therapy. All misadministrations of drug or therapy (whether increase or decrease in prescribed dose) should also be reported to the IRB COT to ensure reporting to federal regulatory agencies, as appropriate. All other protocol deviations should be submitted through the Modification module in RASCAL.

The IRB will review protocol deviations to determine whether the risk/benefit ratio of the protocol has increased as a result of the deviation. Potential or real harm to the subject will be assessed. A corrective plan should be submitted by the researcher with the protocol deviation and will be reviewed by the IRB to ensure that adequate steps are being taken to avoid recurrence of the deviation.

4. Review of Emergency Use Requests

Emergency use is defined by the FDA as the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval (21 CFR 56.102(d)). This does not include the “off-label” uses of approved medical products in the practice of medicine (i.e., not in a research context). Such uses are not considered research, but rather the practice of medicine for the treatment of patients with non-FDA-approved products. The data from such uses may not be used for research purposes.

In general, emergency use of an investigational agent may only be authorized once. If future need for use of the test article under similar circumstances is anticipated, a full protocol should be submitted to the IRB for review.

Refer to section VI.D.10 for provisions regarding emergency research.

a. Initial Notification to the IRB

Emergency use of a test article under the conditions specified in 21 CFR 56.102(d), 21 CFR 56.104, and 21 CFR 312.36 does not require prospective IRB review. However, written IRB acknowledgment of notification by a clinician of the proposed emergency use of a test article, and receipt of a consent document, if available, may be required by the manufacturer of the product to permit shipment of the investigational product to the institution.
When the IRB office is notified of proposed emergency use of an investigational agent, a letter will be provided to the investigator from the IRB acknowledging the proposed use and advising the clinician of the need for a follow-up report to the IRB within 5 days. See Working Practice 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.

Waiver of informed consent in conjunction with emergency use is discussed under Informed Consent below.

b. Consent Requirements for Emergency Use of a Test Article

If the use involves the individual emergency administration of an FDA regulated article under 21 CFR Parts 50 and 56, the requirement for prior consent may appropriately be waived, as provided for in 21 CFR 50.23(a)-(c), 56.104(c), and 56.102(d) and these written procedures. The IRB will acknowledge rather than approve the waiver.

The obtaining of 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 legal representative; 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 shall be submitted to the IRB within 5 working days after the use of the test article.

c. Follow-up Report

Within 5 working days after emergency use, the physician responsible for the use must notify the IRB office of its use and outcome. The report should document the following:

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1) an explanation of the life-threatening situation necessitating the use of the test article and the patient’s initials;

2) if not provided earlier, the name of the investigational product, and the IND number, BB-IND number, or IDE number, as applicable;

3) a copy of the consent document that was used or an explanation of why obtaining consent was not possible (i.e., details in item b above); also, if the patient was a child whether assent of the child was obtained;

4) concurrence from another physician who is not otherwise involved in the use of the investigational product stating that the situation was life-threatening and that no alternative standard treatment was available;

5) an indication of whether additional uses are anticipated, in which case a protocol and consent form must be submitted for Board approval.

If a protocol for additional uses is submitted, the Board will prospectively review, at a convened Board meeting, proposals for the treatment (FDA 21 CFR 312.34 and 312.35) or compassionate use of a test article under applicable FDA regulations and the principles of research ethics presented in Ethical Principles and Guidelines for the Protection of Human Subjects of Research (The Belmont Report) (Appendix I). Data collected from these activities, when the proposed activities have been reviewed by the convened Board, may be used for research purposes.

5. Facilitative Review

Facilitative review will occur when CU is relying upon the review of another IRB, in accordance with the terms of an IRB Authorization Agreement. The type of reviewer and extent of review required is dependent upon the specific Agreement, as described in Working Practice Document #05.

6. Continuing Review

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. 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.
Continuing review should occur within the 60 days prior to the study’s expiration date. Review of a change in the study does not routinely alter the date by which continuing review must occur. However, if a modification is submitted that requires review of all study procedures and documents, to the extent that all information required for consideration of renewal is requested and found to be acceptable, the Board may consider review of the modification to be equivalent to a continuing review and recalculate the expiration date for IRB approval of the protocol.

Each Board has authority to determine, at their discretion, 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 and sudden increase in risk to subjects, FDA audits, site visits conducted by authorized personnel, reports from “whistleblowers,” etc (45 CFR 46.103(b)(4); (FDA 21 CFR 56.108(a)(2)). Verification may be obtained through contact with the sponsor, FDA, or cooperative group, as applicable, (e.g., to verify protocol version dates), by audit of the investigator’s files, and via requests for information from a coordinating center or monitoring board.

Further explanation of how continuing review serves an important function in oversight monitoring is provided in Section IX.

a. Continuation Past Expiration of IRB Approval

Applicable regulations require that each non-exempt protocol be reviewed at least annually. The IRB cannot extend a study’s approval beyond the expiration date, 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 must be suspended pending re-approval of the research by the IRB.

2) Where failure to continue study procedures would seriously adversely affect the safety or well-being of enrolled subjects, the IRB Chair can 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). 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 HHS regulations, in accordance with HHS guidance.

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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 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. Some situations that the Board should consider for a shorter approval time include:

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);

3) the need for increased monitoring to evaluate potential noncompliance or for projects conducted by investigators who have previously failed to satisfy IRB requirements.

When initial review was conducted by a convened meeting of the IRB, and the procedures have not substantively changed, continuing review will also be conducted at a convened meeting (45 CFR 46.108(b); 46.109(e)), with the exception of the limited circumstances described by expedited review categories (8) and (9). (See List of Expedited Review categories, Appendix IX.) If study procedures have evolved, whether through modifications or completion of active intervention, such that all remaining procedures meet the criteria for one or more of the expedited review categories, continuing review may be conducted via an expedited review process.

For full Board reviews, the maximum approval interval shall be one year from the date of the convened meeting at which the study was approved, either unconditionally or with specific conditions which the IRB Chair or his/her designee can verify.

When initial review was conducted by an expedited review procedure, continuing review will also be conducted via an expedited process, provided all study procedures continue to fall within one or more of the federal categories of expedited review.

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.

Each Board has 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.
Any suspension or IRB-initiated termination will be reported promptly to the investigator, and to the EDHRPP, who will inform the appropriate IO. The EDHRPP 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.

7. Review of Termination Requests

Requests by researchers for closure of an approved project are reviewed by a primary reviewer prior to presentation at a convened meeting. The reviewer will evaluate information provided about number of subjects enrolled, unanticipated problems, and study results to determine whether closure is appropriate, and 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 adverse events or outcomes should be reported to the IRB.

8. Suspension 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 an unfavorable risk/benefit ratio, or is not being conducted in accordance with stipulations previously imposed on the research activity by the IRB Board.

The EDHRPP 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; such actions should occur when, in the judgment of the EDHRPP or IRB Chair, it would be inappropriate to wait until the next meeting of the IRB or Executive Committee of the IRB.

Any suspension or termination will be reported promptly to the investigator and, if the action was initiated by the Chair, the EDHRPP, who will notify the appropriate IOs, the FDA, if applicable, and OHRP of the suspension or termination (45 CFR 46.108(a); 21 CFR 56.113).

There is no regulatory authority for appeal of Board decisions in suspending or terminating approval of research.
D. Review of Specific Types of Research

1. Review of Research involving Investigational Drugs

For studies involving investigational drugs, or approved drugs used off-label, IRB staff will perform the following functions:

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 FDA documentation if necessary.

b. If the regulatory status is not clear, staff will request one of the following from the investigator or sponsor:
   1) A letter from FDA that documents the status;
   2) A copy of the sponsor’s protocol or Investigator’s Brochure that reflects the IND number;
   3) Other appropriate documentation of the need for an IND or exemption thereof.

During its review of the proposed research, the IRB will consider, in addition to the review criteria previously described that applies to all reviews:

a. Whether an IND is required, if one has not been obtained;

b. Whether the investigational drug is being dispensed in accordance with the NYPH Investigational Drug Policy (Working Practice Document #18);

c. Whether specific information regarding birth control measures must be provided to subjects with reproductive capacity;

d. Whether special handling is required by research staff, subjects, or others.

2. Review of Research involving Medical Devices

For studies involving medical devices, IRB staff will perform the following functions:

a. Determine whether the regulatory status of the device is clearly indicated in the materials submitted for Board review, with appropriate FDA documentation if necessary.

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 Investigational Device Exemption (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.

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 Investigational Device Exemption (IDE) by the FDA (21 CFR 812.2 (b)(1)).

b. Research involving a medical device for human use that does not qualify as NSR device and is not exempt is classified as a Significant Risk (SR) Device. Research involving SR devices (unless the device is banned) cannot begin until the FDA issues an IDE and approval is granted by an IRB (21 CFR 812.30 (a)).

A significant risk device means 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 Board will determine if the device is a SR Device, an NSR Device, or whether the research use of the device is exempt from the IDE regulations.

a. If the Board 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.
b. If the FDA has issued an Investigational Device Exemption (IDE) for the proposed use of the device, then it is, in most cases, considered to be an SR device.

c. If the FDA has not issued an IDE for the proposed use of the device, then the Board shall consider the following elements in determining if the device is SR:

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.

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 proof 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 proof 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 an SR/NSR determination. Also, if the investigation involves a device that is cleared for marketing through the 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 an SR/NSR determination.

3. **Review of Humanitarian Use Devices**

Humanitarian Use Devices (HUDs) are intended to benefit subjects in the treatment or diagnosis of diseases or conditions that affect or manifest in fewer than 4,000 individuals in the United States per year. HUDs are considered by the FDA to be approved for marketing.

The degree of safety and efficacy testing required for FDA approval of an 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 research involving HUDs will be reviewed at a convened meeting of the full Board at both the initial and continuing reviews.

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:

1) determine that the FDA has granted a Humanitarian Device Exemption (HDE) to the sponsor.

2) determine that the investigator intends to use the HUD according to its FDA approved use.

After the Board has determined that the FDA has granted an HDE, the Board may proceed to review the proposed activities and investigator 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 an HUD in accordance with its FDA approved indication. However, the Board may require consent in such instances at its discretion.

b. Use Not in Accordance with the HDE

When use of an HUD for research is proposed, the IRB should consider all factors relevant to use of an investigational device, as well as the IRB review criteria defined in 45 CFR 46.111. The Board will require informed consent for any research use of the HUD (i.e., outside of the FDA-approved indications) of an HUD.

4. Review of Research involving Pregnant Women 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.

When the Boards consider research involving pregnant women and fetuses, they will ensure that all requirements of 45 CFR 46 Subpart B are met prior to approval of the research. In addition to applying the criteria for IRB review identified in 45 CFR 46.111, they will ensure that:

- there is adequate expertise on the Board to evaluate the risks and benefits related to the inclusion of pregnant women, fetuses and neonates, engaging consultants where necessary;
- the determinations required by Subpart B are documented appropriately in the IRB record;
- the proposed involvement of pregnant women or fetuses meets all requirements for inclusion as stated in 45 CFR 46.204;
- the proposed involvement of neonates meets all requirements for inclusion as stated in 45 CFR 46.205;
- 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;
- informed consent is obtained per provisions of Subpart B for pregnant women who have reached the age of majority or are legally emancipated;
- informed consent is obtained per provisions of Subparts B and D for pregnant minors (where research is related to prenatal care, consent of the pregnant minor may be acceptable);
- consent documents contain information regarding risks of breastfeeding, when risks to the pregnant woman or neonate is determined to be greater than minimal;
- 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 (Working Practice 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.

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. When a convened Board reviews research involving prisoners, the prisoner representative will be present at the meeting and count toward quorum for these protocols. The reviewer form for prisoner research (Working Practice Document #94) will be completed for each review by the prisoner representative.

In addition to its other responsibilities prescribed in these Written Procedures, the Board shall approve research involving prisoners only if it finds that all requirements described in 45 CFR 46.300 (Subpart C) are met.

Human subjects research may involve prisoners as subjects only if the Board has approved the research, considering the above requirements, and the proposed research involves solely research permitted per the federal regulations.

For research involving prisoners, the definition of minimal risk is different than for research not involving prisoners, in that the risk is relative to that encountered in the daily lives of healthy individuals. The following definition of minimal risk will be applied to research involving prisoners:

- the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

The Board will determine that the research under review represents one of the categories of the research permissible under 45 CFR 46.306(a)(2).

Any research involving prisoners that the IRB determines not to represent one of the categories of research permissible under 45 CFR 46.306(a)(2) and that is not federally supported shall have a separate special panel review conducted at CU. The panel will be established by the IRB office.
and will include individuals with appropriate scientific and ethical expertise to review the given research project. IRB approval of such research may not proceed without approval from the special panel.

Details of the IRB review for any research project involving prisoners that is federally-supported or conducted will be given to the EDHRPP or AD promptly after review, with a draft letter for submission to OHRP. The EDHRPP, AD, or designee, will prepare a report for submission to OHRP to satisfy the certification requirements described in 45 CFR 46.305(c).

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 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 in consideration of Subpart D of the applicable HHS and FDA regulations, New York state law, and institutional policy. When appropriate, requirements for involvement of minors in research postulated by the New York City Administration for Children’s Services (ACS), and/or Department of Education, are also considered. Working Practice Document #107, Research involving Children, provides additional information.

Information provided by the investigator regarding level of risk, prospect of direct benefit (when applicable), assent and parental permission, and inclusion of wards/foster children is evaluated by the IRB, which may concur with the investigator’s determinations, make alternative determinations, or impose additional requirements.

Use of the Subpart D Reviewer Form (Working Practice Document #100), currently being implemented, will help to ensure that all necessary elements are considered by the IRB reviewer.
a. Determination of Risk/Benefit Category

When a Board (or qualified reviewer for research that is eligible for expedited review) reviews research involving children, it will determine 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 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.

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.

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.

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.

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 the research is supported by HHS 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 EDHRPP or AD. The EDHRPP, AD, or designee will prepare a report for submission to OHRP to request a panel review as described in 45 CFR 46.407 or 21 CFR 50.54, as applicable.

Research in this category that is not federally funded and does not involve FDA-regulated products will be reviewed by a special panel convened by the IRB office to make the determinations that would be considered by HHS or FDA when evaluating research in this category.

The permission of both parents is required for research in this category, unless one parent cannot reasonably provide permission, as allowed per Subpart D. The assent of the minors involved is required unless the Board determines that some or all are not capable of providing assent.

b. Assent Determination

After the Board makes the risk/benefit determination, they must consider the issue of child assent, as described in 45 CFR 46.408(a) (Subpart D). The Board must decide whether assent is necessary, and also whether and how it will be documented if it is necessary.

Among the formats the Board may consider are the following:

1) waiver of assent;

2) determination that the children lack the ability to provide assent;

3) verbal assent, without documentation;

4) verbal assent, with documentation by the investigator and/or the legally authorized representative(s);

5) written assent form, with subject signature; or

6) subject signature block on consent form (for older children only).

The federal regulations do not require that assent be sought from children starting at a specific age, but that their assent should be sought when, in the judgment of the IRB, the children are capable of providing their assent. IRBs are to take into account the ages, maturity, and psychological state of the children involved (see 45 CFR 46.408(a)).

When the research offers the child the possibility of a direct benefit that is important to the health or well-being of the child and is available only in the context of the research, the IRB may determine that the assent of the child is not necessary (45 CFR 46.408(a)).
c. **Inclusion of Wards in Research**

Special protections must be considered whenever children who are wards of the state or any other institution, agency, or entity are considered for inclusion in research that is greater than minimal risk with no prospect of direct benefit. Of primary concern are consent issues, i.e., who has authority to enroll a child who is a ward in research. Responsibility for ensuring that appropriate individuals provide permission rests with the PI, and must be in compliance with applicable statutes and the process described in the protocol that was approved by the IRB.

Federal regulations do not require special provisions for wards enrolled in research that is either minimal risk or greater than minimal risk with the prospect of direct benefit. However, the Board may impose additional requirements if the research and/or status of the child(ren) warrant additional safeguards. New York state laws and New York City Administration for Children’s Services (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 46.406) 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.

The CU policy, “Research Involving Children” (Working Practice Document #107), provides detailed information regarding the protections required when children are subjects in research.

7. **Review of Research involving Other Vulnerable Adults**

When all or some of the subjects in proposed research are vulnerable adults, and their vulnerability stems from factors other than pregnancy or incarceration, the Boards will ensure that additional protections are included where necessary to uphold the principles of respect for persons, justice, and beneficence. Specific requirements for the inclusion of pregnant women and prisoners are described elsewhere in these written procedures.

Adults may be considered to be vulnerable for a variety of reasons, including but not limited to:

- a. impaired cognitive capacity, either temporary or permanent;
- b. economic or educational disadvantage;
- c. inability to speak or understand English;
d. medical condition;

e. relationship to researcher.

When the Boards find that the subjects in a research protocol are vulnerable, the Boards will consider additional safeguards on a case-by-case basis (21 CFR 56.111(b); 45 CFR 46.111(b).

For studies involving the possibility of consent by legally authorized representatives for adult subjects, the Boards must consider how to document that the subject is capable of providing his/her own consent, who may legally provide consent if the subject is not capable, and the issue of subject assent. The Boards must determine whether assent is necessary, and how it will be documented if it is necessary.

The IRB must first consider whether the research must be done with the particular group of vulnerable subjects. If yes, appropriate justification needs to be made for the inclusion of these subjects in any research that will not directly benefit these subjects. Even with such justification, additional safeguards should be included to minimize the vulnerability of such individuals.

8. Review of Research involving Non-English Speaking Subjects

The Belmont Report identifies “justice” and “respect for persons” as two fundamental ethical principles that must underlie the conduct of all human subjects research. The principle of justice requires that the burdens and benefits of research are equitably distributed. The principle of respect for persons requires that “adequate standards for informed consent are satisfied” so that subjects are provided with sufficient meaningful information to decide whether they want to enroll in a research study.

In the review of a protocol the IRB will evaluate the “special populations” information entered in RASCAL by the research team and determine the number or percentage of non-English speaking subjects that are expected to be enrolled. Determinations will be made regarding the need for translation of study instruments and consent documents, in accordance with federal regulations and the CU IRB policy, “Enrollment of Non-English Speaking Subjects” (Working Practice 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.

9. Review of Research involving International Sites

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. Physical, social and psychological risks may vary from those in the immediate New York City communities. Assessing the risks and benefits of research conducted internationally may raise challenges if there is not adequate knowledge of the local setting. 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 International Conference on Harmonization (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, “IRB Review of Research” 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 underdeveloped countries. If the research is greater than minimal risk, then the research should be designed to provide potential benefit to the subjects and/or to the local community. If a research study is not designed accordingly, the investigator should provide satisfactory justification as to why the study is proposed to be conducted in the given setting(s).

b. In an effort to gain knowledge of the local setting, the IRB should consider the most appropriate means of obtaining this information. The type of research, level of risk, study population, location of the research and whether collaborative efforts are involved are all factors that will affect the means of obtaining the knowledge of the local setting.

For all international research studies, researchers should provide details of the local context within the protocol to provide a basis for the IRB review.

The IRB may obtain local knowledge from literature, documentation, or available written information, or by inclusion of a consultant knowledgeable of the local setting, in accordance with OHRP guidance (IRB Knowledge of Local Research Setting, August 1998). For review of minimal risk studies, this level of knowledge may be adequate.

For 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 local setting. One source of potential international ethical review committees or IRBs is provided in the list of IRBs registered with ORHP at: http://ohrp.cit.nih.gov/search/asearch.asp#IORG.
IRBs should recognize that international ethical review committees may not be willing to review research conducted by investigators outside their institution. Access to local ethical review committees may be facilitated when CU researchers collaborate with researchers at the local institution.

The local ethical review committee or IRB should comply with the IRB composition requirements of 45 CFR 46.107 or 21 CFR 56.107, as applicable. In order to increase efficiency, review and approval by the local ethics committee or IRB should usually be obtained after review by the CU IRB or designated IRB on the FWA.

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 CU IRB review.

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.

If the legal age of an adult differs in another country from NY State Law (e.g., 18 years of age), the IRB should accept the local age of majority when considering who may provide their own consent.

d. When consent and recruitment documents have already been translated into a language other than English, the researcher should provide a copy of the document in English, a copy in the language to be used in the foreign location, and certification from an appropriate individual that the translated version of the document is complete and does not contain information that is not presented within the context of the approved English version of the document.

When the CU IRB-approved informed consent document 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.

e. When the research will be conducted in an institution or organization, 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 stationary and carry an original signature.

f. The research study should provide a plan for oversight of the research that will be conducted in an international setting, particularly when the CU research staff will not be present at the foreign site.
g. The research study should also provide a plan for data collection, protecting the confidentiality of the data, and transport of the data back to CU, or elsewhere in the U.S. or another region.

1) If data will be collected by an individual(s) other than those on the Columbia research team, that(those) individual(s) must be identified and letters of agreement to protect confidentiality should be presented to the IRB. 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, 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 CDC website at: http://www.cdc.gov/od/ohs/biosfty/imprtper.htm.

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, then a permit is not required for importation.

The IRB recognizes that there are instances for which parts of the guidance cited above would be inappropriate, such as with ethnographic research, 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 Research in Emergency Care Settings

Emergency research refers to the study of acute, life threatening clinical situations. Often, informed consent from the subjects is not feasible because the subject lacks the capacity to provide their own consent (e.g., unconscious) and/or there is insufficient time because treatment must be promptly administered. The conduct of planned research in life-threatening emergent situations requires special consideration by the IRB, including consideration of whether consent
may be waived. The specific conditions under which prospective consent of the subject may be waived 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 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 FDA if the research involves an investigational or FDA-approved product. 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 plan must be submitted to the FDA under an emergency IND/IDE by the sponsor or PI responsible for the IND/IDE. The community consultation and the public disclosures, however, generally do not have to be completed prior to submission for FDA approval.

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

a. Emergency Research Consent Waiver

The Boards may waive the requirement for informed consent for research involving emergency medical situations if it finds and documents that the requirements of 21 CFR 50.24 are met.

In order to approve an emergency research consent waiver, the Boards shall find and document that:

1) The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

2) Obtaining informed consent is not feasible because:

   a) Subjects will not be able to give informed consent because of their medical condition;
b) The intervention under investigation must be administered before consent from the subject’s legally authorized representative is feasible; and

c) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

3) Participation in the research holds out the prospect of direct benefit to the subjects because:

a) Subjects are facing a life-threatening situation that necessitates intervention;

b) Appropriate animal and other pre-clinical studies have been conducted, and the information derived from those studies and related evidence supports the potential for the intervention to provide a direct benefit to the individual subjects; and

c) Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

4) The clinical investigation could not practicably be carried out without the waiver.

5) The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative for consent within that window rather than proceeding without consent. The investigator will summarize the efforts made to contact legally authorized representatives and make this information available to the Board at the time of continuing review.

6) The Board has reviewed and approved informed consent procedures and a consent document consistent with 45 CFR 46.116 and 21 CFR 50.25. These procedures and the consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The Board has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject’s participation in the clinical investigation consistent with paragraph 7(e) of this section.

7) Additional protections 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 legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window, a family member of the subject who is not a legally authorized representative, and asking whether he or she objects to the subject’s participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the Boards at the time of continuing review.

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 legally authorized representative of the subject, or if such a representative is not reasonably available, a family member:

1) of the subject’s inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document;

2) that he or she may discontinue the subject’s participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

If a legally authorized representative or family member is informed about the clinical investigation, and the subject’s condition improves, the subject is also to be informed as soon as feasible.

If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative 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.

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 Investigational New Drug Exemption (IND) or Investigational Device Exemption (IDE) will be obtained by the sponsor or the investigator, even for marketed products.
The Board will promptly notify in writing the investigator and sponsor when it determines that it cannot approve an emergency consent exception study. The notice shall include the reasons for the disapproval.

The Board may require additional protections for subjects in an emergency research consent waiver study as appropriate.

11. Review of Research that involves Stem Cells

Research that involves stem cells must be reviewed by the University Stem Cell Committee prior to review by the IRB. In cases where the Stem Cell Committee determines that the research does not meet the criteria in 45 CFR 46 to be considered “human subjects research”, additional review by the IRB is not required. Review by the IRB of research that involves stem cells will be conducted in accordance with the IRB Review Criteria described in 45 CFR 46 and additional criteria identified in Section VI.B., “IRB Criteria for Review”, items 8 through 10, of these written procedures.

E. Review of Specific Types of Documents

1. Review of Recruitment Material

Any item which is intended to be used to encourage a potential subject to consider volunteering for a research study must be reviewed and approved by the IRB before being used. The FDA Guidelines indicate that advertising is considered to be an extension of the informed consent process, and thus subject to Board review. Refer to the FDA Information Sheet, “Recruiting Study Subjects”, for additional information.

The IRB defines as advertising 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.)

Advertising materials for new protocols that are submitted with the study materials will generally be included in the initial full Board or expedited review.
Advertising material submitted after initial approval of research will generally be reviewed by expedited review. The Board member who is conducting the expedited review can approve the material, require modifications before approval, or refer the proposed materials to full Board for consideration.

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.

The manual approval stamp will indicate the IRB number, the date of approval and expiration, and the initials of the person stamping the document.

Board review of advertising that will be presented as audio or video advertising will involve both scripts and copies of the tape prepared according to the script. Actual tapes 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.

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 ensure that all funded procedures are included in the research protocol.

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 Investigator Brochure

The Investigator Brochure 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 Brochure will occur during both initial and continuing reviews, and when a modification includes revision of the document. (Working Practice Document #8)
VII. IRB Convened Board Meetings: Organization and Management

A. Schedule of Meetings

Regularly scheduled meetings of each Board are held, with additional meetings scheduled as necessary. The schedule of meetings is available on Columbia’s IRB website.

B. Packet Preparation

Members of the Board to which a protocol is assigned have electronic access to all submitted materials for any given event via RASCAL. As necessary and/or requested, Board members are provided with hard copy of specific materials, determined by type of event, as described below.

IRB staff prepare packets of the material that will be reviewed at convened meetings for distribution to scheduled Board Members and Alternates approximately one (1) week before the meeting. Details of the packet preparation process are included in Working Practice Document #21.

Each packet includes a copy of the preliminary agenda, administrative notes and copies of the previous meeting’s minutes, if the Board has elected to review minutes in paper rather than online in RASCAL. If changes have been made after the Board packets have been distributed, members receive a copy of the final agenda when they arrive for the meeting.

1. Initial Review

a. Every packet at a minimum includes a copy of the protocol Data Sheet, Study Description Data Sheet, and proposed informed consent documents, for each new review request. Copies of advertising and recruitment materials submitted with the initial review request are also included in the packet.

b. The Board members also receive copies of correspondence between the Investigator and the IRB related to the protocols under review.

c. The assigned primary reviewer(s) for each new review item and the Chair also receive the Investigator Brochure (or other relevant background information on the investigational article), sponsored project proposal (e.g., grant application and/or sponsor’s protocol), research measures, and other supporting documentation, as appropriate.

2. Continuing Review

a. Every packet at a minimum includes a copy of the Data Sheet, Study Description Data Sheet, informed consent documents, and Renewal Information form.
3. **Modification**
   
a. Every packet at a minimum includes the Data Sheet (which includes the modification summary), Study Description Data Sheet, and informed consent documents, if they have been modified since the previous submissions.

b. The assigned primary reviewer(s) for each modification and the Chair also receive a copy of all new supporting documentation submitted with the modification request. These may include, but are not limited to, modified research measures, adverse event reports, revisions to the investigator’s brochure, new funding proposals, and reports from data and safety monitoring units.

4. **Adverse Event Report**
   
a. Every packet at a minimum includes the Report of the Adverse Event and supporting documentation attached by the researcher.

b. The assigned primary reviewer(s) for the event and the Chair also receive a copy of the Data Sheet, and current Informed Consent Forms.

C. **Primary Reviewer Assignments**

Events that require review by the convened IRB or are eligible for expedited review will be assigned to a primary reviewer. The Chair may elect to serve as the primary reviewer or designate this responsibility to another qualified Board member.

Details of the primary reviewer process may be found in the Process section (Section V.F.) of these written procedures.

D. **Voting Requirements**

No official action may be taken at a convened meeting unless a quorum is present either in person or via teleconference, and at least one non-scientist is present. Quorum is defined as more than one half of all voting members listed on the IRB roster. The IRB will ensure and document that a quorum is present for review of each event that requires full Board review.
A motion that is seconded, then carried or denied by a majority of the voting members present is required for acting on approvals, deferrals to Chair (referred to as “pending” in RASCAL), deferrals to Board (referred to as “returned” in RASCAL), suspension, and acknowledgement (where applicable). The Board does not have to vote to defer a protocol 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.

No member who has a conflict of interest with respect to the research under consideration may vote on any action related to that research project. The member will also not count towards the quorum for that study. When necessary to ensure adequate expertise and/or understanding of the research question, a member with a conflict of interest, such as a member who is a PI or holds other status on a research project, may present the study to the Board and answer the Board’s questions prior to recusing him/herself and leaving the meeting room for the rest of the discussion and vote for that study.

E. Minutes

1. Recording of Minutes at the Convened Meeting

The minutes for a convened Board meeting must contain sufficient information to comply with regulatory requirements and to serve as the documentation of attendance and actions taken at the meeting.

Assigned IRB staff will be responsible for preparation of the minutes, and will follow the standard Board guidelines, described in Working Practice Document #100. The minutes will, at a minimum, clearly show the following:

a. Date and time of the meeting;
b. Identification of the individual who served as Chair, attendance and voting status of members/alternate members (and for whom each alternate served), attendance of staff and guests, and for guests, the purpose of their attendance;
c. Any changes in attendance (people called away, coming in late, etc.) and voting status;
d. Agenda categories brought before the Board, and clear identification of each item and/or investigator the Board considers;
e. For each item reviewed:
   1) Title and PI;
   2) Name of primary reviewer(s);
   3) A summary of discussion of controverted issues, with resolution;
   4) The basis for requiring changes in or disapproving research;
   5) Any additional conditions required by the Board that may be satisfied after approval of the project but must be adequately addressed before approval of the withheld item is
provided, (i.e., receipt of approved Certificate of Confidentiality before a consent form may be released, or completion of educational requirements before an individual may participate in the research);

6) A clear indication of the Board action taken for each item with a statement of the vote, the number voting for, against, and abstaining, total number voting, and identification of the members who abstained;

7) Determination of risk level for new protocols, and those events for which the risk level has changed since the last review.

f. For items that are returning to the Board after having been deferred back to the Board, a statement of the area(s) that required significant revision and/or the area(s) of primary concern;

g. For research involving minors, the applicable category of research per HHS and FDA regulations, as applicable, the basis for the determination, requirements for parental permission and assent, requirements for documentation of assent, determination of number of parents who must provide permission for Section 406 and 407 research, 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;

l. For emergency research when informed consent will not be obtained, reference to 21 CFR 50.24 (exception to informed consent requirement), basis for determination that the requirements of 21 CFR 50.24(a)(1-7) are satisfied, and summary of the IRB review of plans for community consultation per 21 CFR 50.24(b);

m. Summary of discussion of noncompliance incidents and other new or old business items.
2. Board Approval of Minutes

Minutes that have been approved by the Chair are distributed to Board members in their meeting packets, or members are notified by email that the minutes have been approved, with instructions for reviewing the minutes in RASCAL and/or an attached copy of the minutes. Minutes are ratified, or revisions requested, as applicable, by the full Board at a subsequent meeting of the Board.

3. Notification of Board Action

The Board notifies the investigator and IOs (and the sponsor, when appropriate) in writing of its actions in approving, disapproving or requiring changes to (in order to approve) the research.

Investigators are notified electronically via RASCAL correspondence. Hard copy letters of approval (Working Practice Document #93) and disapproval (Working Practice Document #96) letters are also generated and forwarded to investigators. Hard copy letters may be signed by a Team Manager, AD, or EDHRPP.

A disapproval notice shall include the basis for the disapproval and provide an opportunity for the investigator to respond to the Board in person or in writing regarding its action.

A summary of the number of items reviewed, compliance matters, and controverted issues is included in the cover memo (Working Practice Document #104) that accompanies the minutes when forwarded to the IOs.

4. Appeal of IRB Decision

If the Board decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person and in writing.

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 file may serve as retention of records as a back-up or for some records that were not uploaded in the RASCAL system).

Documentation of the following IRB activities is maintained:

1. Copies of all research proposals reviewed;
2. Scientific evaluations, if any, which accompany the proposals;
3. Approved consent documents;
4. Statements of significant new findings provided to subjects as required by 45 CFR 116(b)(5), 21 CFR 50.25(b)(5);
5. Copies of all modifications or amendments to protocols;
6. Reports of adverse events;
7. Records of continuing review activities;
8. Progress reports submitted by research investigators;
9. Minutes of IRB meetings (see Section VI: Meeting Preparation and Follow Up);
10. Documentation of IRB review (e.g., Notes, correspondence, IRB reviewer form);
11. Copies of all correspondence between the IRB and the research investigators;
12. List of Board members and their alternates identified by:
   a. Name;
   b. Earned degrees;
   c. Representative capacity;
   d. Indications of experiences such as board certifications, licenses, etc.;
   e. Information sufficient to describe each member’s chief anticipated contributions to the IRB deliberations;
   f. Any employment or other relationship between the member and the institution;
10. Copies of Board member curriculum vitae, appointment letters, and other relevant correspondence involving member service;
11. Emergency use reports.
B. IRB Files

Each protocol is assigned a unique number and is maintained in an individual file in RASCAL. Records of protocols may also exist in paper form in file cabinets located in the IRB office area. Any original IRB record shall not be removed from the IRB office without the written approval of the EDHRPP or AD.

C. Record Retention Term

Records relating to a specific research activity are maintained for at least 3 years after completion of the research (45 CFR 46.115(b); 21 CFR 56.115(b)).

D. Confidentiality of Records

IRB records, including records relating to specific research protocols, are kept private to the extent possible and allowed by law. However, authorized representatives of sponsors, federal regulatory agencies, University officials, IRB staff, and IRB Board members may review, inspect, and/or copy records.

E. Inspection of Records

IRB records are accessible for inspection and copying by authorized representatives of the Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), and other agencies, when appropriate jurisdiction exists, at reasonable times and in a reasonable manner (45 CFR 46.115(b); 21 CFR 56.115(c)). Requests for photocopying and release of any IRB records must be received in writing and approved by the EDHRPP or AD.

F. Off-site Storage of IRB Files

Study files may be stored offsite if they meet the following qualifications:

- The study has been terminated and no submissions for the file are pending a review; or
- The study was disapproved; or
- The study was never approved due to failure to respond satisfactorily to IRB requests.

Offsite 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.

Shipment or retrieval of any item to or from off-site storage may occur only after approval is provided by the EDHRPP or AD.
IX. Oversight Monitoring

The Columbia HRPP assures oversight monitoring of human subjects research by various means, such as: 1) continuing review of the research by the IRB and brief inquiries with investigators or research records following concerns raised by IRB review; 2) IRB review of adverse events; 3) data and safety monitoring by either an internal or external committees; 4) compliance oversight initiatives including for-cause and not-for-cause investigations; 5) additional reviews, investigations or monitoring by the Research Pharmacy, Radiation Safety Office (RSO) or Institutional Biosafety Committee (IBC); and 6) additional reviews conducted by either the Clinical Trials Office (CTO) or Research Administration (RA). Furthermore, Quality Improvement efforts provided by the IRB office, as described in Section XI, serve as additional mechanism to provide oversight monitoring of human subjects research.

A. Continuing Review

As described in Section VI.C.6, continuing review serves a key role in oversight monitoring of all human subjects research that is not exempt. By reviewing the progress of the study during the past approval period, the IRB receives information and insights to the risks associated with the study and the quality of study management. Through these insights the IRB is often able to make determinations that additional oversight monitoring may be necessary and in such cases, may refer a given study to the Compliance Oversight Team for further investigation or audit.

B. Review of Adverse Events

The review of adverse events provides an important role in the oversight of human subjects in research. The process for IRB review of adverse events is described in sections VI.A.4 and VI.C.2. IRB review of adverse events depends on the severity, relationship to the test article and whether the event occurred under the auspices of Columbia or at another site that relies on another IRB for review of the event(s). Depending on these criteria, the CU IRBs review the events either promptly or at 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 VI.B.6. During the course of the study, the IRB will review and/or solicit information from the applicable data and safety monitoring board or committee to address any relevant IRB concerns. The IRB will also rely on the data and safety monitoring boards and/or the sponsor to provide assessments of the adverse events or unanticipated problems involving risks to subjects that may occur during the study.
D. Reviews or Monitoring by the Research Pharmacy, Radiation Safety, or Institutional Biosafety Committee

For oversight of human subjects research providing specific risks from radiation, hazardous materials (including research with human organs, tissues, or fluids), the IRB may also rely on additional oversight provided by the Joint Radiation Safety Committee, the Radioactive Drug Research Committee, Radiation Safety Office (which provide administrative support to both committees) or the Institutional Biosafety Committee. 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 compliance oversight or oversight monitoring by these other groups either in lieu of, or as an adjunct to the oversight monitoring provided by the IRB.

E. Reviews by Clinical Trials Office or Research Administration

The Clinical Trials Office, Research Administration (at CUMC) and Office of Sponsored Programs (at CU-MH) each provide additional oversight of human subjects research during their routine review of contracts or grants. Each of these offices will communicate with the IRB office to resolve issues regarding IRB review of human subjects research. Issues commonly addressed range from assuring IRB review of grants as appropriate, review of subcontracts by the appropriately designated IRB, resolution of conflicts of interest issues, payment for research related injuries, and miscellaneous issues that could be identified during their routine review of contracts or grants.

F. Compliance Oversight

Compliance oversight procedures cover two types of Noncompliance: Research Noncompliance and IRB Noncompliance. “Research Noncompliance” means Noncompliance by anyone other than the EDHRPP or any member of the IRB staff or the IRB (in his/her capacity as such). “IRB Noncompliance” means Noncompliance by the EDHRPP of the IRB or any member of the IRB staff or the IRB (in his/her capacity as such).

For purposes of IRB policy, “Noncompliance” means a failure to comply with University policy or applicable federal and state laws, regulations and policies governing the protection of human subjects in research.

A response to an allegation of Noncompliance consists of three phases, each of which is explained in more detail in the CU “Noncompliance with Human Subject Regulations” policy (Working Practice Document #89):

**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 should be brief and not involve a substantive analysis of any information, but should determine whether the PI is actually conducting, or has conducted, the study,
whether the information presented in the allegation appears to be potentially relevant, affiliation of the source of the allegation with the University, and whether any documents should be sequestered;

**Investigation**: following an Inquiry, the further investigation of facts with respect to whether Noncompliance has occurred (an “Investigation”); and

**Outcome**: following an Investigation, the determination as to whether Noncompliance has occurred and what corrective actions, if any, are required (an “Outcome”).

Related concepts of appeal, reconsideration, and notification to regulatory agencies are also addressed in the CU “Noncompliance with Human Subject Regulations” policy (Working Practice Document #89), as are guidelines for safeguards for the complainant and respondent, and measures to ensure confidentiality, preserve evidence, and sequester documents.
X. **Education & Training**

A. **Research Community**

The CU IRB considers ongoing education of IRB staff, Board members, and investigators to be of utmost importance towards effective protection of human subjects research conducted under the auspices of the institution.

The following media are used to keep the entire research community at Columbia up to date on matters related to human subjects research:

1. Web site;
2. Email listserv;
3. Group meetings with research personnel and other individuals involved in the Human Research Protection Program.

To the extent possible, documentation of educational activities supported by the IRB and/or attended by staff and IRB members will be maintained. See Working Practice Document #105 for a list of educational events.

To facilitate communication between the IRB administrative office and the research community, the IRB maintains an email account for receipt of inquiries related to the protection of human subjects. The account is monitored, and responses are generated, by IRB staff. Analysis of the inquiries that are received may identify areas in which additional education is necessary.

B. **Board Members & 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, and IRB policy.

The following material is distributed or made available to all newly appointed Board Members:

1. Columbia University IRB Policies and Procedures;
2. OHRP IRB Guidebook;
3. “Protecting Study Volunteers in Research” (Dunn & Chadwick).

All Board Members and Chairs are required to have the following certifications:

1. Appropriate Columbia University Good Clinical Practices course;
2. Columbia University HIPAA course;
3. OHRP Assurance Training module.

Hard copy documentation of the above and any other relevant certifications is maintained by the IRB staff.

All members are exposed to ongoing educational opportunities such as regional or local IRB conferences and CU IRB sponsored events. An educational retreat is held periodically for all Board Members and staff. Continuing education information is distributed to the Board members on an ongoing basis, and is posted on the IRB web site for future reference.

All Board members and Chairs will have access to publications related to the protection of human subjects in research, such as:

1. Newsletters;
2. Relevant articles;
3. Literature.

C. Administrative Staff

The IRB administrative office holds regular education sessions for IRB staff. These sessions address all facets of human subjects protections.

The following material is distributed or made available to all IRB Staff:

1. Copy of the Columbia University IRB Policies and Procedures;
2. OHRP IRB Guidebook;
3. “Protecting Study Volunteers in Research” (Dunn & Chadwick).

All IRB Staff are required to have the following certifications:

1. Columbia University Good Clinical Practices course;
2. Columbia University HIPAA course.

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

1. Attending local and national IRB conferences;
2. Access to the CITI online training program;
3. Access to publications related to the protection of human subjects in research, such as:
   a. Newsletters;
   b. Relevant articles;
   c. Literature.

All eligible staff are encouraged to pursue the Certified IRB Professional (CIP) status, which is obtained through successful completion of a comprehensive exam administered by the Council for Certification of IRB Professionals (CCIP). Details regarding eligibility, the content of the exam, and registration may be obtained from the CCIP website: <http://www.ptcny.com/clients/CCIP>.

D. Researchers

All key personnel involved in human subjects research are required to have the following training:

1. Appropriate Columbia University Good Clinical Practices certification:
   a. Protection of Human Research Participants for Patient-oriented Clinical Research (CUMC);
   b. Protection of Human Research Participants for Epidemiology and Social and Behavioral Sciences (CUMC);
   c. Protection of Human Subjects (CU-MS);

2. Columbia University HIPAA certification;

3. If children will be involved as subjects, the CITI Biomedical Research with Children online module.

The IRB administrative office holds regular educational sessions for all researchers. Educational opportunities are also available through departmental and divisional meetings.

Investigators are apprised of new or revised policies, procedures, and regulations by email notification via the IRB listserv and posting on the IRB website.

Explanation for required changes in correspondence transmitted when submitted materials are returned to the investigators provides another avenue for education on a protocol-specific basis.
XI. Quality Improvement Program

The CU IRB is committed to the improvement of the quality, performance and efficiency of its reviews and internal processes, and those of University research teams in regards to the conduct of research with human subjects. Towards these ends, the CU IRB Quality Improvement Program (QIP) is charged with the responsibility of conducting quality assurance, quality improvement, and continuous quality improvement to ensure excellence.

The focus of the QIP is on providing optimal customer\(^1\) service by enhancing the ethical conduct of research while also meeting and exceeding the needs of our research community. The CU IRB QIP is administered by the IRB Central Review Team (CRT), which is responsible for collecting and processing data that enables the IRB office to quantify and assess performance and efficiency of the IRB and University researchers.

A. QIP for Internal Assessment and Improvement

The CRT prepare and forward reports to the Quality Improvement Committee (QIC) for review. The QIC is composed of members of the CRT, the Team Manager or designee of each IRB, the AD, and the EDHRPP.

The QIC is responsible for the assessment of data and other information that is collected on the quality and performance of the overall IRB operation. Assessments and recommendations made by the QIC for specific reviews or events are forwarded to the relevant individuals, e.g., IRB Team Manager, Chair, staff. More general recommendations and comprehensive reports made by the QIC are forwarded to the EDHRPP, the AD, IRB Team Managers, IRB Chairs, and, 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.

1. Strategies to Improve Quality

Information related to individual reviews or actions that were not conducted in accordance with institutional or IRB policies and procedures or applicable Federal Regulations are collected on the Event Reporting Form (ERF) (Working Document #106). Less-than-optimal handling of any action or process is reported on the ERF by IRB staff, members, or Chairs, and is submitted to the CRT for tracking and monitoring.

The information collected on the form is entered into a database and stratified based on submission type (e.g., new study, modification, continuing review, adverse event, protocol deviation, IRB minutes), level of review (e.g., full board, expedited, exempt), and whether the

\(^1\) Customer is defined as Principal Investigators, research staff, human subjects, or any individual or entity of the Columbia Human Research Protection Program (HRPP).
event involved internal (i.e., IRB staff, members, Chairs) and/or external (i.e., researchers other University employees) individuals.

The CRT prepares the ERFs and aggregate data reports for review by the QIC, which will meet at least monthly. Recommendations for corrective actions, improvement in processes, or educational training initiatives will be provided by the QIC to the Executive and ADs of the IRB, and when appropriate, to the IRB Executive Committee.

2. Strategies to Improve Performance and Efficiency

Reports that measure many functions performed by the IRB staff and members are generated for the purposes of assessing and managing such processes. The CRT prepares and distributes regular reports to the IRB Chairs, Team Managers, EDHRPP and/or AD for such purposes. The weekly reports include the following:

a. Pre-Review Tracking report: Measures the number and timeliness of pre-reviews of new protocol submissions by the IRB professional staff (distributed to EDHRPP and AD only).

b. Administrative C Queue report: Measures the number and timeliness of responses from individual IRB reviews to the researchers in the RASCAL system (distributed to IRB Chairs, Team Managers, EDHRPP and AD).

c. Resubmission Review by Team report: Measures the number and timeliness of reviews of the responses from researchers to previous IRB correspondence or action (distributed to IRB Chairs, Team Managers, EDHRPP and AD).

d. 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 (distributed to IRB Chairs, Team Managers, EDHRPP and AD).

Monthly and quarterly reports of pre-reviews of new protocols, approval of IRB meeting minutes, and IRB turnaround time are also provided.

B. QIP for External Assessment and Improvement

Researchers and research subjects will be surveyed to determine levels of satisfaction and to identify areas in need of improvement.

Informed consent processes will be randomly monitored. Adverse event reporting will be monitored for timeliness of adverse event reporting and compliance to the Columbia Adverse Event Reporting policy.
When appropriate, quality action teams, comprised of PI(s), research staff, members of the IRB staff (e.g., clerks, administrative aides, team manager), IRB Chair(s), IRB members, and a member of the RASCAL Information Technology team will be formed to brainstorm solutions to problems and implement planned improvements.

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 subject rights, and issues that an individual should consider prior to enrolling in a research study, are posted on the IRB website:
<http://www.cumc.columbia.edu/dept/irb/>

B. Subject Advocacy Program

A program to assess the experiences of subjects who participate in research conducted by University personnel is currently under development. Proposed modules for an online program would collect data from subjects on:

♦ The informed consent process;
♦ Medical care that was received;
♦ Interactions with medical personnel;
♦ Interactions with support staff;
♦ Logistics of visiting CUMC;
♦ Communication about the progress of the study;
♦ Contact with the IRB office.

Feedback would then be provided to the various entities in the Human Research Protection Program, to enable each unit to improve their procedures as necessary to encourage further participation.
Appendices

Appendix I  The Belmont Report; Ethical Principles and Guidelines for the Protection of Human Subjects of Research

Appendix II  Department of Health and Human Services (HHS) Regulations for the Protection of Human Subjects

Appendix III  United States Food and Drug Administration (FDA) regulations for the Protection of Human Subjects

Appendix IV  Department of Education FERPA (Family Educational Rights and Privacy Act) regulations

Appendix V  New York State Laws 2440/441

Appendix VI  New York State Law Article 7, Section 79-1 Confidentiality of Genetic Tests

Appendix VII  AAHRPP Accreditation Standards

Appendix VIII  International Conference on Harmonization (ICH) “Guidance for Industry-E6 Good Clinical Practice: Consolidated Guideline”

Appendix IX  HHS/FDA List of Expedited Review categories
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Email from GG, “Addition of new expedited review category in RASCAL”
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### Glossary of Abbreviations and Terms

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<td>AAHRPP</td>
<td>Association for the Accreditation of Human Research Protection Programs</td>
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<tr>
<td>AD</td>
<td>Associate Director, IRB</td>
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<tr>
<td>AE</td>
<td>Adverse event</td>
</tr>
<tr>
<td>BB-IND</td>
<td>Investigational New Drug Exemption for biologic</td>
</tr>
<tr>
<td>CIP</td>
<td>Certified IRB Professional</td>
</tr>
<tr>
<td>CFR</td>
<td>Code of Federal Regulations</td>
</tr>
<tr>
<td>COI</td>
<td>Conflict of Interest</td>
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<tr>
<td>Columbia</td>
<td>Columbia University</td>
</tr>
<tr>
<td>CU</td>
<td>Columbia University</td>
</tr>
<tr>
<td>CUMC</td>
<td>Columbia University Medical Center</td>
</tr>
<tr>
<td>CU-MS</td>
<td>Columbia University – Morningside campus</td>
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<tr>
<td>DCA</td>
<td>Dean for Clinical Affairs</td>
</tr>
<tr>
<td>HHS</td>
<td>United States HHS</td>
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<tr>
<td>DNA</td>
<td>Deoxyribonucleic Acid</td>
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<tr>
<td>EDHRPP</td>
<td>EDHRPP, Human Research Protection Program</td>
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<td>EU</td>
<td>Emergency Use</td>
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<td>Events *</td>
<td>RASCAL term for submissions to the IRB for review (e.g., new protocol, modification, renewal)</td>
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<tr>
<td>EVPR</td>
<td>Executive Vice President for Research at Columbia University</td>
</tr>
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<td>Executive Committee *</td>
<td>Committee comprised of IRB Chairs, ED, AD, and VPRO at Columbia University</td>
</tr>
<tr>
<td>FDA</td>
<td>United States Food and Drug Administration</td>
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<tr>
<td>FWA</td>
<td>Federalwide Assurance</td>
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<tr>
<td>GCP</td>
<td>Good Clinical Practice</td>
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<td>HCP</td>
<td>Health Care Proxy</td>
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<td>HDE</td>
<td>Humanitarian Device Exemption</td>
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<td>HHS</td>
<td>Federal Department of Health and Human Services</td>
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<td>HIPAA</td>
<td>Health Information Portability and Accountability Act</td>
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<td>HRPP</td>
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<td>Institutional Biosafety Committee</td>
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<td>ICH</td>
<td>International Council for Harmonization</td>
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<td>IDE</td>
<td>Investigational Device Exemption</td>
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<td>IND</td>
<td>Investigational New Drug</td>
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<td>Institutional Review Board</td>
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<td>Information Technology</td>
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<td>JRSC</td>
<td>Joint Radiation Safety Committee at Columbia University</td>
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<tr>
<td>LAR</td>
<td>Legally Authorized Representative</td>
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<tr>
<td>Acronym</td>
<td>Definition</td>
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<td>LOA</td>
<td>Letter of Approval</td>
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<tr>
<td>LOD</td>
<td>Letter of Disapproval</td>
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<td>National Institutes of Health</td>
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<td>Nonsignificant Risk designation for medical device</td>
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<td>NY</td>
<td>New York</td>
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<td>NYPH</td>
<td>New York Presbyterian Hospital</td>
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<td>OGC</td>
<td>Office for General Counsel at Columbia University</td>
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<td>OHRP</td>
<td>United States Office for Human Research Protection</td>
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<tr>
<td>PI</td>
<td>Principal Investigator</td>
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<tr>
<td>PRMC</td>
<td>Protocol Review and Monitoring Committee at the Herbert Irving Comprehensive Cancer Center at Columbia University</td>
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<tr>
<td>QIP</td>
<td>Quality Improvement Program</td>
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<td>RAC</td>
<td>Recombinant DNA Advisory Committee at NIH</td>
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<td>RASCAL</td>
<td>Electronic protocol submission and tracking system at Columbia University</td>
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<tr>
<td>RDRC</td>
<td>Radioactive Drug Research Committee at Columbia University</td>
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<tr>
<td>SR</td>
<td>Significant Risk designation for medical device</td>
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