

Columbia University
Human Research Protection Program
Executive Summary
December 23, 2008

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 Federalwide 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 (ED), who is also responsible for the management of all Institutional Review Boards (IRBs) at CU. This Executive Summary outlines and summarizes 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. Subjects may include healthy volunteers, as well as patients, and other individuals who may be considered vulnerable due to medical, cognitive, emotional, economical, educational, age, or other factors. Although much of the research is conducted in the New York City area and on Columbia campuses, faculty members also actively conduct research at other sites both domestic and international. Furthermore, many Columbia faculty members collaborate on projects with investigators at other institutions. The Columbia HRPP accounts for approximately 1,400 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, and NYPH. The EVPR is responsible for central oversight of the entire Columbia HRPP and also serves as the Institutional Official on the FWA for CU-MH. Each Institutional Official 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 Institutional Official(s) of CUMC and NYPH, the Vice President of Research Operations (VPRO), and the ED 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 other Institutional Officials of CU-MH, 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 Institutional Officials, 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 bi-weekly 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 of the IRB (AD), and the ED. 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) Educational 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.

A. Institutional Review Boards

There are four IRBs 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-MS. Additional IRBs may be added as necessary to ensure adequate and timely review of research proposals submitted for consideration.

All CU 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 regulations, 45 CFR Part 46, Subparts A (Common Rule), B, C, and D; 2) the U.S. Food and Drug Administration (FDA) Regulations, 21 CFR Parts 50, 56, 312, 600, and 812; 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 CU IRBs are charged with the responsibility of providing review, approval, and oversight monitoring to ensure that all human research under the auspices of the Columbia HRPP is conducted: 1) ethically; 2) in a manner that protects human subjects, and 3) in accordance with the above mentioned regulations, laws, policies, and standards.

The mission of the CU IRB is to enhance and facilitate the ethical conduct of human subjects research conducted by Columbia, and by Columbia faculty, regardless of location. The CU IRB will perform this mission through its review of human subjects research, its educational and training initiatives, and its compliance oversight and quality improvement programs.

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, who have the authority to restrict research that cannot be supported by resources, principles, or policies of the respective institutions, regardless of whether it has been approved by one of the CU IRBs.

The IRBs act independently and consider research proposals from the perspective of protection of the subjects who may be involved. While approval from other CU offices or committees may be necessary per institutional policy, the decision of whether to approve or disapprove a submission is made autonomously and is not influenced by potential funding, prestige, or other benefit that may accrue to the University.

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 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), CU-MS, and the Biomedical Research Alliance of New York to rely on reviews by their IRBs for certain types of research projects. Details regarding each agreement are provided in the IRB Policies and Procedures. The CU IRB 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.

The decision to enter into an agreement with another institution for reliance of both institutions on one of the IRBs is made after: a) evaluation of the non-CU institution's IRB policies and procedures (when CU will delegate review); b) consideration of whether regulatory compliance and CU standards may be upheld through the relationship; c) analysis of whether an efficient process may be implemented to conduct the reviews; d) discussions between IRB administrators from each institution; and e) consultation with the CU Office of the General Counsel.

C. IRB Staff Teams

Each IRB is administered by a team of staff composed of an IRB 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 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 for

the given study for the most recent IRB approval period to ensure that all prior actions were appropriately handled and that any outstanding items will be addressed at the upcoming IRB review. If there has been a lapse in IRB approval or an indication that the study is not proceeding as planned, the review may cover a longer period. 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 involving risks to subjects or others that are submitted to the CUMC IRBs. The pre-review ensures that these reports meet the Reporting to the IRB of Unanticipated Problems Involving Risks policy and cases are identified that require immediate attention. For such reports that satisfy Columbia's reporting policy, the CR staff conducts the preliminary review to determine if the informed consent document needs 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.

CU-MS IRB staff conduct the pre-reviews for renewals, modifications, and reports of unanticipated problems submitted for protocols reviewed by the CU-MS IRB.

E. Compliance Oversight Team

The Compliance Oversight Team (COT) is responsible for investigating and handling all allegations of noncompliance and complaints with respect to the protection of human subjects in research. Allegations of noncompliance may be received from IRBs, faculty, research staff, Institutional Officials, departmental administrators, research subjects, federal and state regulatory agencies, the media, or the general public. All allegations of noncompliance are logged into a tracking system by the COT, which promptly notifies the ED 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 Institutional Official(s), the EVPR, the respective IRB, and when appropriate, with the appropriate regulatory agency.

F. 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 include both mandatory and voluntary initiatives.

G. 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 the one of 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.

H. Accreditation Committee

The Accreditation Committee was established in 2004 within the IRB Office and is charged with the 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.

I. 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 the 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. CU Office of Sponsored Programs Administration (SPA)

The Office of Sponsored Programs Administration (SPA) is responsible for the administration of all sponsored research conducted by Columbia. The Office works closely with the IRB staff to ensure that all human subjects research has obtained appropriate IRB approval. Any potential noncompliance with the regulations for human subjects protection that is identified by an SPA staff member is promptly reported to the ED.

SPA also provides administrative assistance to, and works closely with, the CUMC Conflicts of Interest (COI) Committee in accordance with Columbia's COI policy. All Columbia faculty must complete a COI form when they are hired and must update this form annually. In addition, all Principal Investigators, co-Investigators, and other key personnel on human research proposals must complete a protocol-specific conflict of interest form prior to submission of a research study for IRB approval. The RASCAL system facilitates the management of conflicts of interest by identifying any positive response for conflicts in either the Columbia annual COI disclosure statement or the protocol specific COI form.

IV. Clinical Trials Office

The Clinical Trials Office (CTO) was formed by both NYPH and CUMC to negotiate and manage all contracts involving any clinical trial. The CTO fosters the ethical conduct of research by establishing important provisions and policies that are relevant for the protection of human subjects. For example, in its contract negotiations, the CTO addresses issues such as ensuring

prospective IRB review, payment for research procedures and test articles, compensation for research related injuries, and the protection of confidentiality of research data. All negotiated contracts that are ready for approval are then forwarded to SPA for signature by the appropriate officer.

The Medical Director of the CTO works closely with the IRB and serves on one of the IRBs. In this capacity, the Medical Director provides working knowledge of issues for the protection of human subjects relevant to both the IRB and the CTO. This individual also provides training for investigators both in development of research protocols for submission to the IRB, as well as in the RASCAL system.

Any potential noncompliance with the regulations for human subjects protection that is identified by a CTO staff member is promptly reported to the ED.

A. Research Pharmacy

The Research Pharmacy (RP) is responsible for the storage, handling, accounting and distribution of investigational drugs to research investigators. The RP reports to the CTO. The Director of the RP has been an active, long-term member of the IRB. One other research pharmacist also serves on the IRB and another serves as an alternate. This close working relationship between the Research Pharmacy and the IRB not only provides pharmacy input to the IRBs, but also helps ensure that the handling of investigational drugs is in compliance with federal regulations and institutional and IRB policies.

Any potential noncompliance with the regulations for human subjects protection that is identified by the Research Pharmacy is promptly reported to the ED. This includes dosing errors that may have occurred with the administration of investigational products.

B. Spanish Translation Center

The Spanish Translation Center (STC) provides translation into Spanish of research documents such as consent forms, recruitment letters, and advertisements for potential research subjects. The STC serves a vital role in Columbia's human research protection program because CUMC and NYPH are located in a community with a predominantly Hispanic population. Any document that will be translated by STC for IRB approval must first be approved in English by the IRB. Final approval by the IRB is granted after review and approval by the STC.

Any potential noncompliance with the regulations for human subjects protection that is identified by the STC is promptly reported to the ED.

V. Research Compliance and Training Office

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

The RCTO also provides several compliance oversight efforts. One such effort is to administer and manage the handling of any noncompliance involving research integrity (i.e., fabrication,

falsification, or plagiarism). Another compliance effort is to administer and manage the review of all conflicts of interests involving research conducted by Columbia.

The RCTO works closely with the Columbia IRB office to foster the ethical conduct of research at Columbia.

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

The Joint Radiation Safety Committee (JRSC) was created in 1991 by an Agreement between the College of Physicians and Surgeons of CU, NYPH, and NYSPI. The JRSC, in accordance with New York City (NYC) regulatory requirements, is responsible for oversight of the use of all sources of radiation and licensed radioactive material at these institutions. As delegated by the NYC Department of Health, the JRSC is responsible, on the basis of safety and with regard to training and experience, for approving or disapproving any individual as a Responsible Investigator or Authorized User for the use of radiation or radioactive materials in human subjects research or in diagnosis or therapy, respectively.

The Columbia Radioactive Drug Research Committee (RDRC), created in the 1950s, is delegated by the FDA to review and approve the use of radioactive drugs that are recognized as safe and effective in human subjects during the course of research projects. Such use is limited to obtaining basic information regarding human metabolism, physiology, and biochemistry.

The Radiation Safety Office (RSO) is the professional, technical and administrative arm of the JRSC. In accordance with NYC regulatory requirements, the Radiation Safety Office: assists the JRSC in the performance of its duties and briefs management regarding the radioactive materials program; establishes, implements and maintains written policies and procedures for the safe use of radioactive material; investigates overexposures, misadministrations, accidents, spills, thefts, unauthorized receipts, uses, transfers, and disposals, and other deviations from approved radiation safety practice; and implements corrective actions as necessary.

Any research proposal that involves the administration of radiation or an investigational product containing radioactivity to human subjects must be approved by either the JRSC or RDRC, as appropriate, prior to final approval by the IRB. The administration of radiation or radioactive materials to human subjects may only be performed by, or under the supervision of, a Responsible Investigator or Authorized User approved by the JRSC.

Any potential noncompliance with the regulatory requirements for the use of radiation or radioactive materials in research involving human subjects must be promptly reported to the: JRSC or RDRC, as appropriate; RSO, and ED. Likewise, any potential noncompliance with the regulations for human subjects protection that is identified by the JRSC, RDRC, or the RSO is also promptly reported to the ED.

VII. Institutional Biosafety Office

The Institutional Biosafety Committee (IBC) is responsible for the review and approval of the handling of hazardous materials in research, such as potentially infectious tissues or bodily

samples, and research involving gene transfer. The RASCAL system prompts researchers to identify potential hazardous materials during the creation of a protocol submission to the IRB and does not permit a protocol that requires IBC approval to be approved by the IRB prior to IBC approval.

Any potential noncompliance with the regulations for human subjects protection that is identified by the IBC is promptly reported to the ED.

VIII. Protocol Review and Monitoring Committee

The Protocol Review and Monitoring Committee (PRMC) serves as the scientific review committee for the Herbert Irving Comprehensive Cancer Center on the CUMC campus. Any research proposal involving cancer in any manner at CUMC requires review and approval by the PRMC prior to review by the IRB, whether or not such research is conducted within the Cancer Center. The PRMC conducts an initial review of all cancer research, review of all modifications to the research study, and an annual re-review of the research. The PRMC forwards notification of its scientific reviews to the IRB for consideration during the IRB review of cancer-related protocols.

Any potential noncompliance with the regulations for human subjects protection that is identified by the PRMC is promptly reported to the ED.

IX. Irving Institute for Clinical and Translational Research

The Columbia Irving Institute for Clinical and Translational Research has been awarded the Clinical and Translational Science Award (CTSA). This Institute formerly administered the General Clinical Research Center (GCRC), and was formerly known as the Irving Center for Clinical Research; an operation that had been in existence for over 30 years and supported approximately 150 research protocols a year involving more than 3,000 subjects.

The Irving Institute for Clinical and Translational Research currently provides resources to foster and support new, collaborative, multidisciplinary human subjects research at Columbia. Some of the resources provided include consultation for biomedical informatics, research design and biostatistics, and regulatory considerations. The Institute also administers the Clinical Research Center which allows investigators to conduct both inpatient and outpatient studies involving adults and children. All research conducted at the CRC is first reviewed by a scientific review committee called the CRC Advisory Committee. The ED serves as an ex-officio member of the CRC Advisory Committee.

Any problems or concerns raised during the CRC scientific review are forwarded to the IRB, as appropriate. Likewise, any potential noncompliance with the regulations for human subjects protection that is identified by the CRC is promptly reported to the ED.

X. NYPH Pharmacy

The NYPH Pharmacy works closely with the CUMC Research Pharmacy and the IRB Office to ensure that all investigational drugs, including those administered for emergency use, are administered in accordance with federal regulations, accreditation standards, and IRB and institutional policies. Towards this end the NYPH Pharmacy, the CUMC Research Pharmacy,

and the IRB Office work together to develop policies for the proper dispensation and handling of investigational drugs, as well as the documentation of such processes.

The NYPH Pharmacy promptly reports any potential noncompliance with the regulations for human subjects protection, and/or dosing errors involving investigational drugs to the ED.

XI. NYPH Patient Services Administration

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

XII. Center for Bioethics

The Center for Bioethics provides an inter-disciplinary, inter-professional forum to advance scholarly work on, and public understanding of, contemporary issues in biomedical ethics. One direct benefit for investigators and research administrators is that the Center provides educational training conferences and seminars in the area of bioethics. These educational initiatives provide substantive training opportunities for the IRB Chairs, members, and staff. Additionally, the Director, Center for Bioethics serves as a Policy Advisor to the IRB Office.

XIII. Department Chairs, Faculty, Research Investigators, and Staff

The Department Chairs and Faculty are responsible for ensuring that all research involving human subjects is conducted in accordance with ethical principles, institutional policies, and federal and state regulations. The leadership provided by the Department Chairs, Faculty, and Administrators helps ensure that research at Columbia is conducted with high quality and in an ethical manner. The research investigators and staff are at the forefront of human research protections, as they are best positioned to directly ensure that research is conducted ethically.

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