IX. Oversight Monitoring

The Columbia HRPP assures oversight monitoring of human subjects research by various means, such as:

1) continuing review of the research by the IRB and inquiries with investigators and/or into research records following concerns raised by IRB review;
2) IRB review of UPs;
3) requiring data and safety monitoring by either an internal or external committee, when applicable;
4) compliance oversight initiatives by the COT, including for-cause and not-for-cause investigations, and oversight monitoring of studies that had prior compliance concerns;
5) additional reviews, investigations or monitoring by the RP, JRSC, RDRC, or IBC;
6) oversight monitoring activities conducted by the Cancer Center Research Management Office (CRMO);
7) COT’s review of any audit conducted by a federal agency (e.g., FDA, NCI) or external organization (e.g., audits performed by cooperative oncology groups); these reports are forwarded to the COT; and
6) additional reviews conducted by either the CTO or RCT.

Furthermore, quality improvement efforts provided by the IRB office, as described in Section XI, serve as additional mechanisms to provide oversight monitoring of human subjects research.

A. Renewal (Continuing Review)

As described in Sections III.D.3, V.A.2, and VI.A.7, continuing review serves a key role in monitoring of all human subjects research that is not exempt. By requiring submission of a report of the progress of the study during the past approval period, the IRB receives information about and insights into the risks associated with the study and the quality of study management. Through these insights, the IRB may make determinations that additional oversight monitoring may be necessary and, in such cases, consider what additional measures may be needed. The IRB may require the study team to provide additional reports, or may refer a given study to the COT for further investigation or audit.

IRB staff and members are mindful of the expiration dates of IRB approval during the review process, particularly when subjects are actively participating and an interruption in the conduct of study procedures may pose an increase in risk to those subjects. While the IRB may not extend the IRB approval period without additional review, consideration by the IRB Chair may be given to allowing the continued participation of enrolled subjects to prevent harm or an increase in risk of harm. Investigators are advised to submit renewal requests sufficiently in advance of the expiration date to ensure sufficient time for review.
B. Review of Unanticipated Problems Involving Risks to Subjects or Others (including Adverse Events)

The review of UPs (e.g., adverse events, risks, or problems that were not expected at the onset of the research or at the time of the most recent IRB review, related to the research and suggest an increase in risk of harm) provides an important role in the oversight of human subjects in research. The process for IRB review of UPs is described in Sections V.A.4 and VI.A.3. Timing of and action subsequent to IRB review of UPs depends on the severity, relationship to the test article, and whether the event occurred under the auspices of Columbia or at another site that relies on a non-Columbia IRB for review of the event(s). Depending on how these criteria apply to the situation, the CU IRBs review reports of UPs promptly, with a summary required at the time of continuing review.

C. Data and Safety Monitoring

The IRB will review a data and safety monitoring plan for certain research studies as described in Section V.B.6. During the course of studies conducted by Columbia (either at Columbia or elsewhere), the IRB will review and/or solicit information from the applicable data and safety monitoring board or committee to address any relevant IRB concerns. The IRB will also rely on the data and safety monitoring boards and/or the sponsor to provide assessments of the adverse events and other UPs that may occur during the study.

D. Reviews or Monitoring by the Research Pharmacy, Radiation Safety Committees, or Institutional Biosafety Committee

For monitoring of human subjects research providing specific risks from radiation, hazardous materials (including research with human organs, tissues, or fluids), or investigational drugs and devices, the IRB may also rely on oversight provided by the RP, JRSC, RDRC, RSO (which provides administrative support to both radiation committees) or the IBC. The Columbia HRPP provides for effective partnering and communication between each of these committees or offices and the IRB as appropriate. The IRB may rely upon either the COT or oversight monitoring by these other groups in lieu of, or as an adjunct to, the oversight monitoring provided by the IRB.

To enhance the oversight of human subjects research/clinical investigations involving ionizing radiation, communication between the IRB and radiation safety committees (i.e., JRSC and RDRC) includes:

1) For any study involving human subjects and an investigational radiopharmaceutical that requires RDRC review, the IRB will forward a copy of the IRB approval to the RDRC.

2) For any study involving human subjects and a radiographic procedure that is not standard practice (or the frequency of the procedure is greater than standard practice), the IRB will forward a copy of the IRB approval to the JRSC.
3) For continuing review of any study covered in items 1 or 2 above, the IRB will forward a copy of continuing review (i.e., renewal) IRB approval to the RDRC or JRSC, as appropriate.

4) For any UP related to an investigational radiopharmaceutical, radiation therapy or a radiographic procedure, the IRB will forward the UP report along with the IRB review of the event to the RDRC or JRSC, as appropriate.

5) Any IRB approval of a modification or amendment to a protocol that involves or affects procedures involving ionizing radiation will be forwarded to the RDRC or JRSC, as appropriate.

6) Any closure (i.e. “Termination”) of a study that is approved by the IRB or study that is suspended by the IRB will also be reported to the RDRC or JRSC, as appropriate.

When ionizing radiation exposure beyond that required for clinical care is proposed for research purposes, IRB approval to commence the research, at least for the component of research involving radiation, is not granted until RDRC or JRSC approval, as appropriate, has been issued.

E. Reviews by Research Administration Offices

The CTO (including the IAP), RCT, and SPA each provide additional oversight of human subjects research during their routine review of contracts or grants. Each of these offices will communicate with the IRB office to resolve issues regarding IRB review of human subjects research. Issues commonly addressed include assurance of IRB review of grants, review of subcontracts by the appropriately designated IRB, resolution of conflict of interest issues, terms of payment for research related injuries, and miscellaneous issues that could be identified during the routine review of contracts or grants.

F. Compliance Oversight

Compliance oversight procedures address two types of Noncompliance: Research Noncompliance and IRB Noncompliance.

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

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

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

The COT is responsible for the management of all investigations of potential non-compliance. The COT determines, with the direction of the ED, which incidents of potential
noncompliance require investigation. If an IRB staff member finds and determines that noncompliance is minor based on established criteria in Appendix 1 of the IRB Noncompliance with Human Subject Regulations” policy (Reference Document #89), the findings are entered by the appropriate IRB staff into a central IRB database for tracking purposes and aggregate review by the COT. The COT relies on this information to evaluate patterns or behaviors that may suggest poor management or regulatory oversight of a study by the research team.

All other incidents of potential noncompliance are reported to the COT. Based on the seriousness of the allegations, the COT will determine whether an onsite investigation is required and whether a full or targeted audit is appropriate.

The response to an allegation of noncompliance consists of one to three phases, each of which is explained in more detail in the CU “Noncompliance with Human Subject Regulations” policy (Reference Document #89).

**Phase 1 - Inquiry:** the gathering of preliminary information and fact-finding to assess whether an allegation has substance and, if so, whether an Investigation is warranted (an “Inquiry”); this phase is brief and does not involve a substantive analysis of any information, but determines whether the PI is actually conducting, or has conducted, the study, whether the information presented in the allegation appears to be potentially relevant, affiliation of the source of the allegation with the University, and whether any documents should be sequestered.

**Phase 2 - Investigation:** following an Inquiry, the further investigation of facts with respect to whether Noncompliance has occurred (an “Investigation”). This phase may involve an audit/review conducted by the COT. Upon completion of all COT investigations of potential serious noncompliance, a report is released to the PI, and copied to the ED, AD, applicable IRB, applicable department chair and departments, appropriate IO(s), EVPR and, when appropriate, the relevant regulatory agency and sponsor. Determinations that allegations are unfounded are also reported to all relevant parties.

**Phase 3 - Outcome:** following an Investigation, the determination as to whether Noncompliance has occurred and what corrective actions, if any, are required (an “Outcome”).

If, at any point in the three phases, serious noncompliance is discovered, the noncompliance is reported to the appropriate regulatory agencies. When an investigation is complete, a follow-up or final letter is sent to the applicable regulatory agencies.

Not-for-cause audits are also conducted by the COT to randomly review IRB-approved research or records and activities for compliance with federal regulations as well as institutional policies. Not-for-cause audits focus primarily on investigator-initiated studies and studies that have little, if any, external oversight.
Additional oversight may consist of ongoing monitoring visits conducted by the COT in cases where a follow-up audit/review may be necessary to confirm that certain necessary corrective actions have been initiated/completed or appropriate follow-up to COT reports has occurred. Regular ongoing monitoring visits by the COT may be conducted in cases where serious noncompliance was identified.

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