GUIDELINES FOR THE USE OF RADIATION IN RESEARCH STUDIES INVOLVING HUMAN SUBJECTS

These Guidelines describe what a principal investigator (PI) needs to know if he/she intends to use ionizing radiation in a research study involving human subjects under the auspices of the Joint Radiation Safety Committee (JRSC) of Columbia University (CU), NewYork-Presbyterian Hospital (NYPH) and New York State Psychiatric Institute (NYSPI).

I. What Research Is Covered?

Any research study (JRSC Research) involving human subjects that will use radiation must be approved by the JRSC prior to enrolling subjects in the study if the use of radiation goes beyond that established for the applicable standard of care. It is assumed that, for purposes of these Guidelines, unless specifically indicated otherwise, use of radiation in JRSC Research does not constitute standard of care. Studies using radiation can fall into two general categories:

- Studies using radiopharmaceuticals
- Studies using radiographic or therapeutic radiation such as x-rays (including mammograms, DEXA scans and dental scans), CT scans, radiotherapy (including brachytherapy) and fluoroscopy (including cardiac catheterization)

A study may use more than one form of radiation in different procedures under that study. As discussed further below, the Application for the Use of Radiation in Research Studies Involving Human Subjects (the Application) is organized using these two categories. The Application form can be found in the Hazardous Materials section of Rascal as Appendix H [link].

Note: There are a limited number of basic research studies using radiopharmaceuticals that may be conducted under the auspices of the Columbia University Radioactive Drug Research Committee (RDRC). Such studies are described in the Guidelines for Conducting Research Under the Auspices of the Columbia University Radioactive Drug Research Committee (the RDRC Guidelines) which can be found on the Radiation Safety Program website at http://www.ehs.columbia.edu/RadiationFormsMC.html.

II. What Steps are Needed to Obtain JRSC Approval?

You must take the following steps in order to obtain approval of JRSC Research:

A. As indicated above, certain basic research studies using radiopharmaceuticals may be approved by the RDRC without the need to file an Investigational New Drug Application (IND) with the FDA. If, after reviewing the RDRC Guidelines, you believe that your study may qualify for review by the RDRC, you should notify the Director of the Radiochemistry and Radiopharmaceutical Laboratories (collectively, the Laboratory) at the Columbia University PET Center (the PET Center) that your study might constitute a RDRC study. The Director of the Laboratory and you will determine whether the particular study should be conducted under an IND or with RDRC approval. If the Director of the Laboratory agrees that the study can be conducted with RDRC approval, you may proceed with the steps described in the RDRC Guidelines.
B. A Clinical Authorized User is a physician who is an expert in the clinical use of radiation or radioactive materials, has the requisite training and qualifications for such use and has been authorized by the JRSC to prescribe the administration of radioactive materials to humans. If your study involves the administration of radioactive materials to humans and you are not yourself a Clinical Authorized User, select a Clinical Authorized User from the list of Clinical Authorized Users that can be found on the Radiation Safety Program website in the category of study to which the protocol relates (http://www.ehs.columbia.edu/RadiationHumanResearch.html) and obtain his/her approval to act as the Clinical Authorized User on your study.

C. If your study involves the use of radiographic procedures only and you are not yourself a licensed physician, you must select a physician (a Physician Liaison) to order such radiographic procedures prior to filing the Application and receive the consent of the Physician Liaison to act as such.

D. Complete the Application. A link to the Application can be found in Section I and the Application will be further described below. If you need assistance in filling out the Application, you may contact the Radiation Safety Program Office at (212) 305-0303.

E. Prior to filing the Application with the JRSC, if applicable, have the Clinical Authorized User or the Physician Liaison approve the Application in Rascal.

F. Submit the Application as Hazardous Materials Appendix H to the related Columbia University or New York State Psychiatric Institute IRB protocol (the Protocol). The IRB review process will run parallel to the JRSC process, but IRB approval will not be granted until the JRSC has approved your Application.

Note: If you are using any radiation in your study, even if such use is standard of care, you must check the box on the IRB protocol indicating the same.

G. Make sure that your and each of your Co-Investigators’ C.V.s are attached to the Application.

III. What Information Does the JRSC Need In Its Review?

This Section describes what information must be reviewed by the JRSC before approval may be given. Approval may be given only if the JRSC is satisfied that these requirements have been met. Most of this information is provided to the JRSC in the Application. The section of the Application to which each requirement relates is referenced below.

A. IRB Protocol [Application, Section I]. As indicated above, the Application, Protocol and related Informed Consent Form (ICF) must be submitted together. You should use the same study title on both the Application and the Protocol. The IRB and JRSC processes will be undertaken in parallel tracks, but there will be communication between the JRSC and the IRB during the course of the review so that each Committee will be up to date on issues that may arise prior to approval and the language that must be included in the ICF.
B. Intent of Study/Justification/Proposed Use [Application, Section I]. No study may be approved by the JRSC unless it concludes that the use of radiation is necessary and appropriate given the intent of the study. Therefore, you must:
- Provide a description of the study, a rationale for the use of radiation and a description of the proposed use.
- Confirm that the radiation dose to research subjects is sufficient and no greater than necessary to obtain valid measurements.
- Verify that the number of research subjects is sufficient and no greater than necessary for the purpose of the study.

C. Personnel [Application, Section II]. List the Principal Investigator, any Co-Investigators and, if applicable, the Clinical Authorized User or the Physician Liaison.

D. Studies Using Radiopharmaceuticals for Research [Application, Section III]. You should complete this Section only if your study uses radiopharmaceuticals for research. You should not include procedures ordered as routine standard of care. However, standard of care procedures that would not have been ordered except as a requirement of the Protocol should be included.

1. Radiopharmaceuticals to be Used [Application, Section III(A)]. In the table in Section III(A), you are asked to identify for each radiopharmaceutical used in the study, the name of the radiopharmaceutical (i.e., F-18, Tc-99m, etc.), the chemical form (i.e., Sestimibi), the minimum pharmacologic dose (i.e., the lowest dose at which any pharmacologic effect has been found), the physical amount of radiation to be administered to the subject and the supplier.

2. Radiation Doses to Subjects from Research Study Procedures [Application, Section III(B)]. In the table in this Section, you are asked to provide dose calculations for the following unless dosimetry data on the particular tissue or organ is not available:
- The three organs or tissues receiving the highest doses
- Active blood-forming organs such as bone marrow
- Lens of the eye
- Gonads.

In addition, you are asked for the whole body “effective dose” which is used to compare the stochastic risk of non-uniform exposure to radiation to the risk caused by uniform whole body exposure.

The amount of radioactive material to be administered may not exceed the smallest radiation dose with which it is practical to perform the study without jeopardizing the benefits to be obtained from the study. You must therefore provide radiation dose calculations based on biologic distribution data from published literature or other valid studies.
The Application calls for information applicable to a “representative subject in your study”. In many cases, the actual individual radiation dose can only be estimated using standard adult and child reference models published by organizations such as the Society of Nuclear Medicine’s Medical Internal Radiation Dosimetry (MIRD) Committee, the British Health Protection Agency (formerly the National Radiological Protection Board) for x-ray sources, including CT, and the FDA for conventional x rays. The determination of radiation dose to specific tissue or organs using currently accepted methods, such as the system set forth by the MIRD Committee, or the system set forth by the International Commission on Radiological Protection, is sufficiently accurate for estimating radiation risk from radionuclides used in JRSC Research.


If you need assistance in estimating doses, call the Columbia University Medical Center Radiation Safety Program office at (212) 305-0303.

With limited exceptions, all radiopharmaceuticals used in JRSC Research at Columbia must be produced in the Laboratory. In certain circumstances, investigators will be permitted to use radiopharmaceuticals produced by an external radiopharmaceutical manufacturer or pharmaceutical company (a Vendor). Therefore, either the Laboratory or the Vendor will be responsible for producing such radiopharmaceuticals in accordance with all regulatory standards.

If the radiopharmaceutical is produced in the Laboratory under an IND, a Quarterly Quality Assurance Report (Lab QA Report) will be delivered to you within 10 days following the end of each calendar quarter for each of your studies for which radiopharmaceuticals were produced during the preceding quarter. The Lab QA Report will identify radiopharmaceutical release and administration data for all batches produced by the Laboratory, including both radiopharmaceuticals injected and radiopharmaceuticals not injected due to cancellation or production failure.

**E. Studies Using Radiographic or Therapeutic Radiation for Research [Application, Section IV].** You should complete this section if your study uses radiographic or therapeutic radiation, such as x rays, CT scans, radiotherapy and fluoroscopy either alone or with radiopharmaceuticals. Many studies have ancillary radiation scans that are in addition to the primary use of radiation. You should not include procedures ordered as routine standard of care, unless such procedures would not have been ordered except as a requirement of the Protocol.
F. Summary Dosimetry Tables [Application, Section V]. The information asked for in the first table is the total radiation dose from the study (i.e., the sum of the doses from the procedures listed in Sections III(B) and IV). If you are using only one form of radiation in your study, this table will be the same as the table in Section III(B) or IV, as applicable.

There is also a table in this Section that asks you to provide total radiation doses over a 12-month period from not only the study being considered by the JRSC, but also from any other study conducted by you or known to you that would result in the subject getting additional exposure to radiation outside the study being considered by the JRSC. The information about studies other than your own need be provided only if you know of them; you are not under any obligation to investigate whether the subject will be in any other studies.

If the sum of the doses from the research study procedures and from clinical standard of care used in conjunction with such procedures would result in injury to a subject, you should describe such potential injury. Any such additional risk should also be included in the ICF.

G. Human Research Subjects [Application, Section VI]. Although the IRB is responsible for assuring the protection of human research subjects, including that proper consents are obtained, the JRSC reviews certain criteria, as follows:

1. Women of Childbearing Potential. The JRSC requires that a woman of childbearing potential state in writing that she is not pregnant, or, on the basis of a pregnancy test, be confirmed as not pregnant, before she may participate in a JRSC study. The absence of pregnancy should be confirmed by a pregnancy test. Lack of pregnancy in women of childbearing potential is usually confirmed by a negative urine pregnancy test.

2. Pediatric Subjects. The JRSC requires that subjects should be at least 18 years of age and legally competent unless there is sufficient justification for the use of minors in the study.

The FDA recommends that risk assessment of proposed pediatric studies include consideration of the magnitude, probability, and duration of each protocol intervention, the age-related changes in risk profile, and factors such as the use of venipuncture (both the frequency and total blood volume needed for the study), the use of enclosed or confining equipment, the length of any proposed immobilization (including the possibility that the immobilization may be prolonged), concomitant medications, any additional protocol interventions, and the need for sedation (if any). You may be asked by the IRB to provide this data.

IV. What Ongoing Responsibilities Does a PI Have During the Course of a Study?

After approval by the JRSC and the IRB, you may commence the study. During the course of the study, you as PI will have certain ongoing responsibilities, which are described below.
A. **Annual Reports.** You must submit to the JRSC at the time the related Protocol is submitted to the IRB for renewal, an Annual Report in paper format summarizing certain information with respect to your study during the previous year. The Annual Report can be found at [http://ehs.columbia.edu/RadiationHumanResearch.html](http://ehs.columbia.edu/RadiationHumanResearch.html).

B. **QA Reports.** You must submit to the JRSC by the 15\textsuperscript{th} day of the first month following the end of each calendar quarter a certified copy of each Lab QA Report that you receive from the PET Center. If no radiopharmaceuticals were administered under an IND during the quarter, you should so notify the JRSC.

C. **Adverse Events, Adverse Reactions and Unanticipated Problems.** You must forward to the JRSC copies of (1) any adverse event or adverse reaction report submitted to a sponsor or a governmental agency or (2) any report of an unanticipated problem involving risks to subjects submitted to the IRB, in each case resulting from the use of radiation or a radiopharmaceutical in your study, promptly after submission of such report.

D. **Modifications.** If you wish to modify any information in the Application for this study, you should provide the JRSC with a revised Application at the same time that the related IRB Protocol Modification is submitted to the IRB. The Application is amended by creating a clone of the original Application and revising the clone. You must indicate the changes in the Application and the rationale for each change in the Rascal Notes. A copy of each IRB Protocol Renewal or Modification that involves a change to the research radiation exposure should also be sent to the JRSC upon submission to the IRB.

Each of the foregoing Reports will be uploaded into Rascal by the Radiation Safety Committee Coordinator.