University of Colorado
Denver | Anschutz Medical Campus

RDRC SOP on Review Criteria

Regulatory Statement

Radioactive drugs, as defined by the regulations, are generally recognized as safe and effective when administered, under the conditions specified in the FDA regulations, to human research subjects during the course of a research project intended to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of a radioactivelabeled drug or regarding human physiology, pathophysiology, or biochemistry. The use of these drugs is not intended for immediate therapeutic, diagnostic, or similar purposes or to determine the safety and effectiveness of the drug in humans to carry out a clinical trial. Certain basic research studies, such as those to determine whether a drug localizes in a particular organ or fluid space and to describe the kinetics of that localization, may have eventual therapeutic or diagnostic implications, but the initial studies are considered to be basic research within the meaning of this section

The conditions under which use of radioactive drugs for research are considered safe and effective are:

Approval by Radioactive Drug Research Committee

(ii) The radiation dose is within the limits set forth below

(iii) The radiation exposure is justified by the quality of the study being undertaken and the importance of the information it seeks to obtain

(iv) The study meets the other requirements set forth below regarding qualifications of the investigator, proper licensure for handling radioactive materials, selection and consent of research subjects, quality of radioactive drugs used, research protocol design, reporting of adverse reactions, and approval by an appropriate Institutional Review Committee

And

(v) The use of the radioactive drug in human subjects has the approval of the RDRC

Limit on Pharmacological Dose

The amount of active ingredient or combination of active ingredients to be administered shall be known not to cause any clinically detectable pharmacological effect in human beings. If the same active ingredients (exclusive of the radionuclide) are to be administered simultaneously, e.g., under an "Investigational New Drug Application" or for a therapeutic use in accordance with labeling for a drug approved under the FDA's regulations, the total amount of active ingredients including the radionuclide shall be known not to exceed the dose limitations applicable to the separate administration of the active ingredients excluding the radionuclide

Limit on Radiation Dose

The amount of radioactive material to be administered shall be such that the subject receives the smallest radiation dose with which it is practical to perform the study without jeopardizing the benefits to be obtained from the study

Under no circumstances may the radiation dose to an adult research subject from a single study or cumulatively from a number of studies conducted within 1 year be generally recognized as safe if such dose exceeds the following:

Whole body, active blood-forming organs, lens of the eye, and gonads	**Rems**
Single dose	3
Annual and total dose commitment	5
Other organs	
Single dose	5
Annual and total dose commitment	15

For a research subject under 18 years of age at last birthday, the radiation dose shall not exceed 10 percent of that set forth in the table above.

All radioactive material included in the drug either as essential material or as a significant contaminant or impurity shall be included when determining the total radiation doses and dose commitments. Radiation doses from x-ray procedures that are part of the research study (*i.e.*, would not have occurred but for the study) shall also be included. The possibility of follow-up studies shall be considered for inclusion in the dose calculations.

Numerical definitions of dose shall be based on an absorbed fraction method of radiation absorbed dose calculation, such as the system set forth by the Medical Internal Radiation Dose Committee of the Society of Nuclear Medicine, or the system set forth by the International Commission on Radiological Protection.

In making the determination the RDRC shall consider the following requirements and assure that each is met.

(1) ***Radiation dose to subjects***. To assure that the radiation dose to research subjects is as low as practicable to perform the study and meet the required criteria, the Radioactive Drug Research Committee shall require that:

(i) The investigator provides absorbed dose calculations based on biologic distribution data available from published literature or from other valid studies

(ii) The investigator provides an acceptable method of radioassay of the radioactive drug prior to its use to assure that the dose calculations actually reflect the administered dose

(iii) The radioactive drug chosen for the study has that combination of half-life, types of radiations, radiation energy, metabolism, chemical properties, etc., which results in the lowest dose to the whole body or specific organs with which it is possible to obtain the necessary information

(iv) The investigator utilizes adequate and appropriate instrumentation for the detection and measurement of the specific radionuclide

(2) ***Pharmacological dosage***. To determine that the amount of active ingredients to be administered does not exceed the limitations, the committee shall require that the investigator provide pharmacological dose calculations based on data available from published literature or from other valid human studies

(3) ***Qualifications of investigators***. Each investigator shall be qualified by training and experience to conduct the proposed research studies

(4) ***License to handle radioactive materials***. The responsible investigator or institutions shall, in the case of reactor-produced isotopes, be licensed by the Nuclear Regulatory Commission or Agreement State to possess and use the specific radionuclides for research use or be a listed investigator under a broad license, or in the case of non-reactor-produced isotopes, be licensed by other appropriate State or local authorities, when required by State or local law, to possess and use the specific radionuclides for research use

(5) ***Human research subjects.*** Studies involving human subjects must have appropriate IRB review and approval. The responsible investigator shall obtain the consent of the subjects or their legal representatives in accordance with the regulations and the IRB's approval. The research subjects shall be at least 18 years of age and legally competent. Exceptions are permitted only in those special situations when it can be demonstrated to the committee that the study presents a unique opportunity to gain information not currently available, requires the use of research subjects less than 18 years of age, and is without significant risk to the subject.

Studies involving minors shall be supported with review by qualified pediatric consultants to the RDRC.

Each female research subject of childbearing potential shall 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 any study

(6) ***Quality of radioactive drug***. The radioactive drug used in the research study shall meet appropriate chemical, pharmaceutical, radiochemical, and radionuclidic standards of identity, strength, quality, and purity as needed for safety and be of such uniform and reproducible quality as to give significance to the

research study conducted. The RDRC shall determine that radioactive materials for parenteral use are prepared in sterile and pyrogen-free form. Therefore, the protocol shall be based upon a sound rationale derived from appropriate animal studies or published literature and shall be of sound design such that information of scientific value may result.

The projected number of subjects shall be sufficient but no greater than necessary for the purpose of the study. The number of subjects shall also reflect the fact that the study is intended to obtain basic research information and not intended for immediate therapeutic, diagnostic or similar purposes or to determine the safety and effectiveness of the drug in humans for such purposes (*i.e.*, to carry out a clinical trial).

(7) ***Adverse reactions***. The investigator shall immediately report to the RDRC all adverse effects associated with the use of the radioactive drug in the research study.

The RDRC shall report all adverse reactions probably attributable to the use of the radioactive drug in the research study to the Food and Drug Administration

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History of SOP	Date
Initial approval	12/16/15
Review by the RDRC	
Re-review:	