

Radioactive Drug Research Committee (RDRC)

The Food and Drug Administration (FDA) mandates that all research studies that involves the use of radioactive material in or on humans, be reviewed and approved by the RDRC. The RDRC will review all research protocols that involve the use of radioactive material in or on human subjects regardless of the amount of radioactivity. The RDRC only approves research studies that are intended to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of radioactive labeled drugs or regarding human physiology, pathophysiology, or biochemistry. The RDRC would not review and approve studies that are 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). Approval of the RDRC, the RSC and the Institutional Review Board (IRB) are required prior to initiation of any research on human by the use of radioactive drugs.

The RDRC will review and approve a research protocol, if it considers that the scientific knowledge and benefits are likely to result from such study. Therefore, a protocol should be based upon a sound rationale derived from appropriate animal studies or published literature and must be designed such that the information of scientific value may result. The radiation dose should be minimized and should be no greater than is necessary to obtain valid measurement. The projected number of human subjects should be sufficient but no greater than is necessary for the purpose of the study.

The RDRC submits an annual report on or before January 31 of each year to the FDA. The annual report s includes the names and qualifications of the members of, and of any consultants used by, the RDRC, and, for each study conducted during the preceding year. The RDRC activities are monitored and reviewed periodically by the FDA. The FDA may monitor by reviewing the RDRC annual reports, or by reviewing full protocols for certain studies, and/or by on-site inspections.

RDRC MEMBERSHIP

- The RSC will appoint the members and chairperson of the RDRC.
- The RDRC have at least five members that includes:
 1. The Radiation Safety Officer
 2. A physician recognized as a specialist in nuclear medicine,
 3. An individual qualified by training and experience to formulate radioactive drugs, and
 4. An individual with special competence in radiation dosimetry.
 5. The remainder of the membership may consists of individuals that have special training and experience in various disciplines pertinent to the need of committee in reviewing the research project. These individuals may be from field of radiology, internal medicine, clinical pathology, hematology, endocrinology, radiation therapy, radiation physics, radiation biophysics, health physics, cardiology, pediatric and radiopharmacy and other fields related to safe use of radioactive drugs.
- Membership is sufficiently diverse to permit expert review of the technical and scientific aspects of proposals submitted to the committee.
- If needed consultants will be used from other medical disciplines.

- FDA's approval of the qualifications of the members of the committee is required. Changes in membership and applications for new members would be submitted to the FDA as soon as, or before, vacancies occur on the committee.

RDRC Functions

- The chairperson will sign all applications, minutes and reports of the committee.
- The Committee will meet at least once in each calendar quarter in which research activity has been authorized or conducted.
- One-half of the members would constitute the quorum including the RSO, or her designee, nuclear medicine physician and individual qualified to formulate radioactive drugs.
- Minutes that include numerical results of votes on protocols would be kept.
- The RDRC members can not vote on the protocol in which he/she is an investigator or co-investigators.

Charge of RDRC

The RDRC requires that:

- The investigator be qualified by training and experience to conduct the proposed research studies.
- The responsible investigator be an authorized user approved by the RSC in use of the specific radionuclides.
- The investigator select the appropriate human subjects and to submit the protocol to obtain a review and approval of IRB.
- The investigator obtain the consent of the human subjects or their legal representatives. (The research subjects are 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).
- The investigator obtain a written statement from each female research subject of potential childbearing age that she is not pregnant, or, on the basis of a pregnancy test is confirmed as not pregnant, before she may participate in any study.
- The investigator provide absorbed dose calculations based on biologic distribution data available from published literature or from other valid studies.
- The investigator provide an acceptable method of radioassay of the radioactive drug prior to its use to assure that the dose calculations actually reflect the administered dose.
- The investigators utilize adequate and appropriate instrumentation for the detection and measurement of the specific radionuclide.
- The radioactive drug chosen for the study has a combination of half-life, types of radiations, radiation energy, metabolism, chemical properties, etc., that result in:

1. The smallest radiation dose to whole body or specific organs of subject, which is practical to perform the study without jeopardizing the benefits that are to be obtained from the study.
2. The radiation dose to an adult research subject from a single study or cumulatively from a number of studies conducted within 1 year does not exceed the following:

Research Subject	Single dose rem	Annual and total dose commitment Rem
Adult		
Whole body, active blood-forming organs, lens of the eye, and gonads	3	5
Other organs	5	15
Minor under age of 18		
Whole body, active blood-forming organs, lens of the eye, and gonads	0.3	0.5
Other organs	0.5	1.5

3. All radioactive material included in the drug either as essential material or as a significant contaminant or impurity are included in 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) are also included.
 4. The possibility of follow up studies shall be considered for inclusion in the dose calculations.
 5. Numerical definitions of dose should 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.
- The investigator provide pharmacological dose calculations based on data available from published literature or from other valid human studies. The pharmacological dosage that the amount of active ingredient or combination of active ingredient should not known to cause any clinically detectable pharmacological effect in humans, and the total amount of active ingredient without radionuclide shall be known not exceed the dose limitations.
 - The radioactive drug used in the research study meet the appropriate chemical, pharmaceutical, radiochemical, and radionuclide standards of identity, strength, quality, and purity as needed for safety and is of such uniform and reproducible quality as to give significance to the research study conducted. The investigator must assure the committee that the radioactive drugs are prepared in sterile and pyrogen-free form for the parenteral use.
 - The investigator immediately report all adverse effects associated with the use of the radioactive drug in the research study. All major adverse reactions probably attributable to the use of the radioactive drug in the research study must be immediately reported by the RDRC to the FDA

The RDRC reviews the protocols for the following:

1. The radiation exposure is justified by the quality of the study being undertaken and the importance of the information it seeks to obtain;
2. The safe use of radioactive material in human related to good Radiation Safety Practices;
3. The qualification and experience of the principle investigators and co-investigators in performing the radiation study in humans;
4. The consent forms;
5. The adverse reactions, and approves the adverse reactions related to radiation use and the statement related to the radiation exposure;
6. selection and consent of research subjects and
7. research protocol design.

Reports To FDA on Research Use of Radioactive Drug

- The RDRC should submit an annual report on or before January 31 of each year to the FDA. The annual report should include the names and qualifications of the members of, and of any consultants used by, the RDRC, and, for each study conducted during the preceding year, a summary of information presented in the following format:
- Report on Research Use of Radioactive Drug
 1. Title of the research project.
 2. Brief description of the purpose of the research project.
 3. Name of the investigator responsible.
 4. Pharmacological dose:
 - a. Active ingredients.
 - b. Maximum amount administered per subject.
 5. Name of the radionuclide(s) used, including any present, as significant contaminants or impurities.
 6. Radiation absorbed dose. Provide the maximum dose commitment to the whole body and each organ that was received by a representative subject and the calculations or references that were used to estimate these maximum dose commitments.
- The report should include the dose contribution of both the administered radionuclide(s) and any X-ray procedures associated with the study. If the study elicits data on the uptake or excretion of the radioactive drug pertinent to the estimation of dose commitment, report the mean value and range of values. For each subject the report should provide:
 1. Age, sex, and approximate weight.
 2. Total activity of each radionuclide administered for each radioactive drug used in the study. Report each X-ray procedure used in conjunction with the study.
 3. If the subject has participated in other radioactive drug research studies, report the name of the radioactive drug used in these other studies, the date of administration, and the total activity of each radionuclide administered. If any X-ray procedures were used, identify the X-ray procedure(s) and include an estimate of the absorbed radiation doses.

4. If more than one administration of a radioactive drug per subject, cumulative radiation dose and dose commitment, expressed as whole body, active blood-forming organs, lens of the eye, gonads, and other organ doses from the administered radionuclides.
- Any approved protocols which involves exposure either of more than 30 research subjects, or of any research subject under 18 years of age, the RDRC should immediately submit a report to the FDA
 - All adverse reactions probably attributable to the use of the radioactive drug in the research study must be immediately reported by the RDRC to the FDA

Packaging And Labeling of Radioactive Drug

The label of the immediate container and shielded container, if any, should bear the following:

- The statement "Caution: Federal law prohibits dispensing without prescription";
- The statement "To be administered in compliance with the requirements of Federal regulations regarding radioactive drugs for research use";
- The established name of the drug, if any;
- The established name and quantity of each active ingredient;
- The name and half-life of the radionuclide, total quantity of radioactivity in the drug product's immediate container, and amount of radioactivity per unit volume or unit mass at a designated referenced time;
- The route of administration, if it is for the other than oral use;
- The net quantity of contents;
- An identifying lot or control number from which it is possible to determine the complete manufacturing history of the package of the drug;
- The name and address of the manufacturer, packer, or distributor;
- The expiration date, if any;
- If the drug is intended for parenteral use, a statement as to whether the contents are sterile;
- If the drug is for other than oral use, the names of all inactive ingredients, except that:
 1. Trace amounts of harmless substances added solely for individual product identification need not be named.
 2. If the drug is intended for parenteral use, the quantity or proportion of all inactive ingredients, except that ingredients added to adjust pH or to make the drug isotonic may be declared by name and a statement of their effect; if the vehicle is water for injection, it need not be named.

- If the container is too small to accommodate a label with sufficient space to bear all information listed above, the above information may be placed on the shielded container only.