Radioactive Drug Research Committees- Do you have one? Do you need one? Do you want one?

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Disclaimers

- I have no conflicts of interest to report
- I am not a nuclear medicine physician
- I am not a nuclear pharmacist

Objectives

- Understand what a Radioactive Drug Research Committee (RDRC) is and what types of studies need RDRC review.
- Overview of the requirements of an RDRC
- If you don't have an RDRC and decide you don't want one, what are the alternatives?

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What is an RDRC?

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What is NOT an RDRC

- **It is not a radiation safety committee**
- **It is not an IRB**
- **It is not a substitute for the FDA in the approval of investigational drugs**

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FDA's RDRC Program

- 21 CFR 361.1 permits basic research using radioactive drugs in humans **without** an investigational new drug application (IND) when the drug is administered under certain conditions

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FDA's RDRC Program

- Conditions include:
  - Research is approved by an RDRC that is approved by FDA
  - Dose to be administered must be known not to cause any clinically detectable pharmacological effect in humans
  - Total amount of radiation to be administered must be the smallest radiation dose practical to perform the study without jeopardizing the benefits of the study, and must be within specified limits

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FDA's RDRC Program

What is Basic Research?

- Intended to obtain basic information regarding the metabolism (including kinetics, distribution, dosimetry, and localization) of a radioactive drug or regarding human physiology, pathophysiology, or biochemistry,
- Not intended for immediate therapeutic, diagnostic or similar purposes
- Not intended to determine the safety and efficacy of a drug in humans

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Setting up an RDRC

- An FDA approved RDRC is one that fulfills the requirements for:
  - Membership
  - Function
  - Reporting
  - Approval
  - Monitoring

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RDRC Application to the FDA

- An application must be submitted to an approved by FDA before an RDRC may approve research studies.
- Application includes
  - Names and qualifications of proposed RDRC members (Form 2914)
  - CVs for each proposed members and a summary statement describing each member's specific training and experience relative to one of the three required committee positions
  - A statement that the RDRC agrees to comply with the requirements set forth in §361.1

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RDRC Membership

- Minimum of 5 members. Must include:
  - **Physician who specializes in nuclear medicine**
    - Substantial training or experience in nuclear medicine
    - Certification by American Board of Nuclear Medicine
    - Certification by Board of Radiology, Pathology or Internal Medicine with appropriate additional training and experience in nuclear medicine

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RDRC Membership

- **Person qualified by training and experience to formulate radioactive drugs**
  - Board certified nuclear pharmacist
  - Pharmacist with special training and 2 years experience in formulation and quality control of radioactive drugs
  - Chemist holding a graduate degree who can demonstrate association with a clinical medical program and who has 2 years experience in the formulation and quality control of radioactive drugs

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RDRC Membership

- **Person with competence in radiation safety and radiation dosimetry**
  - Medical physicist or scientist with training in radiation safety and substantial experience in calculating organ doses from radiopharmaceuticals and x-ray sources

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RDRC Membership

- **Individuals qualified in various disciplines pertinent to the field of nuclear medicine**
  - Radiology, internal medicine, clinical pathology, hematology, endocrinology, radiation therapy, radiation physics, radiation biophysics, radiopharmacy

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RDRC Membership

- Other considerations:
  - FDA guidance recommends a clinical pharmacologist be a member of the RDRC
  - Membership must be sufficiently diverse to permit expert review of technical and scientific aspects of protocols
  - While members may meet more than one of the membership categories, the member should only represent one category for the review of the protocols
  - There may be a need for consultants to provide oversight for specific studies (i.e. pediatric specialist)
  - Administrative or management personnel may be included as non voting members of the RDRC

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Change in RDRC Membership

- Change in membership and applications for new members must be submitted to FDA as soon as, or before, vacancies occur and new members are appointed to the committee.
- Chair must notify FDA before new members assume committee responsibilities
- New RDRC membership must be approved

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RDRC Function

- Chairperson
  - Members of the RDRC select a chairperson
  - Chairperson must sign all applications, minutes and reports of the RDRC

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RDRC Function

- Meetings
  - Must be held at least one in each quarter in which research activity has been authorized
  - Must have a quorum (more than 50% of members) with appropriate representation of the three required fields of specialization
  - Meetings must include discussion of ongoing studies to ensure that they do not evolve into research projects that no longer meet the criteria for approval under an RDRC

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RDRC Function

- Minutes
  - Must keep minutes that include a numerical vote on new protocols involving human subjects
  - Must include discussion of the criteria for the evaluation of new protocols

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RDRC Function

- Special Summary
  - RDRC must submit a special summary to FDA no later than 7 days after a proposal is approved that involves:
    - More than 30 research subjects (or when a previously approved protocol is expanded to include more than 30 subjects)
    - Exposure to a research subject less than 18 years of age

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Setting up an RDRC

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RDRC Reporting

- Annual Report
  - RDRC must submit an annual report to FDA on or before January 31st of each year
  - Report includes names and qualification of the members and any consultants used (Form FDA 2914)
  - Summary of study information for each study conducted during the preceding year (Form 2915)
  - Current CVs should be included or reference to the date the CV was previously submitted can be provided if there are no changes

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RDRC Reporting

- Annual Report includes information such as:
  - Basic information about the research project
  - Pharmacological dose
  - Active ingredients
  - Maximum amount administered per subject
  - Name of radionuclide used
  - Radiation absorbed dose (max dose commitment to the whole body and each organ specified that was received by the subject). Calculations used are required

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RDRC Approval Criteria

- Approval criteria for RDRC studies can be found in §361.1(d)
- RDRC must find that the protocol meets the approval requirements and document that determination in the minutes

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RDRC Approval Criteria

(1) Radiation dosimetry parameters are as a low as practicable to perform the study and meet the criteria of §361.1(b)(3)

(b)(3) provides the radiation dose limits for studies that are conducted under RDRC approval

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RDRC Approval Criteria

(2) The amount of active ingredient is known not to cause a clinical detectable pharmacological effect based on published data from human studies cited in the protocol or from other valid human studies

This means that RDRC protocols cannot include the use of drugs that have no documented previous human experience!!

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RDRC Approval Criteria

(3) The study investigators are qualified by training and experience to conduct the study

(4) The medical facility is properly licensed to handle radioactive materials

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RDRC Approval Criteria

(5) Selection and consent of research subjects is appropriate

- Research with minors requires reduced radiation dose
- Females of childbearing potential must state in writing that they are not pregnant or have a negative pregnancy test

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RDRC Approval Criteria

(6) Quality of the radioactive drug to be administered meets appropriate standards as needed for safety, and be of such uniform and reproducible quality as to give significant to the research study conducted

* RDRC must determine appropriate production standards for meeting Current Good Manufacturing Practice requirements

(7) Protocol design has scientific worth and is based on a sound rationale

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RDRC Approval Criteria

(8) Protocol includes provisions for reporting of adverse events to the RDRC and then immediately, but no later than 7 calendar days, to the FDA

(9) Protocol receives concurrent approval by an appropriate institutional review board

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Labeling

- In addition to the approval criteria, the RDRC is required to confirm that the packaging, label and labeling of the radioactive drug are in compliance with Federal, state and local laws on radioactive materials
- There are 12 statements that must be on the label. List can be found at §361.1(f)

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Setting up an RDRC

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  - Monitoring

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RDRC Monitoring

- Monitoring of ongoing RDRC studies is required
- Meetings must include discussion of ongoing studies to ensure they have not evolved into research projects that no longer meet the criteria for approval under an RDRC
- Progress reports should be required
- Adverse events should be monitored
- Protocol amendments must be approved

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Do You Want One?

- If you need an RDRC and decide you want one, the FDA has published resources to assist with compliant set up and management of an RDRC
  - Guidance document
  - Sample Review Criteria Checklist
  - List of active RDRC sites- Phone a Friend!

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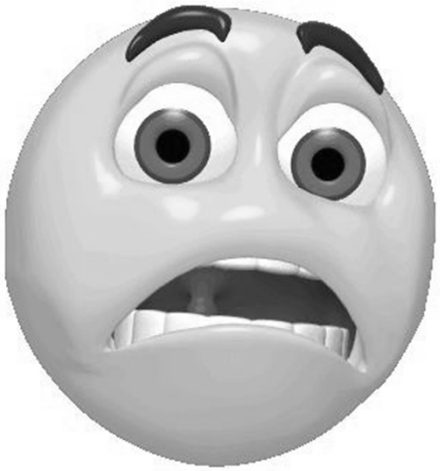

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What are the Alternatives to RDRC?

- Don't do this type of research!
- Apply for an IND!
- Joint RDRC

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Questions??

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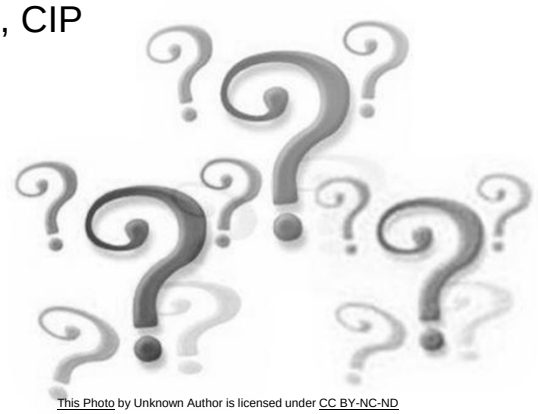

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