

**West Virginia University Hospitals**

**Radioactive Drug Research Committee**  
**(WVUH-RDRC)**

**POLICIES AND PROCEDURES**

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## **I. Charter**

Food and Drug Administration (FDA) regulations at 21 CFR 361.1 entitled “Prescription Drugs For Human Use Generally Recognized as Safe and Effective and Not Misbranded: Drugs Used In Research” provide for a mechanism that allows the use of radioactive drugs in human research under certain specific conditions. The human research use of radioactive drugs that meet these specific conditions can be performed without the need for an FDA-approved New Drug Application or an FDA-accepted Investigational New Drug (IND) exemption. Among the conditions specified at 21 CFR 361.1 is the requirement that each research project be approved and monitored by a Radioactive Drug Research Committee (RDRC) that is itself approved by the FDA.

To achieve compliance with these regulations, West Virginia University Hospitals submitted an application to re-establishment of its Radioactive Drug Research Committee in November 2018. This committee (Radioactive Drug Research Committee No. 185 at West Virginia University Hospitals) was re-instated by the FDA in December of 2018.

The WVUH-RDRC is responsible for the review of basic science research protocols using radioactive drugs or biological products (hereinafter referred to as “radioactive drugs”) in humans that are subject to 21 CFR 361.1 that are conducted at West Virginia University Hospitals. Approval of a research study by the WVUH-RDRC is based on assurance that the following requirements are met:

- Appropriate limit on the radiation dose;
- Appropriate limit on the pharmacologic dose;
- Qualified study investigators;
- Medical facility properly licensed to possess and handle radioactive materials;
- Appropriate selection and consent of research subjects;
- Appropriate quality of radioactive drug administered;
- Sound research protocol design;
- Reporting of adverse events by the investigator to the WVUH-RDRC; and

## **II. Membership**

21 CFR 361.1 (c) (1) outlines the requirements for membership of an RDRC. The Committee must be composed of the following individuals: (1) a physician recognized as a specialist in nuclear medicine; (2) a person qualified by training and experience to formulate radioactive drugs; (3) a person with special competence in radiation safety and radiation dosimetry; and (4) other

members qualified in various disciplines pertinent to the field of nuclear medicine (e.g., radiology, internal medicine, clinical pathology, hematology, endocrinology, radiation therapy, radiation physics, radiation biophysics, health physics and radiopharmacy). The Committee must consist of at least 5 members, and the membership should be diverse enough to permit expert review of the technical and scientific aspects of proposals submitted to the Committee. Note that although one individual may have expertise in more than one category, an individual should only represent one category for the review of protocols. Consultants in other pertinent medical disciplines will be included, as necessary, for review of specific studies. Additionally, an RDRC will include pediatric consultants when it reviews research studies (under the authority of 21 CFR 361.1) that involve subjects less than 18 years of age, as described in Section IV.B.1.

Changes in membership and applications for new members Form FDA 2914 (Appendix D) must be submitted to the FDA as soon as, or before, vacancies occur and new members are appointed to the WVUH-RDRC [21 CFR 361.1].

The WVUH-RDRC has a designated chairperson (“Chair”). The Chair signs all applications, minutes, and reports of the WVUH-RDRC [21 CFR 361.1]. All committee action letters are signed by the Chair.

The current *voting* and *non-voting* members of the WVUH-RDRC and their respective disciplines are shown in Appendix A.

### **III. Responsibilities**

The WVUH-RDRC reviews and approves all research investigations conducted at West Virginia University Hospitals that involve the administration of radioactive drugs to human subjects for scientific objectives, when these radioactive drugs do not already have FDA approval and/or are not being used under an IND. Studies involving a routine clinical procedure that uses an FDA approved tracer offered by the Nuclear Medicine or Nuclear Cardiology service are also excluded from RDRC review. The Committee’s preeminent objective is to ensure that the RDRC studies are scientifically sound and are conducted safely and result in radiation exposures no greater than are necessary to fulfill the scientific objectives of the research. For those research studies subject to the requirements of 21 CFR 361.1, the RDRC is responsible for ensuring that the studies are approved and conducted in accordance with the applicable FDA regulations. Additionally, the WVUH-RDRC seeks to ensure that all human research investigations conducted at West Virginia University Hospitals involving non-FDA approved radioactive drugs are conducted in compliance with applicable regulations of the U.S. Nuclear Regulatory Commission.

## **IV. Policies and Procedures**

### **A. Meetings**

The WVUH-RDRC is required by FDA regulations to meet at least once each calendar quarter. In order to facilitate the timely review of protocols and amendments, the WVUH-RDRC meets quarterly. Applications and amendments must be submitted for each meeting no later than one month prior to the meeting. At the request of the Chair, ad hoc meetings may be convened to review time-sensitive applications or amendments.

The quarterly meeting may be cancelled if, in the quarter, all of the following conditions have been met:

- No subjects have been admitted to any of the approved studies;
- No progress reports have been received on ongoing studies;
- No reports of adverse reactions have been submitted;
- No protocol amendments have been submitted for approval;
- No responses are due on committee recommendations or questions concerning pending research protocols; and
- No new protocols have been submitted.

If the meeting is cancelled, the WVUH-RDRC records will document the reason for the cancellation.

The Chair may review and administratively approve unchanged renewal applications that might expire before a scheduled meeting, and minor amendments (those that do not involve changes radiotracer preparation, radiation exposure, or application) throughout the year.

The Chair administratively approves some WVUH-RDRC applications, as described below. A brief summary of the administrative approval action is distributed to Board members after the action has been taken. The item is reported on the next agenda and minutes for the meeting.

#### **1. Quorum**

A quorum is constituted by more than 50% of the voting members of the Committee. However, when applications subject to the requirements of 21 CFR 361.1 are to be considered by the Committee, there must be appropriate voting member

representation of the required fields of specialization (i.e., nuclear medicine; formulation of radioactive drugs; and radiation safety/radiation dosimetry).

## **2. Minutes**

Minutes of the meetings of the committee are prepared and signed by the Chair. The minutes include the results of votes on new research protocols and protocol amendments involving the use of human subjects. No member of the Committee votes on a protocol for which he or she participates as an investigator/collaborator, and any such abstentions will be recorded in the minutes. Minutes will be reviewed and approved by the committee members.

## **3. Committee Actions**

Protocols reviewed by the WVUH-RDRC may be approved, disapproved, or found to be approvable pending Radiological Safety Committee (RSC) approval and pending resolution of other contingencies, if applicable. Investigator responses to substantive contingencies will be reviewed at a subsequently convened Committee meeting. For all protocols involving greater than 30 subjects, the WVUH-RDRC Chair will notify the FDA of final WVUH-RDRC approval following resolution of any contingencies.

## **B. Review Procedures**

### **1. New Applications**

As all new applications will undergo full-committee review by the WVUH-RDRC, the more detailed form, “**Application to Involve Human Subjects in Biomedical Research that Includes use of Radioactive Drugs not covered under an IND (2019-1)**” (Appendix B), must be used. Additional documents that need to be submitted along with the application form are specified on these forms.

All investigators who submit research applications to the WVUH-RDRC must be qualified by training and experience to conduct the proposed research. In addition, the Authorized User (AU) shall be authorized under West Virginia University Hospitals U.S. Nuclear Regulatory Commission license to possess and use the specific radioactive drugs proposed in the research. At West Virginia University Hospitals, this is accomplished via application to the

West Virginia University Hospitals Radiation Safety Department and approval by the Radiation Safety Committee.

All applications submitted to the committee should contain complete answers to all of the questions in the application. Pertinent portions of grants, as well as a detailed protocol that outlines the entire research procedure, should be submitted.

All new submissions are initially screened by the WVUH-RDRC administrator to determine whether all required documents have been submitted. Each protocol requiring full review by the WVUH-RDRC is reviewed prior to a committee meeting by at least three committee members, including; one physician with expertise in nuclear medicine, a reviewer with expertise in radiation dosimetry, and a reviewer with radiochemistry/radiopharmacy expertise. In addition, all new protocols involving new PET radiosyntheses will be reviewed by a member of the committee with expertise in PET.

Protocols subject to the requirements of 21 CFR 361.1 that involve administration of radioactive drugs to research subjects under 18 years of age are also reviewed by one or more *ad hoc* pediatric consultants to the committee, who report their assessment of the protocol in writing.

WVUH-RDRC will perform full review of all protocols involving new radioactive drugs used for basic physiological or pathophysiological investigations under the conditions specified at 21 CFR 361.1. Such drugs are defined as “generally recognized as safe and effective” (GRASE) and thus exempt from the new drug provisions of the Food, Drug, and Cosmetic Act. This is the specific category of drugs that the RDRC is chartered to approve by the FDA.

The WVUH-RDRC will review, approve and maintain institutional Drug Master Files (IDMFs) for the radioactive drugs produced by the commercial pharmacy working in conjunction with the West Virginia University Cyclotron Facility. Each IDMF includes, in one place, the required information concerning the chemistry and manufacturing control information for the radioactive drug, as well as documentation of the “no clinically detectable pharmacological effect” level and the radiation dosimetry for the radioactive drug.

## **2. Amendments to Approved Protocols**



Any significant alteration of the original proposed research plan requires submission of a request for an amendment to the Committee, the form, “**Application to Involve Human Subjects in Biomedical Research that Includes use of Radioactive Drugs not covered under an IND (2015-1)**” (Appendix B), must be used. An amendment is required for any changes in the protocol on annual renewal that has an impact on radiotracer administration. Amendments will be pre-reviewed by representatives on the committee with expertise in the area of change prior to the meeting.

### **3. Review of Changes in Radioactive Syntheses**

Any changes in the radioactive synthesis must be submitted for review by the full committee, and those changes must be outlined in application amendment.

## **C. Monitoring Procedures**

The WVUH-RDRC will monitor all active protocols through review of bi-annual reports provided by the PI. Content of these reports are listed below. Amendments in any protocol are also reviewed at the regularly held meeting, which will occur at least quarterly.

## **D. Reporting Procedures**

### **1. Adverse Reaction Reporting**

The investigator must immediately, but no later than 7 calendar days, report to the WVUH-RDRC all adverse effects associated with the use of the radioactive drug in the research study [21 CFR 361.1]. The WVUH-RDRC chair must immediately, but no later than 7 calendar days, report to FDA all adverse reactions determined to be probably attributable to the use of the radioactive drug in the research study. Any adverse reactions reported by the WVUH-RDRC to the FDA will also be reported to the RSC. All adverse reactions will be reviewed by the committee at the next meeting.

### **2. Biannual Reporting**

For all protocols subject to the requirements of 21 CFR 361.1, effective January 2019, in addition to annual reporting the principal investigator must report on the progress of the research before July 15 (Reporting Period January 1 – June 30) and January 15 (Reporting Period (July 1 - December 31) of each year to the RDRC. This is performed by submission of a



form entitled “**Biannual Progress Report For RDRC-Approved Research Protocol Subject to Requirements of 21 CFR 361.1**”. This interim document will need to include:

- A summary of all patients recruited into each protocol and subgroup;
- The number of extra doses of radiopharmaceuticals administered due to technical failures as part of proposed protocol contingencies;
- Any issues related to radiochemistry production and quality assurance; and
- Any adverse events. An Adverse Event is defined as all events associated with the radiotracer that are not clearly defined in the protocol as expected side effect of other drugs, which may be used in the protocol.

### **3. FDA Reporting Requirements**

#### **a. Annual Report**

FDA regulations require that the responsible investigator submit an annual report to an RDRC using Form FDA 2915, “**Report on Research Use of Radioactive Drug**” (Appendix C).

Completed annual reports must be submitted to the WVUH-RDRC by 15<sup>th</sup> of January each year, so that these forms can be reviewed by the Chair, and other committee members as necessary, and forwarded by the RDRC to the Food and Drug Administration by 31<sup>st</sup> of January. This report contains the following information:

- Name of institution
- RDRC committee number
- Title of the research project
- Study ID number and approval/termination dates
- Brief description of the purpose of the research project
- Name of responsible investigator
- Pharmacological dose (including the name of the nonradioactive drug, maximum mass dose of the nonradioactive drug administered per subject in a single dose and per year and per protocol,
- No-observed-effect level mass dose and route of administration),
- Names of radionuclide(s) used (including any present as significant contaminants)
- Radiation absorbed dose for a representative subject (including the maximum dose commitment to the whole body and to blood-forming organs, lens of the eye, and gonads
- Calculations or references that were used to estimate these maximum dose commitments
- The report shall include the dose contribution of both the administered radionuclide(s) and any x-ray procedures associated with the study)

- Listing of the following information for each subject enrolled during the year:
- Age, sex, approximate weight, the total activity of each radioactive drug administered and other associated procedures
- Total absorbed dose per single administration for each radioactive study drug and the total dose per organ per year.

The WVUH-RDRC will add the names and qualifications of members of the committee and any consultants used by the WVUH-RDRC during the review of studies over the past year to the annual report submitted to the FDA using Form FDA 2514, “**Report on Research Use of Radioactive Drug Membership Summary**” (Appendix D).

**b. Special Summary Report**

For any protocol subject to the requirements of 21 CFR 361.1 that involves either more than 30 subjects or subjects under 18 years of age, a special summary must be submitted to the FDA no later than 7 calendar days post WVUH-RDRC approval, using FDA Form 2915 as outlined above (Appendix C). The responsible physician must provide the WVUH-RDRC with a completed FDA Form 2915 for each such protocol as a condition for final approval by the WVUH-RDRC.

**E. WVUH-RDRC Record Retention**

WVUH-RDRC records will be retained for five (5) years after closure of a protocol or, for those studies subject to the requirements of 21 CFR 361.1, for five (5) years after FDA was notified of closure of the protocol by submission of FDA Form 2915. After protocol closure, records may be retained either as original paper documents or as scanned electronic documents (pdf files).

**V. Revision History**

<b>Version</b>	<b>Description of Changes</b>	<b>Release Date</b>
1.0	Initial Draft	2019

## **APPENDICES**

**Appendix A. WVUH-RDRC Membership**

**Appendix B. WVUH-RDRC Application**

**Appendix C. FDA Form 2915**

**Appendix D. FDA Regulations 21CFR361.1**

**Appendix A**  
**West Virginia University Hospitals RDRC Membership**

***Voting Members***

**Required Specialties:**

**Nuclear Medicine**

Gary D. Marano, MD

**Radioactive Drug Formulation**

Glen F. Palmer, RPh

**Radiation Safety and Radiation Dosimetry**

Nasser Razmianfar, EdD

Stephen I. Root, MS

R. Alfredo C. Siochi, PhD - Chair

**Other Voting Members:**

Raymond R. Raylman, PhD

Robert Callery, PhD

**Non-Voting Members:**

Benjamin Parker RT (R) (N)