**YALE UNIVERSITY**

 **RADIOACTIVE DRUG RESEARCH COMMITTEE (RDRC)**

**RADIOACTIVE INVESTIGATIONAL DRUG COMMITTEE (RIDC)**

**Application to Involve Human Subjects in Biomedical Research with Ionizing Radiation**

Complete this section in its entirety. A principal investigator submitting for the first time will need to contact the Yale University Radiation Safety Committee for a new-PI meeting.

## SECTION I: GENERAL INFORMATION

|  |
| --- |
| **Title of Research Project:** Click or tap here to enter text. |
| **HIC Protocol Number:** Click or tap here to enter text. |
|  |  |
| **Principal Investigator:**Click or tap here to enter text. | **Title/Department:**Click or tap here to enter text. |
| **Campus Address:** Click or tap here to enter text. |
| **Campus Phone:** Click or tap here to enter text. | **E-mail:**Click or tap here to enter text. |
|  |
| **Authorized User (AU):** Choose or tap to add your own. |
| **Campus Address:** Choose or tap to add your own. |
| **Campus Phone :**Choose an item. | **E-mail**Choose an item. |
| **Has this Authorized User been previously approved by the RDRC/RIDC:** [ ] **YES** [ ]  **NO** |

*General Notes: Approval of a protocol can only be obtained if i) the AU has been approved, and ii) the use of radioactive drugs has been approved.*

*For help in filling out these forms for PET Center studies, please consult the guide on the PET Center web site:* [*https://medicine.yale.edu/pet/informationforinvestigators/*](https://medicine.yale.edu/pet/informationforinvestigators/)

## SECTION II: Committee Oversight

1. Is the radioactive drug/product FDA approved or will the radioactive drug/biological product be used under an IND?

[ ] **YES**: The research will be reviewed by Yale RIDC and RSC. Upload the FDA submission cover letter in the Supporting Documents page in IRES IRB. Move to section II A and skip section II B. **Answer all questions in Sections III, IV, V, and VI.**

[ ]  **NO**: Move to section II B to determine whether the protocol meets criteria for RDRC oversight. Skip section II A. **Answer all questions in Sections III, IV, V, and VI.**

## SECTION II A: RADIOACTIVE INVESTIGATIONAL DRUG COMMITTEE (RIDC)

1. **Type of Submission:** [ ] Initial [ ] Amendment

 *If Amendment, specify type and highlight amendment in sections below:*

[ ] Change in the number of subjects in current study cohort(s)

[ ] Addition of a new aim with a new study cohort

[ ] Increase in the number of injections of previously approved radiopharmaceuticals

[ ] Addition of a new radiopharmaceutical

[ ] Change/Addition of low dose CT and/or transmission scans, x-rays or fluoroscopy

[ ] Other: Click or tap here to enter text.

1. **Type of Radiopharmaceutical Used in the Study:**

[ ] IND:

**IND#** Click or tap here to enter text.

**Holder of the IND:**

 [ ] Yale Principal Investigator-held IND

 [ ] PET-Center held IND

 [ ]  Manufacturer-held IND

 [ ] Other: Click or tap here to enter text.

[ ] FDA Approved Drug Used According to the Label

[ ] Other: Click or tap here to enter text.

Date of Initial IND submission to the FDA (submit Study May Proceed Letter if available):

Has this version of this protocol been submitted to the IND yet?

 [ ]  Yes, date: Click or tap here to enter text.

 [ ]  No, to be submitted upon IRB approval

## SECTION II B: RADIOACTIVE DRUG RESEARCH COMMITTEE (RDRC)

1. **Does this study meet the criteria for RDRC review listed below?**
2. Basic research designed to study: the metabolism of a radioactive drug or to gain information about human physiology, pathophysiology, or biochemistry. [ ] YES [ ] NO
3. This research is **not** **intended** for immediate therapeutic, diagnostic, or similar purpose:

 [ ]  YES [ ]  NO

1. This research is **not intended** to determine the safety and effectiveness of the radioactive drug:
 [ ]  YES [ ] NO

If you answered NO to any of the 3 questions above, an IND will be required. Please, contact Amy Hummel (amy.hummel@yale.edu) Associate Director, IND/IDE Management Office in YCCI to discuss the project and the FDA submission requirements. RIDC will review the research instead of the RDRC. Revise this application and submit it along with the IRB application.

1. **Type of Submission**:[ ]  Initial [ ]  Amendment

 ***If Amendment, specify type and highlight amendment in sections below:***

[ ] Change in the number of subjects in current study cohort(s)

[ ] Addition of a new aim with a new study cohort

[ ] Increase in the number of injections of previously approved radiopharmaceuticals

[ ] Addition of a new radiopharmaceutical

[ ] Change/Addition of low dose CT and/or transmission scans, x-ryas or fluoroscopy

[ ] Other: Click or tap here to enter text.

## SECTION III: Study Methodology

1. **Statement of Purpose:** Briefly state the scientific aim(s) of the study, specifically involving radiation exposure. Cross-reference IRB protocol, if appropriate. If there are different parts to the protocol with different radiation exposures (e.g., one part with 2 tracer injections and one part with 3 tracer injections), please identify these parts individually:

Click or tap here to enter text.

1. **For an Amendment:** Describe the Protocol Changes relevant to radiation exposure. Add the amended information with the date of the amendment request in the relevant sections below:

Click or tap here to enter text.

## SECTION IV: Human Subjects

1. **Total Number of Subjects** Click or tap here to enter text.

**If the study is conducted under RDRC oversight (see Section IIB above), answer questions 1A, 1B, and 2 about the number of subjects.**

**Answers to questions 1A and 1B are not required if the study is conducted under RIDC purview (skip to question # *2. Study Population*).**

**1a.** **Do the total # of subjects in the study exceed 30?** [ ] YES [ ]  NO

*If Yes, please contact: Donna McMahon (203-785-5005 or rdrc\_admin@yale.edu) for information on the completion of an FDA 2915 special summary for inclusion with this RDRC submission.*

 **If the # of subjects in any subject population exceed 30:**

**1b. State reason for exceeding 30 subjects** (this may include the study of multiple subpopulations related to age, sex or disease types):

 Click or tap here to enter text.

1. **Subject Population(s):** Include all cohorts for each objective of the research.

**Objective 1:**

**Number of Subgroups:**Click or tap here to enter text.

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| **Subgroup 1** |  |
| Diagnosis: |
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| **Subgroup 2** |
| Diagnosis: |
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| **Subgroup 3** |
| Diagnosis: |

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| Age Range |
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| Number of Subjects |
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| Number of Subjects |
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| Number of Subjects |

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**Objective 2:**

**Number of Subgroups:**Click or tap here to enter text.

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| **Subgroup 1** |  |
| Diagnosis: |
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| **Subgroup 2** |
| Diagnosis: |
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| **Subgroup 3** |
| Diagnosis: |

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| Number of Subjects |
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| Number of Subjects |
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| Number of Subjects |

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**Objective 3:**

**Number of Subgroups:**Click or tap here to enter text.

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| **Subgroup 1** |  |
| Diagnosis: |
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| **Subgroup 2** |
| Diagnosis: |
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| **Subgroup 3** |
| Diagnosis: |

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| Age Range |
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| Number of Subjects |
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| Number of Subjects |
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| Number of Subjects |

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1. **Pregnancy**
	1. Are women of child-bearing potential included in this study? [ ] YES [ ]  NO
	2. If Yes, will pregnancy testing be performed? [ ] YES [ ]  NO
	3. If Yes, at what time points will pregnancy testing be performed?

[ ] Screening Type of Test: [ ] Serum [ ] Urine

 [ ]  Prior to Each Administration Type of Test: [ ] Serum [ ] Urine

 of Radioactivity

 [ ] Other: Click or tap here to enter text. Type of Test: [ ] Serum [ ] Urine

1. **I acknowledge the following Reporting Requirements (check all applicable boxes):**

**RIDC and RDRC Protocols**

[ ] Adverse reactions will be reported to the RDRC or RIDC and RSC immediately[[1]](#footnote-1).

**Please, review Adverse Event Reporting Requirements in** [**940 GD.1 Guidance on Committee Reviews Required for Human Subjects Research Protocols Using Radiation**](https://your.yale.edu/policies-procedures/other/940-gd1-research-using-radiation)**, section 7**.

[ ] The RDRC/RIDC will be notified when a dose infiltration occurs.

[ ] The RDRC/RIDC will be notified if a subject receives a contingent dose.

**RDRC Protocols Only**

[ ] Quarterly reports will be submitted by the deadline:

* + Q1: Due date - April 15th (Reporting Period - January 1st –March 31st)
	+ Q2: Due date - July 15th (Reporting Period - April 1st – June 30th)
	+ Q3: Due date – October 15th (Reporting Period – July 1st – October 30th)
	+ Q4: Due date – January 15th (Reporting Period – September 1st – December 31st)

[ ] FDA Annual Report

* + Submit FDA 2915 form
	+ Due Date – January 15th (Reporting Period – January 1st – December 31st)

## SECTION V: RADIATION SOURCES

Prevent errors that may delay the approval process. Avoid copy and paste errors, be sure to use the complete radiopharmaceutical name, use complete and current references, and correct mass dose. Current list can be found in the IRES IRB library.

1. **Radioactive Drug List**

|  |  |  |  |
| --- | --- | --- | --- |
| **#** | **Radioactive Drug**  | **Supplier of Drug** | **Location of Use**  |
| **1** | Choose or add your own |  | Choose or add your own |
| **2** | Choose or add your own |  | Choose or add your own |

**Radioactive Drug Specifics and Dosimetry**

|  |  |
| --- | --- |
| **1.** | **Radioactive Drug 1 Name:** Choose or add your own |
| **a.** | Route of Administration | [ ]  I.V.[ ] P.O.[ ] Other Click to enter |
| **b.** | Maximum Mass Dose of non-radioactive drug administered per subject (μg)—RDRC only; for RIDC, enter “IND” |  |
| **c.** | Minimum Radioactivity per Dose (mCi) |  |
| **d.**  | Maximum Radioactivity per Dose (mCi) |  |
| **e.** | Maximum Number of Injections |  |
| **f.** | Does the number of injections include a contingent dose? | [ ]  Yes [ ]  No |
| **g.** | **Dosimetry for Drug:** Ensure dosimetry section is included in submission. In addition, please provide below: |
| The Effective Dose (mrem) per mCi | Click to enter text mrem/mCi |
| The Effective Dose for Maximum Administered Dosage | Click to enter text mrem |
| Indicate Reference Source Used for Dosimetry (complete literature citation or relevant documentation, such as Investigator Brochure) | Reference:  |

|  |  |
| --- | --- |
| **2.** | **Radioactive Drug 2 Name:** Choose or add your own |
| **a.** | Route of Administration | [ ]  I.V.[ ] P.O.[ ] Other Click to enter |
| **b.** | Maximum Mass Dose of non-radioactive drug administered per subject (μg)—RDRC only; for RIDC, enter “IND” |  |
| **c.** | Minimum Radioactivity per Dose (mCi) |  |
| **d.**  | Maximum Radioactivity per Dose (mCi) |  |
| **e.** | Maximum Number of Injections |  |
| **f.** | Does the number of injections include a contingent dose? | [ ]  Yes [ ]  No |
| **g.** | **Dosimetry for Drug:** Ensure dosimetry section is included in submission. In addition, please provide below: |
| The Effective Dose (mrem) per mCi | Click to enter text mrem/mCi |
| The Effective Dose for Maximum Administered Dosage | Click to enter text mrem |
| Indicate Reference Source Used for Dosimetry (complete literature citation or relevant documentation, such as Investigator Brochure) | Reference:  |

**Ionizing Radiation Specifics**

|  |  |
| --- | --- |
| **1.** | **Ionizing Radiation Source 1** (CT, X-ray, Transmission Scan, etc..)**:** Click or tap here to enter text. |
| **a.** | Number of scans: |  |
| **b** | Does the number of scans include those needed with a contingent injection dose? |  |
| **c.** | Indicate Equipment to be Used and Location |  |
| **d.** | Indicate equipment parameters to be used (keV, mA, etc..) include Pitch and Rotation Speed for CT scans.                 |  |
| **e.** | Maximum Exposure Received by Subject per Scan: |  |
| **f.** | Total Exposure Received by Subject from Source (include contingent scans, if appropriate) |  |
| **g.** | Indicate Reference Used for Dosimetry and include as an attachment the estimated total and/or annual exposure to organs. | Reference:  |

|  |  |
| --- | --- |
| **2.** | **Ionizing Radiation Source 2** (CT, X-ray, Transmission Scan, etc..)**:** Click or tap here to enter text. |
| **a.** | Number of scans: |  |
| **b.** | Does the number of scans include those needed with a contingent injection dose? |  |
| **c.** | Indicate Equipment to be Used and Location |  |
| **d.** | Indicate equipment parameters to be used (keV, mA, etc..) include Pitch and Rotation Speed for CT scans.                           |  |
| **e.** | Maximum Exposure Received by Subject per Scan: |  |
| **f.** | Total Exposure Received by Subject from Source (include contingent scans, if appropriate) |  |
| **g.** | Indicate Reference Used for Dosimetry and include as an attachment the estimated total and/or annual exposure to organs. | Reference:  |

## SECTION VI: Dosimetry

1. Summarize the total and/or annual effective dose from both the radioactive drug(s) and other research related procedures involving ionizing radiation that the subject will receive during the course of this study. Upload a completed spreadsheet with dosimetry calculations in Supporting Documents page in IRES IRB.

Complete this section following the template wording below. Include contingent radiotracer injection and ionizing radiation scans, as appropriate. Ensure mrem units are used and consistent in the consent form.

## SECTION VII: Radiation Risk Template

Please use the template below for the consent form and radiation risk language. Insert the appropriate committee (RDRC or RIDC), # of transmission scans, # of injections, and the radiotracer name.

Include contingent radiotracer injection and ionizing radiation scans, as appropriate. Ensure mrem units are used and consistent in the consent form.

*This research study involves exposure to radiation from PET imaging. If you take part in this research, you will be exposed to a small to moderate dose of radiation from the radiolabeled probes used for the PET scans and associated with the transmission scans. Please note that this radiation exposure is****not****necessary for your medical care and is for research purposes only. The**Yale University Radiation Safety Committee (RSC) and [insert correct committee: Radiation Investigational Drug Committee (RIDC); Radioactive Drug Research Committee (RDRC)] have both reviewed the use of radiation in this research study and have approved this use as**involving slightly greater than minimal risk and necessary to obtain the research information desired.*

*The total amount of radiation you will receive in this**study is from [insert #] low dose CT scan - used to optimize the PET scan - and [insert #] injection[s] of radioactive material (XX mCi insert radiotracer name). This radiation is in addition to what you may get as part of your regular medical care and what you receive from natural radiation in our environment. Everyone is exposed to low levels of natural radiation, called ‘background radiation.’ This background radiation comes from outer space and from rocks and minerals in the soil, and is greater at higher altitudes. The average yearly background radiation in the United States is about 300 mrem. The amount of additional radiation you will get from participating in this study is about [insert # of mrem] mrem. This is equal to about [insert # of years] years’ worth of natural radiation.*

*The amount of radiation involved in this research is small, but may slightly increase your risk of getting cancer. Scientists are not certain about the actual cancer risk at these low doses, and there may be no risk at all, but to be conservative we assume that any amount of radiation may pose some increased cancer risk.*

## SECTION VIII: Supporting Information

# **Overview of the process for moving a protocol through RIDC or RDRC**

The institutional committees RIDC (Radioactive Investigational Drug Committee, [RIDC website](https://your.yale.edu/research-support/human-research-protection-program/yale-ridc-yale-university-radioactive)) and RDRC (Radioactive Drug Research Committee, [RDRC website](https://your.yale.edu/research-support/human-research-protection-program/yale-rdrc-yale-university-radioactive-drug)) are charged with evaluating human use protocols involving the use of radioactive radiotracers (radiopharmaceuticals).

Regulations covering the study of radiopharmaceuticals in humans require that the safety of the material has been established, and that the radioactive drug used must meet appropriate standards of identity, strength, quality and purity, and that parenteral products must be prepared in sterile and pyrogen-free form. For studies conducted under an IND (investigational new drug) application, FDA approval (“study-may-proceed” documentation) of the IND study provides this support, and the Yale RIDC function is to ensure that the appropriate IND is referenced. For studies conducted under RDRC (radioactive drug research committee), the Yale RDRC directly evaluates information provided by the investigator and Yale PET Center.

**Reference: IRB Policy 940.1 - Guidance on Committee Reviews Required for Human Subjects Research Protocols Using Radiation**

<https://your.yale.edu/sites/default/files/940_gd.1_guidanceoncommitteereviewsrequiredforhumansubjectsresearchusingradiation_clean.pdf>

# **New Principal Investigator**

An investigator submitting a protocol for the first time to the RDRC or RIDC will need to contact the Yale University Radiation Safety Committee to complete the new investigator training.

# **Application Completion and Submission Instructions:**

* + - 1. Download the Radiation Safety submission forms from IRES IRB, which are located in the IRES Library under “Other Forms”. In addition to the current form, this includes the Yale RSC Coversheet and the Dosimetry Calculator (filename: Dosimetry Calculator\_Yale University).
			2. The Authorized User (AU) at the Yale University PET Center is Ming-Kai Chen, MD, PhD. If another Authorized User will be listed, they must be an approved AU listed on the Yale University NRC materials license.
			3. If unknown, contact shannan.henry@yale.edu at the PET Center to verify if your study will be conducted under the purview of the RDRC or under an IND (RIDC review).
			4. Complete the current form based on type of study (RIDC or RDRC).
			5. For radiotracer information, refer to the dosimetry reference document. If the radiotracer included in your research protocol is not present, or additional information is needed, contact the PET Center for guidance.
			6. Complete the dosimetry calculator. To do this:
1. Choose the radiotracer from the “source” dropdown menu. Input the correct dose. For some tracers, both male and female options are included. Choose the option with the more conservative (higher) effective dose (ED), if you are studying both genders.
2. Include a separate column for each injection in the study design.
3. Include contingent injections; i.e., if the protocol specifies that participants may receive an additional injection in the event of scan failure, these injections must be included.
4. Add other radiation sources (HRRT transmission scans or low dose CT scans). Dose for HRRT or CT scan should be “1” or at most “2”, as these should be listed per PET scan.
5. The Effective Dose (ED) is the radiation exposure value that should be used in your protocol and consent form. Please ensure the dose is consistent across the protocol, consent, the RDRC/RIDC application, and the dosimetry calculator.
6. If your protocol includes multiple Aims, include a dosimetry calculator for each aim.
	* + 1. If your study contains any radiation related procedures that will be conducted at Yale-New Haven Hospital, an application will need to be submitted to the Yale-NHH RSC for approval of those procedures. Refer to the IRES Library under “Other Forms” for that application.
			2. In IRES IRB, upload the following under Supporting documents:
				1. RDRC-RIDC Application (current form)
				2. Dosimetry Calculator
				3. Yale RSC Coversheet

9. Once all documents are submitted, the protocol will be routed by the IRB regulatory analyst to

 the appropriate committees for review. When RDRC/RIDC/YU RSC reviews are complete,

 response letters will be uploaded in IRES IRB.

# **Responding to a request for clarification or additional information**

Prepare a point-by-point response reply to a contingent approval or deferral letter, which must include:

* The Committee finding being responded to
* Detailed description of the changes made
* The document name
* The page numbers
* Document revisions with track changes

# **Errors to Avoid**

* **Copy and Paste Errors**

It is common to reuse or copy text from an existing or previous protocol for a new submission. Although this may be a time-saving strategy in preparation of the proposal, it may delay the review and approval process, as errors propagate through copy-and-paste (e.g., the reference for dosimetry) or changed requirements are not met because of using out-dated information (e.g., the language in informed consent forms).

* **Incomplete or Inconsistent Radiotracer Name Used**
	+ Spell out the full radiotracer name as specified on the Yale PET Center label; don’t use abbreviated names (e.g. use [11C]FLB457, not FLB).
	+ If the name of the tracer in the application is not the same as the Yale PET Center label, include the Yale PET Center name as an alias the first time the tracer name is referenced in each document (e.g. [11C]UCB-J aka [11C]APP311).
	+ Ensure the radiotracer names are consistent throughout all documents.
* **Incorrect or Incomplete Dosimetry Reference**

Confirm the current reference is being used with sufficient detail to allow finding the citation. A current list can be found in the IRES IRB library.

* **Wrong Mass Dose**

The mass dose may differ between an RDRC protocol and an RIDC protocol. For an RDRC study, confirm the correct mass dose with the Yale PET Center. Mass dose is not required for an RIDC application; enter “IND” in the space for mass dose.

* **Inconsistencies across documents**

Commonly seen errors are inconsistencies among the radiation safety cover sheet, the application, informed consent forms, and protocol.

* **Excessive use of acronyms and abbreviations**

Using too many study-specific acronyms and abbreviations makes it difficult to review the documents. All but common medical acronyms and abbreviations should be spelled out at first use in each document.

1. Report immediately, but no later than 24 hours with a follow up, if necessary, within 3 calendar days, but no later than 7 calendar days to rdrc@yale.edu or ridc@yale.edu. [↑](#footnote-ref-1)