NIH RADIOACTIVE DRUG RESEARCH COMMITTEE (RDRC)
APPLICATION FOR HUMAN SUBJECT RESEARCH USING RESEARCH RADIOACTIVE DRUG
(PER FDA 21 CFR 361.1)

Please complete the following sections and submit this application, along with a complete copy of the protocol, NIH form 88-23(a), and consent documents to the NIH RDRC Chair. This form may be expanded or collapsed as necessary.

1. PRINCIPAL INVESTIGATOR (PI):

Name:

ICD:

_____ _____

Signature of Principal Investigator Date

2. PROTOCOL TITLE:

Please also indicate the IRB approval status of this protocol.

3. RESEARCH RADIOACTIVE DRUG:

Please state the maximum quantity of RDRC radioactive material per single administration and the total amount for the duration of the research study.

4. QUALIFICATIONS OF INVESTIGATOR:

Please indicate the training and experience, and/or the approval/licensing authority of the investigator to use the proposed research radioactive drug.

5. INTENDED USE OF RADIOACTIVE DRUG:

Must be to obtain basic information regarding the metabolism of a radioactively labeled drug or regarding human physiology, pathophysiology, or biochemistry, but 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). Please be sure to mention the scientific knowledge and benefit likely to result from use of the research radioactive drug.

6. HUMAN SUBJECT POPULATION:

Appropriate human subjects must be selected. Research subjects must be at least 18 years or age and legally competent. Exceptions are only permitted in special situations and require additional ad hoc review. Each female research subject of childbearing potential shall be confirmed as not pregnant prior to study participation. Please identify and justify the selection (patient and/or healthy controls) and number of subjects that will receive the research radioactive drug in the proposed study. Note that for protocols approved which involve more than 30 subjects, the RDRC is required to immediately submit to the FDA a special summary of the information using FDA Form 2915. If more than 30 subjects are requested, please also attach a justification and a completed FDA Form 2915.

7. PHARMACOLOGICAL DOSE EFFECTS AND LIMITS:

For the research radioactive drug, please specify the maximum amount of active ingredient or combination of active ingredients to be administered per single administration and the total amount for the duration of the research study. The amount of active ingredient or combination of active ingredients administered must be known not to cause any clinically detectable pharmacological effects in humans and the pharmacological dose is within the limits determined to be safe. Please specify these limits for the research radioactive drug requested). Also, please include documentation and attach other relevant information.

8. HUMAN RADIATION DOSIMETRY ESTIMATES:

Note the following regulatory restrictions:

- *The radiation exposure must be justified by the quality of the proposed study and the importance of the information the study seeks to obtain.*
- *Note that the biological distribution data must be from published literature or from other valid studies. Please indicate the source of this data.*
- *The dose limit for adults is 3 rem per single administration and 5 rem per year to the whole-body, lens of the eye, red bone marrow, and gonads; 5 rem per single administration and 15 rem per year to all other organs.*
- *The dose limit for minors (under the age of 18 years) is 10% of the adult limits.*
- *Include ancillary radiation doses from x-ray procedures or scans that are part of the proposed research study. Note that the total dose estimates must also include the ancillary doses and that the total must be within the limits specified.*

Please cite and include references. If MIRDOSE or OLINDA dosimetry code was used to generate estimates, please include a copy of the output data.

9. HUMAN SAFETY DATA:

Please include relevant information to demonstrate the safety of the non-radioactive drug or component in humans.

10. ADVERSE EVENTS:

Note that the investigator is required to immediately report to the RDRC all adverse effects associated with the use of the radioactive drug in the research study. All adverse reactions probably attributable to the use of the radioactive drug in the research study will be immediately reported by the RDRC to the FDA as required in 21 CFR 361.1. Please indicate a commitment to reporting adverse events immediately to the RDRC.

11. REFERENCES:

Please list or attach relevant references to the research radioactive drug or proposed study.

12. QUALITY CONTROL OF THE RESEARCH RADIOACTIVE DRUG

"The radioactive drug must meet appropriate chemical, pharmaceutical, radiochemical, and radionuclidic 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 conducted. Additionally, the radioactive materials for parenteral use must be prepared in sterile and pyrogen-free form."

A. Who will supply the material? If available, please attach a copy of the manufacturers MSDS (Material Safety Data Sheet).

B. In what format will the materials be supplied? (Bulk or unit doses).

C. Who/What Department at the NIH will perform the quality control?

Please be aware that the RDRC may occasionally request to review all relevant records related to the approved use of RDRC materials and protocols.

The table on the next page lists tests that are related to commonly used production methods for typical research radioactive drugs. In the event that the production method (1) does not use a component listed below or (2) uses an alternate method of production or (3) produces additional impurities, appropriate tests, acceptance criteria, procedures, and a testing schedule that is more appropriate for such production should be proposed, and stated in this section of the application. Please complete and revise the table specific to the research radioactive drug requested in this protocol.

TEST	ACCEPTANCE CRITERIA	PROCEDURES	TESTING SCHEDULE
Radionuclidic identity	The measured half-life is _____	Measurement of a sample in a dose calibrator over _____ period.	Test completed prior use of new target design and annually thereafter
Radionuclidic purity	NMT[1] 1.0% impurities at TOI[2]	Gamma spectroscopy of decayed sample (____).	Test completed prior use of new target design and annually thereafter.
Radiochemical identity	Co-elution with authentic Standard	HPLC QC Procedure	Test completed prior to release of drug product
Radiochemical purity	NLT[3] 90 %	HPLC QC Procedure	Test completed prior to release of drug product
Chemical Purity	NLT 90 %	HPLC QC Procedure	Test completed prior to release of drug product
Specific activity	No carrier added NLT 500 Ci/mmole	HPLC QC Procedure	Test completed prior to release of drug product
Residual Solvent Acetonitrile Ethanol	NMT 0.04% (wt/v) NMT 10% (wt/v)	Gas Chromatography w/ Flame Ionization Detection	Validation and on annual batch thereafter
Assay (radioconcentration)	1.0 mCi to 30 mCi / mL @ EOS	USP	Test completed prior to release of drug product
pH	Specify limits (refer to USP)	pH paper	Test completed prior to release of drug product
Sterility testing	Sterile	NIH Microbiology, Bldg 10, Clinical Center	Test initiated within 192 hours of preparation
Membrane Filter Integrity	Sterile 0.22 □ filters are used once. Each membrane tested at maximum system He pressure (128 kPa) for pressure drop.	Pressure drop in gauge measurement.	Test completed prior to release of drug product
Bacterial endotoxins (LAL)	NMT[1] 175/V USP EU mL of the injection, in which V is the maximum recommended total dose in mL, at the expiration time	LAL Test Kit Procedure (Enclosure)	On each Batch

1. NMT = No More Than
2. TOI = Time of Injection
3. NLT = No Less Than
4. EOS = End of Synthesis
5. *V* = Total volume of the batch of radioactive drug injection produced

13. RDRC LABELING REQUIREMENTS

Radioactive drugs prepared, packaged, distributed and primarily intended for use in accordance with the requirements of the RDRC regulations (21 CFR 361.1) are exempt from other such Federal, State and local laws regarding radioactive materials and labels of the immediate containers and shielded containers if specific conditions are satisfied (listed below).

Please indicate if the RDRC labeling requirements, as described on the next page, will be followed. If not, please identify and explain (or attach) the proposed labeling procedures.

YES: _____

NO: _____

EXPLAIN

RDRC LABELING REQUIREMENTS

Radioactive drugs prepared, packaged, distributed and primarily intended for use in accordance with the requirements of the RDRC regulations (21 CFR 361.1)…the labeling must contain the following:

(1) The statement ``Rx only``;

(2) The statement ``To be administered in compliance with the requirements of Federal regulations regarding radioactive drugs for research use (21 CFR 361.1)``;

(3) The established name of the drug, if any;

(4) The established name and quantity of each active ingredient;

(5) 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;

(6) The route of administration, if it is for the other than oral use;

(7) The net quantity of contents;

(8) An identifying lot or control number from which it is possible to determine the complete manufacturing history of the package of the drug;

(9) The name and address of the manufacturer, packer, or distributor;

(10) The expiration date, if any;

(11) If the drug is intended for parenteral use, a statement as to whether the contents are sterile;

(12) If the drug is for other than oral use, the names of all inactive ingredients, except that:

a. Trace amounts of harmless substances added solely for individual product identification need not be named.

b. (ii) 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. Provided, however, That in the case of containers too small or otherwise unable to accommodate a label with sufficient space to bear all such information, the information required by paragraphs (f)(1) and (12) of this section may be placed on the shielded container only.

RDRC OFFICAL USE SECTION

RDRC Review Date:

Approval Status:

- ○ **Approved**
- ○ **Approved w/Comments**
- ○ **Approved w/Stipulations**
    - ○ **Stipulations Satisfied**
- ○ **Not Approved**

_____ _____

RDRC Chair **Date**