Instructions for Completing HUSC-RSC Form 1002, “Information Required in Support of the Research Use of a Non-Approved (F.D.A.) Radioactive Drug”

A. General Instructions

1. Responses to the requests for information should be type-set (i.e., handwritten responses will not be accepted).

2. Use of supplementary pages or appendices is permitted if additional space is required.

3. One completed HUSC-RSC Form 1002 for a given radioactive drug may serve as a “Master File” for multiple research projects involving the administration of that radioactive drug. Each new submission of a research protocol should specifically cite the current Master File for the applicable radioactive drug.

B. Specific Instructions

1. Identity of the Radioactive Drug
   a. Identify the (radionuclide)-active ingredient/carrier (e.g., [C-14] glucose)
   b. Identify the non-radioactive ingredients that appear within the final dosage form (e.g., 10% V/V ethanol in 0.9% Sodium Chloride for injection, U.S.P.)

2. Route of Administration
   a. Indicate the proposed route of administration.

3. Estimated Radiation Dose to Human Subjects
   a. Absorbed dose calculation:
      - Provide radiation absorbed dose estimates for the radioactive drug. At a minimum, radiation dose estimates must address the effective dose equivalent and absorbed doses to the total body, gonads, active blood-forming organs, critical organ, and lens of the eye. (The latter may be assumed to be equivalent to the total body dose unless specific eye uptake of the radioactive drug has been demonstrated or is expected). Submit a complete list, to include absorbed doses to other organs, when respective data is available. These dose estimates must take into account the contribution of any significant radionuclide contaminant(s) present in the final product.
      - Specify the literature reference from which the biodistribution data for calculation of the radiation absorbed dose estimates were obtained; or, if not published, provide a summary of the biodistribution data and identify the laboratory and personnel involved in its collection.
      - Specify the individual or entity responsible for calculation of the radiation absorbed estimates and the methodology (e.g., MIRD or ICRP absorbed fraction) utilized; or, if taken from a published source, include a copy of the respective reference.
b. Method of radioassay:

Specify the method by which the radioactive drug will be assayed prior to use so as to ensure that the administered radioactivity dosage and corresponding absorbed dose estimated are as stated in the research proposal.

c. Assay instrumentation quality control:

Indicate the procedures that will be performed to ensure accurate operation of the instrumentation used to assay the radioactive drug.

4. Pharmacological Dosage of Active Ingredient

a. For an FDA-approved (i.e., NDA) radiopharmaceutical prepared using a non-approved method and/or used for a non-approved (i.e., off-label) indication: Provide supporting statements to address the requirement that deviation(s) from the approved product labeling will not significantly increase the risk to the research subject.

b. For a radioactive drug prepared and administered under the authority of 21 CFR 361.1: Provide data, based on published or other valid human studies, in support of the requirement that the amount of active ingredient/carrier in the proposed dosage of the final radioactive drug will not cause any clinically detectable pharmacological effects. (Append copies of key referenced publications or cited human studies.)

5. Quality of the Radioactive Drug

a. Method of preparation/dispensing:

- Identify the individual(s) or entity that will be responsible for the preparation, repackaging, and/or dispensing of the radioactive drug.
- Describe, in detail, the procedures that will be used in the preparation, repackaging, and/or dispensing of the radioactive drug. (May be appended in the form of a master formula card.)

b. Minimum acceptance criteria:

Delineate minimum acceptance specifications for the final radioactive drug, addressing each of the criteria listed below:

- Visual appearance
- pH
- Radiochemical purity
- Chemical purity
- Specific activity
- Radionuclide purity of identification:
- Pyrogens or bacterial endotoxins (limited to parenteral administration)
- Sterility (limited to parenteral administration)

c. Preclinical validation studies:

Summarize the outcome of any preclinical validation studies that have been performed to confirm that the final radioactive drug will meet the designated minimum acceptance criteria when prepared/repackaged according to the indicated procedures. Such validation studies may include procedures performed on site and/or data obtained from the supplier of the radioactive drug.
d. Routine quality control procedures:

- Indicate the testing procedures that will be performed on each batch of the radioactive drug to ensure that it meets the designated minimum acceptance criteria.

- Note that because of test complexity it may not be possible or practicable to address each of the designated minimum acceptance criteria on each batch of the radioactive drug. In such an event, compliance of the radioactive drug with the applicable minimum acceptance criterion should be addressed in the preclinical validation studies. For certain criteria (e.g., sterility, pyrogens/bacterial endotoxins), it may be a requirement (i.e., based on the physical half-life of the radionuclide) that testing be completed following release of the radioactive drug for human use.

- Indicate the individual(s) or entity that will be responsible for routine quality control testing of the radioactive drug.

e. Expiration dating:

Specify an expiration period, post preparation or repackaging of the radioactive drug, wherein there is evidence that each of the designated minimum acceptance criteria will be retained. Summarize the studies that have been performed or provide a literature reference justifying this expiration period.

6. Labeling

The final container for the radioactive drug shall be labeled to include the following:

- The statement “Caution: Federal law prohibits dispensing without a prescription.”
- The statement “To be administered in compliance with the requirements of Federal regulations regarding radioactive drugs for research use (21 CFR 361.1).”
- Identity of the radioactive drug to include the name and half-life of the radionuclide.
- The identity and quantity of the active ingredient.
- The total quantity of radioactivity within the immediate container at a designated reference time.
- The amount of radioactivity per unit volume or unit mass at a designated reference time.
- The net quantity of contents.
- The route of administration if it is for other than oral use.
- An identifying lot or control number from which it is possible to determine the complete preparation/repackaging history of the batch of radioactive drug.
- The name and address of the manufacturer, preparer, repackager, or distributor.
- The expiration date.
- If the drug is intended for parental use, a statement as to whether the contents are sterile.
- If the drug is for other than oral use, the identity of all active ingredients.