**Radiation Safety Committee Review of Research Protocols Involving**

**The Administration of Radiation to Human Subjects**

**Revision 4**

**Approved by UCI Health RSC on April 14, 2022**

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**Submission Instructions and Guidance**

Determine if Review Required

1. If *all* radiological procedures are standard of care (i.e., the subject would undergo all these procedures even if they were *not* enrolled in the research study), then there is no review needed by the RSC. The standard of care determination is normally made by the Principal Investigator (PI), unless the PI is not a physician, in which case, the determination shall be made by a physician in the appropriate specialty and who is a part of the protocol research team.
2. If *any* radiological procedures are not standard of care, the protocol, informed consent, and the attached Application and Radiological Procedures Form must be submitted to the UCI Health Radiation Safety Officer (bhamrick@uci.edu), so that it may be delivered to the Radiation Safety Committee (or designated Subcommittee) for review.

Submission Materials

1. If the protocol requires review by the Radiation Safety Committee, the following documents must be submitted:
	1. The master protocol (or, the UCI-specific protocol, if the study is investigator-initiated);
	2. Informed consent documents;
	3. A copy of any special imaging procedures or imaging manual (e.g., where the sponsor or investigator requires information in addition to that included in a standard radiology report, or requires imaging parameters different than the standard radiology protocols, or includes other special instructions involving the preparation of the patient for imaging or special collection or processing of the imaging data);
	4. Radiological Procedures Form (see page 3);
	5. If using a *radiopharmaceutical* that is either: *not approved*, or *used off-label*, also submit the Form for Use of Radiopharmaceuticals That Are Investigational or Used Off-Label (see page 4);
	6. For therapeutic applications of radiation, detailed dosimetry from the sponsor must be submitted, as well as the Form for Investigational Radiotherapy (see page 5);
	7. The IND number for any investigational drugs used in the study.
2. Submit the above to the UCI Health Radiation Safety Officer (Barbara Hamrick). Documents should be submitted to her at bhamrick@uci.edu. She can be reached by telephone at 714-456-5607.

About the Review

Once all materials are provided to the UCI Health Radiation Safety Officer (RSO), the RSO makes a determination whether the protocol may be submitted to a Subcommittee of the full Radiation Safety Committee (RSC), or must be presented to the full RSC.

In general, the following protocols must be reviewed by the full RSC:

1. Subjects are minors and the total radiation dose from non-standard of care (non-SOC) procedures is greater than 0.1 millisievert (mSv);
2. Subjects are normals and the total radiation dose from non-standard of care (non-SOC) procedures is greater than 0.5 millisievert (mSv), *except* where the following is true:
	1. The protocol involves imaging with an approved nuclear medicine (including PET) radiopharmaceutical;
	2. The *only* off-label use is the use in a population that does not meet the indications on the approved label (i.e., the use is in a normal study population);
	3. Subjects are all 50 years or older;
	4. The protocol includes no more than two radiological procedures;
	5. The total dose does not exceed 20 mSv.
3. Subjects are adult patients with *no known* advanced cancer and the total radiation dose from non-standard of care (non-SOC) procedures is greater than 50 millisievert (mSv);
4. Subjects are adult patients with *known* advanced cancer and the total radiation dose from non-standard of care (non-SOC) procedures is greater than 100 millisievert (mSv), with the following exception:
	1. The non-SOC procedures are all procedures typically used in the patient populations treatment (e.g., CT scans of the chest, abdomen and pelvis; or FDG-PET), but will be at an increased frequency, and will not result in more than an additional 100 mSv per year of the study.
5. Any protocol that includes the use of an unapproved radiopharmaceutical or off-label use of an approved radiopharmaceutical (except as noted in Item 2, above);
6. Any protocol that includes the non-SOC therapeutic use of radiation.

All other protocols may be reviewed by the Subcommittee.

The RSC and Subcommittee review the protocols, informed consent documents, and any specialized imaging or therapeutic radiation procedures to 1) ensure the use of radiation is necessary and appropriate, 2) assess the total dose to individuals in the study population from non-SOC radiological procedures, 3) ensure the appropriate level of information relating to radiation risk is included in the informed consent documents, and 4) assess whether the radiological procedures are within the capabilities of the Department of Radiological Sciences (e.g., where special equipment or equipment qualification is required by the sponsor) or Department of Radiation Oncology (if non-SOC radiological therapeutic procedures are included in the protocol).

Note:If you have any questions about the submission process you should consult with the UCI Health Radiation Safety Officer.

UCI Health Radiation Safety Officer

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RADIOLOGICAL PROCEDURES FORM

Table 1. Diagnostic Machine-Produced Radiation

|  |  |  |
| --- | --- | --- |
|  | Type of Procedure (include as much detail as possible) | Number and timing of *non-SOC* scans |
| Sample 1 | CT scan of chest, abdomen, pelvis w/o contrast | 7 total: 1 at screening, and 1 every 4 weeks for six months |
| Sample 2 | Standard Chest X-ray w/2 views | 1 at screening |
|  | Click here to enter text. | Click here to enter text. |
|  | Click here to enter text. | Click here to enter text. |
|  | Click here to enter text. | Click here to enter text. |
|  | Click here to enter text. | Click here to enter text. |
|  | Click here to enter text. | Click here to enter text. |

Table 2. Diagnostic Nuclear Medicine Scanning

|  |  |  |
| --- | --- | --- |
|  | Type of Procedure (include as much detail as possible, and specifically, the isotope and compound) | Number and timing of *non-SOC* scans |
| Sample 1 | F-18 FDG PET Brain Scan | 2 total: 1 at screening and 1 at end of treatment |
| Sample 2 | Tc-99m MDP Bone Scan | 1 at screening if patient has not had one in last 28 days |
|  | Click here to enter text. | Click here to enter text. |
|  | Click here to enter text. | Click here to enter text. |
|  | Click here to enter text. | Click here to enter text. |
|  | Click here to enter text. | Click here to enter text. |
|  | Click here to enter text. | Click here to enter text. |

Therapeutic: Submissions that include the non-SOC therapeutic use of radiation must include detailed treatment plans.

FORM for USE OF Radiopharmaceuticals

That are INVESTIGATIONAL OR used OFF-LABEL

HS No. Click here to enter text. Lead Researcher: Click here to enter text.

Study Title: Click here to enter text.

Name of radiopharmaceutical(s) used in this study:

Name of drug: Click here to enter text. Isotope: Click here to enter text.

IND No. Click here to enter text. Sponsor: Click here to enter text.

Name of drug: Click here to enter text. Isotope: Click here to enter text.

IND No. Click here to enter text. Sponsor: Click here to enter text.

Provide the name of the authorized user (AU) physician that will order the radiopharmaceutical, and supervise the administration of the radiopharmaceutical. The AU physician must be 1) named on the UCI Health (UCI Medical Center) radioactive materials license or on a Radiation Use Authorization issued by UCI, 2) authorized to perform the procedure involving the radiopharmaceuticals used in this study, and 3) included as a member of the research team. The physician must agree in writing to this participation, by co-signing this application below.

By signing below, I affirm that I am named on the University of California Irvine (UCI) or UCI Medical Center radioactive materials license and am authorized to perform the procedure involving radiopharmaceuticals in this study, and understand I will be included as a co-researcher on this protocol:

|  |  |  |  |
| --- | --- | --- | --- |
| Authorized User (Print Name) | Authorized User (Signature) | Date | Radioactive Material License |
| Click here to enter text. |  | Click here to enter a date. | UCI [ ]  UCIMC [ ]  |
| Click here to enter text. |  | Click here to enter a date. | UCI [ ]  UCIMC [ ]  |

Please sign below:

By signing below, I affirm that the above information relating to the protocol and investigational drug/device is true and correct.

|  |  |  |
| --- | --- | --- |
| Principle Investigator(Print Name) | Principle Investigator (Signature) | Date |
| Click here to enter text. |  | Click here to enter a date. |

FORM for INVESTIGATIONAL RADIOTHERAPY

HS No. Click here to enter text. Lead Researcher: Click here to enter text.

Study Title: Click here to enter text.

Type of Radiotherapy:

Name of drug/device: Click here to enter text. Isotope: Click here to enter text.

IND/IDE No. Click here to enter text. Sponsor: Click here to enter text.

Name of drug/device: Click here to enter text. Isotope: Click here to enter text.

IND/IDE No. Click here to enter text. Sponsor: Click here to enter text.

Provide the name of the authorized user (AU) physician that will order the radiopharmaceutical, and supervise the administration of the radiopharmaceutical. The AU physician must be 1) named on the UCI Health (UCI Medical Center) radioactive materials license or on a Radiation Use Authorization issued by UCI, 2) authorized to perform the procedure involving the radiopharmaceuticals used in this study, and 3) included as a member of the research team. The physician must agree in writing to this participation, by co-signing this application below.

By signing below, I affirm that I am named on the University of California Irvine (UCI) or UCI Health (UCI Medical Center) radioactive materials license and am authorized to perform the procedure involving radiopharmaceuticals in this study, and understand I will be included as a co-researcher on this protocol:

|  |  |  |  |
| --- | --- | --- | --- |
| Authorized User (Print Name) | Authorized User (Signature) | Date | Radioactive Material License |
| Click here to enter text. |  | Click here to enter a date. | UCI [ ]  UCIMC [x]  |
| Click here to enter text. |  | Click here to enter a date. | UCI [ ]  UCIMC [x]  |

Please sign below:

By signing below, I affirm that the above information relating to the protocol and investigational drug/device is true and correct.

|  |  |  |
| --- | --- | --- |
| Principle Investigator(Print Name) | Principle Investigator (Signature) | Date |
| Click here to enter text. |  | Click here to enter a date. |

**Sample Risk Language for Informed Consent Documents**

Below are some examples of risk language that may be used to develop language for the Protocol Narrative and Informed Consent documents related to your research protocol. Please note that these are examples only, and the actual risk language you use must address the specific type and number of research related radiological procedures your study subjects will undergo. You must also provide the radiation dose from each research related procedure, and the total projected dose to the maximally exposed individual.

The highlighted language in the examples below must be revised to reflect the actual type and number of research related radiological procedures a subject will undergo, as well as the actual radiation dose to which they will be subject, and the correct number of days, months or years of background radiation that is equivalent to that total dose.

INFORMED CONSENT

EXAMPLE: SINGLE NON-SOC CHEST X-RAY

In this study, you may have a chest x-ray. This x-ray is solely for the purpose of this research study. A chest x-ray exposes you to a small dose of radiation. The amount of radiation from one standard chest x-ray is about the same as you receive in 10 days from the natural radiation in our environment.

EXAMPLE: SINGLE NON-SOC CT SCAN

In addition to any scans you may have as a part of your normal medical care, you may have 1 additional CT scan of your chest, abdomen and pelvis.  This scan is solely for the purpose of this research, and you would not have this additional scan if you do not enroll in this study.  CT uses radiation to see inside of your body.  The radiation from a single CT scan of your chest, abdomen and pelvis is about 20-25 millisievert.  A millisievert is a measure of radiation dose.  The average person in the United States receives about 3 millisievert per year from natural sources of radiation in our soils, water and air.  The total dose from 1 CT scan (of your chest, abdomen and pelvis) is equivalent to about 6-9 years of radiation exposure from natural sources.

EXAMPLE: MULTIPLE NON-SOC CT SCANS

In addition to any scans you may have as a part of your normal medical care, during the first two years of this study, you may have 8 additional CT scans of your chest, abdomen and pelvis, and up to 5 additional CT scans of your head and neck.  These scans are solely for the purpose of this research, and you would not have these additional scans if you do not enroll in this study.  CT uses radiation to see inside of your body.  The radiation from a single CT scan of your chest, abdomen and pelvis is about 20-25 millisievert, and the radiation from a single CT scan of your head and neck is about 7 millisievert.  A millisievert is a measure of radiation dose.  The average person in the United States receives about 3 millisievert per year from natural sources of radiation in our soils, water and air.  The total dose from 8 CT scans (of your chest, abdomen and pelvis), and 5 CT scans of your head and neck could deliver up to 195-215 millisievert over two years.  A dose of 195-215 millisievert is equivalent to about 65-70 years of radiation exposure from natural sources.  Radiation exposure at this level may be associated with an increased risk in cancer.  For an average person in the U.S., with no history of cancer, a total dose of 195-215 millisievert may increase their risk of cancer from about 40% to about 42%.  There are many factors that contribute to an individual’s personal risk of a second future cancer, and your increased risk may be higher or lower than the average person.  You may wish to discuss radiation risk further with your study doctor or radiologist.

EXAMPLE: NUCLEAR MEDICINE BONE SCAN WITH Tc-99m

In addition to any scans you may have as a part of your normal medical care, you may have 1 additional nuclear medicine bone scan using a radioactive element, technetium-99m.  This scan is solely for the purpose of this research, and you would not have this additional scan if you do not enroll in this study.  Nuclear medicine uses radioactive material to take pictures inside of your body.  The radiation from a single nuclear medicine bone scan is about 4-5 millisievert.  A millisievert is a measure of radiation dose.  The average person in the United States receives about 3 millisievert per year from natural sources of radiation in our soils, water and air.  The total dose from 1 nuclear medicine bone scan is equivalent to about one and a half years of radiation exposure from natural sources.

After the bone scan, you will still have some radioactivity in the body, which will go completely away in the following 24 - 48 hours. The risk to others is very low, but you may cause sensitive radiation detectors used for security to alarm in the first 1 – 10 hours after the scan.

**Human Subjects and Radiation Dose**

When a research protocol involves the exposure of human subjects to radiation, there are a number of issues of which the Principal Investigator should be aware.

For most imaging procedures involving radiation (e.g., nuclear medicine scans or computed tomography scans) there are no known short-term health or side effects associated with the radiation exposure. The risk associated with these exposures is a theoretical increased risk in future cancer development over the next 10-40 years. For certain imaging procedures (e.g., those used in interventional radiology and cardiology) there may be a wide range of acute and long-term effects (from mild skin erythema to chronic radiation-induced dermatitis to deep ulcerations requiring skin grafts), as well as the increased risk of a future cancer.

In order to convey the potential risks to a study subject, it is important to estimate the dose or dose range from the radiological procedures involved. In general, the UCI Health Radiation Safety Committee (RSC) relies on the available scientific literature to estimate doses from common procedures. In particular, for CT scanning, the RSC will typically use a range of dose from a given exam as reported in *“Radiation Doses in Consecutive CT Examinations from Five University of California Medical Centers,”* (Smith-Bindman, et al., *Radiology,* Vol. 277, Issue 1, October 2015).

For total dose (from all non-standard of care radiological procedures in a study) below 200 millisievert, it is sufficient to provide a dose estimate and a comparison to natural background radiation. In the United States, the average dose from natural sources is about 3.1 millisievert per year. For total dose greater than 200 millisievert, it is generally appropriate to also provide an estimate of increased risk of future cancer. Below is language that is typically recommended in a protocol with dose in excess of 200 millisievert:

“A dose of 185-215 millisievert is equivalent to about 60-70 years of radiation exposure from natural sources.  Radiation exposure at this level may be associated with an increased risk in cancer.  For an average person in the U.S., with no history of cancer, a total dose of 185-215 millisievert may increase their risk of cancer from about 40% to about 42%.  There are many factors that contribute to an individual’s personal risk of a second future cancer, and your increased risk may be higher or lower than the average person.  You may wish to discuss radiation risk further with your study doctor or radiologist.”

In addition, for nuclear medicine procedures, the informed consent should provide a statement regarding the fact that radioactive material will remain in the body after the exam. While most nuclear medicine procedures will result in small dose rates after the exam that do not pose a risk to others, they may be sufficient to set off very sensitive radiation detection devices, such as at large-venue events (e.g., the Super Bowl) or in public buildings (e.g., court houses or other government buildings). Subjects should be made aware of this possibility.

If the protocol involves a therapeutic administration of radiation (from a sealed radioactive source, or machine-produced radiation), a radiation oncologist and medical physicist should be included as research team members, and consulted regarding all aspects of the treatment planning and dose projections, as well as other aspects associated with the treatment, pursuant to California regulations and the terms and conditions of the UCI and UCI Health radioactive materials licenses.