

# POLICIES REGARDING RESEARCH PROTOCOLS ENTAILING HUMAN SUBJECT EXPOSURE TO IONIZING RADIATION

## A. General

1. Any research project that is subject to approval by the VA Research and Development Committee and a VA IRB, and that entails exposure of subjects to ionizing radiation for research purposes, also needs the approval of the VA Radiation Safety Committee (RSC). This includes projects entailing ordinary x-rays, CT scans, PET or other nuclear medicine scans, injection of radioactive materials for tests without imaging, external beam radiation therapy and radionuclide therapy. No such project can be initiated until it has all necessary approvals including that of the RSC. There is an exception to this requirement when it can be established to the satisfaction of the committees that the use of radiation is limited to procedures that are consistent with the customary standard of clinical care.

2. The Radiation Safety Committee is charged with safeguarding individuals with respect to the risks of radiation exposure. The concerns of this Committee include the magnitude of risk (including whether it is excessive and whether it reaches the level of concern for specific risks like skin burns from fluoroscopy), potential danger to a fetus or breast-feeding child, the manner in which the risks are represented in the consent form, and possible excess cumulative radiation exposure if a subject has participated in other research projects.

3. The Radiation Safety Committee is obliged to determine if the radiation risk is so high as to call into question whether the project should be approved. This would normally become an issue with projects that entail radiation absorbed dose to whole body, gonads, bone marrow or lens of the eye exceeding 5 rems, or a dose to other body organs exceeding 15 rems. These values are rough guidelines, as every project will be considered individually. Projects with unusually high radiation exposure may, in any case, call for some extra elaboration of the representation of risk. Projects utilizing radiation such that there is a concern for skin burns from fluoroscopy warrant special consideration.

4. With regard to VA RSC Form 313, "[Part V: Application for Authorization to use Radioactive Materials for Research](#)", completion of this form is needed if the investigator is directly using radioactive materials, for human or non-human purposes, as in a research laboratory. Otherwise, it is not needed. Part V is specifically not needed by investigators who are incorporating in their research nuclear medicine studies (PET scans or otherwise) on human subjects when they are performed in an established nuclear medicine (or PET) department by qualified employees of that department.

5. The following is a **CHECK-LIST** of what is necessary for a submission, with references to relevant portions of this document. *(Note: checkboxes will appear when you print a copy of this section for your use in reviewing the documents and components of your protocol related to Human Exposure to Ionizing Radiation necessary for a complete submission).*

a. **Documents to submit (F)**

- The protocol
- Consent (C; E)
- One-page summary including radiation aspects (F,1)
- Letters of approval (F,3).

b. **Special items in protocol and/or consent**

- Include sentence about exclusion for prior research radiation in protocol (D).
- Address pregnancy and/or breast-feeding issues in protocol and consent (B; E,2).
- Address prior radiation exposure as part of medical care in consent (C,3; E).
- Follow general scheme of examples (E).

c. **Radiation risk representation for nuclear medicine procedures, including PET**

- Formulate consent to include comparison with annual allowed whole body exposures for radiation workers, with a routine procedure like a bone scan, and with the amount of radiation an average person receives under normal circumstances (C,1; E,3).

d. **Radiation risk representation for routine radiological examinations**

- Formulate consent to include comparison with annual allowed exposure for radiation workers to most sensitive organs, with a routine procedure like a chest x-ray, and with the amount of radiation an average person receives under normal circumstances (with qualification) (C,1; C,2; E,1; E,4).
- When relevant (e.g. skull x-ray), radiation risk for cataracts should be addressed (E,1).

e. **Highlighting**

- Highlight radiation-relevant portions of submission.

## **B. Pregnancy and breast-feeding**

1. It is important to exclude subjects who are pregnant from projects involving radiation exposure in order to avoid radiation to the fetus. The favored pregnancy test is a serum test (beta subunit of human chorionic gonadotrophin) rather than a urine test, because the urine test is considerably less sensitive and can take two or more weeks to become positive. If the radiation exposure consists only of simple x-rays of parts of the body remote from the pelvis, thus entailing a very low risk to the fetus, a urine test for pregnancy will be considered acceptable, provided that it is performed no more than two days before the radiation exposure and provided that the subject has not had sexual relations without contraception since four weeks before the pregnancy test. These considerations do not apply to patients without childbearing capability, e.g. by virtue of being post-menopausal or having had a sterilizing procedure. Breast-feeding is generally a contraindication to participation only when the research involves administration of radioactive material that might be secreted in breast milk (e.g. PET scans). A breast-feeding woman may be allowed to participate if she will refrain from breast-feeding for a suitable period after the procedure, to be determined according to the specific radiopharmaceutical used.

2. MRI studies present a special problem with respect to pregnancy screens. They are not, strictly speaking, under RSC jurisdiction because they do not entail ionizing radiation. Pregnancy excludes subjects from MRI's, not because of a known risk, but because the risk is unknown. These procedures are of concern to the RSC because (a) the MRI may (in selected cases) need to be preceded by a screening x-ray for metal and (b) protocols involving MRI will often also involve procedures with radiation such as PET scanning. When MRI and possible screening x-ray are components of a project that also includes PET scans or other procedures for which the exclusion of pregnancy is critical, the serum test for pregnancy will be required.

## **C. Informed Consents: general principles**

1. Informed consents should make several comparisons to help patients understand the radiation risk from the experimental procedures.

- The first comparison should be with allowed annual limits for radiation workers.
- In cases of administration of radiopharmaceuticals, the comparison should be with allowed whole body exposures, as it is possible to calculate a whole body dose equivalent that makes this comparison valid.

For x-ray procedures, the comparison should be:

- (1) with allowed limits to the most sensitive organs, as the exposure during these procedures is localized and we can determine the exposures only in terms of local entrance doses and not in terms of whole body dose equivalents.
- (2) with a routine procedure that is familiar to the subject, such as “chest x-ray” when the investigation entails x-rays and “bone scan” when the investigation entails PET or other nuclear medicine scans.
- Finally, a comparison with the amount of radiation an average person receives per year to the whole body under normal circumstances should be made (about 0.3 rem mainly from background radiation). However, when x-rays are compared with this whole body exposure, we need to explain that this comparison exaggerates the risk, because the subject’s radiation exposure will be to a limited area.

2. The following tables will help you assess radiation exposures and make valid comparisons. The radiograph (x-ray) exposures were determined for the specific conditions of tests performed at VAPHS.

<b>ENTRANCE SKIN EXPOSURE (ESE) OF ROUTINE RADIOGRAPHS</b>	
<b>Radiograph</b>	<b>ESE (mrem)</b>
Chest (PA and lateral)	25
Skull (AP)	133
Skull (lateral)	86
Cervical spine (AP)	117
Cervical spine (lateral)	78
Cervical spine (oblique)	110
Thoracic spine (AP)	157
Thoracic spine (lateral)	846
Thoracic spine (oblique)	364
Lumbar spine (AP)	446
Lumber spine (lateral)	868
Lumbar Spine (oblique)	423
Pelvis (AP)	213
Pelvis (lateral)	846
Pelvis (oblique)	305
Sacrum (AP)	294
Sacrum (lateral)	783
Abdomen (AP)	138
Abdomen (lateral)	516
IV cholangiogram (PA)	213

IV cholangiogram (oblique)	357
CT head	2,800 - 4,800
CT body (spiral)	12,700 - 28,900
Dental (panoramic)	2,000 - 5,000
Dental (bite film)	100 - 500

<b>EFFECTIVE DOSES FOR ROUTINE NUCLEAR MEDICINE STUDIES</b>			
<b>Nuclear medicine scan</b>	<b>Activity (mCi)</b>	<b>Radiopharmaceutical</b>	<b>Effective dose (mrem)</b>
Brain (PET) <sup>2</sup>	50	O-15 water	170
Brain <sup>3</sup>	20	Tc-99m HMPAO	690
Bone <sup>2</sup>	20	Tc-99m MDP	440
Kidney <sup>1</sup>	20	Tc-99m DTPA	310
Kidney <sup>2</sup>	20	Tc-99m MAG3	520
Heart <sup>2</sup>	30	Tc-99m sestamibi	890
Heart <sup>3</sup>	30	Tc-99m tetrofosmin	845
Various PET <sup>2</sup>	10	F-18 FDG	700

References:

1. NCRP Report 100; 1989
2. ICRP Publication 80; 1999
3. ICRP Publication 62; 1993

**3.** Prior medically indicated radiation exposure (as distinct from radiation experienced as a volunteer, and not necessarily of benefit to the subject) has not been considered a contraindication to participation in a project involving radiation. However, the consent form should indicate that the participant might wish to take into account prior medically indicated radiation before deciding on participation in the research.

**4.** When a project involves different groups of subjects and the specifics of radiation exposure differ between the groups, it will often be preferable to have separate consent forms for the different groups, so that the subjects are not confused reading material that does not apply to them. However, since there may be other considerations affecting the number of different consent forms, the RSC may submit a recommendation to the IRB in this matter, and the IRB will have final jurisdiction.

**D. Sample wording to be included in protocols involving Human Subject Radiation Exposure:**

**1.** “Subjects will be excluded who have participated in other research protocols such that their cumulative radiation absorbed dose to whole body, gonads, bone marrow or lens of the eye would exceed 5 rems, or the dose to other body organs would exceed 15 rems in the preceding 12 months.

## **E. Sample wording to be included in Consent Form for protocols involving Human Subject Radiation Exposure:**

### *1. Representative Consent Form paragraph for MRI screening x-ray:*

“If there is reason to suspect that your body contains metal fragments that would make you ineligible for a MRI test, an x-ray to check for the fragments is needed and involves exposure to radiation. The needed x-ray varies, but, in a typical case, would be x-rays of the skull. The maximum amount of radiation exposure that you will receive from the x-ray exam is approximately 0.3 rem (a unit of radiation exposure) to the area of the body evaluated, with minimal exposure of other areas of your body. There is no minimal level of radiation exposure that is recognized as being totally free of the risk of causing genetic mutations or cancer. However, the risk associated with the amount of radiation exposure that you will receive from this additional x-ray exam is considered to be low and comparable to everyday risks. It is 1.5% of the annual radiation exposure (20 rems) that federal regulations permit radiation workers to receive when their exposure is concentrated exclusively in the organs that are most susceptible to genetic defects or cancer. Compared to a common routine diagnostic test, it is equivalent to about 13 routine sets of 2-view chest x-rays. It is about the same as the amount of radiation that an average person normally receives to the whole body during the course of a year; however this comparison exaggerates the risk, because the radiation exposure of your test will be to a limited area.

Exposure to the lens of the eye relates to the risk of cataract formation; the exposure from the test X-ray is 0.3 rem, which may be compared to the annual limit for radiation workers of 15 rems. Women capable of bearing children must have a negative blood test for pregnancy no more than two days before this x-ray, and must not have had sexual relations without contraception for four weeks before the pregnancy test and continuing through the x-ray. You will not be charged for the pregnancy test.

If you have had radiation exposure as part of your medical care, you may wish to take this into account or discuss it with your physician before deciding if you wish to participate in this project.”

*2. Representative Consent Form paragraph regarding pregnancy screen, adaptable according to the specific procedures. X-ray exposure does not mandate exclusion of breast-feeding women:*

“No MRI or PET studies will be performed on pregnant women and no PET studies will be performed on breast-feeding women. Women capable of bearing children must have a negative blood test for pregnancy no more than two days before the MRI scan and before each pair of PET scans, and must not have had sexual relations without contraception for four weeks before the pregnancy test through the completion of the MRI or PET tests. You will not be charged for the test.”

*3. Representative Consent Form paragraph for nuclear medicine scan, e.g. PET scan:*

“Participation in this research study involves exposure to radiation. The total effective radiation dose that you will receive from the 4 PET transmission scans and the 4 injections, 5 millicuries of <sup>18</sup>F-FDG each, is equivalent to 2.2 rems (a unit of radiation exposure). There is no known minimal level of radiation exposure that is recognized as being totally free of the risk of causing genetic defects or cancer. However, the risk associated with the amount of radiation exposure that you will receive from this study is considered to be low and comparable to everyday risks. It is less than one half of the annual radiation dose (5 rems) allowed, by Federal regulation, to a radiation worker during the course of his or her normal work activities. It is about the same as the amount of radiation that an average person normally receives to the whole body over 7 to 8 years. The radiation exposure from your PET scans are equivalent to that from about five bone scans. You will be asked to drink fluids and to urinate frequently after each PET scan to further reduce your radiation exposure. It is important that you inform the investigators of your participation in any other research studies during the past year in which you have been exposed to radiation. If you have had radiation exposure as part of your medical care, you may wish to take this into account or discuss it with your physician before deciding if you wish to participate in this project.”

*4. Representative Consent Form paragraph for x-rays; in this example, a fluoroscopic swallowing study:*

“The amount of radiation exposure that you will receive to the head and neck region is approximately 1.4 rems (a unit of radiation exposure), with minimal exposure to other body areas (based on 3 seconds of exposure per swallow). There is no known minimum level of radiation exposure that is recognized as being totally free of the risk of causing genetic defects or cancer. However, the risk associated with the radiation dose that you will receive from this study is considered to be low and comparable to everyday risks. It is seven percent (7%) of the annual radiation exposure (20 rems) that federal regulations permit radiation workers to receive when their exposure is concentrated exclusively in the organs that are most susceptible to genetic defects or cancer. It is about the same as the amount of radiation that an average person normally receives to the whole body over 4 to 5 years; however, this comparison exaggerates the risk, because the radiation exposure of your test will be to a limited area.

Compared with a common routine diagnostic test, your test is equivalent to about five percent (5%) of an upper GI series. No studies will be performed on pregnant, nursing, or potentially pregnant women. Women capable of bearing children must have a negative serum test for pregnancy no more than two days before the fluoroscopy, and must not have had sexual relations without contraception since four weeks before the pregnancy test. You will not be charged for the test. It is important that you inform the investigators of your participation in any other research studies during the past year in which you have been exposed to radiation. If you have had radiation exposure as part of

your medical care, you may wish to take this into account or discuss it with your physician before deciding if you wish to participate in this project.”

#### **F. Application procedure; requirements of Radiation Safety Committee**

1. Submissions should include the protocol and consent form(s) with highlighting and referencing of parts that deal with exposure to ionizing radiation, PET scans, nuclear medicine scans, x-rays including CT scans, and MRI scans, radiation therapy, injection of radioactive materials not for imaging, pregnancy screen procedure, and screening for prior involvement in research that entails exposure to radiation. There should also be a summary of less than one page that describes the project including all aspects that pertain to radiation exposure as detailed above.

2. Any letters of approval or letters stating conditions for approval from other committees of the VA or the University of Pittsburgh should be included in the submission.

3. As needed, assistance with the details regarding radiation exposure may be obtained by consulting the Radiation Safety Officer, Mitch Belanger, MSHP, (132N-U), University Drive, (412) 360-3221, mitch.belanger@va.gov.

4. The above materials should be submitted to the Chairperson of the Radiation Safety Committee, Barry H. Kart, M.D., FACR, Radiology Program (132X-U), University Drive, (412) 688-6105) Barry.Kart@med.va.gov. Submission by electronic means or floppy disk is acceptable.

5. Submission to the VA Radiation Safety Committee is acceptable, before, concurrently with, or after submission to the other committees, **however, work may not begin without RSC and R&D committee approval** The RSC meets quarterly, but every effort will be made to expedite action, if necessary by consulting members between regular meetings.