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**Radiation Ethics Form**

for external sponsors

The Radiation Ethics form is intended to assess the **additional** radiation dose related to a subject‘s participation in medical scientific research involving ionizing radiation. This additional radiation dose can, e.g., be the result of new procedures and/or additional time points in existing radiological procedures. Radiation dose as a result of standard medical care does not count as additional dose and therefore these procedures should not be listed on this form. To judge whether a procedure is part of standard medical care, the generally accepted directives for the relevant conditions should be used (if applicable and available). The resulting dose assessment will subsequently be judged by the medical review and ethics committee METC Oost-Nederland.

**How to use this form:**

* The coordinating investigator completes the non-marked questions on the procedures.
* A medical physicist/radiation expert completes the marked questions and must check the form for optimization measures and provide radiation dose calculations.
* The coordinating investigator completes the ethical consideration.
* The coordinating/principal investigator and medical physicist/radiation expert sign the form.

## General information

|  |  |
| --- | --- |
| 1. Protocol ID |  |
| 1. Protocol title |  |
| 1. Sponsor |  |
| 1. Principal investigator |  |
| 1. Coordinating investigator   (Contact person) |  |

## Dose Results

**Result** (*to be completed by the medical physicist/radiation expert)*

This table provides information on the extra radiation dose (effective dose [mSv]) per subject as a result of participation in the study, the corresponding risk category and minimum required level of benefit. This result follows from information and calculations provided in question 6 to 16. Radiation dose that results from standard of care is not included.

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| --- | --- | --- | --- |
| **Effective dose (mSv)** | | **Risk category1** | **Level of benefit2** |
|  | <0.1 | I (< 5·10-6) | Acquisition of knowledge |
|  | 0.1-1 | IIa (5·10-6 – 5·10-5) | Acquisition of knowledge, resulting in health benefit |
|  | 1-10 | IIb (5·10-5 – 5·10-4) | Acquisition of knowledge, directly aimed at prevention or cure of disease |
|  | 10-20 | IIIa (5·10-4 – 10-3) | Acquisition of knowledge, directly aimed at prevention or cure of serious disease |
|  | >20 | IIIb (> 10-3) | Acquisition of knowledge, directly aimed at saving lives or mitigation of serious diseases |

1 According to ICRP 62, total detriment

2 The information in appendix A can be used for the interpretation of ‘Level of Benefit’

**Dose Assessment**

**Procedures** *(to be completed by the investigator)*

**7.** Required procedure(s) involving additional ionizing radiation (procedure(s) listed in the study protocol that are not standard of care)3

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| --- | --- | --- | --- | --- |
| **Required procedure(s) (e.g. 18F-FDG, (low-dose, contrast enhanced) CT, etc.)** | **Goal of procedure (short)** | **Scanning range (e.g. thorax, abdomen, etc.) or reference to clinical standard** | **Number of procedures per patient** | **Specify procedure (e.g. administered activity, minutes per bedposition, CT specific protocols (contrast etc.), other parameters)** |
|  |  |  |  |  |
|  |  |  |  |  |
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3 Please contact a Radiologist or Nuclear Medicine physician if unsure which procedure is required for the study and whether procedures are not standard of care and therefore should be listed.

**8.** Please specify the age requirements for subjects participating in this study, according to the inclusion/exclusion criteria.

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9. Please provide a justification on the number of volunteers needed (this information can be copied from the study protocol’s sample size section):

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**10.** Will subjects of the study be informed that it is not desirable to participate in other research studies involving exposure to radiation? Yes No

**Dose assessment** (*to be completed by the medical physicist/radiation expert)*

**11.** Specification of the dose involved for the required procedure(s)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **A. Nuclide / Compound** | **Activity per administration [MBq]** | **e504**  **[mSv/MBq]** | **Effective dose per administration [mSv]** | **Number of administrations** | **Committed effective dose E50 [mSv]** |
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|  |  |  |  |  |  |
| **B. Type X-ray apparatus  E.g. (mobile) X-ray, mobile C-arc, angiosuite, cathlab, CT or CT part of PET-CT or SPECT-CT examination** | **X-ray / fluoroscopy: DAP [Gycm2] or  CT: DLP [mGy.cm]** | **Conversion factor5 [mSv/(Gy.cm2)] or [mSv/(mGy.cm)]** | **Effective dose per procedure [mSv]** | **Number of procedures** | **Effective dose**  **[mSv]** |
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|  |  |  |  |  |  |
|  |  |  |  | **Total dose A+B [mSv]:** |  |

4,5 References:

ICRP 128: e50 [mSv/ MBq]

ICRP 102: DLP [mSv/ DLP]

IAEA website: [mSv/ DAP]

**12.** References on the used coefficients if other than the IAEA of IRCP publications mentioned above:

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**13.** Radiation dose after correction for relative detriment:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Research group** | **Relative detriment factor**  **ICRP 62 Used6** | | **Total dose A+B**  **[mSv]** | **Relative dose for detriment assessment (Relative detriment factor × Total dose A+B) [mSv]** |
| Children (< 18 years) | 2-3 |  |  |  |
| Adults (18-50 years) | 1 |  |  |  |
| Adults (> 50 years) |  |  |  |  |
| Patients with terminal disease |  |  |  |  |

6 NCS publication 26, table 4 can also be used.

**14.** Explain if another factor is used than is advised by ICRP 62/ NCS 26: (*to be completed by the medical physicist/radiation expert)*

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| **15.**Will the threshold dose (mGy) from ICRP 118 for tissue and/or organ effects be exceeded? Yes No |

**16.** If yes is answered at question 15, please provide numbers and clarification on estimated absorbed dose per relevant organ/tissue. If not provided in ICRP 118, please provide estimated threshold dose and literature reference.

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## Ethical consideration

***This section should be completed by the researcher after the medical physicist’s assessment of the additional radiation dose related to participation in the study (above) or after prior consultation with a medical physicist.***

**17**. The dose results as indicated at the beginning of this form show the additional effective radiation dose to a subject participating in this study. For each risk category the Results table further provides a corresponding “Level of benefit” to balance the associated radiation risk. For the purpose of ethical review, please explain the balance between the radiation risk and the level of benefit to be reached by performing the study as indicated in the protocol. If ‘yes’ is answered in question 15, please also specify the additional burden in relation to disease status. More information on the interpretation can be found in the appendix A.

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## Signatures

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| **Approval responsible investigator**  The responsible researcher declares that all information given in this Radiation Ethics Form is accurate.  Name responsible researcher:  Date:  Signature: |

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| **Approval medical physicist/radiation expert**  The medical physicist/radiation expert declares that the assessment of the radiation dose based on the Researcher’s information is correct and that possible optimization in terms of the ALARA concept has been included and advised.  Function:  Name:  Date:  Signature: |

## References

NCS publication 26 (Relative Detriment factor)

[http://radiationdosimetry.org/ncs/documents/human-exposure-to-ionising-radiation-for-clinical-and-research-purposes-radiation-dose-risk-estimates](https://radboudumc.zenya.work/management/hyperlinkloader.aspx?hyperlinkid=10609f32-506e-4e30-8bc7-3cd3525f4ca7)

IAEA website: (DAP [mSv/ DAP])

[https://rpop.iaea.org/RPOP/RPoP/Content/InformationFor/HealthProfessionals/4\_InterventionalRadiology/patient-staff-dose-fluoroscopy.htm](https://radboudumc.zenya.work/management/hyperlinkloader.aspx?hyperlinkid=0be0ba38-1a76-4f3d-8a88-2a7a10d283dd)

ICRP-62 (Relative Detriment factor)

[http://www.icrp.org/publication.asp?id=ICRP%20Publication%2062](https://radboudumc.zenya.work/management/hyperlinkloader.aspx?hyperlinkid=3f88790e-0e88-4164-bc48-a96e23b3af68)

ICRP-102 (DLP [mSv/ DLP])

[http://www.icrp.org/publication.asp?id=ICRP%20Publication%20102](https://radboudumc.zenya.work/management/hyperlinkloader.aspx?hyperlinkid=bdd10538-c47f-4436-beda-3007f9d198cc)

ICRP-118 (threshold dose [mGy])

[http://www.icrp.org/publication.asp?id=ICRP%20Publication%20118](https://radboudumc.zenya.work/management/hyperlinkloader.aspx?hyperlinkid=1e53386a-b97e-44d6-8974-39329627d533)

ICRP-128 (e50)

[http://www.icrp.org/publication.asp?id=ICRP%20Publication%20128](https://radboudumc.zenya.work/management/hyperlinkloader.aspx?hyperlinkid=2908740b-3704-4804-8571-4444d8a5c15f)

NCS rapport 26 (Interpretation of effective dose with corresponding risk category and associated level of benefit, advisory document by the ‘Nederlandse commissie voor stralingsdosimetrie’)

[http://radiationdosimetry.org/documents/ncs/human-exposure-to-ionising-radiation-for-clinical-and-research-purposes-radiation-dose-risk-estimates?worker=add\_footer&text=The+NCS+report+has+been+&file=files/documents/0000096/264-ncs-report-26-radiation-dose-and-risk-estimates.pdf](https://radboudumc.zenya.work/management/hyperlinkloader.aspx?hyperlinkid=83a08da9-0182-4cc1-bfa9-de0087d6d6bd)

## Interpreting risk categories

***The text below is based on the NCS rapport 26 from the Dutch Committee for dosimetric calculations (Human Exposure to Ionising Radiation for Clinical and Research Purposes: Radiation Dose & Risk Estimates; Publication of the Netherlands Commission on Radiation Dosimetry; May 2016)***

Communication of the risks associated with the radiation dose received by a patient or healthy volunteer is a task of the (clinical) investigator. To put these risks into perspective, it is useful to consider the annual background radiation level in the Netherlands (~2.5 mSv), and to be aware that those levels in other European countries and elsewhere can be in the order of 10 mSv or even higher ([http://www.world-nuclear.org](https://radboudumc.zenya.work/management/hyperlinkloader.aspx?hyperlinkid=af8aa05e-2039-48a3-b98e-08bff85d1b0c)). It should be noted that the risk categories listed in Table 3 apply to normal healthy adults. In case of children or elderly volunteers, correction factors as indicated in section 4.1 should be applied before using Table 3. On the basis of the data presented in Tables 2 and 3, age and gender adjusted risk categories and corresponding dose constraints are given in Table 4. In addition, case specific correction factors for patients with a short life expectancy may be required. For the latter it should be noted that the anticipated time-to-event for cancer induction is more than ten years. Both life expectancy and time-to-event should be taken into account before communicating radiation risks to patients.

*Category I*

This is the lowest risk category with a statistical probability of less than five in a million to develop radiation induced cancer, to be compared with the natural incidence of cancer, which is about 30%. The dose in this category is less than 0.1 mSv. Each member of the public in the Netherlands will receive this dose within a few weeks, just from natural background radiation. In addition, this dose is equivalent to that received during a transatlantic return flight.

Only a minor level of benefit is sufficient for approval of research in this category, including investigations that aim to increase knowledge.

*Category IIa*

This category represents an intermediate level of risk. The range of 0.1 to 1 mSv corresponds with a maximum risk of five in hundred thousand and is less than the annual background dose.

To justify these risks a research proposal should at least lead to potential health benefit for future patients. Examples are repeated mammography procedures or X-ray examinations of the thorax to gather data for prospective cohort studies.

*Category IIb*

This category represents a moderate level of risk. The range of 1 to 10 mSv corresponds to a maximum risk of five in ten thousand, and is of the same order of magnitude as the annual natural background radiation in various parts of the world.

To justify these risks a moderate benefit is required, which will be more directly aimed at the diagnosis, cure or prevention of diseases in the future. Examples are the following studies in both patients and healthy controls that use investigational or routine CT/PET/SPECT scans: drug development studies (i.e. imaging studies before and after administration of a therapeutic drug), studies needed for better understanding of pathophysiological mechanisms underlying disease (e.g. the study of cognition from healthy controls to patients with dementia, blood pressure in relation to hypertension, body weight in relation to obesitas, etc), and studies primarily intended for the development of novel imaging procedures, including the evaluation of new radiopharmaceuticals. Preclinical data should support the value of such studies.

*Category IIIa*

Category IIIa represents a substantial level of risk. The range of 10-20 mSv corresponds with a maximum risk of one in a thousand. To place this level into context, the maximum allowed dose for radiological workers is 20 mSv per year.

To justify research in this category, its benefit has to be related directly to prevention or cure of serious diseases in the future. Examples are repeat CT/PET/SPECT scans and scans using tracers labelled with long lived radionuclides, such as 89Zr labelled monoclonal antibodies.

*Category IIIb*

Category IIIb exceeds the maximum allowed dose level that radiological workers may receive annually. To justify research in this category, the benefit will have to be directly related to saving lives or mitigating serious diseases in the future. For this category benefits also have to be weighed against possible tissue reactions that may be induced (Table 1). These effects should be communicated explicitly to the subject, along with the stochastic effects. Examples are studies in cancer patients who receive radiotherapy, such as repetitive PET/CT scans during radiation treatment, and extensive PET/CT response monitoring scans (with or without 89Zr labelled monoclonal antibodies) during experimental chemotherapy in terminal cancer patients who

themselves may or may not benefit from the treatment.

The risk categories mentioned above assume that the subject has not undergone research studies involving exposure to radiation within a year preceding inclusion in a research protocol associated with one of the categories. In particular for healthy volunteers, it is their own responsibility to report any exposure to radiation within the preceding 12 months. Nevertheless, it is the responsibility of the investigator to explicitly ask subjects for such exposure. In case of healthy volunteers, it is advised to incorporate a statement concerning previous exposure in the Informed Consent Form. The dose associated with that exposure should be taken into account in the risk evaluation. As a general principle, each investigator should emphasize that it is undesirable for the same healthy volunteer to repeatedly take part in studies involving exposure to radiation.