National Institutes of Health

Radiation Safety Committee

IMPROVING INFORMED CONSENT for RESEARCH RADIATION STUDIES

Endorsed and approved for distribution by the NIH Human Subjects Research Advisory Committee (HSRAC) and the NIH Medical Executive Committee (MEC).

October 17, 2001

SUMMARY

The NIH Clinical Center supports approximately 950 clinical protocols for intramural research. Most protocols use radiation as *medically indicated*, i.e., for diagnosis or treatment when such use is considered to be standard medical procedure for the clinical management of the patient. In approximately 150 of these protocols, the radiation exposure is described as *indicated for research* whereby the radiation use does not meet the criteria of "medically indicated" and, therefore, must be reviewed and approved by the NIH Radiation Safety Committee (RSC). Also, all exposures of healthy clinical research volunteers must be approved by the RSC. Additionally, the Radioactive Drug Research Committee (RDRC), a subcommittee of the RSC, must also approve protocols conducted with certain radioactive research drugs (radiopharmaceuticals that are neither FDA-approved drugs nor used under an IND or NDA).

To increase the efficiency of the protocol review and approval process, reduce stipulations to approvals, and improve the communication of information to prospective subjects, the RSC completed the following initiatives:

- Pre-submission assistance and review service
- Electronic dissemination of protocol applications and communications
- Adoption of effective dose to quantify and compare radiation risk
- Revision of radiation exposure guidelines for research subjects
- Development of informed consent language templates that simplify presentation of radiation risk
- Development of a supplementary informational pamphlet for research subjects, and
- Creation and continuous development of a protocol assistance website.

These services are now available. Investigators are encouraged to use these services and materials. In addition, reference materials and documents cited in this report are available for viewing and printing at the RSC Protocol Assistance Center. The URL for this site will be distributed as soon as it is available.

New dose guidelines and consent language statements are currently incorporated into new protocol applications and submissions for amendment or triennial review. Principal Investigators may elect to incorporate the revised dose guidelines and consent language sooner than at the time of triennial review or need for amendment. Applications and questions may be directed to the RSC Clinical Protocol Administrator, Lisa Coronado, at coronado@mail.nih.gov.

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PRE-SUBMISSION ASSISTANCE AND REVIEW SERVICE

Investigators assembling a protocol application for submission to the RSC for the first time, or those in need of assistance in amending or preparing the triennial review and renewal application are encouraged to consult the RSC Protocol Assistance Center. Additional information and resource material is available by contacting the RSC Clinical Protocol Administrator, Lisa Coronado, at Coronado@mail.nih.gov or by calling 301-496-2253.

Investigators may submit a single copy of the application (i.e., NIH form 88-23(a), protocol and consent documents) to the Clinical Protocol Administrator for review *prior* to official submission to the RSC. Use of this review service has demonstrated a significant reduction in the number of stipulations to protocol approval, and results in a more efficient and expedient process. Please note that pre-review materials must be submitted *at least* two weeks prior to the scheduled RSC meeting. Official submissions, with 13 copies, are due at least one week prior to the meeting.

ELECTRONIC SUBMISSION AND DISSEMINATION

The RSC now accepts electronic submission of protocol applications and related documents. For applications requiring review by the full Committee (i.e., new, amendment and triennial review), investigators are encouraged to submit one copy electronically for pre-review, and, after receipt of pre-review comments and changes (if needed), submit the remaining copies (13) via interoffice mail or deliver to the RSC Clinical Protocol Administrator in Building 21, Room 233. Please note that original signatures are required on page 1 of the NIH form 88-23(a), *"Application for Authorization to use Radiation in Research Involving Human Subjects",* and, therefore, cannot be transmitted electronically. Please send this page via delivery or interoffice mail.

In addition, stipulation memos, triennial review reminders and approval notices are now transmitted electronically. Original approval documents and copies of the pink approval form will continue to be distributed, via interoffice mail, to the Protocol Coordination Services Center, Authorized User, Principal Investigator, respective IRB Chair and, if appropriate, the CC Radiopharmacy. Please note the applicant's response to stipulation memos may also be transmitted to the RSC electronically.

ADOPTION OF EFFECTIVE DOSE

SUMMARY

Although not perfect, many radiation safety experts, in particular, the Medical Internal Radiation Dosimetry (MIRD) Committee, endorse the concept of effective dose (E) as an appropriate method to convey the potential risk associated with radiation exposure for volunteers participating in investigational protocols (Poston, 93). In addition, effective dose provides a *single* number (or magnitude) of risk from participating in a research radiation study that can be easily compared to the risk associated with other types of radiation-related procedures or sources of exposure (e.g., natural background). Thus, from the subject's perspective, this comparison is simple and conveys the risk in a meaningful way. Therefore, the RSC will now require the calculation and reporting of the total effective dose (E) for all *research* radiation studies, with the exception of radiation therapy studies. The effective dose shall be included on the NIH form 88-23(a) dose table, and cited in the consent document.

RSC CONSIDERATIONS FOR ADOPTION OF EFFECTIVE DOSE

The responsibility of making a risk-versus-benefits analysis is inherent in the medical decision to perform a specific test. This responsibility is magnified when the test will offer no benefit to the subject. The research subject must be informed of the risks in easily understood language. When the research involves radiation exposure, there is the added challenge to produce an informative consent risk statement.

Analyzing and presenting risk information associated with radiation exposure is difficult. Many of the data used to derive risk factors were generated from *uniform whole-body* external exposure situations. This is not the typical exposure situation encountered in a clinical research setting. Many of the exposures associated with research studies, such as radiographic and fluoroscopic exams, are *partial-body* exposures. In addition, studies involving radiopharmaceuticals produce *nonhomogeneous* exposure to the whole body, in which the dose for each organ varies greatly depending on the biokinetics of the material.

Often, the concept of ***total-body dose*** or ***whole-body dose*** (i.e., the total energy deposited in the body divided by the mass of the body) was used to evaluate the risks of different nuclear medicine

procedures. However, the total body dose does not account for the varying radiosensitivities of the different organs and tissue. The concept of ***effective dose equivalent*** **(H_E)**, first described by ICRP Publication 26 (ICRP 26) and endorsed in ICRP Publication 52 (ICRP 52), was then accepted as a better way to evaluate the total risk of a procedure. The calculation of effective dose equivalent involves multiplying individual organ doses by risk weighting factors and summing the individual contributions into a single value. However, some have criticized this measure primarily because the tissue weighting factors used in the calculation were intended for use in the radiation worker population, not the general population.

In 1991, the ICRP, in Publication 60 (ICRP 60), and later updated in ICRP Publication 73 (ICRP 73), developed tissue weighting factors based on the *entire population* and introduced the quantity of ***effective dose (E)***. Note that the main difference between effective dose and effective dose equivalent is in the weighting factors used in the calculation. The RSC believes that the use of effective dose is more suitable for evaluating risk for subjects participating in clinical studies that involve research radiation. However, the RSC acknowledges that citing and using *only* an effective dose results in a loss of important specific organ dose information. This limitation to effective dose is often not recognized nor appreciated. Specific organ dose information is important when considering the varying sensitivity of organs to potential effects, particularly acute effects that may be possible in radiation therapy studies. Furthermore, the risk coefficients used in calculating effective dose were intended to apply to low doses and low dose rate scenarios. Radiation therapy studies generally involve high organ doses or high dose rates in which the predominant concern is with acute organ effects rather than the delayed effects of secondary cancer. Therefore, it is deemed inappropriate to use effective dose for radiation therapy studies (Poston, 93 and Toohey).

The RSC will now require the calculation and reporting of the total effective dose (E) for all *research* radiation studies, with the exception of radiation therapy studies. For these latter studies, the risk discussion will focus on the acute organ effects, specific to the study and subject population. In all other studies, the effective dose value shall be included in the NIH form 88-23(a) dose table, and cited in the consent document(s). For illustration purposes, an example of effective dose calculation follows. Assistance with calculating effective dose is available by consulting the RSC Assistance Center or by contacting the RSC Clinical Protocol Administrator.

EXAMPLE: CALCULATION OF EFFECTIVE DOSE

The effective dose is the sum of the weighted equivalent doses in all the tissues and organs of the body. It is given by the expression:

$$E = \Sigma_T (w_T \times H_T)$$

Where:

E = the effective whole body dose

w_T = the tissue weighting factor for tissue T

H_T = the equivalent dose in tissue or organ T; absorbed dose averaged over a tissue or organ and weighted for the radiation quality. The radiation quality factor for clinical radiation (photons, x-rays) is 1; thus, the equivalent dose is equal to the absorbed organ dose.

TISSUE WEIGHTING FACTORS (ICRP 73, 1996)[1]

Tissue or Organ	**Weighting factor, w_T**
Gonads	0.20
Bone Marrow (red)	0.12
Colon	0.12
Lung	0.12
Stomach	0.12
Bladder	0.05
Breast	0.05
Liver	0.05
Oesophagus	0.05
Thyroid	0.05
Skin	0.01
Bone Surfaces	0.01
Remainder	0.05[2,3]

[1] The values have been developed from a reference population of equal numbers of both sexes and a wide range of ages. In the definition of effective dose, they apply to workers, to the whole population, and to either sex.

[2] For purposes of calculation, the remainder is composed of the following additional nine tissues and organs: adrenals, brain, small intestine, kidney, muscle, pancreas, spleen, thymus and uterus. The list includes organs that are likely to be selectively irradiated. Some organs in the list are known to be susceptible to cancer induction. If other tissues and organs subsequently become identified as having a significant risk of induced cancer they will then be included either with a specific w_T or in this additional list constituting the remainder. The latter may also include other tissues or organs selectively irradiated.

[3] In those exceptional cases in which one of the remainder tissues or organs receives an equivalent dose in excess of the highest dose in any of the twelve organs for which a weighting factor is specified, a weighting factor of 0.025 should be applied to that tissue or organ and a weighting factor of 0.025 to the average dose in the rest of the remainder as defined above.

CALCULATION OF EFFECTIVE DOSE

Material: *F-18 FDG*

Administered Quantity *10 mCi per scan*

Subject Age: *ADULT*

		ICRP 73 (1996)	
Organ	**Dose (rem)**	**Weighting Factor (w_t)**	**Effective Dose**
Adrenals	0.480	remainder	
Brain	0.700	remainder	
Breasts	0.340	0.050	0.017
Esophagus [1]	0.440	0.050	0.022
Gallbladder Wall	0.490		
GI-tract: Lower Large Intestine	0.510		
Small Intestine	0.470	remainder	
Stomach	0.470	0.120	0.056
Upper Large Intestine	0.460		
Colon [2]	0.482	0.120	0.058
Heart Wall	2.200	0.025	0.055
Kidneys	0.740	remainder	
Liver	0.580	0.050	0.029
Lungs	0.640	0.120	0.077
Muscle	0.390	remainder	
Ovaries	0.530	0.200	0.106
Pancreas	0.960	remainder	
Red Marrow	0.470	0.120	0.056
Bone Surfaces	0.410	0.010	0.004
Skin	0.300	0.010	0.003
Spleen	1.400	remainder	
Testes	0.410	(ovaries dose is greater)	
Thymus	0.440	remainder	
Thyroid	0.390	0.050	0.020
Urinary Bladder Wall [3]	3.200	0.050	0.160
Uterus	0.620	remainder	
REMAINDER AVE	0.689	0.025	0.017
EFFECTIVE DOSE		1.000	**0.680**

NOTES:

[1] Since no dose is explicitly tabulated for esophagus, thymus dose is used (as per ICRP 80)

[2] Colon Dose estimated by [0.57 ($Dose_{ULI}$) + 0.43 ($Dose_{LLI}$)] (as per ICRP 80).

[3] Dynamic urinary bladder model used; void interval of **_1.5__ hours**

Top three highest-dosed organs are highlighted

DOSIMETRY SOURCE: Coronado, L. (F-18)FDG Internal Rad.Dosim. for Research Protocols, NIH, 10/30/91.

RISK ESTIMATION

Members of the NCI Radiation Epidemiology Branch and Radiation Effects Branch were consulted to identify the most reasonably appropriate risk estimates to use for determining the increase risk of cancer fatality for subjects participating in research radiation studies (Gilbert, 01). The following estimates, from the International Commission on Radiological Protection (ICRP), publication 60 (p. 22), were recommended:

NOMINAL PROBABILITY COEFFICIENTS FOR STOCHASTIC EFFECTS

Detriment x 10^{-4} per rem

Exposed Population	***Fatal Cancer***	***Non-fatal Cancer***	***Severe Hereditary Effects***	***Total***
Children (0-19)	8.0	1.6	1.6	11.20
Adult workers (20-60)	4.0	0.8	0.8	5.60
Geriatric (over 50)	1.0	0.2	0.65	1.46
Whole Population (0-90)	5.0	1.0	1.3	7.30

These estimates are intended to apply to low doses and dose rates. They were developed by reducing linear estimates from the Atomic bomb survivors by a factor of two in order to reflect reduction in risk for dose received at low doses and dose rates. These risk coefficients are age and sex averaged, and for the age group of adult workers the risk is reduced to 80% of that for the whole population. For children, the risks is 2-3 times greater than for adults, while for persons aged 50 years or over, the risk is $1/5^{th}$ to $1/10^{th}$ of that for younger adults (ICRP 60 and Mountford, 95).

The additional fatal cancer risk for a subject group, participating in a research radiation study, can be estimated by the following expression:

(Total effective dose for the study, in rem) X (fatal cancer risk per rem for age group)

As illustrated in the previous effective dose calculation (FDG scan of 10 mCi), the additional *estimated* increase in fatal cancer risk for the adult subject is as follows:

(0.680 rem) (4.0 x 10^{-4} per rem) = 0.00027 = 0.027 %

Note that the natural incidence of fatal cancer is 25%. Therefore, the theoretical total risk of fatal cancer for the group of adult subjects participating in this example study is predicted as 25.027 %, or, rounded to 25.03%. It is important to remember that effective dose is a theoretical quantity; no organ or system, including the total body, actually receives the calculated dose.

REVISION OF DOSE GUIDELINES

In response to comments and feedback from the NIH clinical investigator community, the RSC has revised the radiation dose guidelines for subjects participating in research radiation studies. The revised guidelines are now based upon total effective dose instead of an organ or tissue dose value. In addition, the quarterly organ guideline value of 3 rem is eliminated; the annual (i.e., 12 consecutive months) guideline value of 5 rem is retained, and defined as a total effective dose. The guideline value for pediatric subjects (under the age of 18 years) remains at $1/10^{th}$ the adult value, or 0.5 rem per year.

Note that the RSC dose guideline values are separate and distinct from the FDA (Food and Drug Administration) radiation dose limits applicable to the use of "radioactive research drugs", as defined in 21 CFR 361.1. Radiation exposure to adult subjects participating in RDRC (Radioactive Drug Research Committee) reviewed and approved studies must be within the regulatory limits of 3 rem to the whole body, active blood-forming organs, lens of the ye, and gonads from a single administration, and 5 rem annually. Limits of exposure for pediatric subjects (under the age of 18 years) are $1/10^{th}$ of the adult limits.

CONSENT LANGUAGE TEMPLATES

SUMMARY

The previous *"Guidelines for Informed Consent Statements for Clinical Research Protocols Involving Radiation Exposure for Research Purposes and Not for the Medical Benefit of the Subject (Patients and Normals)"* have been revised and expanded. The RSC now offers and strongly encourages informed consent language templates that more clearly present the radiation risk associated with the research radiation exposure than previous statements. Risk for this purpose is defined as the increased possibility of fatal cancer. The template chosen by the investigator for inclusion in the consent document is dependent upon the total effective dose associated with the study:

TEMPLATE A

- Total effective dose is less than or equal to 0.100 rem (or 100 mrem).
- No need to list the 3 highest organ doses; include only the single highest dosed organ.
- Use of "minimal risk" instead of "safe" to describe the radiation exposure.
- Increased fatal cancer risk from 0.1 rem effective dose is calculated as:

  $(4.0 \times 10^{-4}$ per rem) x (0.1 rem) = 0.00004 = 0.004 % for adults

TEMPLATE B

- Total effective dose is greater than 0.100 rem (or 100 mrem) and equal to or less than 5 rem.
- Retained requirement to list the 3 highest organ doses.
- Use of "minimal risk" instead of "safe" to describe the radiation exposure.
- Increased fatal cancer risk from 5.0 rem effective dose is calculated as:

  $(4.0 \times 10^{-4}$ per rem) x (5 rem) = 0.002 = 0.2 % (adults)

TEMPLATE C

- Total effective dose is greater than 5 rem.
- Typically used in radiation therapy studies in which the total effective dose is much greater than 5 rem.
- Use of "acceptable risk" instead of "safe" to describe the radiation exposure.
- Risk discussion shall focus on the acute and chronic organ effects. Statements shall be developed specific to the study and subject population.

TEMPLATE A *(Total effective dose less than or equal to 100 mrem)*

This research study involves exposure to radiation from (*insert type of procedure or procedures*). Please note that this radiation exposure is **not** necessary for your medical care and is for research purposes only. The total amount of radiation you will receive in this study is from (*insert maximum number*) injections (*scans or repetitions*) of (*insert quantity of radioactive material, in units of millicuries; or type of x-ray procedure).* The NIH Radiation Safety Committee[1] has reviewed the use of radiation in this research study and has approved this use as involving minimal risk and necessary to obtain the research information desired.

Using the standard way of describing radiation dose, from participating in this study, you will receive a total of (*XX)* rem to your *(insert highest-dosed organ)*. All other parts of your body will receive smaller amounts of radiation. Although each organ will receive a different dose, the amount of radiation exposure you will receive from this study is equal to a uniform whole-body exposure of less than (*insert total effective dose value*). This calculated value is known as the "effective dose" and is used to relate the dose received by each organ to a single value. The amount of radiation you will receive in this study is below the dose guideline established by the NIH Radiation Safety Committee for research subjects. This guideline is an effective dose of 5 rem (or 5,000 mrem) received per year[2].

For comparison, the average person in the United States receives a radiation exposure of 0.3 rem (or 300 mrem) per year from natural background sources, such as from the sun, outer space, and from radioactive materials that are found naturally in the earth's air and soil. The dose that you will receive from participation in this research study is about the same amount you would normally receive in *(insert number)* months from these natural sources. If you would like more information about radiation and examples of exposure levels from other sources, please ask the investigator for a copy of the pamphlet called, *An Introduction to Radiation for NIH Research Subjects*.

(INCLUSION OF THIS PARAGRAPH IS OPTIONAL) The effects of radiation exposure on humans have been studied for over 60 years. In fact, these studies are the most extensive ever done of any potentially harmful agent that could affect humans. In all these studies, no harmful effect to humans has been observed from the levels of radiation you will receive from taking part in this research study. However, scientists disagree on whether radiation doses at these levels are harmful. Even though no effects have been observed, some scientists believe that radiation can be harmful at any dose - even low doses such as those received during this research.

One possible effect that could occur at these doses is a slight increase in the risk of cancer. Please be aware that the natural chance of a person getting a fatal cancer during his/her lifetime is about 1 out of 4 (or 25 percent). The increase in the chance of getting a fatal cancer, as a result of the radiation exposure received from this research study, is less than 1 in 25,000 (or much less than $1/100^{th}$ of a percent). Therefore, the total risk of fatal cancer may be estimated to increase from 25 percent to 25.01 percent. This additional risk is too small to be measured and is generally regarded as insignificant.

(INCLUSION OF THIS PARAGRAPH IS OPTIONAL) Another concern some people may have about radiation exposure is the effect on fertility or on the possibility of causing harm to future children (i.e., genetic effects). The doses you will receive in the study are well below the levels needed to affect fertility. In addition, genetic effects have not been seen in humans who have been exposed to radiation. The information on genetic effects currently available is based on animal studies using much larger doses of radiation than the amount you will receive in this study.

Please tell your doctor if you have taken part in other research studies or received any medical care at the NIH or other places or hospitals that used radiation. This way we can make sure that you will not receive too much radiation. Consider x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

If you are pregnant or breast feeding, you may not be able to participate in this research study. It is best to avoid radiation exposure to unborn or nursing children since they are more sensitive to radiation than adults.

TEMPLATE B *(100 mrem < Total effective dose = < 5 rem)*

This research study involves exposure to radiation from *(insert type of procedure or procedures)*. Please note that this radiation exposure is **not** necessary for your medical care and is for research purposes only. The total amount of radiation you will receive in this study is from (*insert maximum number*) injections (scans or repetitions) of (*insert quantity of radioactive material, in units of millicuries; or type of x-ray procedure).* The NIH Radiation Safety Committee[1] has reviewed the use of radiation in this research study and has approved this use as involving minimal risk and necessary to obtain the research information desired.

Using the standard way of describing radiation dose, from participating in this study, you will receive a total of *XX* rem to your (*insert highest-dosed organ*), *XX* rem to your (2^{nd} *highest-dosed organ*), and *XX* rem to your (3^{rd} *highest-dosed organ*). All other organs will receive smaller amounts of radiation.

Although each organ will receive a different dose, the amount of radiation exposure you will receive from these procedures is equal to a uniform whole-body exposure of (*insert effective dose value, in rem*). This calculated value is known as the "effective dose" and is used to relate the dose received by each organ to a single value. The amount of radiation received in this study is within the dose guideline established by the NIH Radiation Safety Committee for research subjects. The guideline is an effective dose of 5 rem (or 5,000 mrem) received per year[2].

For comparison, the average person in the United States receives a radiation exposure of 0.3 rem (or 300 mrem) per year from natural background sources, such as from the sun, outer space, and from radioactive materials that are found naturally in the earth's air and soil. The dose that you will receive from this research study is about the same amount you would normally receive in (*insert number)* years from these natural sources. If you would like more information about radiation and examples of exposure levels from other sources, please ask the investigator for a copy of the pamphlet called, *An Introduction to Radiation for NIH Research Subjects*.

(INCLUSION OF THIS PARAGRAPH IS OPTIONAL) The effects of radiation exposure on humans have been studied for over 60 years. In fact, these studies are the most extensive ever done of any potentially harmful agent that could affect humans. In all these studies, no harmful effect to humans has been observed from the levels of radiation you will receive by taking part in this research study. However, scientists disagree on whether radiation doses at these levels are harmful. Even though no effects have been observed, some scientists believe that radiation can be harmful at any dose - even low doses such as those received during this research.

One possible effect that could occur at these doses is a slight increase in the risk of cancer. Please be aware that the natural chance of a person getting a fatal cancer during his/her lifetime is about 1 out of 4 (or 25 percent). The increase in the chance of getting a fatal cancer, as a result of the radiation exposure received from this research study, is *(insert percent increase)*. Therefore, the total risk of fatal cancer may be estimated to increase from 25 percent to *(insert new rate)*. This change in risk is small and cannot be measured directly. Compared with other everyday risks, such as flying in an airplane or driving a car, this increase is considered slight.

(INCLUSION OF THIS PARAGRAPH IS OPTIONAL) One concern some people may have about radiation exposure is the effect on fertility or on the possibility of causing harm to future children (i.e., genetic risk). The doses you will receive in the study are well below the levels that affect fertility. In addition, genetic effects have not been seen in humans who have been exposed to radiation. The information on genetic effects currently available is based on animal experiments studies using doses of radiation much higher than the amount you will receive in this study.

Please tell your doctor if you have taken part in other research studies or received any medical care at the NIH or other places/hospitals that used radiation. This way we can make sure that you will not receive too much radiation. Consider x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

If you are pregnant or breast feeding, you may not participate in this research study. It is best to avoid radiation exposure to unborn or nursing children since they are more sensitive to radiation than adults.

TEMPLATE C *(Total effective dose > 5 rem)*

This research study involves exposure to radiation from *(insert type of procedure or procedures)*. Please note that this radiation exposure is **not** necessary for your medical care and is for research purposes only. The total amount of radiation you will receive in this study is from (*insert maximum number*) injections (scans or repetitions) of (*insert quantity of radioactive material, in units of millicuries; or type of x-ray procedure)*. The NIH Radiation Safety Committee[1] has reviewed the use of radiation in this research study and has approved this use as involving acceptable risk and necessary to obtain the research information desired.

Using the standard way of describing radiation dose, from participating in this study, you will receive a total of *XX* rem to your (*insert highest-dosed organ*), *XX* rem to your (*2nd highest-dosed organ*), and *XX* rem to your (*3rd highest-dosed organ*). All other organs will receive smaller amounts of radiation. The amount of radiation received in this study exceeds the dose guideline established by the NIH Radiation Safety Committee for research subjects. The guideline is an effective dose of 5 rem (or 5,000 mrem) received per year[2].

(*Include discussion about possible acute and chronic organ effects of radiation therapy, specific to study and subject population*).

If you would like more information about radiation and examples of exposure levels from other sources, please ask the investigator for a copy of the pamphlet called, *An Introduction to Radiation for NIH Research Subjects*.

Please tell your doctor if you have taken part in other research studies or received any medical care at the NIH or other places/hospitals that used radiation. This way we can make sure that you will not receive too much radiation. Consider x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

If you are pregnant or breast feeding, you may not participate in this research study. It is best to avoid radiation exposure to unborn or nursing children since they are more sensitive to radiation than adults.

NOTES FOR THE CLINICIAN DRAFTING THE CONSENT FORM:

FOOTNOTES:

1. *Optional* inclusion statements to further identify the RSC.

   The RSC is comprised of individuals from different scientific specialties (nursing, radiation therapy, diagnostic radiology, the NIH Radiation Safety Officer, radiation dosimetrists, science administrators, health-physicists, psychologists, laboratory research scientists, physicists and physicians). Members are appointed by the director of NIH and charged with the responsibility to review all studies involving human subjects, which require radiation exposure for research purposes. *(If applicable, also cite the NIH Radioactive Drug Research Committee).*

2. Relate the radiation doses to the appropriate guideline or regulatory limit:

   a. NIH Radiation Safety Guideline for adults (aged 18 and older), both patients and normal subjects, is a total effective dose of 5 rem per year (12 consecutive months). The guideline for minors (under age 18) is 1/10 of the adult values (i.e., 0.500 rem per year).

   b. FDA regulatory limits for exposure to research subjects from the use of "radioactive research drugs" also require approval by the NIH Radioactive Drug Research Committee (RDRC). These limits are 3 rem per single administration or study to the whole body, blood-forming organs, lens of the eye, and gonads; and 5 rem annually. For other organs, the limits are 5 rem per single administration or study, and 15 rem annually. For minors (under the age of 18), limits are $1/10^{th}$ the adult values.

PAMPHLET: *"An Introduction to Radiation for NIH Research Subjects"*

The RSC developed a tri-fold informational pamphlet for prospective subjects to serve as a companion to the informed consent document or for discussion during the consent process. This pamphlet addresses the following frequently asked questions:

- What is radiation?
- Typical radiation doses.
- Limits for radiation exposure.
- Risks from exposure.
- Concerns regarding exposure and study participation.
- Who reviews these studies?
- What is the benefit to me?
- Glossary of terms and definitions.

A copy of this pamphlet is attached to this report. Additional copies may be printed from the RSC Protocol Assistance Center or obtained by contacting the Radiation Safety Branch Training Office by calling at 301-46-2254.

REFERENCES

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