RADIOISOTOPE SAFETY MANUAL

VETERANS ADMINISTRATION MEDICAL CENTER

DURHAM, NORTH CAROLINA

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VETERANS ADMINISTRATION MEDICAL CENTER

DURHAM, NORTH CAROLINA

A MANUAL OF GUIDELINES FOR SAFE HANDLING OF RADIOACTIVE MATERIALS

FORWARD

I. INTRODUCTION: The United States Nuclear Regulatory Commission (NRC) grants to qualified institutions specific licenses of broad scope for medical use, i.e., licenses authorizing multiple quantities and types of byproduct radioactive material for unspecified uses. The terms of such licenses require that such uses take place within an organized radiation safety program. This manual constitutes the formal set of rules, recommendations, and procedures for procurement and safe handling of radioisotopes within this institution as established by the Radioisotope Committee in compliance with the directives of the U.S. Nuclear Regulatory Commission. The purpose of this manual is to provide descriptions of policies and procedures deemed essential for the safe use of radioactive material.

II. ORGANIZATION:

A. Radioisotope Committee. The Durham VA Medical Center Radioisotope Committee is constituted as required by the NRC requirements on Medical Isotopes Committees, and is composed of persons having training and experience in the use of ionizing radiation. It is responsible for the safe use of radioactive materials at the Durham VA Medical Center.

B. Radioactive Drug Research Committee. Additional to regulatory actions of the NRC, administration of radioactive material to patients or research subjects is regulated by the Food and Drug Administration (FDA). FDA regulations require that radioactive administrations to human subjects be approved by a radioactive drug research committee. The Duke University Medical Center Radiation Control and Radioactive Drug Research Committee serves Durham VA Medical Center in this regard, and works in cooperation with the Durham VA Medical Center Radioisotope Committee.

C. Radiation Safety Officer. The Radiation Safety Officer (RSO) is the on-the-job representative of the Radioisotope Committee for providing information and assistance on radiation safety matters and to ensure adherence to regulations established by the Radioisotope Committee. The RSO also serves as a consultant to the Medical Center Safety Committee, as required by JCAH standards.

D. Authorized User. Any person authorized by the Radioisotope Committee to use and/or supervise the use of radioactive materials.

III. PHILOSOPHY: Maintaining occupational radiation exposure and releases of radioactive effluents to the environment as low as reasonably achievable (ALARA) is an important element in radiation safety practice. The Durham VAMC is formally committed to the ALARA concept. The regulations established by the Radioisotope Committee are not intended to harass, hinder or obstruct the use of radioactive materials, but rather to ensure that such use is directed towards the protection of health and the minimization of hazard to life or property through the ALARA concept.

IV. EXPLANATION: This manual is composed of three major sections:

A. Section I describes those policies and procedures common to all uses of radioactive material, to include responsibilities, duties, procurement, disposal and record maintenance.

B. Section II is comprised of several annexes, each of which is specifically relevant to a particular operation, activity or department.

C. Section III contains copies of forms to be used in applying for use of radioactive material and for disposal of radioactive waste.

Veterans Administration Medical Center

Durham, North Carolina

RADIOISOTOPE SAFETY MANUAL

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Section I

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Veterans Administration Medical Center

Durham, North Carolina

RADIOISOTOPE SAFETY MANUAL

SECTION 1

I. Responsibilities, Duties, and Functions:

A. Radioisotope Committee. The Radioisotope Committee is responsible for establishing procedures and policies for the procurement, use and disposal of radioactive materials (including discrete and sealed sources) located at the Durham VA Medical Center. The committee shall:

1. Determine the adequacy of the training and experience of persons utilizing and/or supervising the use of radioactive materials.

2. Review all applications for radioactive materials to determine the adequacy of associated equipment, facilities and radiological safety procedures.

3. Establish maximum permissible occupational radiation levels.

4. Require any individual user to submit to such examinations as may be deemed necessary to assure safe operation.

5. Determine whether the use of radioactive materials duplicates or conflicts with established clinical procedures at this station.

6. Require cessation of any operation involving radioactive materials upon a determination of inadequate safety procedures.

7. Meet periodically to review all matters relating to radiological safety, and receive a status report on such matters from the Radiation Safety Officer.

8. Meet at the call of the Chairman to resolve matters of an emergency nature relating to health and safety arising from the use of radioactive material.

B. Radiation Safety Officer. The Radiation Safety Officer shall:

1. Ensure adherence to all regulations issued by the Radioisotope Committee.

2. Maintain personnel dosage records of all persons, other than

patients, exposed to ionizing radiation resulting from materials or devices possessed by the Durham VA Medical Center.

3. Assure recording of radioisotope procurement.

4. Assure recording of radioisotope disposal.

5. Perform radiological surveys.

6. Perform leak tests on sealed sources requiring such tests.

7. Review all requests for radioisotopes to determine compliance with possession limits.

8. Provide assistance, advice, and training on radiological safety procedures.

C. Authorized User. Each individual authorized user shall:

1. Furnish all information requested by the Radioisotope Committee or Radiation Safety Officer concerning his qualifications, facilities, equipment and safety procedures.

2. Perform all tests required by the Radioisotope Committee.

3. Maintain records as required by this manual.

4. Comply with the applicable portions of this manual.

5. Administration of radioisotopes to human being requires the physical presence of the authorized individual user unless specified otherwise by the Radioisotope Committee.

II. Procurement:

A. Approval. The procurement of all radioactive material must be approved by the Radioisotope Committee or Radiation Safety Officer. Approval of usage is based upon the adequacy of the safety procedures to be exercised. Three principal factors will be considered: (1) the experience and ability of the applicant to cope with hazards involved (2) the adequacy of equipment and facilities, and (3) the thoroughness and attention given to safety precautions.

B. Requests. Requests for projects requiring the use of radioactive materials are prepared on RSO Form #1 and forwarded to the Radiation Safety Officer.

C. Requisitions. Upon approval of a particular project, requisitions for radioisotopes to be used in the project shall be submitted through the office of the Nuclear Medicine Service.

D. Notification. The office of the Nuclear Medicine Section shall be notified by the Supply Service of all radioactive materials received.

E. Records.

1. Each authorized individual user shall maintain a record of all radioactive material received, on RSO Form #2.

2. RSO Form #2 shall be forwarded to the RSO on the last working day of each month. Negative reports are required.

III. DISPOSAL:

A. SPECIAL NOTE - - DATE OF CURRENCY: 21 JAN. 1980

Because of serious and frequent interruptions in the availability of commercial sites for disposal of low-level radioactive waste, local rules and regulations for disposal of such waste may change frequently and with short notice. THE SITUATION IS CRITICALLY SERIOUS AND THE RULES AND PROCEDURES DESCRIBED HEREIN MUST BE FOLLOWED WITHOUT EXCEPTION. THESE RULES HAVE NOT BEEN GENERATED LOCALLY OR ARBITRARILY; THEY DERIVE FROM REQUIREMENTS STATED BY THE DISPOSAL SITES AND ARE BINDING UPON USERS AND SHIPPING FIRMS.

REPEATED FAILURE TO FOLLOW THE PROCEDURES STATED HEREIN, REVISED AS NECESSARY BY THE RSO, WILL RESULT IN WITHDRAWAL OF AN INDIVUDAL USER'S RADIOACTIVE MATERIAL AUTHORIZATION.

B. General.

1. Radioactive wastes will be described in one of the following categories:

a. solid

b. absorbed liquid

c. scintillation vials

d. in-vitro counting vials (e.g. non-scintillation gamma counting vials such as T-3, T-4 vials containing I-125)

e. biologic vials (e.g. those containing blood, tissue, bone, etc.)

2. Radioactive waste shall be packaged in barrels provided by the RSO and in such a manner that contamination of personnel handling them is unlikely.

3. All radioactive waste except animal carcasses and biologic vials will be packaged in fiberboard drums (called barrels herein). Animal carcasses will be packaged in steel 30-gallon drums (also called barrels) for subsequent containment in 55-gallon drums.

Biologic vials do not have to be emptied, but must be capped and placed in separate steel barrels provided by the RSO.

4. Each barrel must be labeled to show:

   a. radionuclide(s)

   b. activity

   c. chemical form(s)

   d. date of assay

   e. toxicity of substance(s)

   f. percentage of chelating agents in solution

   g. individual user's name

   NOTE: This information is required by shippers and disposal sites. Failure by users and the institution to be able to supply accurate information will have serious consequences, including loss of disposal privileges and punitive actions. Forms for this purpose are attached to the top of each barrel by the RSO, with a different color for each class of material.

5. Waste disposal fees are based on volume. Waste materials must be packed to obtain maximum use of each barrel.

6. Classes of materials must be segregated.

7. Absorbed liquids must truly be absorbed. Barrels exhibiting leakage from unabsorbed liquids will not be accepted for disposal. The responsibility for re-packaging shall rest upon the indivudal user.

8. Barrels exhibiting exposure levels in excess of 1 mr/hr should not be placed on loading docks, but instead reported to the RSO for special pick-up instructions.

9. Full barrels should be placed on loading docks JUST prior to pick-up (i.e. 10:00 AM Wednesdays and Fridays) to reduce wetting from rain and to reduce accessibility to unauthorized persons.

C. Procedures.

1. Solid waste (white form)

   a. place polyethylene liner in barrel

   b. add solid radioactive wastes, e.g. contaminated paper, pipettes, gloves, dry syringes, etc.

c. Complete form on top of barrel.

d. Place full barrel at designated pick-up point by 10:00 AM Fridays.

2. Carcasses (pink form)

a. The RSO, through the Duke Division of Laboratory Animal Resources will provide a 30-gallon steel barrel having a liner and a layer of diatomaceous earth and lime.

b. Animal carcasses are to be placed within the barrel and the liner folded over, not tied.

c. Replace the barrel lid and complete the attached form.

d. Contact Duke Laboratory Animal Resources for pick-up of barrel. (684-2797, 684-6745)

3. Biologic counting vials (pink form)

a. Place polyethylene liner in barrel.

b. Put 2 inches of diatomaceous earth in bottom of barrel.

c. Place capped biologic vials in barrel, avoiding breakage.

d. Complete form on top of barrel.

e. Place barrels at designated pick-up point by 10:00 AM Wednesdays.

4. Scintillation vials (green form)

a. Place polyethylene liner in barrel.

b. Put 2 inches of diatomaceous earth in bottom of barrel.

c. Place capped scintillation vials in barrel, avoiding breakage.

d. Complete form on top of barrel.

e. Place barrels at designated pick-up point by 10:00 AM Wednesdays.

5. In-vitro counting vials (blue form)

a. Place polyethylene liner in barrel.

b. Put 2 inches of diatomaceous earth in bottom of barrel.

c. Place capped in-vitro counting vials in barrel, avoiding breakage (50 ml maximum).

d. Complete form on top of barrel.

e. Place barrels at designated pick-up point by 10:00 AM Wednesdays.

6. Contaminated liquids (yellow form)

a. Obtain 1-gallon milk jugs from Duke Biochemistry Storeroom.

b. Put 3 inches of diatomaceous earth in jug.

c. Add contaminated solutions and more earth until jug is full. LIQUIDS MUST BE TRULY ABSORBED

d. Mark jug with a piece of "Caution-Radioactive Material" tape and a number.

e. Place filled jugs in barrels marked "Absorbed Liquids Only" and complete form on top of barrel.

f. Place barrels at designated pick-up point by 10:00 AM Wednesdays.

Disposal Records.

1. Each individual authorized user shall maintain a record of disposition of radioactive material. RSO Form #2 shall be used for this purpose.

2. RSO Form #2 shall be forwarded to the Radiation Safety Officer on the last working day of each month, provided any disposals had been made during the period covered. Negative reports are required.

IV. PERSONNEL MONITORING:

A. Personal Badges.

1. All persons exposed to X- and/or gamma radiation, from radioactive material, on a routine basis shall be required to wear a film or thermoluminescent dosimeter (TLD) badge. Persons whose hands are exposed repeatedly to high levels of X- or gamma radiation may, at the direction of the RSO, be required to wear wrist or finger-ring badges. Persons exposed to beta radiation may be required to wear monitoring badges at the direction of the RSO.

2. Film or TLD badges shall be processed on a monthly basis.

3. Film or TLD badge readings on workers shall be reported to the appropriate Service Chiefs by the RSO. Reports shall include

monthly reading, quarter-to-date and year-to-date totals.

4. Records of personnel exposures shall be maintained by the RSO.

5. Each individual to whom a badge is issued has the responsibility to ensure its proper wear and use.

B. Pocket Dosimeters. A pocket dosimeter may be worn at the discretion of the user, but will not be used in lieu of a film or TLD badge. Under certain circumstances, the use of both a badge and pocket dosimeter may be required.

C. Bioassays. Individuals involved in activities that use, at any one time, more than 100 milliCuries of hydrogen-3 in a non-contained form, other than metallic foil, shall have bioassays performed within one week following a single activity, and at weekly intervals for continuing activities. Bioassays may be required by the Radioisotope Committee on individuals conducting operations with other radionuclides. Reports of bioassay results shall be forwarded to the RSO.

D. Thyroid Monitoring. Individuals using quantities of iodine-125 and/or iodine-131 in excess of 10 milliCuries in a single operation or 20 milliCuries in a 30-day period shall be subject to periodic thyroid monitoring by external detection. Frequency and scheduling of such examinations shall be determinated by the RSO.

V. MAXIMUM PERMISSIBLE EXPOSURE:

A. External.

1. Whole body; head and trunk; active blood forming organs; lens of the eyes; or gonads -- 1.25 Rems/calendar quarter.
Note: Above value can be increased to 3.0 Rems per calendar quarter provided total accumulated exposure does not exceed 5 (age 18).

2. Hands and forearms; feet and ankles -- 18.75 Rems/calendar quarter.

B. Internal. Tissues, organ systems and organs not specified above -- 5 Rems/calendar quarter.

C. Air and Water Concentrations. Concentrations of radioactivity in air and water shall not exceed the limits specified in the U.S. Code of Federal Regulations 10 CFR Part 20. In keeping with the ALARA concept, it is desirable to limit air and water concentrations of radioactivity to 10% of 10 CFR Part 20 specifications.

VI. EMERGENCIES:

A. Definition. Any circumstances or events that have caused or threatened to cause abnormal exposure of persons to radiation, or

loss of containment of radioactive material shall be termed a radioactivity emergency.

B. All radioactivity emergencies shall be reported immediately to:

Assistant Medical Center Director VA Extension 6210

and

Radiation Safety Officer
Rms. 06-09 Research Park IV
Duke University Medical Center
684-2194 Home: 544-1954
DUMC beeper No. 395

VII. GENERAL RADIOACTIVITY SAFETY PROCEDURES:

A. Restricted Areas. Supervisors of laboratories or rooms containing radioactive material shall:

1. Instruct all individuals working in or frequenting any portion of a restricted area in the health protection problems associated with exposure to radiation or radioactive materials. Female workers and those who may supervise or work with them should be given specific instruction about prenatal exposure risks to the developing embryo and fetus.

2. PROHIBIT eating, drinking, smoking, or application of cosmetics within that area of the laboratory where radioisotopes are stored or used.

3. PROHIBIT pipetting or the performance of any similar operation by mouth suction.

4. PROHIBIT the routine exposure of pregnant employees to ionizing radiation.

B. Contamination Control.

1. Surveys. Each individual user utilizing unencapsulated radioisotopes should perform periodic radiological surveys of each area in which such material is used and/or stored, to include a determination of contamination levels. Tests for contamination may consist of wiping work areas with absorbent material and checking the swipe with an appropriate detection instrument. Monthly radiological surveys shall be performed by the RSO.

2. Personnel. Each person associated with the handling of unencapsulated radioisotopes shall wash hands thoroughly before eating, smoking or leaving the work area and shall utilize appropriate detection instrumentation to ensure lack of contamination on hands, feet and/or clothing.

3. Hoods. Work involving aerosols, dusts or gaseous products, or procedures which might produce airbone contamination, shall be conducted in a hood, dry box, or other suitable closed system.

4. Work Surfaces. All work areas (bench tops, hood, floors, etc.) should be covered at all times with stainless steel, uncracked glass plates, plastic trays or absorbent paper.

5. Decontamination. Preparations for decontamination should begin promptly. Determine the extent and hazard of contamination prior to commencing clean-up. The Radiological Safety Officer will assist in this evaluation upon notification. The individual responsible for the contamination will be expected to perform the necessary clean up, under the supervision of the RSO. After decontamination, the area or equipment shall be considered contaminated until declared otherwise by the RSO.

C. Leak Tests.

1. Each sealed source containing radioactive material with a half-life of greater than 30 days and in any form other than gas, shall be tested for leakage and/or contamination upon receipt and at intervals not to exceed 6 months.

2. The test shall be performed on the source surfaces, or on those surfaces on which one would expect contamination should there be leakage.

3. Test shall be sufficiently sensitive to detect 0.005 microCuries of removable radioactive material.

4. Leak tests and record maintenance shall be performed by the RSO.

VIII. RECAPITULATION:

The following is a summary of the forms and records required by this manual. Each item is referenced to that portion of the manual containing further information:

1. To obtain approval of a project utilizing radioactive material:

   Complete RSO Form #1, VA Forms 10-1152 and 10-1153 and forward to RSO (See paragraph II, A and B).

2. To order radioisotopes:

   Forward requisitions through VA Nuclear Medicine office. (See paragraph II,C).

3. Records to be maintained by individual users:

   Record of "Radioisotope Receipt and/or Disposal", RSO Form #2 (See paragraph II, E and III, B).

SECTION I

ANNEX A

PREREQUISITES FOR AUTHORIZED USE OF RADIOACTIVE MATERIAL

I. QUALIFICATIONS OF AUTHORIZED INDIVIDUAL USERS OF RADIOACTIVITY IN HUMANS

A. Individual must be a physician licensed to dispense drugs in the practice of medicine by a State or Territory of the United States, the District of Columbia, or the Commonwealth of Puerto Rico.

B. If the individual has not previously been issued a Byproduct Material License by NRC or a medical license to use radioactive material in humans by an Agreement State and if the individual's qualifications are not completely documented as noted below, the individual may be requested to appear before the Durham VA Medical Center Radioisotope Committee.

C. Training and experience criteria for individual physicians to participate in medical use of radiopharmaceuticals are set forth by the Nuclear Regulatory Commission in paragraph 35.12. (c) of 10 CFR Part 35. Paragraph 35.100 of 10 CFR Part 35 establishes five groups of uses of byproduct material for medical purposes; at Durham VA Medical Center, radiopharmaceuticals containing accelerator-produced radionuclides will be subject to the same classification and requirements for use. These groups may be classed generally thus:

Group I: Use of diagnostic agents with an approved New Drug Application (NDA) by the Food and Drug Administration (FDA) in uptake, dilution and excretion tests.

Group II: Use of agents with an FDA - approved NDA in imaging and tumor localization.

Group III: Use of generators and reagents in preparation of radiopharmaceuticals.

Group IV: Use of agents with an FDA-approved NDA in therapeutic procedures in which the patient is not hospitalized.

Group V: Same as Group IV, but where patient is hospitalized.

D. To qualify as adequately trained to use or directly supervise the use of radioactive material listed above (and accelerator-produced counter-parts in well-established use), the physician should have

"basic isotope training", "experience with material for which application is made" and "supervised clinical training" as elaborated below.**

1. Basic isotope training (200 hours) includes handling techniques, radiation physics and instrumentation, radiation protection, mathematics and dose calculations, radiation biology and radiopharmaceuticals.

2. Experience in actual use (500 hours) of radioactive material of the type and quantity for which application is made or equivalent satisfactory to the Radioisotope Committee.

3. Supervised clinical training (500 hours), including:

   a. Examination of patients to determine the suitability for radioisotope diagnosis and recommendation on prescribed dosage.

   b. Collaboration in calculation, calibration and administration of the radiopharmaceutical.

   c. Study of case histories with discussion with preceptor to establish most appropriate diagnostic procedures, limitations, contraindications, and interpretation of results, and

   d. Follow-up and management where required.

4. The above may be satisfied concurrently in a three-month training program IF all three areas are integrated into the program.

E. Certification by the American Board of Nuclear Medicine may be accepted as evidence of adequate training for use of Groups I, II and III. Certification by the American Board of Radiology in Diagnostic Radiology with Special Competence in Nuclear Radiology may be accepted as evidence of adequate training for uses in Groups II and III.

F. Training requirements to use or directly supervise uses in Groups IV and V with radiopharmaceuticals include 80 hours of basic isotope handling techniques and calculations (scope as defined in D. I. above) and clinical training in specific therapy procedures (see ANNEX B). For use in therapy procedures with sealed sources, the applicant should show training as in D. I. plus three years of use of such sources in therapeutic radiology.

** For a more detailed description of training requirements, see U.S. NRC Regulatory Guide 10.8, January 1979

G. Details of an applicant's training, experience and participation in clinical studies shall be indicated (and confirmed by preceptor) on RSO Form #1.

II. APPLICATION FOR AUTHORIZED USE OF RADIOACTIVITY IN HUMANS

A. General. The administration of radioactive material to humans is regulated by the FDA and NRC. At Durham VA Medical Center, FDA and NRC regulations are carried out by the Radioisotope Committee and the Duke University Medical Center Radiation Control and Radioactive Research Drug Committee. Requests for approval of human use of radioactive material must be sufficiently detailed to enable a determination of compliance with current regulations and policies.

B. Application. Requests for approval of human use of radioactivity may be submitted to the D.U.M.C. (Radiation Control and) Radioactive Drug Research Committee, which will forward the application to the Radioisotope Committee with its recommendation. Alternatively, requests may be submitted to the Chairman, Radioisotope Committee, who will refer them to the Radioactive Drug Research Committee for review and recommendations to the Radioisotope Committee.

C. Categories. Each human use shall be determined to fall into one of the following categories.

1. Basic Research. The use of radioactive drugs to obtain basic research information, but not intended for immediate therapeutic, diagnostic or similar purpose.

2. Well-established Medical use. Those radioactive drugs which through previous use, (primarily in Nuclear Medicine) have proven to be safe and effective in diagnosis and/or therapy.

3. Non-Routine Medical use. The proposed human use of any radioactive drug which is not identified in paragraphs 1 or 2 above.

D. Required Specific Information by Category.

1. Category 1 - Basic Research

a. Definition: Projects intended to obtain basic research information regarding the metabolism (including kinetics, distribution and localization) of a radioactively labeled drug or regarding human physiology, pathophysiology or biochemistry; but not intended for immediate therapeutic, diagnostic, or similar purposes.

b. Conditions for use: The amount of active pharmaceutical ingredient or combination of pharmaceutical ingredients to be administered shall be known not to cause any clinically detectable pharmacological effect in humans.

c. Radiation dose shall be the smallest practical to perform the study. Under no circumstances shall the whole body dose exceed:

Single exposure	3 Rem
Quarterly cumulative	3 Rem
Yearly cumulative	5 Rem

Critical organ dose shall not exceed:

Single exposure	5 Rem
Quarterly cumulative	5 Rem
Yearly cumulative	15 Rem

d. Normally, children and pregnant females will not be subjected to non-routine studies with radioactivity. Female research subjects of child-bearing potential shall state in writing that they are not pregnant, or be given a pregnancy test before participating in any study.

e. Information to be submitted:

1. Pharmacological dose calculations based on data available from published literature or from other valid human studies.

2. Absorbed dose calculations based on biologic distribution data available from published literature or other valid studies.

3. Investigator's qualifications through training and experience to conduct the proposed research studies.

4. Copy of consent form (see ANNEX D) and, when applicable, method of pregnancy determination.

5. Procedure for determining that radioactive material for parenteral use is sterile and pyrogen-free.

6. The research protocol must be based on a sound rationale derived from appropriate animal studies or published literature and must be of such sound design that information of scientific value may result.

7. Confirmation that all adverse reactions associated with the use of the radioactive drug will be reported immediately to the Radioisotope Committee.

8. Types and numbers of research subjects to be employed in the study.

2. Category - 2 Well-Established Medical Use

a. Definition: The use of a radioactive drug for diagnosis or

therapy which is identified on the list of "well-established medical uses" issued by the NRC or FDA, is under an active Investigational New Drug (IND) evaluation or is under an NDA issued by the FDA.

b. Conditions for use:

1. The radionuclide and its chemical form, dose and use is as stipulated on the list of well-established medical uses, an IND or NDA.

2. The applicant has training and experience of the type described in Section I of this Annex, commensurate with the objectives of the application.

c. Information to be submitted:

1. Applicants training and experience qualifications.

2. Procedure for determining that radioactive material for parenteral use is sterile and pyrogen-free.

3. Category 3 - Non-routine Medical Use

a. Definition: The use of radioactive material in humans which is not included on the list of well-established medical uses nor meets the definition of basic research.

b. Conditions for Use: Non- routine medical uses of radioactive material are classified into one of two phases of development:

1. Clinical Research applied to a new use in humans -- little or nothing is known about the procedure and little or nothing has been published on the subject. The basis for proceeding with the new use in humans is derived from knowledge obtained from animal studies. This phase of development includes the initial introduction into humans and initial trials on a limited number of patients.

2. Clinical Evaluation applies to the planned testing of a new diagnostic or therapeutic agent or procedure in an appropriate series of control and diseased humans. The procedure and results of Clinical Research will ordinarily have been reported in the literature or at meetings. If adequate information has been published, the applicant should have spent sufficient time with those who have developed the test to be thoroughly familiar with the details of its use.

c. Information to be submitted:

1. Title and purpose of study. Indicate whether the study is to be Clinical Research or Clinical Evaluation and explain why.

2. The plan of investigation in sufficient detail to permit a critical evaluation of the methods for conducting the experiments and the controls established.

3. A statement as to whether any planned complementary drug or radioisotope administration is contemplated in conjunction with the study.

4. A statement about the expected fate of the radionuclide administered, and if the administration is for therapy, a statement of expected results.

5. (a) IF THE APPLICATION IS FOR CLINICAL RESEARCH, an outline of related work conducted in laboratory animals and in humans, including data on localization, organ and body clearance, and absorbed radiation dose. If work has been conducted in animals, explain why. Pertinent references and a brief abstract prepared by the applicant from published or unpublished material should be submitted. (The brochure of a commerical supplier is not a satisfactory submission for this purpose.)

   (b) IF THE APPLICATION IS FOR CLINICAL EVALUATION, pertinent references and a brief abstract prepared by the applicant of published or unpublished material, including information on localization, organ and body clearance and absorbed radiation dose. (The brochure of a commerical supplier is not a satisfactory submission for this purpose.)

6. A description of the human subjects to be studied:

   a. Persons without manifest disease - number, method of selection and age range.

   b. Persons with manifest disease - number, nature of pathology, method of selection and age range.

   c. Pregnant women shall ordinarily be excluded from any study not involving a condition of the pregnancy itself. Specify whether pregnant women will be studied and why.

7. The range of radioactivity (microCuries or milliCuries) to be administered and the method of administration.

8. Calculations of the radiation doses delivered to the whole body and to the critical organ(s). The calculations shall include information concerning:

   a. Expected half-time in various organs.

   b. The relationship between the retained radioactivity and the permissible body burden for occupational exposure (except for therapy).

c. The rational for using the amount of radioactivity selected, and

d. The absorbed radiation dose due to simultaneous or accompanying radioactivity that may be administered.

9. A statement of the institutional resources available to support the study, including:

a. Physical facilities and equipment especially suited to the study under consideration.

b. Availability of clinical material, and

c. Types of consultation or collaboration available, including the name of the sponsor of the study if other than the applicant.

10. Qualifications of the individual physician who will be responsible for the study, including a summary of research training and experience and pertinent training and experience in the use of radioactive material.

11. Estimated time needed to complete the study.

12. A schedule for reporting the results of the study, and an outline of the type of information to be included in the report. The schedule can be in terms of time intervals or number of subjects studied. If studies are to be long-range, interim reports would be provided.

13. Copy of consent form (see ANNEX D).

14. Confirmation that all adverse reactions associated with the use of the radioactive material will be reported immediately to the Radioisotope Committee.

III. APPLICATION FOR USE IN ANIMALS OR in vitro

A. General. The applicant should have "basic isotope training" and "active participation" (See Section I, Paragraph D. 1. of this Annex) appropriate to the work contemplated. The active participation shall be carried out in a program using radioactive material in experimental situations comparable to those for which approval is sought.

B. Applications. Applications may be made by letter to the Chairman of the Radioisotope Committee, and will be subject to review by the Radioisotope Committee. Applications should include the following:

1. Applicant's training and experience.

2. Nature and amount of radioactivity to be used in the study.

3. A description of facilities, including radioactivity - measuring equipment, in which the work is to be carried out.

IV. APPLICATIONS FOR AMENDMENTS TO RADIOACTIVE MATERIAL AUTHORIZATIONS

Applications to add certain radioactive materials to previously approved Radioactive Material Authorizations (RMAs) may be addressed to the Chairman of the Radioisotope Committee, who, with the Radiation Safety Officer, will review the application. If a significant increase in the hazards of radioactive material use is a likely result of the contemplated work, the application will be reviewed by the Radioisotope Committee. If the increase in hazard is minimal or insignificant, the Chairman and the RSO may grant approval of the application.

ANNEX B

MINIMUM REQUIREMENTS FOR ACTIVE PARTICIPATION

I. Groups I, II and III (see Annex A, I. C.):

There are no specific requirements for participation in stated numbers of specified procedures in these Groups. Acceptable training experience will inherently involve the applicant in currently performed clinical studies and activities. The applicant for authorized use may use Supplement B to RSO Form #1 to indicate involvement in specific procedures. (Supplement B is identical to NRC Form 313M Supplement B; Supplement A is contained within RSO Form #1.)

II. Groups IV and V (see Annex A, I. C.):

The following are minimum requirements for active participation:

Procedure	Requirements
1. Iodine-131 for treatment of hyperthyroidism and/or cardiac conditions:	Clinical experience in the diagnosis of thyroid function and active participation in the treatment of 10 patients.
2. Phosphorus-32 for treatment of polycythemia vera, leukemia and/or bone metastases:	Treatment of 3 patients with any combination of these conditions.
3. Colloidal phosphorus-32 intracavitary treatment:	Active participation in the treatment of 3 patients.
4. Iodine-131 for treatment of thyroid carcinoma:	Clinical experience in the diagnosis of thyroid function and treatment of hyperthyroidism and/or cardiac function and active participation in the treatment of 3 patients with thyroid carcinoma.
5. Use of sealed sources of by-product material for interstitial, intracavitary, or surface treatment of cancer:	Active practice in therapeutic radiology with a minimum of 3 years experience.

ANNEX C

NOTES ON NURSING CARE OF PATIENTS CONTAINING RADIOISOTOPES*

I. GENERAL

A. Purpose. To provide instruction to all hospital personel who may come in contact with patients who have received diagnostic or therapeutic doses of radioisotopes.

B. Hazards of Radioactive Isotopes. Hazards may arise from three sources:

1. Irradiation of the person by radiations emitted by radioactive isotopes in the patient.

2. Accidental contamination of the skin by radioactive materials in the course of patient care.

3. Accidental ingestion of radioactive material (possibly by smoking when the hands are contaminated).

C. Tracer or Diagnostic Doses. There is no radiation hazard from patients who have received tracer or diagnostic doses of radioactive isotopes. No special precautions need be taken in caring for them.

1. There is no external radiation hazard from patients who have received not more than 5 milliCuries of any radioisotopes. If such a patient vomits or is incontinent within the first 24 hours, care should be taken to avoid contaminating the skin during cleanup. Rubber gloves should always be worn when there is any possibility of skin contamination.

2. The hazards increase with increased levels of dose. General instructions for care of patients who have received more than 5 milliCuries of an isotope are given in the following sections.

II. PRINCIPLES OF PROTECTION

A. Skin contamination or ingestion or inhalation of radioactive material can be avoided by practicing good housekeeping, clean work habits, and frequent hand washing.

B. Radioactive materials should not be allowed to come in contact with the skin. Rubber gloves should be worn whenever such contact is possible. Personnel should not smoke or eat when there is any possibility that the hands are contaminated.

*This material was obtained from Appendix 3, SAFE HANDLING OF RADIOISOTOPE IN MEDICAL PRACTICE, Edith H. Quimby, Sc. D.

C. External irradiation from patients may be reduced to a minimum of time close to patients who have received therapeutic doses. Appropriate instructions will be posted on patient's door by the RSO.

III. GENERAL PRECAUTIONS

A. Time spent close to patients should be regulated. If the hazard is high, the RSO or doctor in charge will issue special instructions.

B. Hands should be washed after contact with a patient, particular attention being given to the fingernails.

C. Burnable materials, such as paper handkerchiefs, that are contaminated, should be put into non-porous garbage bags and reported to the RSO for disposal.

D. Articles or utensils suspected of being contaminated should be monitored by the RSO prior to final disposition.

E. No special precautions are necessary for dishes, instruments, or utensils, unless contaminated by vomiting, or incontinence is known to have occurred.

F. It is not usually necessary to limit visitors, within the general rules of the institution. If any restrictions are necessary for the first few days, special instructions will be issued by the doctor in charge.

IV. GENERAL NURSING CARE

A. Equipment.

1. A metal can with laundry bag inside should be provided to collect linen where there is danger of contamination by vomiting, incontinence, or profuse perspiration.

2. Items such as bedpans, urinals, and basins should be thoroughly washed with soap and running water. The same items should be used for an individual patient until his treatment is terminated. If these items were used for a patient who had received a large dose of iodine-131, they should be monitored before being returned to general stock.

3. Heavy rubber gloves should be worn while cleaning possibly contaminated equipment. These gloves should be washed with soap and running water while on the hands, and dried before removal. They should be monitored periodically by the RSO.

4. A designated sink on the floor should be used for washing possibly contaminated equipment. After each use, this sink should be washed with soap and water and scrubbed with a brush, to prevent collection of radioactivity and subsequent dissemination.

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B. Bath. Unless specifically ordered by the doctor, the bath should be postponed for the first 48 hours. In this period, the radioactivity of patients treated with iodine-131 will have decreased by almost 50%. The possibility of iodine-131 contamination in perspiration, saliva, or excreta is over.

C. Excretions. Rubber gloves should be worn whenever handling excreta of patients or contaminated material, such as soiled bedding.

1. Urine. Accurate urine collections are frequently desired by the laboratory or the doctor in charge. Great care should be taken not to lose any part of the specimen. In the case of iodine therapy, the urine collection bottles with special shields will be provided by the Nuclear Medicine Section whose personnel will collect them. The patient should be encouraged to take care of his own urine collection, if possible. If the urine is not to be collected, it may be disposed of in the usual way.

2. Stools. Usually there is very little radioactivity in stools. They may be disposed of in the usual way unless collection is specifically requested.

3. Sputum, Vomitus and Perspiration. If the radioactive isotope has been administered by mouth, any vomitus expelled during the first 24 hours should be collected in a waterproof cardboard container and sent to the Nuclear Medicine Section. For iodine-131 therapy patients, excessive sputum should be collected in a similar manner for the first 24 hours. For intravenous administration, no precautions are necessary, except with iodine-131 during the first 24 hours, when excessive sputum should be collected, and if there is excessive perspiration, sheets should be monitored for contamination. After 24 hours no precautions are necessary.

D. Soiled Tissues and Sponges. All such soiled material should be placed in a non-porous garbage bag attached to the patient's bed, and later reported to the RSO for disposal.

E. Incontinence. If there has been a large spill of urine, the RSO or Nuclear Medicine Section personnel should be notified immediately. The damp bedclothes should not be handled without rubber gloves.

F. Drainage. In the event of drainage from the site of injection of phosphorus, the nurse should not attempt to change the dressing, but should immediately notify the doctor in charge and the RSO.

G. Special Orders or Instructions. The doctor in charge, or the resident, will write any of the following orders which may be applicable:

1. Room or bed restrictions.

2. Special restrictions on nursing time.

3. Visitor restrictions.

4. Instructions for collection of excreta or bathroom privileges.

5. Diet.

6. Special medication.

7. Special nursing care, including special attention to dressings.

ANNEX D

INFORMED CONSENT FOR PROCEDURES INVOLVING RADIOACTIVE MATERIAL IN CLINICAL INVESTIGATIONS

I. INTRODUCTION; The Duke University Medical Center Radiation Control and Radioactive Drug Research Committee, which reviews human-use applications for the Durham VA Medical Center Radioisotope Committee has adopted the following requirements regarding the expression of radiation dose to patients or research subjects. Informed consent forms constructed in support of any research application should be as simple and understandable as possible.

II. REQUIREMENTS

A. The investigator shall calculate the anticipated exposure to the whole body and the critical organ(s) where appropriate. Calculations should include the dose from the initial administration and, if applicable, quarterly and yearly cumulative exposures due to subsequent procedures.

B. The calculated dose shall be expressed as a fraction or percentage of the allowable occupational exposure level for the whole body or critical organ, whichever is more restrictive.

C. The informed consent form shall include a statement of the relationship of the anticipated dose to the occupational exposure level as described in B. above.

D. To assist the patient in understanding the meaning of "occupational exposure levels", the following is suggested:

> "The National Committee on Radiation Protection has set 'occupational radiation exposure limits' for the many radiologists, technologists, and scientists who work with radiation and are exposed nearly every day. These limits are defined as ' the dose of radiation that, in the light of present knowledge, is not expected to cause appreciable bodily injury to a person at any time during his lifetime.' The risks of this amount of occupational exposure to radiation are thus considered to be very small and, at these levels which have been in effect since, there is no indication of harmful effects to the worker or his offspring."

ANNEX E

CARE OF ANIMALS CONTAINING RADIOACTIVE MATERIAL

I. GENERAL

All appropriate radiological safety techniques and procedures will be observed in the administration of radioactive materials to animals and shall have prior approval by the Radiation Safety Officer.

II. SPECIFIC INSTRUCTIONS

A. Each cage containing experimental animals will be tagged so as to show the isotope, amount, name of investigator and date of injection.

B. Animals will be kept in an isolated area within the animal building and remain caged until excretions contain only background amounts of radioactivity or until sacrifice of the animal.

C. Non-metabolic animal cages will contain sufficient wood shavings to absorb all liquid excreta. All dry waste, including contaminated shavings, will be collected and deposited in labeled radioactive waste drums.

D. Contaminated carcasses will be labeled and freezer-stored until disposal in accordance with current procedures.

E. Cages having a dose-rate greater than 1 mr/hr must be reported to the RSO. The RSO will survey the animal room for contamination periodically.

F. Cages will be decontaminated with normal methods by personnel wearing rubber or vinyl gloves.

SECTION III

APPLICATION FOR USE OF RADIOACTIVE MATERIAL

VETERANS ADMINISTRATION MEDICAL CENTER, DURHAM, NC

1. Name of Applicant (Name, title and department of individual who will use or directly supervise use of radioactive material).
2. Location at which radioactive material will be used. (Building and room number (s))
3. Previous license number. (Duke, State, or NRC)
4. Radioactive material. (Elements and mass numbers)
5. Activity to be possessed. (Maximum activity to be possessed for each radionuclide listed in Item 4).

6. A description of the purposes for which radioactive material will be used. (Include experimental design; identification of types of labeled compounds; approximate activity per experiment; specify laboratory animals, if appropriate. If material is for "human use", complete Supplement A and Supplement B.

TRAINING IN RADIOLOGICAL SAFETY PRACTICES OF INDIVIDUAL NAMED IN ITEM #1

7. Type of Training	Where Trained	Duration of Training	On the job (circle answer)	Formal Course (circle answer)
1. Principles & practices of radiological health safety			yes no	yes no
2. Radioactivity measurement standardization & monitoring techniques & instruments			yes no	yes no
3. Experience with Radioisotopes. Actual use of radioisotopes in the types and quantities for which application is being made, or equivalent experience				

PHYSICAL FACILITIES, EQUIPMENT, AND RADIATION INSTRUMENTATION

8. RADIATION DETECTION INSTRUMENTS (USE SEPARATE SHEET IF NECESSARY)

Type of instruments (include make & model number of each)	Manufacturer's Model	Radiation detected	Sensitivity range (mr/hr)	Window thickness (mg/cm^2)
a) Monitoring & Surveying instruments				
b) Counting Instruments				

9. Methods, frequency and standards used in calibrating instruments listed in item 8.

10. Film badges, dosimeters and other personnel monitoring devices; including bioassay procedures.

11. Facilities and equipment. (Laboratory facilities, remote handling equipment, storage containers, shielding, fume hoods; etc.)

12. Radiation protection program. (Describe control measures from receipt to disposal of radioactive material, including survey and waste disposal procedures.)

Signature of individual named in Item 1.

_____ (Signature)

_____ (date)

13. If byproduct material is for "human use" (internal administration of byproduct material or the radiation therefrom to human beings), complete this supplement and attach to the application for byproduct material license.

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14. The using physician indicated above is licensed to dispense drugs in the practice of medicine by a state or territory of the United States, the District of Columbia, or the Commonwealth of Puerto Rico.

(Circle Answer) Yes No

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15. A Supplement A-Human Use--(statement of using physician's clinical radioisotope experience) is submitted in support of this application. If answer is NO, use reverse side of this page to explain or refer to other application or related documents on which this information appears.

(Circle Answer) Yes No

PROPOSED DIAGNOSIS OR TREATMENT

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16. (a) Describe purpose for which byproduct material will be used including specific conditions or disease to be diagnosed or treated: (Use reverse side if necessary).

(b) Chemical form administered:

(c) Describe procedures which will be observed to minimize hazard from handling, storage, and disposal of the byproduct material:

(d) Description and sketch of any special devices to be used for administering byproduct material to human beings are

(1) Attached (Literature references will suffice
CIRCLE ANSWER Yes No

(2) On file with Committee refer to Application No: _____
CIRCLE ANSWER Yes No

PROPOSED DOSAGE SCHEDULE

(a) In millicuries for internally administered byproduct material other than discrete fixed source; and in roentgens or rads, as appropriate, for internal or external irradiation from discrete fixed sources (gold seeds, cobalt needles, etc.; state separately for each condition or disease.

(b) Investigative proposal for experimental, new or human uses is attached. (Attachment should include outline of conditions to be evaluated, including data from anumal studies and/or abstract of literature reference, if any, and number and type of patients (i.e., age group, moribund, etc.)

CIRCLE ANSWER Yes No

18. If byproduct material will not be obtained in precalibrated form for oral administration or in precalibrated and sterilized form for parenteral administration, describe identification, processing, and standardization procedures:

19. The proposed use of byproduct material has been, or will be, approved by the medical isotope committee.

CIRCLE ANSWER Yes No

This page may be completed by the physician's preceptor (if any) in the medical use of radioisotopes.

20. (a) Using Physician's name

(b) Name & address of applicant (if different from 20 (a)

SUPPLEMENT TO APPLICATION FOR AUTHORIZED USE OF RADIOACTIVE MATERIAL TO HUMANS, TO DOCUMENT TRAINING AND EXPERIENCE

PRECEPTOR STATEMENT

Supplement B must be completed by the applicant physician's preceptor. If more than one preceptor is necessary to document experience, obtain a separate statement from each.

1. APPLICANT PHYSICIAN'S NAME AND ADDRESS

FULL NAME

STREET ADDRESS

CITY | STATE | ZIP CODE

KEY TO COLUMN C

PERSONAL PARTICIPATION SHOULD CONSIST OF:

1-Supervised examination of patients to determine the suitability for radioisotope diagnosis and/or treatment and recommendation for prescribed dosage.

2-Collaboration in dose calibration and actual administration of dose to the patient including calculation of the radiation dose, related measurements and plotting of data.

3-Adequate period of training to enable physician to manage radioactive patients and follow patients through diagnosis and/or course of treatment.

2. CLINICAL TRAINING AND EXPERIENCE OF ABOVE NAMED PHYSICIAN

ISOTOPE A	CONDITIONS DIAGNOSED OR TREATED B	NUMBER OF CASES INVOLVING PERSONAL PARTICIPATION C	COMMENTS *(Additional information or comments may be submitted in duplicate on separate sheets.)* D
I-131 or I-125	DIAGNOSIS OF THYROID FUNCTION		
	DETERMINATION OF BLOOD AND BLOOD PLASMA VOLUME		
	LIVER FUNCTION STUDIES		
	FAT ABSORPTION STUDIES		
	KIDNEY FUNCTION STUDIES		
	IN VITRO STUDIES		
OTHER			
I-125	DETECTION OF THROMBOSIS		
I-131	THYROID IMAGING		
P-32	EYE TUMOR LOCALIZATION		
Se-75	PANCREAS IMAGING		
Yb-169	CISTERNOGRAPHY		
Xe-133	BLOOD FLOW STUDIES AND PULMONARY FUNCTION STUDIES		
OTHER			
Tc-99m	BRAIN IMAGING		
	CARDIAC IMAGING		
	THYROID IMAGING		
	SALIVARY GLAND IMAGING		
	BLOOD POOL IMAGING		
	PLACENTA LOCALIZATION		
	LIVER AND SPLEEN IMAGING		
	LUNG IMAGING		
	BONE IMAGING		
OTHER			

PRECEPTOR STATEMENT *(Continued)*

2. CLINICAL TRAINING AND EXPERIENCE OF ABOVE NAMED PHYSICIAN *(Continued)*

ISOTOPE A	CONDITIONS DIAGNOSED OR TREATED B	NUMBER OF CASES INVOLVING PERSONAL PARTICIPATION C	COMMENTS *(Additional information or comments may be submitted in duplicate on separate sheets.)* D
P-32 *(Soluble)*	TREATMENT OF POLYCYTHEMIA VERA, LEUKEMIA, AND BONE METASTASES		
P-32 *(Colloidal)*	INTRACAVITARY TREATMENT		
I-131	TREATMENT OF THYROID CARCINOMA		
	TREATMENT OF HYPERTHYROIDISM		
Au-198	INTRACAVITARY TREATMENT		
Co-60 or Cs-137	INTERSTITIAL TREATMENT		
	INTRACAVITARY TREATMENT		
I-125 or Ir-192	INTERSTITIAL TREATMENT		
Co-60 or Cs-137	TELETHERAPY TREATMENT		
Sr-90	TREATMENT OF EYE DISEASE		
	RADIOPHARMACEUTICAL PREPARATION		
Mo-99/ Tc-99m	GENERATOR		
Sn-113/ In-113m	GENERATOR		
Tc-99m	REAGENT KITS		
Other			

3. DATES AND TOTAL NUMBER OF HOURS RECEIVED IN CLINICAL RADIOISOTOPE TRAINING

4. THE TRAINING AND EXPERIENCE INDICATED ABOVE WAS OBTAINED UNDER THE SUPERVISION OF:

a. NAME OF SUPERVISOR

b. NAME OF INSTITUTION

c. MAILING ADDRESS

d. CITY

5. MATERIALS LICENSE NUMBER(S)

6. PRECEPTOR'S SIGNATURE

7. PRECEPTOR'S NAME *(Please type or print)*

8. DATE