

INSTRUCTIONS MANUAL
APPLICATION FOR NEW INVESTIGATIVE STUDY (January 2004)

The following forms must be completed when submitting an Application for New Investigative Study at the Bronx VAMC.

Please note that all the following forms are for VA use only and will not be accepted by the MSSM GCO/IRB. Many of the forms are similar for both institutions please file appropriate paperwork with appropriate institution. If you are submitting to both VA and MSSM you must complete the VA application for the HSSC and the MSSM IRB application for the MSSM IRB.

**** If a consent form is being submitted as part of the application, the FULL 10-1086 VA consent form must be submitted, simply attaching the VA signature page to the Mount Sinai Consent which was prior accepted practice will no longer be acceptable effective 1/5/04.**

- I. Face Page
- II. Part I - Services Questionnaire
- III. Part II – Research Proposal
- IV. Part III – Information for Human Studies
- V. Protocol Summary
- VI. Waiver of Signed Consent
- VII. Waiver of Informed Consent
- VIII. Assurances
- IX. Adverse Events Form (To be completed during approval period, if applicable)
- X. VHA Handbook 1200.11 Appendix C (Bio Safety Form)
- XI. Consent Form

- I. Face Page: 1) Indicate Title of Project. Title should not exceed 142 spaces.
2) Indicate Principal Investigator's name, social security number and hospital title. (Principal Investigator must be a VA employee).
3) Indicate all co-investigators and collaborators. Please have each co investigator and collaborator sign the face page.
4) Protocols will not be accepted without the signature of the principal investigator and the program director.

II. Part I- Services Questionnaire:

Please complete questions 4 through 12. Indicate in question 12g the funding source. Protocols will not be accepted without appropriate funding source.

III. Part II – Research Proposal:

Complete on separate sheets unless equivalent information is provided in attached grant forms. Describe your research program, succinctly, but with sufficient

information to allow evaluation by an expert consultant in your field. Use the following headings:

- A) Specific aims.
- B) Brief review of results of others and current stage of knowledge
- C) Procedures, methods and experimental design.
- D) Previous work done by you or your collaborators on this or related projects, listing publications.
- E) Significance of this research.
- F) List of key bibliographic references.

IV. Part III – Information for Human Studies:

SECTION I-GENERAL

If this study involves human subjects, or biologic materials obtained from humans, sufficient information must be provided to weigh the risk against the benefits. The “Procedures” Section (IIC) should contain a detailed description of experimental design, methods and procedures.

- A. Basic Information (Even if described under “Procedures”, list the information requested below where pertinent.)
 - 1. What procedures will be used (i.e. biopsy, surgical operation, interview, experimental diet, infusion, drug administration, etc.) and with what frequency?
 - 2. Provide description of these procedures. If pharmacologic agents or radioisotopes are to be administered, give dosages, mode of administration and duration of usage.
 - 3. Describe population to be studied, listing basis for selection or exclusion. Include number to be studied.
 - 4. If subjects are patients, will conventional therapy or diagnostic procedures be withheld or modified for the purpose of this study?
- B.
 - 1. List possible hazards to subjects and/or investigative personnel from the procedures, drugs, or isotopes to be employed.

2. Include estimates of degree of risk with documentation from recent medical literature.
3. What monitoring or other safety precautions will be taken?

C. Possible Benefits

Describe possible benefits from this study and state whether these benefits will be to experimental subject, to others, or both.

Section II – Instruction for Documentation of Informed Consent

A. Consent Document:

1. VA Form 10-1086, Part I and Part II (dated September 1979) “Agreement to Participate in Research Program Under the Direction of the Veterans Administration”, must be completed.

2. VA Form 10-1086, Part I, is read and signed by the subject when he is legally competent to do so. Part II is signed by the subject’s legal guardian or authorized representative in situations where the subject is unable to do so because he has been adjudged incompetent by a court; or as a result of a psychiatric disorder; is unable to comprehend the significance of such action; or is unconscious, or is legally ineligible to give consent (See DM&S Manual M-3, Part I, Par.1.20).

3. VA Form 10-1086, Part I or Part II, when freely executed, will be filed in the patient’s medical record or outpatient treatment folder. A copy will be retained by the investigator and another given to the subject.

B. “Information About” Document and “Long-Form” Consent Procedure:
(See Interim Issue 10-81-44, dated October 8, 1981)

1. When submitting any human investigative study, to the Research Committee or Human Studies Subcommittee, which places subjects at risk of injury, investigators are required to prepare a separate document utilizing the “Long-Form” format. This format consists of a brief document, devoid of any exculpatory language, and written in a way which is easily understood by the subjects. If you are uncertain whether consent may be needed, consult the ACOS-R&D for advice.

2. This document must include the following elements:

- (A) The purpose of the investigation and a general statement as to its nature, i.e., how it relates to other knowledge and what may be made of the results obtained.
 - (B) The procedures to be used, including invasive techniques, restrictions on normal activities or the possibility of receiving inactive material in a double-blind trial.
 - (C) Any known risks, inconveniences or side effects that could be expected and what measures will be taken to minimize any hazard or discomfort or, where applicable, a statement that the risk cannot be predicted.
 - (D) Any benefits that may come to the subject as a result of participation in the trial, including therapeutic benefits, payments or recognition.
 - (E) Any alternate courses of action open to the subject – generally another course of therapy or diagnostic procedure – in lieu of participation in the study.
 - (F) A statement that the subject may withdraw, without prejudice, at any time from participation.
 - (G) The Human Studies requires that investigators list daytime and nighttime phone numbers to that they may be contacted should any study subject have problems needing attention.
 - (H) The following statement should be the last paragraph of the text: “I understand that should I wish to discuss my participation in this project with another doctor or layperson, I can contact the Director of Medical Research, by requesting an appointment (Extension 6007 or 4228; Office, Room 1F-01, First Floor in the Research Building).
3. Each sheet of this document will be headed “Information About”, followed by the title of the study.
 4. The document must be given to each subject who is allowed to read it or have it read, before discussing consent with the investigator. The subject then signs the final page along with the investigator and a witness, and retains one copy for his personal records. Another copy is filed in the medical record and a 3rd retained by the investigator. When the procedure is simple and the explanation is brief, several or all subjects can sign the same document. This document should be retained by the investigator and attached to his file copy of VA Form 10-1086.
 5. In discussing the investigation with the subjects, the investigator may have to go somewhat beyond statements in the information document. There must be, however, no substantive additions, deletions or modifications of the written information. If such a change is necessary for a particular subject, the

information document should be modified in writing and signed or initialed by the investigator and the subject. The information document is tangible evidence of what the investigator tells the patients.

6. As indicated above, consent has two components, VA Form 10-1086 is the consent agreement while the “information about” statement establishes that consent was informed and the nature of the information transmitted. These documents should be attached to one another. This procedure protects the patients rights and confirms that the physician has proceeded according to VA policy and practices.

All pharmaceutical protocols must have a contract with Pharmacy Program.

All protocols containing laboratory test must establish a contract with the Chief of Diagnostic Program.

LABTEST.XLS

	REQUEST FOR LABORATORY TESTS					
DATE						
INVESTIGATOR						
PROJ. TITLE						
PROJ. NO.						
TEST REQUESTED						
# SUBJECTS						
# TEST/SUBJECT						
TOTAL # TESTS						
COST/TEST						
TOTAL COST						
INVESTIGATOR						LAB MANAGER
SIGNATURE						SIGNATURE

V. Protocol Summary: Please complete questions 1 through 20c.

VI. Waiver of Informed Consent:

An investigator may request a waiver of the usual requirement for research subjects to sign a consent form to document that informed consent has been given (waiver of signed consent). To request a waiver of signed consent complete the following questionnaire. **Note:** The Code of Federal Regulations Title 45, Part 46.117 (c) **ONLY** permits an IRB to consider the possibility of approving a consent procedure which does not require a subjects signature when at least one of two specific criteria are met. Your request will be considered on a case by case basis at a convened meeting of the IRB.

VII. Waiver of Informed Consent:

An investigator may request approval of a modification in the requirements for informed consent (waiver of informed consent). To request a waiver of informed consent complete both Parts A and B. **Note:** The Code of Federal Regulations Title 45, Part 46.116 (d) **ONLY** permits an IRB to approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent (i.e. a waiver of informed consent) if four very specific criteria are met. Your request will be considered on a case by case basis at a convened meeting of the IRB.

VIII. Assurances:

The principal investigator as well as the co-investigators must sign an assurance page.

IX. Adverse Events Form:

Should be completed during approval period, if applicable. Definitions of adverse events:

(1) An **Adverse event** (AE) is defined as any untoward medical occurrence in a patient or clinical investigation subject who may or may not be administered a product (i.e., pharmaceutical, medical device, biologic, etc.) and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the investigation, whether or not related to the investigational product (ICH Guideline, Clinical Safety Data Management, March 1, 1995). This would include a change in the frequency or intensity or worsening of a pre-existing condition (a condition present at baseline).

(2) **Serious adverse events (SAE)** is defined (ICH Guideline, Clinical Safety Data Management, March 1, 1995) as any untoward medical occurrence that at any dose or with any product:

- (a) results in death;
- (b) is life threatening;
- (c) requires in-patient hospitalization or prolongation of existing hospitalization;
- (d) results in persistent or significant disability/incapacity;
- (e) **or** is a congenital anomaly/birth defect.

If tests in laboratory animals suggesting a significant risk for human subjects, including any finding of mutagenicity, teratogenicity or carcinogenicity, become available these must be reported to the IRB.

(3) **Unexpected adverse event** is defined (in the ICH Guideline, Clinical Safety Data Management, March 1995) as an adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g. an investigator's brochure for an unapproved investigational product or package insert/summary of product characteristics for an approved product).

(4) **IND Safety Report** is a written report of a serious adverse event that is determined by a sponsor-investigator to be both related to the drug/device under investigation and unexpected in nature.

2. Reporting of Adverse Events

(1) **All serious adverse events** which occur during the study (from patient enrollment through termination), and in a post-study period defined by the given protocol, **regardless of treatment group or relationship to the research**, must be reported to the Institutional Review Board by FAX (718-562-9120) or submit in person within 24 hours of the investigator's awareness of the occurrence of the event. These initial reports must be followed by a full written report (see below). Serious AEs should also be summarized annually in the IRB application for continuation or termination of the research.

(2) **All expected non-serious AEs** that occur at a **greater frequency or severity** than anticipated and **all unexpected non-serious AEs** must be reported to the IRB within 15 working days of the investigator becoming aware of the event. These AEs should also be summarized annually in the IRB application for continuation or termination of the research.

(3) All other AEs should be summarized annually in the IRB application for continuation or termination of the research.

(4) The investigator must include the following in the Bronx VA AE Report Form:

- (a) the project number and investigator's name;
- (b) Patient ID
- (c) a descriptive narrative of the event.
- (d) a descriptive narrative of any further action taken as a result of the event;
- (e) an indication of the outcome of the event;
- (f) a statement as to whether the investigator feels the event was definitely related to the subject's participation in the research, probably related, possibly related, or definitely not related and a statement as to whether the consent form has to be modified to incorporate the adverse event (if not already enumerated).
- (g) if the sponsoring agency (i.e. – industry or government agency) requires that a special form be completed and submitted, the investigator should forward a copy of that form to the Institutional Review Board.

3. Submission of IND Safety Reports

Copies of IND Safety reports that are received from Sponsors or generated from investigator held IND studies must be submitted to the IRB within fifteen (15) working days of receipt.

NOTE: The **IRB Serious Adverse Event/adverse Event/IND Safety Report Form** must be used when submitting adverse events and IND Safety reports to the IRB. Attach the form to the memo or report describing the event. The PI must sign and date the form to acknowledge that he/she is aware of the event and concurs with the assessments made.

X. VHA Handbook 1200.11 Appendix C (Bio Safety Form)

SAFETY OF PERSONNEL ENGAGED IN RESEARCH

1. **REASON FOR ISSUE:** This Veterans Health Administration (VHA) Handbook establishes new, integrated procedures for ensuring personnel safety in the Department of Veterans Affairs (VA) research laboratories by including information relevant to biohazards and establishes procedures for local and VHA Headquarters review of affected research proposals.

2. SUMMARY OF CONTENTS/MAJOR CHANGES

a. Paragraph 1: Delineates range of risks to research workers considered in the Handbook.

b. Paragraph 2. Defines hazard categories.

c. Paragraph 3: Provides general principles for ensuring safety in the major hazard areas.

d. Paragraph 4: Outlines responsibilities of research administrators, Research and Development Committees, Subcommittees on Research Safety, and research investigators for safety of research personnel.

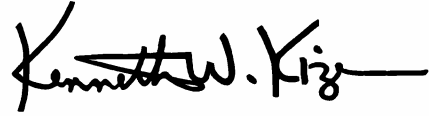
e. Paragraph 5: Provides key safety references.

3. **RELATED ISSUES:** VHA Directive 1200, to be published.

4. **RESPONSIBLE OFFICE:** The Chief Research and Development Officer (12) is responsible for the contents of this VHA Handbook. Questions may be referred to Deanna Robbins, Ph.D. by telephone (410) 605-7132, Fax (410) 605-7906, or e-mail drobbins@umabnet.ab.umd.edu.

5. **RESCISSIONS:** M-3, Part I, Chapter 11, dated March 5, 1985, is rescinded.

6. **RECERTIFICATION:** This document will be recertified on or before August 2002.



Kenneth W. Kizer, M.D., M.P.H.
Under Secretary for Health

DISTRIBUTION: **RPC: 1367 is assigned.**

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SAFETY OF PERSONNEL ENGAGED IN RESEARCH

1. PURPOSE

a. Ensuring personnel safety in Veterans Health Administration (VHA) research laboratories is of primary importance. This VHA Handbook prescribes mandatory procedures with respect to the potential hazards encountered in these settings, including, but not limited to:

(1) Biohazards

(a) Pathogens and/or etiologic agents corresponding to Biosafety Levels 1-4 (see subpar. 5.f.).

(b) Organisms and viruses containing recombinant deoxyribonucleic acid (DNA) molecules (see subpar. 5.g.).

(2) Chemical hazards.

(3) Physical hazards.

b. This Handbook covers only safety issues unique to research; it is not intended to replace general safety policy applicable to all Department of Veterans Affairs (VA) employees, whether or not involved with research.

NOTE: Hazards encountered in research laboratories will vary among medical centers according to the nature of research being conducted.

2. DEFINITION OF HAZARD CATEGORIES

a. **Biohazards.** Biohazards include, but are not limited to, the following:

(1) Pathogens and/or etiologic agents corresponding to Biosafety Levels 1-4 (as defined by subpar. 5.f., Laboratory Biosafety Level Criteria, Section III, pp. 16-67);

(2) Poisonous, toxic, parasitic and venomous animals or plants; and

(3) Recombinant DNA molecules.

(4) Select agents, as specified in Title 42 Code of Federal regulations (CFR) Part 72.

b. **Chemical Hazards.** Chemical hazards include any substance or mixture of substances with properties capable of producing adverse effects on the health and/or safety of humans. The general chemical hazard categories include corrosives, toxic substances (poisons, irritants, asphyxiants), sensitizers, carcinogens, mutagens and/or teratogens, flammables, and explosives.

c. **Physical Hazards.** Physical hazards include excessive levels of ionizing and nonionizing radiation (see App. A), noise, or vibration and extremes of temperature and pressure. Included in this category are explosive, electrical, and mechanical hazards.

NOTE: These definitions are illustrations and are not all inclusive; it is not possible to give complete definitions of even the major occupational hazards in the space available.

3. SCOPE

Research laboratories must have a written occupational safety and health program that is consistent with VA policies, Federal statutes and regulations, and any applicable state and local requirements. This program shall be called the Research Safety Program.

a. **Biohazards.** Each laboratory that will be using biohazardous agents shall include a description of the biohazard controls (i.e., engineering, administrative, and personal protective equipment), as part of the written occupational safety and health program. The laboratory’s occupational safety and health program must adopt the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH) safety and health guidelines (with respect to biosafety) unless an exception is granted by the Designated Agency Safety and Health Official (DASHO).

(1) The risk of exposure to bloodborne pathogens shall be minimized in the research setting by ensuring that all research personnel are aware of, and utilize, universal precautions in the handling of biologic fluids of any type according to the specifications of the Bloodborne Pathogen Standard (see subpar. 5.b.). Likewise, the risk of exposure to airborne pathogens such as *Mycobacterium tuberculosis* must be minimized and strict adherence to all applicable Federal statutes, regulations, and policies be rigorously upheld. Reviews of all research protocols must be submitted as a part of research proposals submitted to the appropriate component of the Office of Research and Development (R&D), e.g., Medical Research Service (121F), including a statement that the facility safety official has concurred.

(2) Recombinant DNA Research

(a) VA medical center investigators planning to conduct recombinant DNA research shall comply with the NIH Guidelines for Research Involving Recombinant DNA Molecules (see subpar. 5.g.), regardless of the source of research funding. These guidelines describe five categories of experiments involving recombinant DNA (see Section III of the NIH Guidelines). For all projects conducted at a VA facility, the following levels of approval are required:

Experiment category	Approval level
(i)	Chief Research and Development Officer (12)
(ii)	Chief Research and Development Officer (12)
(iii)	R&D Committee (after review by Subcommittee on Research Safety)
(iv)	R&D Committee (after review by Subcommittee on Research Safety)
(v)	R&D Committee (after review by Subcommittee on Research Safety)

(b) It should be noted that projects and proposals to be funded by NIH (reviewed and approved according to the procedures described in the NIH Guidelines) must receive local R&D committee approval and, when appropriate, approval from the Office of R&D (12).

b. **Hazardous Chemicals and/or Waste.** This Handbook is not designed to cover either the management of hazardous chemicals and/or waste in depth or to restate other Federal and state requirements applicable to the VA research laboratory setting. However, it assumes that the research laboratory’s occupational safety and health program (within the context of the facility’s safety program) will ensure that these Federal and state requirements are addressed. For example, Federal regulations require the development of a “chemical hygiene

plan” and the administration of this plan by a “chemical hygiene officer” (see subpar. 5.c.). **NOTE:** *Requirements for hazardous waste management are stated in subparagraph 5.c.*

c. **Physical Hazards.** Physical hazards must be addressed in the occupational safety and health program for research laboratories. **NOTE:** *Additional information about the management of radiation hazards is provided in Appendix A and paragraph 5..*

4. RESPONSIBILITIES

a. **Associate Chief of Staff or Coordinator for R&D.** The Associate Chief of Staff or Coordinator for R&D shall ensure that an adequate written occupational safety and health program has been developed, coordinated with the facility safety official, and included in research proposals.

b. **Research and Development Committee.** The R&D Committee shall:

(1) Establish a Subcommittee on Research Safety (SRS) that meets the requirements set forth in Appendix B and carries out the functions detailed in following subparagraph. Alternatively, the R&D Committee may establish more than one subcommittee dealing with different aspects of research safety. These subcommittees will, *in turn*, carry out the functions of the Subcommittee on Research Safety described as follows. Each subcommittee will have at least one member from the parent committee and provide written minutes to the parent committee as detailed in subparagraph 4.c. (8).

(2) Review all R&D proposals and ensure the SRS review of those proposals which involve safety hazards unique to the research environment.

(3) Appoint a Research Safety Coordinator who is responsible for supervising and operating the Research Safety Program. Normally, either the Associate Chief of Staff or the Coordinator for R&D will accept this role. Specific responsibilities for this position shall be specified in the written local policy of the Research Safety Program.

(4) Appoint a Biological Safety Officer if research is conducted at the facility that involves recombinant DNA research at Bio-safety Level(BL)3 or 4, or large scale (greater than 10 liters of culture) research or production activities involving viable organisms containing recombinant DNA molecules (see Section IV-B-3 of the NIH Guidelines). The Biological Safety Officer, who is also a member of the SRS, carries out the duties specified in Section IV-B-3-c of the NIH Guidelines.

(5) Oversee compliance with this Handbook by Principal Investigators conducting research at the facility as specified in subparagraph d. of this paragraph.

(6) Ensure the development and implementation of safety protocols by the Principal Investigator for individual research projects as needed.

(7) Provide the Associate Chief of Staff or Coordinator for R&D, facility safety official, and when appropriate, facility safety committee, information

needed to evaluate the occupational safety and health program for the Research laboratory.

c. **SRS.** The Subcommittee on Research Safety shall:

(1) Review all research proposals which involve safety hazards unique to the research environment for compliance with all applicable directives pertinent to biological, chemical, physical, and radiation hazards. This includes all research proposals to be conducted at the VA facility or by VA personnel off-site. The review (which should focus on the information provided by the Principal Investigator using App. C, or similar format) shall include:

(a) Assessment of the containment levels required for the proposed research.

(b) Assessment of the facilities, procedures, practices, and training and expertise of personnel involved in the type of research to be conducted including recombinant DNA research.

(2) Provide written notification to the R & D Committee and the Principal Investigator of the proposed research of the results of the SRS review.

(3) Certify its approval (or disapproval) of all proposals (which involves safety hazards unique to the research environment), using the format shown on page C-6 of Appendix C or similar format. This certification, along with pages C-1 through C-5 of Appendix C, must be included with any proposal submitted to the Office of Research and Development for funding. For medical research proposals, this document will constitute the Biohazards Statement referred to in M-3, Part II, Chapter5, and subparagraph 4.03t.

(4) Periodically review research conducted at the medical center to ensure compliance with all applicable directives.

(5) Coordinate all safety- related activities in research laboratories including safety training, safety inspections, accident reporting, and liaison activities with other facility safety committees and officials.

(6) Report operational problems (including research- related accidents or illnesses directly affecting the health and safety of Research personnel or others), or violations of directives to the Research Safety Coordinator within 30 days of occurrence or detection unless the SRS determines that a report has already been filed by the Principal Investigator.

(7) Identify need for health surveillance of personnel involved in individual research projects; and if appropriate, advise R&D Committee and Employee Health Practitioner on need for such surveillance.

(8) Maintain adequate documentation of all SRS or equivalent subcommittee activities and distribute minutes of its meetings to the R&D Committee and to the facility safety committee.

(9) Hold meetings at least quarterly.

d. **Principal Investigator or Laboratory Director.** The Principal Investigator or Laboratory Director shall: (1) Prior to initiating the research:

(a) Submit the initial research proposal to the medical center Research Office, which will arrange for review by the SRS.

(b) Include in the proposal:

1. A summary of possible hazards associated with the proposed research (recorded by the Principle Investigator, on App. C, or similar format).

2. References to the occupational safety and health program for the R&D and laboratory;

3. Controls that will be taken to minimize potential hazards; and

4. The actions to be taken in the event of an accident.

(2) After R&D Committee approval, but before initiation of research:

(a) Train employees concerning potential hazards and the occupational safety and health program; coordinate all safety-related training with facility safety officials.

(b) Maintain a record of all personnel who have been trained.

(c) Inform the laboratory staff of the reasons and provisions for any precautionary medical practices advised or requested (e.g. vaccinations or serum collection).

(d) Provide a listing and quantities of hazardous chemicals and Material Safety Data Sheets (MSDS) to the Chemical Hygiene Officer for Research and/or appropriate facility or activity officials.

(3) During the conduct of research:

(a) Supervise the performance of the laboratory staff to ensure that the required safety practices and techniques are employed.

(b) Investigate and report problems pertaining to operation and containment practices and procedures in writing to the facility safety officer (where applicable), the Veterinary Medical Officer (where applicable), the Radiation Safety Officer (if applicable), the R&D Committee, or other appropriate authorities.

(c) Correct work errors and conditions that may result in safety hazards or the release of recombinant DNA material.

(d) Ensure the integrity of the physical containment (e.g., biological safety cabinets) and the biohazards containment (e.g., purity and genotypic and phenotypic characteristics), and

(e) Secure approval of the R&D Committee through the SRS or equivalent subcommittees for any changes to be made in the original research plan.

(4) When planning to close a laboratory check out with all relevant officials, e.g. chemical hygiene officer, industrial hygienist, Radiation Safety Officer, and the SRS to ensure that the laboratory to be closed (vacated) does not contain unidentified chemicals or waste, biological agents, or radiological materials or waste.

5. REFERENCES

a. Title 10, CFR Part 19, Notices, Instructions and Reports to Workers Inspections and Investigations; and Part 20, Standards for Protective Against Radiation; and Part 35, Medical Use of Byproduct Material.

b. Title 29, CFR, Part 1910.1450, Occupational Exposure to Hazardous Chemicals in Laboratories; and Title 29, CFR, Section 1910.1030, The Bloodborne Pathogen Standard.

c. Title 40, CFR, Subchapter I, Solid Waste, Part 260, Hazardous Waste Management System: General et. seq.

d. Title 42, CFR, Part 72, Additional Requirements for Facilities Transferring or Receiving Select Agents.

e. "Radiologic Protection in Biomedical Research," Annals of the ICRP, Vol. 22, No., 3, 1991.

f. Centers for Disease Control and Prevention (CDC)/National Institutes of Health (NIH). Biosafety in Microbiological and Biomedical Laboratories. CDC/NIH, Washington, DC, 1993.

g. "National Institutes of Health Guidelines for Research Involving DNA Molecules," NIH Guidelines. National Institutes of Health, Bethesda, MD, April, 1995.

h. "Implementation of the principle of As Low as Reasonably Achievable (ALARA) for Medical and Dental Personnel," National Council on Radiation Protection and Measurements (NCRP) Report No. 107. National Council on Radiation Protection and Measurements, Bethesda, MD, 1990.

i. "Limitation of Exposure to Ionizing Radiation," NCRP Report No. 116. National Council on Radiation Protection and Measurements, Bethesda, MD, 1993.

j. M-1, Part VII, Chapter 14, Waste Management.

RADIATION HAZARDS

1. The safe uses of radioactive materials are controlled either by implementation of the licensing and regulatory requirements of the Nuclear Regulatory Commission (NRC) or through Veterans Health Administration (VHA) policies for safety and control procedures similar to the NRC's regulations (see subpar. 5.a.). These policies, procedures and regulations collectively control the receipt, uses and disposal of radioactive materials in the VHA research programs.
2. X-Ray devices and their uses, while generally not subject to regulation in Federal facilities, are nevertheless subject to de facto standards of practice and the important recommendations of influential national and international councils and commissions (see subpars. 5.h. and 5.i.). Specific details of local facility requirements are approved and promulgated by a facility Radiation Safety Committee (RSC) and implemented by the Radiation Safety Officer (RSO). The RSC and the RSO are the primary facility resources for ensuring safe and effective uses of ionizing radiation in research and should always be consulted.
3. While Federal regulation and the weight of authoritative commissions establish upper limits for the permissible radiation dose to workers and the public, one of the most effective tools for education on dosage is the facility specific As Low As Reasonably Achievable (ALARA) programs (see subpar. 5.h.). This is a mandatory commitment to maintain individual and collective radiation doses as low as reasonably achievable and requires participation of management, safety personnel, and individual research users.

COMPOSITION OF SUBCOMMITTEE ON RESEARCH SAFETY

It is recommended that the Subcommittee on research Safety (SRS) include member(s) from the facility safety committee, such as the Safety Officer, the Facility Infection Control Committee; the Subcommittee on Animal Studies, the Radiological Safety Officer; and a liaison from an affiliated university Institutional Biosafety Committee. Such individuals may be included in the core five members referred to in subparagraph 1a of this Appendix.

1. Number and Qualification of Members

a. Each SRS will have at least five members, exclusive of ex-officio members. The SRS will include two members not affiliated with the Institution, when the research reviewed involves recombinant DNA not exempt from the current National Institutes of Health (NIH) Guidelines for Research Involving Recombinant deoxyribonucleic acid (DNA) Molecules (VHA Handbook 1200.11, subpar. 4.b.).

b. It will usually be necessary for the SRS to possess expertise in:

- (1) Etiologic agents, including bloodborne and airborne pathogens.
- (2) Chemical carcinogens and other chemical hazards.
- (3) Physical and radiation hazards.

2. Ex-Officio Members

- a. The Administrative Officer for Research and Development (R&D) or other representative from the R&D office.
- b. A liaison member from the local R&D Committee.
- c. An employee union safety representative or other union designee.

3. Representatives from other Medical Center Committees and/or Offices.

NOTE: If the facility conducts research with recombinant DNA, it shall comply with all requirements with respect to composition of an Institutional Biosafety Committee as specified in the NIH Guidelines (see Handbook 1200.11, subpar. 5.g.).

XII. Consent Form

INSTRUCTIONS FOR COMPLETING THE VA RESEARCH CONSENT FORM (10-1086)

1. THE PURPOSE OF THE STUDY AND HOW LONG IT WILL LAST.

Introduce the subject to the nature of the research, why it relates to his condition, and make a specific purpose statement. Also include why the subject qualifies for participation as well as who is sponsoring the study..

2. DESCRIPTION OF THE STUDY INCLUDING PROCEDURES TO BE USED.

- 1. Start this section with: **If you consent to participate in this research study**
- 2. Give a step by step description of the procedures from selection of patients through follow-up. Identify phases, if appropriate.
- 3. Discuss experimental procedures (do not call them investigational procedures). Focus on invasive techniques, restriction of normal activities, long term follow-up, and possibility of receiving inactive materials.
- 4. Make a clear distinction between procedures which are necessary because of the study and those which would be required as part of the subject's usual care. This includes increases in time, complexity, discomfort, and/or prolongation of hospitalization or hospitalization entirely for research purposes.
- 5. If the study involves random assignment, the nature and probability of group assignment must be specified:
Using a procedure like flipping a coin, you will have a 1 in _____ chance of receiving a sugar pill instead of _____.
- 6. If the subject and/or treating physician are to be kept blind to group assignment, this fact must be included.
- 7. When appropriate, the subject's approximate length of involvement in the study shall be indicated.

8. The number of times a procedure is repeated shall be noted.
 9. The duration of lengthy procedures, including questionnaires, should be indicated. This may be summarized for procedures done as a group.
3. DESCRIPTION OF ANY PROCEDURES THAT MAY RESULT IN DISCOMFORT OR INCONVENIENCE
1. If blood is withdrawn, both the frequency of the procedure and the total amount of blood should be indicated in metric measures, followed by teaspoons, tablespoons, ounces, pints, etc., as appropriate. For studies involving a large number of samples to be drawn over an extended time interval, an estimate can be given.
 2. For women of child bearing age:
If pregnant subjects are to be excluded, the following statement is required for all women of childbearing age:
Since this research may have bad effects on an unborn child and should not be done during pregnancy, it is necessary that a pregnancy test be done first. To your knowledge, you are not pregnant at the present time.
 3. If the research extends over more than several days, add a statement to indicate the following:
You also agree to avoid becoming pregnant (use contraceptives, take precautions against becoming pregnant, etc.) during this study
 4. For studies involving investigational (experimental) drugs, devices, or procedures, the following statements must be included:
(a) **Because this is a new (drug, device, procedure) we do not know all of its bad effects. You should contact (name of the VA investigator) at (phone, location) if you have any bad effects. Include this information about the investigator here even if it is repeated elsewhere.**
(b) **We (I) can not guarantee that you will be able to continue receiving this (drug, device, procedure) after this study is over.**
 5. Describe anything unusual about this study that is not covered above.
 6. List the anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

Please note that for Potentially Vulnerable Subjects Groups the following also must be included.

A. Subjects Who May Have Diminished Mental Capacity

In order that a subject give his/her informed consent to enroll in a research project, that individual must fully understand all aspects of the study and his/her rights as a

research participant. This can only be done if subjects have the mental capacity to understand. If there is a possibility that the subjects may have diminished capacity, their mental capacity must be assessed.

For research protocols which involve subjects who may lack the capacity to give informed consent or subjects whose condition creates a reasonable likelihood of development of impaired capacity while on the study, special measures must be instituted to assess capacity initially and/or to monitor it during the study.

In their written submissions the Principal Investigators should employ the following topic headings, or some other device, which will enable the members of the IRB to more easily identify and evaluate how these guidelines are being met. If any study cannot conform to the guidelines, the Principal Investigator must specifically describe the deviation and the reason for it:

1. **Assessment of Capacity:** For individuals who may have diminished mental capacity there must be an assessment of the subject's capacity to consent to participate prior to enrolling subject in the study. For all subjects in studies involving individuals with psychiatric illness, and for any other subject in any other study for whom there is diminished mental capacity or a question of diminished capacity, the assessment should be undertaken by a physician not associated with the study and whose professional training and credentials are suitable given the nature of the subject's illness and the nature of the study. This physician must be completely independent from the study and the physician's name should not appear as an author on any published paper reporting on the study as that might lead to the appearance of a conflict. The protocol must indicate how the assessment of capacity will be undertaken. Factors to be considered in assessing capacity include: the prospective subject's medical condition, the voluntariness of the subject's consent in light of the subject's hospitalization or relationship with the physicians conducting the study, as well as the subject's ability to assess the information provided to him/her and make informed and knowing decisions. **In the event the subject lacks capacity to consent to participate, consent must be given by an individual legally authorized to consent on behalf of the subject.**

2. **Monitoring:** If there is a likelihood that a subject's capacity may become impaired during the course of a study, then the specific mechanisms for monitoring the subjects to determine if there is a decrease in capacity must be detailed in the protocol and/or the consent form.

B. Withdrawing Drugs from Subjects

The Bronx VAMC IRB has developed the following guidelines for any research protocol involving the withdrawal of drugs from human subjects, particularly the withdrawal of neuroleptics from psychiatric subjects. For purpose of these guidelines, withdrawal of medication includes a washout study, a withdrawal study, or a study that entails a washout or drug withdrawal that may be followed by administration of a drug or placebo.

1. **Assessment of Capacity:** If there is any question of the subject's capacity

to give informed consent or the possibility of deterioration and loss of capacity during the study, capacity must be evaluated as detailed above.

2. **Assessment of Clinical Suitability:** A qualified physician/investigator must assess the subject, and determine the subject's clinical suitability to participate in the study.

3. **Enrollment:** At the time of a subject's enrollment in a study, the informed consent process must take place and must be consistent with institutional guidelines for enrolling individuals in studies. Once a subject or surrogate signs the consent form, the subject is considered to be enrolled in the study. Any change in the subject's therapeutic regime, which may be necessary, may only be made after the subject has signed the consent form agreeing to participate in the study.

4. **Monitoring:** The mechanisms for monitoring the subject while on the protocol must be detailed in the research protocol (and the consent form) as described below. Those mechanisms must be appropriate given the subject's clinical condition and the nature of the study. The subject must be seen and assessed by an independent physician with sufficient frequency to assure the subject's health will not deteriorate while on the study. This physician must be completely independent from the study and the physician's name should not appear as an author on any published paper reporting on the study as that might lead to the appearance of a conflict. Any protocol not requiring the periodic personal assessment by an independent physician must specifically state the reason for such omission. For some protocols, particularly outpatient psychiatry protocols, an additional monitor, a "home monitor" should be identified who can evaluate the subject on a more frequent basis. The "home monitor" should be a reliable adult relative or friend who lives in close proximity to the subject and who is capable of reporting changes in the subject's status to the investigators.

The protocol and consent form(s) must indicate:

- (a) who will do the monitoring;
- (b) the frequency of monitoring, including a justification for the intervals between monitoring that is dependent on the disease process;
- (c) the site at which monitoring will be done (clinic, hospital, doctor's office, home); and
- (d) an itemization of the tests, lab data, examinations, etc. that will be used to monitor the subject.

5. **The Content of the Consent Form:** The consent form and the consent process must comply with all the requirements for consent forms in human subject research. In addition, specifically with respect to studies in which a subject will be withdrawn from a therapeutic medication, it is critical that the consent form:

- (1) Identify:
 - (a) the risks associated with the withdrawal from the subject's current medication;

- (b) the risks of being maintained on a placebo (if applicable); and
- (c) the risks of the experimental drug(s).

(2) Describe the symptoms and assess the risks of the occurrence of those symptoms during the period of withdrawal, or while receiving placebo or experimental drug.

(3) If the subject is expected to self-monitor for recurrence of the symptoms, the procedure for such self-monitoring should be clearly set forth. If there will be additional monitoring, the subjects must be told:

- (a) who will do the monitoring,
- (b) the frequency of the monitoring,
- (c) the place where monitoring will be done and
- (d) the specific tests, lab data and/or examinations that will be done for the purposes of monitoring. The actual purpose of monitoring (to assess possible relapse) should be stated and the specific symptoms, which are being looked for, should be listed.

(4) The reversibility of any recurrence of symptoms as the result of medication withdrawal or placebo administration must be specifically described as well as the clinical steps that will be necessary to return the subject to the subject's former baseline.

(5) The threshold for initiating treatment and removal from the study should be described as well as how the decision to return the subject to the subject's medication will be made and by whom.

(6) It must be made clear to the subject that not only does the subject (or an appropriate surrogate) have the right to decide to withdraw from the study, but the subject also has the right to be returned to an appropriate clinical regime. In the event the subject's participation ends because the study ends, the subject and surrogate must be advised whether the subject will be returned to the subject's old medication, and whether the experimental drug, should it be useful, will be available to the subject.

4. EXPECTED RISKS OF STUDY

1. State any known risks, inconveniences, or side effects, with at least a rough estimate of number per 100, 1000, etc. of likelihood for severe events such as, loss of limb, coma, death, hemorrhage, etc.
2. If blood is to be drawn, include the following risks: **Pain, bruising, and rarely, fainting or infection.**
2. Discuss any measures taken to minimize hazards.
4. Note that risks cannot be predicted.

5. Include the effects these risks will have on the person's health or person as a result of participating in the research study.

5. EXPECTED BENEFITS OF STUDY

1. Describe any potential benefits to the subject, society, or future patients with similar conditions. This section should answer the question of how the benefits outweigh the risks and discomforts. It should indicate how fruitful results could not be obtained by other methods or at random. The subject should have a clear understanding of why the experiment is justified, without being coerced.
2. If there are no clear benefits to this subject, include the following:
You may not personally be helped by taking part in this study, but your participation may lead to knowledge that will help others.

6. ALTERNATIVE THERAPY OR DIAGNOSTIC TEST

1. Discuss the consequences of not being involved in the study including whether and how the evaluation/treatment received would be different.
2. Where appropriate, include the consequences of a subject's decision to withdraw from the research.
3. Where appropriate, include the set procedure for safe and orderly termination of participation when abrupt termination would impose risks.

7. USE OF RESEARCH RESULTS

Consider the statements below, as applicable. The wording should be changed only for substantive reasons and without changing the meaning. The intent of the statements and all parts of the statements should be retained.

1. **We (I) will let you and your physician know of any important discoveries made during this study, which may affect you, your condition, or your willingness to participate in this study.**
2. If using scales, which elicit information concerning suicidal intent, depression, or other major clinical findings, indicate when the primary physician will be notified.
3. Include a statement that indicates who will have possession of questionnaires, videos, audio cassettes, who else will have access to them, how they will be secured, and the timing and method of coding and disposal.

4. Include a statement as follows: If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent or No information by which you can be identified will be released or published unless required by law. Your medical records will be maintained according to this medical center's requirements.
5. If an investigational drug, device, or procedure is involved, add: However, there is a possibility that the food and drug administration or (the name of the sponsoring company) may inspect the records.
6. The following standard statement must be included on consent form, "Your identity as a participant in this research study will be kept confidential in any publication of the results of this study. The information obtained during this research (Research Records) will be kept confidential to the extent permitted by law. However, this Research Record and or hospital Medical Records (if any) may be reviewed by government agencies (such as the Food and Drug Administration or the Department of Health and Human Services), the agency sponsoring this research, individuals who are authorized to monitor or audit the research, or the Institutional Review Board (the committee that oversees all research in humans at Bronx VAMC) if required by applicable laws or regulations."

All of the following items must be included in this Section exactly as stated and in the listed order. Modification is allowed in item 3 when applicable. This section represents an affirmation to the subject concerning participation.

8. SPECIAL CIRCUMSTANCES

1. **If you are a patient, a copy of this consent form will be placed in your medical record.**

9. COMPENSATION AND/OR TREATMENT IN THE EVENT OF INJURY

1. Include a statement of who to contact in the event of a research-related injury to the subject.
2. In case of adverse (bad) effects or physical injury resulting from this study, eligible veterans are entitled to medical care and treatment. Compensation may or may not be payable in the event of physical injury arising from this study under applicable federal law. Further information about compensation and medical treatment may be obtained from the medical administration service at this VA medical center. Non-eligible veterans are entitled only to medical emergency care and treatment on a humanitarian basis.

10. VOLUNTARY PARTICIPATION

1. You are not required to take part in this study: your participation is entirely voluntary.
2. You can refuse to participate now or you can withdraw from the study at any time after giving your consent. This will not interfere with your regular medical treatment, if you are a patient.
3. Eligibility for medical care is based upon the usual VA eligibility policy and is not guaranteed by participation in a research study.

11. TERMINATION OF PARTICIPATION

1. You can refuse to participate now or you can withdraw from the study at any time after giving your consent. This will not interfere with your regular medical treatment, if you are a patient.
2. A statement of consequences of subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject is included.
3. A statement of anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

12. CONTACT PERSON

1. Include a statement of whom to contact for answers to questions about the research and the rights of the research subjects.

13. COSTS AND REIMBURSEMENTS

1. There will be no costs to you for any of the treatment or testing done as part of this research study.
2. when applicable, clarify that costs for clinically indicated tests and procedures are the responsibility of the patient.

CONSENT FORM 10-1086 - THE LAST PAGE OF THE CONSENT FORM - AFFIRMATION FROM SUBJECT]

RESEARCH SUBJECTS' RIGHTS: I have read or have had read to me all of the above. Dr. _____ has explained the study to me and answered all of my questions. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

I understand that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled.

The results of this study may be published, but my records will not be revealed unless required by law.

In case there are medical problems or questions, I have been told I can call Dr. _____ at _____ during the day and Dr. _____ at _____ after hours. If any medical problems occur in connection with this study the VA will provide emergency care.

I understand my rights as a research subject, and I voluntarily consent to participate in this study. I understand what the study is about and how and why it is being done. I will receive a signed copy of this consent form.

Subject's Signature

Date

Signature of Subject's Representative*

Subject's Representatives
(print)

Signature of Witness

Witness (print)

Signature of Investigator

*Only required if subject not competent.
“I understand that should I wish to discuss my participation in this study with any other doctor or layperson, I can contact the ACOS-R&D Program by requesting an appointment (718) 741-4228 hospital extension 4228, first floor in the research building, room 1F-01. Questions concerning conduct of a study or of subject research rights, should also be addressed to the ACOS. Medical problems during the course of the study should be addressed to the investigator at the phone listed above”