INVESTIGATIONAL DRUGS AND SUPPLIES

1. REASON FOR ISSUE. This Veterans Health Administration (VHA) Handbook provides specific direction and procedures related to the appropriate handling of investigational drugs and supplies.

2. SUMMARY OF MAJOR CHANGES. This is a new VHA Handbook which incorporates centralized dispensing requirements and appropriate co-pay assessment for investigational drugs and supplies.

3. RELATED DIRECTIVE. VHA Directive 1108 (to be published).

4. RESPONSIBLE OFFICE. The Office of Patient Care Services, Pharmacy Benefits Management Strategic Health Group (119), is responsible for the contents of this Handbook. Questions may be addressed to 202-273-8429.

5. RESCISSIONS: VHA Manual M-2, Part VII, Chapter 6, is rescinded.

6. RECERTIFICATION: This VHA Handbook is scheduled for recertification on/or before the last working day of October 2010.

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INVESTIGATIONAL DRUGS AND SUPPLIES

1. PURPOSE

This Veterans Health Administration (VHA) Handbook provides specific procedures related to the appropriate handling of investigational drugs and supplies.

2. DEFINITIONS

a. **Authorized Prescriber.** An authorized provider is a provider who is authorized to prescribe the investigational drug as a Principal Investigator (PI) or Site Investigator (SI).

b. **Blind.** The term blind refers to the lack of knowledge regarding the identity of the drug treatment. In a clinical trial, patients, investigators, and other personnel may be kept "blinded" to the medication prescribed in order to decrease biases and avoid placebo effect.

c. **Comparator Drug.** A comparator drug is an agent that the investigational drug is being compared to in a clinical trial. A comparator drug may be the current standard of care for the disease state being studied.

d. **Centralized Dispensing Protocol.** A centralized dispensing protocol is a protocol that requires dispensing of the investigational drug(s) and possibly concurrent or comparator medications from a single centralized pharmacy, directly to the study participants.

e. **Cooperative Study.** A cooperative study is a project or program of research at two or more VA health care facilities which utilizes a common protocol, so that data obtained at all participating facilities can be treated as though from a single source.

f. **Investigational Drug.** An investigational drug is a chemical or biological drug that is used in a clinical investigation.

(1) An investigational drug can be:

(a) A new chemical compound, which has not been released by the Food and Drug Administration (FDA) for general use, or

(b) An approved drug that is being studied for an approved or unapproved use, dose, dosage form, administration schedule, or under an Investigational New Drug (IND) application, in a controlled, randomized, or blinded clinical trial.

(2) Concurrent medications, comparators, or rescue medications used in the investigational trial that are not the drug(s) being studied are not defined as investigational drugs unless they are not commercially approved or not available through commercial channels. Prescription drugs, over-the-counter drugs, nutritional supplements, herbal preparations, and legend items used for diagnosis or treatment and meeting the definition in subparagraph 2f(1), are considered

investigational drugs. ***NOTE:*** *The preceding definitions also apply to drugs used for animal research that are stored in or dispensed by pharmacy.*

g. **Investigational Supply.** An investigational supply is any medical or surgical product listed in the National Drug File and is not considered a drug. These products are identified as Department of Veterans Affairs (VA) Class IN-000, and are not subject to co-payment.

h. **Principal Investigator (PI).** A PI is the individual who is accountable for the proposal, the protocol, performance, and culmination of a research or development project. For multi-center clinical trials, the SI at each site is the individual at each clinical site who is accountable for all aspects of conduct of the study at the site. ***NOTE:*** *The terms PI and SI are considered equivalent for the remainder of this Handbook.*

i. **Repass or Retest Date.** A repass or retest date is the date assigned by the manufacturer after which the drug substances need to be examined to ensure that they are within suitable specifications for use in the manufacture of a drug product.

3. CO-PAYMENTS

a. Title 38 United States Code (U.S.C.) 1722A, Co-Payment for Medications, and Title 38 Code of Federal Regulations (CFR) 17.110, Co-Payment for Medications, state that VA medication co-payments will be waived if the medication is provided to the patient as part of a VHA-approved research protocol. This is true even when the sponsor of the investigational study does not provide the medication. However, in those instances when the sponsor does not provide the protocol medications and medical care appropriations are utilized for their purchase, that amount must be reimbursed from the research appropriation. ***NOTE:*** *Neither dispensed supplies nor investigational supplies are subject to co-payment.*

b. Co-payment eligible patients, participating in 38 U.S.C. 7303 third-party funded VHA-approved research projects should not be charged for inpatient or outpatient medications provided through an investigational drug study. However, these individuals are still subject to appropriate co-payment for VHA provided medications for non-research medical care, or for treatment associated with local, non-centralized research projects. To ensure that co-payments are not generated for subjects in approved investigational protocols see subparagraph 4c(9).

4. SCOPE

a. The Investigational Drug Program is the major component of VHA's clinical research program. Investigational protocols can be localized or cooperative in design, but in all instances must have the approval of the Research and Development (R&D) Committee and the Institutional Review Board (IRB) at each medical center where the study is conducted.

(1) Each facility carrying out investigational drug and/or supply studies must ensure through written policies and procedures that adequate safeguards are in place to protect the patient, the staff, the facility, and the quality of the study.

(2) All investigational drug studies must be consistent with applicable laws, regulations and VA policy. They must be conducted by properly qualified investigators under protocols approved by the local R&D Committee and the IRB.

(3) The R&D Committee cannot approve a proposal involving investigational drugs unless the Chief, Pharmacy Service, or the Chief (Manager) for Research Service Investigational Pharmacy documents in writing that pharmacy resources are adequate or that satisfactory provisions have been made to reimburse pharmacy for the services provided. Resources need to consider pharmacist time and associated costs. These costs include, but are not be limited to:

(a) Pharmacist time for protocol review, study start-up, ordering, monitoring, dispensing, and closure;

(b) Space and equipment (i.e., refrigerator or freezer space);

(c) The destruction or return of unused medication or supplies;

(d) Plans for the treatment of non-VA patients; and

(e) Plans for maintaining study medications after completion of the study protocol. ***NOTE:*** *Reimbursement fees may be required.*

(4) The patient or the patient's surrogate must be given complete information regarding the study objectives, risks, and benefits of the study. The patient must then give written, informed consent to participate in the study, unless the informed consent requirement is waived by both the R&D and IRB Committees.

(5) The Pharmacy and Therapeutics (P&T) Committee must review all Quality Improvement (QI) projects (such as Medication Utilization Evaluations (MUE) or Drug Use Evaluations (DUE)) to determine if the project incurs patient risk. The IRB Committee at VA facilities (or their designated University affiliate) may conduct an expedited review of QI projects when it has been determined that the project incurs no more than minimal risk to the patient, or when previously approved research requires only minor changes in accordance with 38 CFR §16.110. This is essential to allow publication and dissemination of the results outside of VHA settings. ***NOTE:*** *This requirement includes approved pharmacy resident research projects.*

(6) During the clinical investigation of a drug, it may be appropriate to use the drug in the treatment of a patient who is not in the clinical trial, in accordance with a treatment protocol or treatment IND.

(a) The FDA criteria permitting an investigational drug to be used for a treatment under a treatment protocol or treatment IND are if:

1. The drug is intended to treat a serious or immediately life-threatening disease;

2. There is no comparable alternative drug or other therapy available to treat that stage of the disease in the intended patient;

3. The drug is under investigation in a controlled clinical trial under an IND in effect for the trial, or all clinical trials have been completed; and

4. The sponsor of the controlled clinical trial is actively pursuing marketing approval of the investigational drug with due diligence (21 CFR §312.34).

(b) If all conditions exist, then the emergent use of an IND may be utilized in accordance with 21 CFR §312.36. Submissions for the institution of treatment (including a treatment protocol submitted by an IND sponsor or a treatment IND submitted by a licensed practitioner) are detailed in 21 CFR §312.35. Informed consent is required unless the conditions for exemption are met. The IRB must be notified within 5-working days when an emergency exemption is used.

(7) All investigational drugs and supplies, as defined in paragraph 2, must be provided by the study sponsor. Commercially available study drugs are to be provided by the study sponsor or procured using research appropriations. They are to be stored in a separate storage area as described in subparagraph 8a.

(8) Concurrent, comparator, or rescue medications that are required by the study sponsor and used for study-related purposes need to be recorded by the dispensing pharmacy as part of the study treatment. These medications are to be stored in accordance with subparagraph 8a. If the study sponsor does not provide these medications and medical care appropriations are utilized for their purchase, that amount must be reimbursed from the research appropriation.

(9) Medications approved for an investigational study must be identified in the drug file as a study medication. If the medication is already listed as a formulary agent, a second entry in the drug file identifying the medication as a study medication or supply is required. ***NOTE:*** *The Investigational Drug Pharmacist, or the Pharmacy Automated Data Processing Applications Coordinator (ADPAC), may be contacted regarding questions relating to the entry of research medications.*

b. VA has contracted the National Committee for Quality Assurance (NCQA) to develop and implement an accreditation program to systematically review all VA Human Research Protection Programs (HRPP). Each year a self-assessment of the institution's HRPP needs to be considered. The findings of this review need to be reported to the P&T Committee, R&D Committee, and the IRB. ***NOTE:*** *A self- assessment tool can be found at:* http://www.phrp.org/show.asp?durki=4864 *under Standards for Accreditation.*

5. PHARMACY RESPONSIBILITIES

a. Pharmacy Service, and/or Research Service Investigational Pharmacy, as part of their function on local research committee(s), are responsible for determining that all investigational studies have received initial approval and funding, prior to ordering, receipt, storage, or dispensing of investigational drugs. Documentation of a properly-approved clinical investigation includes:

(1) Minutes or an approval letter signed by the R&D Chairperson;

(2) Minutes, an approval letter signed by the IRB Chairperson, or VA Form 10-1223, Report of Subcommittee on Human Studies, approved by the IRB or the R&D Committee;

(3) A copy of VA Form 9012, Investigational Drug Record, when appropriate; and

(4) A copy of the approved protocol.

b. Medications approved for an investigational study must be identified in the drug file as a study medication. If the medication is already listed as a formulary agent, a second entry in the drug file identifying the medication as a study medication or supply is required. The Drug Enforcement Agency (DEA) special handling field needs to be noted as investigational for this entry. This is to be accomplished prior to study initiation in order to prevent a veteran's co-payment from being assessed at the time of dispensing.

c. All documentation of the continuing review process or termination for clinical investigations involving investigational drugs must be provided to Pharmacy Service and/or to the Research Service Investigational Pharmacy by the PI.

d. The Chief, Pharmacy Service, or Chief (Manager) for Research Service Investigational Pharmacy, is responsible for the receipt, storage, security, labeling, dispensing, and disposition of all investigational drugs. Investigational drugs must be:

(1) Secured in the pharmacy,

(2) Stored separately from the non-investigational drugs, and

(3) Be clearly identified. ***NOTE:*** *Storage does not require a separate locked area within pharmacy unless the medication has specific storage requirements as identified in subparagraph 8g.*

e. Pharmacy Service and/or Research Service Investigational Pharmacy need to be represented as a member on the local R&D Committee. If this is not possible, another formal mechanism is to be established to inform Pharmacy Service of approved drug research. Pharmacy Service and/or Research Service Investigational Pharmacy must be represented on the IRB or Human Studies Subcommittee.

f. Clinical investigations conducted as part of a "Non-VA Research Cooperative Agreement" (clinical trial research agreements with another Federal agency) require review by the P&T Committee in addition to the IRB. The local P&T Committee (or the Veterans Integrated Services Network (VISN) Therapeutics Management Committee), must review the "Cooperative Research Agreement" to ensure that all medication benefits and costs associated with the clinical trial are realized.

g. Pharmacy Service and/or Research Service Investigational Pharmacy representatives to the local R&D and IRB are required to meet all local educational requirements on ethics and good clinical practice.

6. RESPONSIBILITIES OF PHARMACY SERVICE OR RESEARCH SERVICE INVESTIGATIONAL PHARMACY

a. The Chief, Pharmacy Service, or Chief (Manager) for the Research Service Investigational Pharmacist may delegate in writing the custody of investigational drugs stored outside the pharmacy to the PI. This delegation of custody document is an agreement on the specific procedure that the PI is required to follow.

(1) It must identify the location of the drug and the name of the investigator responsible for the storage and dispensing; be signed by the PI; and maintained in the pharmacy.

(2) In these cases the Investigational Drug Pharmacist must verify that the storage location meets all security and storage requirements. Access to this storage area is to be restricted to appropriate study personnel only.

(3) When investigational drugs are stored outside of the pharmacy a real-time documentation of all drugs dispensed is required. This dispensing log provides a method for Pharmacy Service to inspect the investigational drug inventory and track all dispensing from the storage area.

(4) The PI must comply with all dispensing and documentation requirements and these records must be made accessible to the investigational drug pharmacist when requested. ***NOTE:*** *The storage of investigational drugs outside of the Pharmacy needs to be discouraged when a pharmacy is located within the facility.*

b. Pharmacy Service or Research Service Investigational Pharmacy is responsible for:

(1) Maintaining a file of all studies involving drugs, approvals by the IRB and R&D committees, any sponsor-related correspondence (specific to the drug(s)) to the site investigator and all correspondence from the FDA (and other involved authorities) specific to the investigational drug(s).

(2) Ensuring that a VA Form 10-1086, Informed Consent Form, dated and signed by both the patient and the individual conducting the consent process (i.e., Agreement to Participate in Research By or Under the Direction of VA) is received for each patient, prior to dispensing.

(3) Records involving investigational drugs are retained a minimum of 3 years in accordance with VHA Records Control Schedule 10-1. In some cases, FDA regulations or sponsor requirements mandate record retention for a period of 2 years after the New Drug Application approval, or 2 years after discontinuation of the IND (21 CFR Chap. 1, Sec. 312.62). Records are not to be destroyed until approval by the sponsor has been received. ***NOTE:*** *It is the responsibility of the PI to forward all correspondence to the pharmacist who is responsible for maintaining the file.*

(4) Maintaining a log of all transactions involving receipt, storage, security, dispensing, and disposition of unused stocks of investigational drugs, unless this responsibility has been authorized in writing to the PI as previously outlined. ***NOTE:*** *The PI or SI must provide Pharmacy Service and/or Research Service Investigational Pharmacy information on each patient receiving an investigational drugs through the electronic medical record or other locally approved means. Documentation is to include allergies, toxicities, or adverse drug events related to the investigational drug, or the potential for interaction with other drugs, foods, or dietary supplements (herbals, nutriceuticals).*

7. RECEIPT, STORAGE, AND SECURITY

a. Regardless of the source, all investigational drugs must be delivered to the Pharmacy Service and/or Research Service Investigational Pharmacy for receipt, storage, security, dispensing, distribution, and disposition. Distribution to other locations such as Community-based Outpatient Clinics (CBOC) occurs from the main pharmacy. All investigational drugs must remain under the direction of Pharmacy Service. ***NOTE:*** *Investigational drugs mailed directly to the patient through centralized dispensing protocols do not need to go through the local Pharmacy Service or the Research Service Investigational Pharmacy.*

b. VA Form 10-9012, Investigational Drug Information Record, must be provided to the pharmacy by the PI prior to the time of first dispensing of the investigational drug. Once on file, additional copies are required only if the form requires revision.

(1) VA Form 10-9012 informs the authorized prescribers and other clinical personnel of the side effects and any known antidote of the investigational agent, as well as who is the designated contact person for questions. ***NOTE:*** *A completed VA Form 10-9012 is not required for drugs not meeting the definition of an investigational drug, such as concurrent, rescue, or auxiliary medications. VA Form 10-9012 may contain information for more than one investigational drug if the drugs are commercially available and not blinded.*

(2) The completed VA Form 10-9012 must be made available to the pharmacy and must be in the patient's medical record by written or electronic media.

c. Investigational drugs are not to be obtained from other facilities or PIs without an approved Letter of Understanding (LOU) (see App. A) and adherence to protocol procedures, except where noted under a humanitarian or treatment IND.

d. An LOU can exist between a university affiliate or a VA affiliate and the VA Medical Center (or a parent VA Medical Center and its affiliated satellite clinics). Detailed information as to how drugs are to be dispensed and accounted for must be clearly stated in the Investigational Drug LOU. ***NOTE:*** *All drugs must be delivered to the pharmacy prior to use.*

e. Use of an investigational drug from an outside source for a hospitalized patient may be permitted to ensure the patient's well-being. In this case:

(1) The Pharmacy must obtain the drug and dispense in accordance with FDA guidelines (21 CFR § 312.34) that address these circumstances.

(2) The study PI must be contacted prior to dispensing.

(3) The PI must provide a copy of the signed informed consent, information on the protocol, and all drug-related information (see par. 6) prior to any dispensing.

8. STORAGE AND DISPENSING AT VA MEDICAL CENTER PHARMACIES

a. Investigational drugs must be kept separate from all other drugs. They may be dispensed only after a provider who is authorized to prescribe the drug has submitted a properly written or electronic order.

b. The provider must submit the initial order with an accompanying, signed informed consent for the investigational drug for each patient added to the protocol.

c. Investigational drug prescriptions must be entered into the Computerized Patient Record System (CPRS) by the Investigational Drug Pharmacist at the VA medical center, or by using an approved centralized order entry system.

d. Investigational drugs can only be dispensed directly to the patient, an authorized agent of the patient, or study personnel.

e. An investigational drug log (automated or written), authorized by the facility or clinical investigation sponsor, must be maintained containing the following information:

(1) Name of the drug, dosage form, and strength;

(2) Manufacturer or other source;

(3) Date of receipt of the drug;

(4) Quantity received;

(5) Expiration, retest, or repass date;

(6) Control, lot number, or other identification (ID) number;

(7) Name of site investigator;

(8) Protocol name or number;

(9) Name of subject or other subject identifier for individuals receiving the medication;

(10) Quantity dispensed;

(11) Balance of drug currently available (when amenable to protocol design);

(12) Patient identifier (not the patient's name);

(13) Recorder's initials;

(14) Serial number of the patient and date the protocol was approved; and

(15) A final entry is made when drug therapy for the entire study (at the site) has ended. This entry documents the date of termination of the use of the drug, the quantity remaining, the action taken to dispose of the balance on hand, and the agent or individual responsible for drug destruction or return. ***NOTE:*** *When documentation by the clinical investigation sponsor demonstrates that the expiration date and control number (or lot number) of the medication(s) are monitored centrally, (to maintain blinding procedures or ensure continued stability) this information does not need to be maintained on the investigational drug log.*

f. In addition to the generally required prescription label information and appropriate auxiliary caution or warning labels, all investigational drug labels must include the following legend: "CAUTION – NEW DRUG: LIMITED BY FEDERAL LAW TO INVESTIGATIONAL USE."

g. Clinical investigations involving controlled substances must meet the same storage and accountability requirements in accordance with applicable laws, regulations, and VA policy outlined for routine patient care. In addition to the information required for non-controlled study medications, the following detailed information must be kept for a controlled substance study drug:

(1) Controlled substance inventories;

(2) All controlled substance dispensing;

(3) Controlled substances returned (including drugs drawn up, but not used);

(4) All controlled substance record reconciliation;

(5) Controlled substances wasted; and

(6) Controlled substance use categorized by investigator and/or prescriber.

h. Compounding investigational drugs is to follow applicable United States Pharmacopoeia Standards and Good Clinical Practices (GCP). Methods used for compounding the investigational drug must be clearly described and readily accessible to all pharmacist staff.

i. In certain studies, pharmacists are required to maintain the blind to ensure scientific integrity. In emergency situations in which the blind must be broken, the Investigational Drug Pharmacist, PI, and sponsor must agree on the proper procedure and documentation for unblinding treatment.

j. Medical center management must establish written procedures to ensure that an individual who can break the blind is available 24 hours per day, 7 days per week, and 365 days per year.

9. USE OF APPROVED DRUGS FOR UNAPPROVED INDICATIONS

a. A physician may use a marketed drug in an unapproved manner without obtaining an IND, if it is given for therapeutic rather than investigational purposes (21 CFR § 312.2[d]).
NOTE: *See Off Label Drug Use Guidance at:*
http://vaww.pbm.va.gov/directive/Guidance%20Off%20Label%20Prescribing.pdf

b. The use of the VISN Therapeutics Management Committee, the Chief of Staff, or the medical center Director may apply more stringent controls regarding such drug usage.

10. VA COOPERATIVE STUDIES

a. In the case of a VA Cooperative Study employing investigational drugs, the Cooperative Studies Program Clinical Research Pharmacy Coordinating Center (CRPCC) must prepare VA Form 10-9012, for the PI at the VA medical center.

b. The Cooperative Studies Program (CSP) is responsible for obtaining the investigational drug(s) or when commercially available, reimbursing the cost of the drug(s) and for distributing them to the Pharmacy Service at each authorized participating medical center.

c. Pharmacy Service at each participating medical center must designate an individual to whom the investigational drug(s) must be shipped.

d. The Pharmacy Service of each participating medical center must maintain records on investigational drug(s) including all transactions involving receipt, dispensing, and disposition of unused drug in accordance with paragraph 6 of this Handbook.

e. A copy of all records, describing the return or local destruction of investigational drugs associated with the protocol, must be provided to CRPCC by the Investigational Drug Pharmacist at each participating medical center.

11. CENTRALIZED DISPENSING PROTOCOLS

a. Do to unique circumstances, it may be advisable for investigational drug dispensing to be performed centrally. In these instances, the following procedures apply:

(1) All centralized dispensing of investigational drugs must be approved by the local R&D Committee and IRB.

(2) The IRB committee must validate that the dispensing pharmacy is accredited by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO). This validation is to be forwarded to the local Investigational Drug Pharmacist.

(3) All centralized dispensing of investigational drugs must be accomplished using the VA's pharmacy record system in VistA. This is to ensure that all dispensing is in full compliance with JCAHO standards for patient records review (i.e., medication profile, laboratory results, adverse drug reactions, etc.) prior to dispensing.

(4) Dispensing must adhere to all VistA prescription standards (i.e., the maximum supply is 90 days).

(5) The CRPCC pharmacist performing the centralized dispensing is required to:

(a) Maintain all necessary records and correspondence.

(b) Obtain a signed copy of the informed consent prior to dispensing.

(c) Ensure that all dispensing requirements in subparagraph 8e are followed.

(d) Ensure that all dispensing activity is entered into the patient files at a centralized location using VistA software. This information must be accessible to all VA facilities using the Network Health Exchange. ***NOTE:*** *Alternately, the centralized pharmacy, the local pharmacy, information technology and other key personnel at the study location may jointly elect to provide remote access to the centralized dispensing pharmacist for direct VistA data entry. If this option is mutually agreed upon, the joint recommendation must be submitted to the R&D Committee and IRB as part of the protocol submission.*

(e) Ensure that the PI and a CRPCC dispensing pharmacist, who is familiar with the protocol, are on call 24 hours per day, 7 days per week and 365 days per year.

(f) Ensure that all authorized providers at the study site use CPRS to prescribe the investigational drug.

b. The study investigators must:

(1) Ensure that all protocols are reviewed by their local R&D and IRB Committees.

(2) Ensure that the local P&T Committee has the opportunity to review the protocol prior to initiation when necessary.

(3) Ensure that all prescribing takes place using the VistA access provided to the centralized pharmacy.

(4) Annotate on the local medication profile, under Non-VA Medication, that the patient is on the investigational protocol and how to access information about the investigational drug.

NOTE: *This information is to be updated at least quarterly to reflect the current dispensing status. When dispensing from the centralized pharmacy is discontinued, the authorized provider will indicate this in the "Non-VA Medications" package and in the patient's CPRS record.*

(5) Identify that the patient is to begin the investigational drug protocol and forward copies of the protocol and VA Form 10-9012, for the investigational drug to the local Investigational Drug Pharmacist for future reference.

(6) Communicate the existence of this protocol to all pharmacist staff at the local facility.

12. FORMS FOR USE WITH INVESTIGATIONAL DRUG PROTOCOLS

The following are VA Forms for use in documentation for investigational protocols:

a. VA Form 10-1223, Report of Subcommittee on Human Studies;

b. VA Form 10-1086, Agreement to Participate in Research (by or under the direction of VA (Part I and Part II); and

c. VA Form 10-9012, Investigational Drug Information Record.

13. REFERENCES

a. Title 38 U.S.C. 7303; 1722A.

b. Title 38 CFR Chap. 1, Sections 16.110; 17.110.

c. Title 21 CFR Chap. 1, Sections 56.102 (d); 56.104 (c); 312.2(d); 312.34; 312.35; 312.36; 312.62.

d. JCAHO Standards: MM.1.10; MM.4.10; MM.4.20; MM.7.40.

e. Records Control Schedule 10-1.

f. VHA Handbook 1200.5.

SAMPLE LETTER OF UNDERSTANDING

Medical Center Name: _____

Medical Center Number: _____

"Protocol or Study Name"

This letter reflects the understanding between _____ (hereinafter referred to as "Department of Veterans Affairs (VA) Affiliate") and the VA Medical Center at _____ regarding the circumstances under which the VA Affiliate agrees to provide study drug to the VA Medical Center for the following research study _____, "_____" ("Protocol or STUDY"). A copy of the Protocol, dated ___/___/___, is attached and incorporated herein by reference.

The VA Medical Center Pharmacy Service _____ _____ will serve as a liaison between VA Affiliate and the VA investigator and will act as the central control and distribution center for donated drugs for the STUDY. Pharmacy Service will provide guidance and information regarding study drugs as well as serving as a conduit for communications between the VA Affiliate and the Food and Drug Administration (FDA) when appropriate.

The VA Affiliate will provide _(Insert Drug name and strength)_ and matching placebo (hereafter referred to as "Study Drug") for the STUDY in accordance with the following provisions.

The VA Medical Center at _____ and the VA Affiliate have agreed upon the following operating procedures in connection with the STUDY and this Letter of Understanding:

1. Conduct of the STUDY. The VA Medical Center at _____ will conduct the STUDY in accordance with the terms of Protocol and within VA guidelines with the participation of the VA Affiliate.

2. Drug Supply, Distribution, and Accountability. The VA Affiliate will supply Study Drug for the duration of the STUDY, free of charge, and will include in planning allowances for wastage that may unavoidably occur during dispensing. The VA Affiliate will provide shipment of Study Drug directly to the Pharmacy Service in accordance with the schedule agreed to by both parties. The Pharmacy Service will label and dispense Study Drug and keep all records of drug disposition. The Pharmacy Service warrants that in its processes the Study Drug shall not be adulterated or misbranded, in accordance with the Food, Drug and Cosmetic Act. Pharmacy Service agrees to use the Study Drug supplied by VA Affiliate only for the investigational purposes authorized under the Protocol. No other use of the drug will be permitted by Pharmacy Service. In the event that the Pharmacy Service has unused Study Drug at the time the STUDY is completed or terminated, the Pharmacy Service will dispose of Study Drug in accordance with operating procedures outlined by the VA Affiliate.

3. Safety Information Reporting. The local investigator is responsible for reporting adverse events with respect to Study Drug to the VA Affiliate and/or FDA in conformance with all applicable laws, rules, and regulations in effect.

a. The local investigator must provide to the VA Affiliate any information on any serious adverse event, side effect, injury, toxicity, sensitivity reaction or any unexpected incidence and the severity thereof related to the Study Drug that is associated with its "clinical" use in accordance with the Protocol. "Serious Adverse Events," as used in this context, have the meaning ascribed thereto in the Protocol. All such events deemed to be related to the Study Drug must be reported to the VA Affiliate on Protocol SAE forms within _____ business days of receipt by the local investigator.

b. It is understood and agreed that these adverse events reporting requirement provisions are based upon the VA Affiliate's respective policies and procedures and regulatory reporting requirements. Accordingly, in the event of changes to VA Affiliate's policies and procedures for adverse events reporting, the local investigator agrees to comply with such revised notification requirements as reasonably requested in writing by the VA Affiliate. This is provided that the scope and extent of activity and undertakings are not materially increased. The VA Affiliate agrees to pay all costs associated with this request.

4. Early Study Termination. The STUDY may be terminated at any time by the Investigational Review Board for safety or efficacy reasons if it is thought to be in the best interests of the patients. Either the VA or the VA Affiliate may withdraw support from the STUDY with 90 days written notice only if this agreement has been violated.

5. Patient Confidentiality. Patient confidentiality will be maintained at all times in accordance with applicable law and VA policy. Reports issued for public distribution or to the VA Affiliate will contain only aggregate data with all patient identifiers removed.

6. Selection of Participants. The VA Medical Center at _____ will be responsible for all decisions concerning the selection and/or discontinuation of participants in the STUDY.

7. Record Retention. The VA Medical Center at _____ shall retain all records related to the STUDY for a minimum period of 3 years from the date of the last patient follow-up. At that point the STUDY records will be evaluated for archiving.

8. Term of Agreement. This agreement shall be effective as of the date last signed below and shall expire upon completion of all activities related to the STUDY as defined by the submission of the final STUDY report to the VA Affiliate and the primary publication of the STUDY results.

9. Modification to Agreement. This agreement can only be modified in writing and would require signatures by the VA Medical Center at _____ and VA Affiliate representatives.

10. Approval. The following signatures indicate approval of the terms of this letter of understanding.

_____ _____

(Name and Signature of the PI) (Date)

_____

(Name of the VA Affiliate)

_____ _____

(Name and Signature of the VA Investigator) (Date)

_____

(Name of the VA Facility)