

Version Number: 4	<b>Research &amp; Development Policy 151-01</b>	Supersedes Document Dated: 3/12/12
Effective Date: 2/10/14	<b>Research &amp; Development Committee Standard Operating Procedures</b>	Expiration Date: 2/10/18

## I. INTRODUCTION

The Syracuse VA Medical Center (SVAMC) Research & Development Committee (R&D) Standard Operating Procedures (SOP) is a reference for R&D Committee members, subcommittee members, Principal Investigators, co-investigators and Research Service administrative staff. This SOP details the policies and procedures specifying the functions of the R&D Committee and the regulations and policies governing the R&D Committee's oversight of the research program at the Syracuse/Canandaigua/Bath VAMC, the functions of its subcommittees, and in some instances, review of research proposals.

It is noted that, per the R&D Organizational Committee Reporting Structure, the SVAMC R&D Committee also oversees research activities at the Canandaigua VAMC (CVAMC) and the Bath VAMC (BVAMC).

This document will be reviewed and modified as needed to reflect updated and applicable regulations, policies, and institutional procedures.

## II. RESEARCH & DEVELOPMENT COMMITTEE ADMINISTRATION

### A. The Authority of the R&D Committee

The R&D Committee is responsible through the Chief of Staff to the VA Medical Center Director at each site (Canandaigua, Bath and Syracuse) for advising and assisting in providing oversight, planning and execution of the VA research program, and for maintaining high standards throughout the Research & Development program at each medical center. Those standards include ensuring the scientific and ethical quality of all research, the protection of human subjects in research, the welfare of laboratory animals, the safety of personnel engaged in research, security of VA data, and the security of VHA research laboratories. The R&D Committee focuses on oversight of the local research program rather than individual protocols. This is accomplished by the assigning of scientific review and some administrative responsibilities, including compliance issues, to more appropriate subcommittees and individuals. This allows the R&D Committee to prioritize their deliberations around broad areas of research program development, risk management, and quality and performance activities.

The Medical Center Director is the institutional official responsible for all aspects of the research program at their site. The R&D Committee advises the Medical Center Directors on both professional and administrative aspects of the R&D program. The Medical Center Director delegates the authority to administer the R&D program to the Associate Chief of Staff for Research & Development (ACOS/R&D), who reports to the Chief of Staff (see appendix A – R&D Organizational Committee Reporting Structure).

The R&D Committee is the governing body for all research conducted at the SVAMC, CVAMC, and BVAMC. The R&D Committee is responsible for the overall development of research and maintaining high standards throughout the research program. This is accomplished through the review of actions of its subcommittees, and each subcommittee conducts the review for the scientific quality and appropriateness of all research, which may involve animal and human subjects. In addition, the R&D Committee reviews subcommittee actions on all research projects through approval of subcommittee minutes containing initial review and continuing reviews. The R&D Committee approvals are communicated to research Principal Investigators from the ACOS/R&D.

## **B. R&D Committee Subcommittees**

The R&D Committee acts as the governing body of the Research Service at the SVAMC. It serves as a parent committee to all of its subcommittees and must review and approve subcommittee actions, minutes, and periodic reports. No research may be undertaken without R&D Committee and appropriate subcommittee(s) review and approval. Neither the R&D Committee, nor the Medical Center Director may approve research to be performed that has not been approved by all of the appropriate R&D Committee subcommittee(s) of record. The R&D Committee and higher authority may strengthen requirements and/or conditions, or add other modifications to a protocol approved by all appropriate subcommittee(s). The Institutional Official, Chief of Staff, ACOS/R&D, or any other individual does not have the authority to grant approval to conduct research.

Policies and procedures do not allow the Syracuse VA Medical Center to utilize a commercial IRB for VA Research.

If the R&D Committee requires changes to a protocol, including those which have been reviewed and approved by the appropriate subcommittee, the R&D Committee follows the actions outlined in Section IV. A. of this document. The corresponding subcommittee must approve the changes requested by the R&D Committee before the R&D Committee can give their final approval.

The Syracuse VA Medical Center utilizes its own Institutional Review Board (IRB) for the oversight of all research activities involving the use of human subjects. The R&D subcommittees include: IRB, Subcommittee for Animal Studies (SAS), the Subcommittee on Research Safety (SRS), and the Central IRB.

The members of the IRB are nominated to fulfill three-year terms by the ACOS/R&D, approved and voted on by the R&D Committee and appointed by the Syracuse VA Medical Center Director on an annual basis. Members of the SAS and SRS subcommittees are nominated by their respective subcommittee, approved by the R&D Committee, and are appointed by the SVAMC Director on a triennial basis (excluding chairmanship, which is annually nominated and appointed). Each subcommittee must have at least one member from the R&D Committee. Each subcommittee keeps minutes of its meetings and reports to the R&D Committee, which accepts or rejects its recommendations. Minutes of these subcommittees are reviewed and accepted at the R&D Committee meeting. The membership rosters of each subcommittee are reviewed annually by the R&D Committee. Each subcommittee is responsible for the review of initial and continuing review of studies under their purview.

The R&D Committee has charged the SVAMC Institutional Review Board (SIRB) with the scientific review and oversight of all research activities involving the use of human subjects. The SVAMC IRB shall perform all functions required under 38 CFR 16 (Common Rule) for reviewing and approving human research conducted under the auspices of the Institution's Federalwide Assurance (FWA). This includes, but is not limited to, research supported by the VA or conducted at the SVAMC, CVAMC, or BVAMC and research involving VA patients as research subjects (hereafter "VA research"). These responsibilities include maintaining the assurances of compliance set forth in the FWA obtained from the Office of Human Research Protections (OHRP) and only approving research involving human research subjects in accordance with all applicable federal requirements in the protection of human research subjects and operations of the IRB. IRB review and approval of VA Research shall be conducted in accordance with 38 CFR 16, 45 CFR 46 Subparts A through D, 21 CFR 50 and 56 (where applicable), and all relevant VA rules and policies set forth in writing in VHA Handbook 1200.5.

The R&D Committee oversees the IRB in these responsibilities.

The Department of Veterans Affairs (VA) and other Federal regulations require specific protections for human subjects. The Associate Chief of Staff/Research & Development is responsible for developing, managing and evaluating policies and procedures that ensure compliance with all state and Federal regulations governing research. This includes monitoring changes in state, VA and other Federal regulations and policies that relate to human research protection and overseeing all aspects of the Human Research Protection Program (HRPP) established for human research protections.

VHA Directive 2007-040 states that VHA facility Information Security Officer (ISO) and Privacy Officer (PO) must be appointed as non-voting members of either the facility's IRB or R&D Committee of record. In order to comply, the SVAMC/CVAMC/BVAMC Director will appoint the ISO and PO from each site as non-voting, ex-officio members of the Syracuse VAMC IRB.

VHA Directive 2007-040 states the facilities are encouraged to engage the ISO and PO prior to submission of a protocol for review by the IRB. Therefore, the VAMC ISO, and PO for each site (SVAMC, CVAMC, BVAMC), will be tasked with the review of privacy and data security for all human subjects research conducted at their respective VAMC. The ISO and PO will receive any and all relevant pages of the Initial/Continuing Review forms, the completed Data Security Checklist for Principal Investigators and will review data security and privacy as described in the protocol. Any questions or concerns will be documented and forwarded to the Principal Investigator and will also be presented at the next IRB meeting when the protocol is reviewed. If there are no concerns, the ISO and PO will sign the Data Security Checklist for Principal Investigators for concurrence, and the IRB will be notified that concurrence was given. The IRB will review the entire protocol, taking into account any and all concerns expressed by the ISO and PO and vote for approval, contingent approval or disapproval with documentation in the minutes of the discussion and vote.

The SVAMC IRB Standard Operating Procedures (SOP 151-02) is a reference for IRB members, coordinators, PIs, co-investigators and other individuals associated with the HRPP. The SOP details the policies and procedures specifying the regulations and policies governing human subjects' research and the requirements for submitting research proposals for review by the SVAMC IRB.

1. The R&D Committee has charged the SVAMC Subcommittee for Animal Studies (SAS) with reviewing scientific quality and ensuring compliance with animal research regulations. The R&D Committee oversees the SAS in this responsibility. The SAS adheres to the policies in VHA Handbook 1200.07, the SVAMC's Animal Welfare Assurance, USDA Animal Welfare Regulations, and AAALAC standards. VHA Handbook 1200.07 contains the procedures and principles by which the SAS abides in the review and conduct of research involving animal research subjects.

2. The R&D Committee has charged the Subcommittee on Research Safety (SRS) with ensuring compliance with all applicable regulations, policies, and guidelines pertinent to biological, chemical, physical, and radiation hazards, and with oversight of all research activities involving safety hazards. The SRS adheres to the policies in VHA Handbook 1200.06 and 1200.08. The Syracuse VA Research SOP 151-04 contains the policies and procedures by which the SRS conducts the review of research which will include biohazards and/or chemicals conducted in a research wet lab.

Each subcommittee must maintain adequate records. These records must include the following:

- a. Copies of all research proposal and their amendments (and any accompanying materials) reviewed by the subcommittees.
- b. All continuing review or final reports.
- c. Minutes of its meetings.
- d. Copies of all written correspondence.
- e. A membership list of all voting, non-voting, and ex-officio members including their appointed roles.
- f. Written records documenting actions taken to carry out the subcommittee's responsibilities.
- g. Standard Operating Policy/Procedures.
- h. All communications to and from Principal Investigators, other committees, subcommittees, and other entities or individuals.

Subcommittee meeting minutes are filed in the Research Service offices. Each subcommittee must make available to the R&D Committee a complete, unredacted set of minutes.

The R&D Committee reviews requests and reports involving research space in addition to proposing assignment of research space. The term "research space" refers to all types of space where research is conducted including dry lab space (for programs more dependent on generation, collection and analysis of clinical data), wet lab space (for biomedical experimentation) and any combination or customization of wet or dry lab space to meet the special needs of SVAMC investigators.

### **III. R&D COMMITTEE MEMBERSHIP**

The membership of the R&D Committee, supplemented as needed by advisors or consultants, reflects a broad and balanced representation of all divisions within the SVAMC, CVAMC, and BVAMC. The Syracuse VA strives to maintain balance and expertise on the R&D Committee by appointing members with appropriate scientific background for the review of all research performed at the SVAMC and under SVAMC R&D Committee auspices (CVAMC and BVAMC).

The R&D committee members are nominated by the Associate Chief of Staff, Research & Development or current R&D Committee members. Nominations are voted on by the current R&D Committee, and appointed in writing by the SVAMC Director. Voting members serve terms of 3 years, and may be reappointed without any lapse in time if it is deemed in the Committee's best interest. The terms shall be staggered to provide partial change in membership annually. As the R&D Committee serves the CVAMC and BVAMC, the respective CVAMC and BVAMC Director appoint its own representative(s). Membership rosters of the R&D Committee and its subcommittees are reviewed and approved annually by the SVAMC Director.

**A. Voting Membership:**

The R&D Committee must have at least five (5) voting members, including whenever possible, one member with expertise in biostatistics and research design. Voting members of the R&D Committee must meet the following criteria:

1. All voting members must be compensated full-time or permanent part-time Federal government employees.
2. At least two members from the facility's staff must have major patient care or management responsibilities.
3. At least two members must be VA investigators actively engaged in major R&D programs or able to provide R&D expertise.
4. A member with expertise in animal research techniques and biomedical animal study settings.
5. At least one member must also hold an academic appointment at the SVAMC's affiliated institution, State University of New York at Upstate (SUNY Upstate).

Voting members may fill more than one criterion for membership requirements; for example, a member may have both major patient care or management responsibilities and be actively engaged in major R&D programs. A member of each subcommittee shall serve as a member of the R&D Committee. Membership also must represent diverse backgrounds with consideration given to race, gender, and ethnicity. The current composition of the R&D Committee in terms of members by name, degrees held, and representative capacity is maintained in the SVAMC Research Office. In addition, the membership is summarized in the R&D Committee meeting minutes.

**B. Election of Chairperson:**

The committee members, exclusive of ex-officio members, shall elect a chairperson on an annual or biannual basis. The Chairperson must be approved and officially appointed, in writing, by the medical center Director for a term of 1 or 2 years. The Chairperson may be reappointed without any lapse in time. The Chairperson must not simultaneously chair a subcommittee of the R&D Committee. In the absence of the R&D Committee Chairperson, a temporary R&D Committee Chairperson can be appointed from one of the senior scientific R&D Committee members. This temporary appointment will be voted upon at the beginning of the convened R&D Committee meeting and remains effective during the R&D Committee Chairperson's absence.

**C. Ex-Officio Non-Voting Membership:**

Ex-Officio non-voting members to the R&D Committee include:

1. Medical Center Directors
2. Chief of Staff (COS)
3. Associate Chief of Staff, Research & Development (ACOS/R&D)
4. Administrative Officer, Research & Development (AO/R&D)
5. Representative of the Research Pharmacy

The ex-officio members are non-voting members. Other ex-officio members may be appointed to the R&D Committee if their appointments assist the R&D Committee in fulfilling its responsibilities. If the ex-officio members are not full or permanent part-time compensated VA or Federal employees, they may only provide individual advice to the R&D Committee, or exchange facts and information.

The ACOS/R&D functions as Executive Secretary of the committee.

#### **D. Alternate R&D Committee Members:**

Alternates for the R&D Committee members may be nominated in the same manner as regular members, approved by the R&D Committee and appointed by the Medical Center Director. The alternate member shall serve as an alternate for a specific voting member. The alternate member should have a similar or related work specialty or responsibility as the member he/she represents in their absence. The alternate member's term expires with the term of the individual that he/she is representing. The alternate member may serve on the R&D Committee with less than one year between terms, i.e. a R&D Committee member that is rotating off the committee may serve as an alternate for a new member voted to serve on the committee, since his/her service may be intermittent. The alternate member is only allowed to vote in the absence of the member he/she represents.

#### **E. Ad Hoc Reviewers**

The R&D Committee may, at its discretion, obtain services of ad hoc reviewers when additional expertise is required. Ad hoc reviewers cannot have a conflict of interest (as defined in SVAMC SOP 151-05) with the program or issue they are asked to review. Ad hoc reviewers do not vote with the committee. Such consultants may be asked to submit written evaluations of the programs or, when necessary, to present their recommendations to the committee in person. R&D funds may be used to pay for the services of consultants who are not employed by the Federal Government.

#### **F. Training of R&D Committee Chair and Members**

It is the responsibility of the ACOS/R&D and the Research Service to provide members with an initial orientation to their committee activities and appropriate continuing education related to the R&D Committee. The following training is mandated for all voting R&D Committee members:

1. *Ethical Principles of Human Subjects Protection*
2. *Good Clinical Practice*

This training can be found at:

<http://www.research.va.gov/programs/pride/training/default.cfm>

Both trainings must be completed biannually.

Upon appointment to the R&D Committee, new members will receive a copy of the most current R&D Committee SOP prior to the first meeting with the R&D Committee. All members will receive updated

versions of the R&D committee SOP as they are issued. The ACOS/R&D may provide further guidance when training as needed.

#### IV. RESPONSIBILITIES OF THE R&D COMMITTEE

The R&D Committee serves in an advisory capacity to the Medical Center Directors through the Chief of Staff on the professional and administrative aspects of the research program. The R&D Committee is responsible for oversight of the research program and for maintaining high standards throughout the R&D Program.

##### A. Responsibilities of the Research & Development Committee include:

1. Overall development of research at the SVAMC/CVAMC/BVAMC. This includes shaping of main research directions, overseeing facility development and all other intellectual, physical and regulatory aspects of research.
2. Assuring the continuing high quality of the facility's research and development program.
3. Planning and developing broad objectives of the research and development program so that it supports the patient care mission of the facility.
4. Determining the extent to which the research program has met its objectives.
5. Reviewing all written agreements that establish:
  - a) A committee from another VA or non-VA entity in lieu of a required committee or subcommittee for the R&D Committee; and
  - b) The R&D Committee or one of its subcommittees, as a committee or subcommittee of another VA facility.
6. Annually reviewing and evaluating all subcommittees. A summary of these reviews and evaluations must be sent to the Medical Center Director annually. The review and evaluation of these subcommittees must be an ongoing function of the R&D Committee, and must be accomplished in part by reviewing the minutes of each subcommittee, by close communication with the subcommittees, and through quality assurance and compliance activities in coordination with the Research Compliance Officer. Subcommittees to be reviewed include:
  - a) IRB including HRPP (including resources indentified through training status reports, budget, space, support staff/FTEE, education activities, IRB review statistics, conflict of interest, Regional Counsel, and community outreach activities), quality improvement activities, IRB membership, compliance issues, and yearly goals.
    - a. Quality improvement (QI) will focus on achieving and maintaining compliance with all federal regulations, VHA Handbooks & Directives, and Office of Research Oversight requirements;

- b. QI will be assessed by reviewing the audit results conducted by the Research Compliance Officer(s);
  - c. QI results will be tracked and measured by comparing to prior year HRPP reports to the R&D Committee;
  - d. RCO audit results are reported to the R&D Committee, with findings and tracked trends noted for discussion and/or recommendation(s) for correction.
- b) SAS including inspection reports, membership, arrangements, budgets, space, support staff, training status reports, quality improvement and education activities, compliance issues, and yearly goals. This process will be facilitated by review of the Laboratory Animal Care and Use Program Review and Facilities Inspection Semiannual Report.
- c) SRS including membership, training status reports, support staff, quality improvement and education activities, compliance issues, and yearly goals.

7. Reviewing and declaring approval/disapproval recommendations from its subcommittees; IRB, SAS, and Subcommittee on Research Safety (SRS). This review includes the subcommittee meeting minutes and other subcommittee actions. The minutes and actions of the subcommittees are unofficial until the R&D has approved them. The R&D members review the minutes and voice any objections to the documented minutes prior to approving the subcommittee meeting minutes. The Research and Development Committee will not approve any proposal that has been disapproved by any subcommittee. The R&D Committee along with the Medical Center Director (MCD) and the Office of Research and Development, Washington, DC (ORD), has the authority to disapprove a research activity approved by the IRB, SAS, and SRS.

8. The R&D Committee, MCD, and/or ORD may strengthen requirements and conditions, or add other modifications in order to secure R&D approval. R&D recommended changes must be reviewed by the appropriate subcommittee (IRB, SAS, SRS).

9. Reviewing on an annual basis the subcommittees' Chair and members and the members' qualifications and experiences. Subcommittees include the IRB, SAS, and SRS.

10. Reviewing on an annual basis all Research Service Memorandum and Standard Operating Procedures and making any necessary changes to reflect best practices in research at the VA.

11. Advising the Director on the recommendation to the CRADO/R&D (Chief Research & Development Officer) and of candidates for the position of ACOS/R&D (Associate Chief of Staff for Research & Development). The R&D Committee will form a search committee, when applicable, for the replacement of the ACOS/R&D. The R&D Committee will first approve a candidate for the position of ACOS/R&D, followed by the Medical Center Director and the final approval given by the CRADO.

12. Reviewing from the Subcommittee (IRB, SRS, SAS) Chairs, Co-Chairs, or members any allegations of undue influence. It is expected that all Subcommittees will function independently and should not experience any undue pressure from the R&D Administration, investigators, other study personnel, or any other internal/external sources. Allegations will be submitted as a written report of contact and submitted to the R&D Committee. The R&D Committee will document and forward all such reports to the Research Integrity Officer to initiate an investigation,

which could include but is not limited to: 1) Informal resolution of the issue, 2) conflict of interest investigation, 3) Regional Counsel, 4) QI, 5) Risk Management, and/or 6) request Administrative Investigative Board. The findings of the investigation will be reported to the R&D Committee. If the individual reporting the allegations does not believe the concerns were addressed, then this individual may report any undue influence directly to the VA Medical Center Director, the appropriate federal oversight body (OHRP, OLAW, or the VA Office of Research Oversight in Washington) for resolution.

13. Fulfilling such other functions as may be specified by the Medical Center Director.

### **B. Reviews Required by the R&D Committee**

The Research & Development Committee focuses on oversight of the SVAMC research program, rather than individual protocols. Review of individual protocols, including scientific review, is conducted by the appropriate subcommittee(s). The IRB, SRS, or SAS and other such entities must notify the R&D Committee of project approvals via a written communication signed by a voting member for the subcommittee. Principal Investigators may not initiate a research project until they have been notified by the ACOS/R&D of project approvals via a written communication signed by the ACOS/R&D that the project has been approved by all relevant committees, subcommittees or other entities.

For protocols not meeting criteria for assignment to any subcommittee, the R&D Committee is the review and approving committee of record for initial and continuing review. Please refer to Syracuse VAMC SOP 151-08 for details and forms for Exempt Research protocols. Human research protocols determined to be exempt from IRB approval will be forwarded by the IRB Administrator to the R&D Committee for review after the IRB chair or designated reviewer has approved the Certification of Exemption. The R&D Committee will review exempt protocols at least once yearly. Exception: If a protocol amendment/revision of a previously determined exempt protocol is reviewed by an IRB chair or designee and the protocol is determined to no longer meet exemption criteria, the IRB will assume the annual and ongoing review of the study. The IRB Administrator will notify the R&D Committee Administrator if this occurs.

After initial or continuing review of protocols not meeting criteria for assignment to any subcommittee, if the project receives final approval, the Principal Investigator will be provided with an ACOS/R&D written notification allowing them to initiate the study. In cases of contingent approval, or a tabled decision, the R&D Administrator will notify the PI within three weeks. Once the reviewer has approved the PI's response to contingencies, ACOS/R&D notification allowing the study to be initiated will be sent.

If a research protocol requires review by a non-research entity at the SVAMC, such as the Radiation Safety Committee, this review may be conducted at any time, but the research may not be initiated until the non-research entity and all applicable R&D Committee subcommittees have approved the project, and the Principal Investigator has been notified in writing by the ACOS/R&D.

#### 1. Standing Agenda Items

- (a) Review and approval of R&D Committee minutes of previous meeting.
- (b) Review of Subcommittee meeting minutes. Final minutes must be sent to the R&D Committee

for review and approval when they are available. This may include review of minutes of the VA Central IRB, on an ad hoc basis, when a project to be conducted at the SVAMC has been reviewed and approved by the VA Central IRB. Prior to review of any subcommittee minutes, the R&D Chair will ask the sitting subcommittee member if there are any issues to address or discuss. Should any finding or recommendation of a subcommittee be questioned, the issue will be discussed and recorded in the R&D Committee minutes.

- (c) ACOS/R&D Report – The ACOS/R&D will update the R&D Committee on any current issues facing the Research Service. Committee members are expected to provide feedback and advice. The ACOS/R&D will also provide annual quality assurance reviews, as noted in section VI of this SOP.
- (d) AO/R&D Report – VA budget updates, VA grant submissions, and any information requested by ACOS/R&D or R&D Committee members.
- (e) CNYRC Report – BOD minutes, audits, grant submissions, and general research issues.
- (f) RCO Report - Findings of audits by the Research Compliance Officer are presented here, as well as educational items relevant to VA Research Compliance.
- (g) CIH/COE Monthly Reports
- (h) Results of Electronic Polling for Policies/Procedures (as noted in SOP 151-16).
- (i) Old Business, if unfinished business exists.
- (j) New Business. New business may include: review of the annual budget, Research Pharmacy Activity Report, subcommittee member qualifications, and policies and procedures from the subcommittees.

## 2. Other Agenda Items (as needed)

The R&D Committee may also review, as needed, applications for special initiatives (equipment requests) and for reviews required by other VA handbooks, which may include the following:

- (a) New non-clinical Ph.D. applicants for merit review eligibility;
- (b) Non-clinical Ph.D. applicants for the Career Scientist program;
- (c) Endorsement of new clinicians for the Career Development Program.
- (d) Endorsement of specific projects or awards offered by the Office of Research & Development.

## 2. **Expedited Review**

The IRB utilizes an expedited review process which is outlined in Syracuse R&D SOP 151-02. Following protocol review and approval by the IRB Chair or designee under expedited review, the R&D Committee performs a full review at a convened meeting with a quorum. There is no expedited review process for the R&D Committee.

## V. **RESPONSIBILITIES OF THE MEDICAL CENTER DIRECTOR**

The Medical Center Director, acting in the capacity of the Institutional Official, is responsible for meeting the requirements outlined in VHA Handbook 1200.01. These responsibilities include:

- 1. Serving as the institutional official responsible for all aspects of the research program.
- 2. Ensuring that research in which the facility is engaged is approved by the appropriate R&D Committee subcommittee.

3. Ensuring adequate resources and administrative support, including personnel, space, equipment, and training for the R&D Committee and its subcommittees to fulfill their responsibilities.
4. Ensuring appropriate education and training for members of the R&D Committee, the research administration staff, and other staff involved in research.
5. Ensuring that PIs, co-investigators and study personnel meet all necessary requirements listed in local SOPS, VHA Handbooks and Directives.
6. Appointing the members of the R&D Committee.
7. Ensuring that the IRB functions independently.
8. Ensuring that any Subcommittee (IRB, SAS, SRS) Chair, Co-Chair, or member(s) have direct access to the Medical Center Director for appeal if they experience undue influence or if they have concerns about the particular Subcommittee (IRB, SAS, SRS). This is depicted in the Syracuse VA Medical Center Reporting Structure diagram.
9. Ensuring appropriate auditing of local human subjects research studies to assess compliance with all local, VA and other federal requirements, including but not limited to, VA Office of Research Oversight requirements. This is accomplished by:
  - a. Appointment of a Research Compliance Officer (RCO) whose primary responsibility is auditing and reviewing research projects relative to requirements for the protection of human subjects;
  - b. The RCO conducts annual consent document audits;
  - c. The RCO conducts triennial regulatory audits on all research protocols;
  - d. The RCO reports directly to the Medical Center Director and the RCO activities may not be determined or managed by the Research Service, research investigators, or any other research personnel.

## **VI. RESPONSIBILITIES OF THE ACOS/R&D**

The Associate Chief of Staff for Research & Development (ACOS/R&D) is responsible for:

1. Providing written notification to the Principal Investigator when a research project can be initiated. This notification occurs only after the research project has been approved by all relevant committees, subcommittees, or other entities. The IRB, SRS, or SAS must notify the R&D Committee of project approvals via a written communication signed by a voting subcommittee member for the subcommittee. The R&D Committee must notify the ACOS/R&D of project approval(s) via a written communication signed by a voting R&D Committee member for the committee. The ACOS/R&D will then notify the Principal Investigator that the study may be initiated.
2. Notifying the Principal Investigator of approval after continuing review by the subcommittees or the R&D Committee.
3. Functioning as the Executive Secretary of the R&D Committee.
4. Conducting regular quality assurance reviews of publications assessing the acknowledgement of VA support and affiliation. This shall happen at least annually.
5. Conducting regular quality assurance reviews ensuring that information pertaining to all requests to WOC appointments for research have been appropriately justified and the

appointments are in compliance with all applicable research, Human Resource Management, and other VA policies.

6. Conducting regular quality assurance reviews of research employees involved in VA research to ensure the employees are working within their approved scopes of practice and their privileges allowed by the facility's by-laws and granted to them by the facility. This annual quality assurance review also includes initial verification of credentialing and privileging through the local facility HR and C&P. This shall happen at least annually.
7. Conducting regular quality assurance reviews of Cooperative Research and Development Agreements (CRADAs) and other agreements in support of the research program or specific research projects and an assessment of the impact of these agreements on the research program, when applicable. This shall happen at least annually.
8. Ensuring that all minutes of the R&D Committee and its subcommittees are sent to the medical center Director and Chief of Staff for review and appropriate action. The Director and Chief of Staff may receive such minutes in the meeting materials provided to all voting and *ex officio* members for the R&D Committee meeting.
9. The ACOS/R&D also reviews protocols and discusses individual research projects as background and experience allows for scientific contributions and advisory capacity.

## VII. RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR

The Principal Investigator is responsible for:

1. Confirming with the applicable service chief that they have been awarded the appropriate credentials and privileges to conduct research at VA prior to initiating any research.
2. Confirming that all research personnel working with the Principal Investigator have the appropriate verification of credentials and privileges, and an approved scope of work to conduct research at VA prior to initiating any research activities.
3. Complying with all applicable VHA personnel and other VA requirements.
4. Obtaining the complete approval of all appropriate non-research entities and R&D Committee subcommittees, and written notification from the ACOS for R&D prior to initiating a research project.
5. Developing a research plan that is scientifically valid; minimizes risk to human subjects, animals used in research, and personnel; and contains a sufficient description of the research including all procedures and the plan for statistical analysis, to allow the R&D Committee subcommittees to fully review the research project.
6. Developing and implementing plans for data use, storage, and security that are consistent with VA Directive 6500, Information Security Program, and its implementing Handbooks and other legal requirements.
7. Preparing and submitting information, at least annually or as required, on their research program(s) and on each project to the appropriate R&D Committee subcommittee for continuing review as required by the respective R&D Committee subcommittees.
8. Ensuring that all research proposals submitted for funding, from any source, support the mission of VHA and enhance the quality of health care delivery to Veterans. **NOTE:** *Examples of research that may not support the mission of VHA includes research involving children or prisoners*

## VIII. CONDUCTING R&D MEETINGS

### **A. Convened R&D Committee Meetings**

A majority of the voting R&D Committee members, excluding the ex-officio members, must be present to conduct a convened meeting. An R&D Committee meeting is not convened until a quorum (one half of the voting members plus one) is present. Although it is recommended that members be physically present, if physical presence is not possible, a member may be considered present if they participate through teleconference or videoconference. In cases where video- or teleconference is used, the member must have received all pertinent material prior to the meeting, must be able to participate actively and equally in all discussions, and their participation in that manner will be so noted in the minutes. The R&D Committee will review any other issues brought forth to the R&D Committee at convened meetings at which a quorum of the members are present. If a voting member steps out of the room causing a quorum to be lost during a meeting, no business may be conducted by the R&D Committee until the member returns.

The R&D Committee meets on the second Monday of each month, except for months in which a Federal holiday falls on this date and conflicts with this schedule. In these rare cases, the R&D Committee meeting will be held on the second non-holiday Monday.

Additional meetings may be called by the Chair, as required (for example, to act on compliance issues or meet VA submission deadlines). Any additional meetings must meet the quorum requirements (either in person or via video- or teleconference).

An agenda is developed prior to each meeting of the R&D Committee and is distributed to members prior to the meeting.

## **IX. RECORD RETENTION AND DOCUMENTATION**

### **A. R&D Committee Records**

The R&D Committee records include the following:

1. R&D Committee meeting minutes;
2. Written Standard Operating Procedures;
3. Membership rosters;
4. R&D correspondence to the PI regarding research projects (when necessary) is kept within the appropriate research project file located in the Research Service office;
5. Exempt research project application files, including copies of all research proposals, amendments reviewed, accompanying materials, and continuing and final reports.

### **B. Written Standard Operating Procedures**

R&D Committee members are provided with a copy of the standard operating procedures at the time they join the R&D, and each time the SOP is updated.

The ACO S/R&D, Administrative Officer/R&D, R&DC Administrator, and others, as needed, work together to write and maintain the SOP. The SOP is reviewed and modified as needed to ensure compliance with federal and institutional regulations and policies.

**C. R&D Committee Membership Roster**

The R&D Service maintains the current R&D Committee membership roster. The R&D Administrator is responsible for maintaining an updated R&D Committee roster and R&D Committee alternate membership roster. The rosters include name, degrees held, and representative capacity (e.g., service and SUNY representative) of each member. The R&D Committee membership roster is located in the Research Service office

**D. R&D Committee Correspondence**

Accurate records are maintained of all communications to and from the R&D Committee. The R&D Committee Chair signs R&D Committee correspondence as appropriate. This may include an electronic signature. R&D Committee correspondence includes written correspondence addressed to the Medical Center Director on behalf of the R&D Committee, the Chief of Staff, Principal Investigators and committees or subcommittees.

If necessary based on the nature of a study, copies of correspondence are filed in the appropriate research project file kept in the SVAMC Research Service office. Principal Investigators shall be notified in writing by the ACOS/R&D of the determination of the R&D Committee, and any changes that are required by the R&D Committee. A signed hard copy of the correspondence will be mailed or scanned and electronically mailed to the Principal Investigator for their files. Responses to the R&D Committee should come from the Principal Investigator or a designated study coordinator, and may be communicated electronically or by hard copy.

In cases in which a project being performed at the SVAMC/CVAMC/BVAMC has multiple co-investigators and study team members, correspondence will be sent to the Principal Investigator (PI) responsible for the conduct of the study, who will be responsible for communicating the results to the co-investigators. The PI is ultimately responsible for communicating to the co-investigators and assuring that they comply with R&D Committee requirements. In cases where communication is electronic, upon resolution of the topic of the communication, a hard copy will be generated and filed with the project file by the R&D Coordinator and/or staff.

**E. Research Project Application Files**

Each research project has a separate file. IRB protocols are assigned a unique number from the Manage your Institutional Review Board (MIRB) computer program and a unique grant number for tracking and administration purposes. R&D Committee records which are specific to a project are kept in the file for that project. To decrease redundancy and increase efficiency, some of the required subcommittee records, such as the records for the IRB, SRS and the SAS are also kept in the same project-specific files. In this manner, copies of written subcommittee correspondence to and from VA investigators are available in the VA research office space for each project.

**F. Research Tracking System**

The R&D Service uses a reliable computerized tracking system, the MIRB computer program, which is maintained by the R&D and IRB Administrators. MIRB stores information regarding which documents have been received, when they were reviewed, and the results of that review. Additionally, MIRB tracks changes that are needed, when those changes were received and approved, and the date of continuing review. MIRB also tracks R&D Committee membership and generates meeting

correspondence. The SAS and SRS have unique numbers for each protocol and each amendment. All dates for annual and triennial review are manually tracked.

The R&D Service also uses the VA enterprise project management information system (ePROMISe)

#### **G. R&D Committee Meeting Minutes**

1. R&D Committee minutes are completed by the R&D Administrator. Minutes shall include:
  - (a) Time and date of the convened meeting.
  - (b) Attendance and absence by name of all voting and non-voting members, including ex officio members. If an alternate is present, the minutes include this fact and state the name of the voting member that the alternate member is replacing.
  - (c) The presence of a quorum.
  - (d) Approval of prior meeting minutes.
  - (e) All items of business or information brought before the R&D Committee.
  - (f) Actions taken by the R&D Committee. The minutes shall include a summary of any discussion, any modifications required, all actions taken by the convened R&D Committee and the votes underlying those actions. Actions which require a vote have the votes categorized as the number who voted "for," "against," "abstained," "recused," and "excused." Any individuals who are recused from a vote will be noted by name, and notation will be made on whether or not the person was present during the discussion. When a member is recused, they must not be present for the vote and may not be counted toward a quorum.
  - (g) Summary of controversial issues and their resolutions.
  - (h) Names of persons who excused or recused themselves and reference to a specific issue. (i) Date and time of the next meeting, as well as the meeting location.
2. Minutes of the meeting are reviewed and signed by the R&D Chairperson and the executive secretary (ACOS/R&D).
3. After the meeting, copies of the minutes, together with any comments the Medical Center Director may care to make, will be distributed to all members of the R&D Committee in the agenda materials and VA Sharepoint site for the next meeting, and made available upon request to any investigator.
4. Minutes shall be maintained by the R&D Committee Administrator and the SVAMC Research Service office and made available to VA Central Office upon request.

#### **H. Documentation of Attendance at R&D Committee Meetings**

R&D Committee minutes shall list attendance as follows:

1. Names of members present, including the presiding officer (Chairperson).
2. Names of excused members.  
Members are designated EXCUSED if the Chairman or R&D Committee Administrator was notified in advance.
3. Names of absent members. Members are designated ABSENT if the Chairperson or R&D Committee Administrator was not notified in advance.
4. Names of alternates attending in lieu of specified (named) excused/absent members.

#### **I. Access to Records**

Research records are accessible to Research Service staff, R&D Committee Chairperson and members. Research investigators shall be provided reasonable access to files related to their research.

Research Compliance Officers will also be provided reasonable access to files. Other authorized individuals, such as officials of Federal and state regulatory agencies, including the: Office of Research Oversight (ORO), the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA), and the Office of Laboratory Animal Welfare (OLAW) will have access to R&D Service records for inspection and copying upon determination of appropriateness and necessity at reasonable times and in a reasonable manner. Appropriate accreditation bodies shall be provided access to and may recommend additional procedures for maintaining security of R&D Service records.

A log of such individuals who do access the R&D Service records, besides the R&D Committee members, IRB/SAS/SRS members, Chair and Research Service staff, is kept by the Research Service staff.

The R&D Committee may have access to all of its subcommittees' records.

#### **J. Record Retention**

The records of research studies conducted at the SVAMC are kept according to the VHA records control schedule (RCS) 10-1. In cases where the sponsor or the Food and Drug Administration (FDA) require longer retention, the records will be retained for the longest of the required timelines. The R&D Service maintains all records collected over the course of a study. The R&D Service also maintains documentation of all activities of the R&D Committee, including but not limited to, minutes of the R&D Committee and subcommittees, copies of written correspondence, and membership lists for the R&D Committee and all subcommittees, according to the VHA record control policies.

#### **X. NON-COMPLIANCE**

All Principal Investigators, co-investigators and study team members conducting research as employees or agents in the SVAMC/CVAMC/BVAMC are required to comply with institutional policies regarding research. All issues of non-compliance will be forwarded from the appropriate subcommittee and reviewed by the R&D Committee. The R&D Committee will vote on all recommendations for corrective and educational actions forwarded by the subcommittee to resolve the issue of non-compliance.

**A. Complaints and Allegations of Non-Compliance Pertaining to Human Research** The R&D Committee reviews all issues of non-compliance pertaining to human and animal research brought to the R&D Committee from the IRB, SAS, or Research Compliance Officer. The R&D Committee will vote on all recommendations for corrective action forwarded by the IRB or the SAS.

For the complete policy regarding non-compliance in human research projects, please refer to the Human Research Protection Program SOP 151-02.

**B. Suspension or Termination of R&D Committee Approval of Research** The R&D Committee shall notify the Principal Investigator in writing of such suspensions or terminations and shall include a statement of the reasons for the R&D Committee's actions. The terms and conditions of the suspension must be explicit. The PI shall be provided with an opportunity to respond in person or in writing.

Where the R&D Committee Chairperson determines that such action is necessary to ensure the health or safety of animal or human subjects, the Chairperson may require an immediate, temporary suspension of work with animals, enrollment of new subjects or of continued participation of previously enrolled human subjects, pending review of the situation by the convened R&D Committee.

## **XI. CONFLICT OF INTEREST IN RESEARCH**

The SVAMC advocates full disclosure of all conflicts of interest in research, personal and financial. The R&D Committee is responsible for determining whether or not any conflicts of interest exist between the chair or member of the R&D Committee and the research project to be reviewed, prior to review of the subcommittee's action on that research project. If such conflicts of interest exist, the conflicted member will be recused from the vote on the research project.

A conflict of interest exists when an employee's financial interests or other obligations interfere, or appear to interfere, with the employee's obligations to act in the best interest of the SVAMC and without improper bias. The mere appearance of a conflict may be as serious and potentially damaging to the public trust as an actual conflict. Therefore, potential conflicts must be disclosed, evaluated, and managed with the same thoroughness as actual conflicts.

### **A. Conflict of Interest in VA Research**

Per SOP 151-05 Syracuse VAMC R&D Standard Operating Procedures – Conflict of Interest, the R&D Committee is responsible for the following regarding conflict of interest in human research:

1. Determining whether or not any conflicts of interest exist between the chair or member of the R&D Committee and the research project to be reviewed, prior to review of the subcommittee's report and action on that research project. If such conflicts of interest exist, the conflicted member will be recused from the vote on the research project.

Reviewing all disclosed conflicts of interest identified within the subcommittee's reports and minutes.

- a. Deliberating and voting on all subcommittee recommendations for action to minimize, manage, monitor and/or eliminate all potentially significant financial or other types of conflicts of interest, forwarded by the IRB, SAS, or SRS.

- b. Notifying the Principal Investigator, appropriate subcommittee (IRB, SAS, SRS), ACOS/R&D, and Research Compliance Officer (RCO), and Research Integrity Officer of the decisions of the R&D Committee to minimize, manage, monitor and/or eliminate all potentially significant financial or other types of conflicts of interest.

2. Reviewing R&D Committee and IRB Member Potential Conflict of Interest Assessment Forms received from the SVAMC Compliance and Business Integrity Officer that were determined to have conflicts of interest and deliberating on any corrective action needed.

3. Managing institutional conflict of interest, when a PI's proposed research project involves the PI's invention for which the Dept. of Veterans Affairs has retained rights of the invention.

## XII. PUBLICATIONS

The R&D Committee is responsible to receive and review annually a quality assurance review of publications for reference to VA support. In order to clarify this acknowledgement by VA investigators, there are several ways to acknowledge an institute in a paper:

1. on the title page, where the affiliation of each author is indicated
2. in the methods section, where it spells out where (at which institute) the patients were recruited and of which institute's IRB approved the study
3. at the end of the paper (before the references), there is an acknowledgment section, where it is described who contributed intellectually or technically to the study (if the person is not included among the authors), and which organization / funding agency provided financial support to carry out the study and which institute provided the space and infrastructure for the study.

### a. REFERENCES

VHA Handbook 1200.01, Research & Development Committee Handbook  
 VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research  
 VHA Handbook 1200.07, Use of Animals in Research  
 VHA Handbook 1200.08, Safety of Personnel Engaged in Research  
 MCM. No. 151-01, Establishment of Governing Structure for Research & Development Service  
 SOP 151-01 Human Research Protections Program  
 SOP 151-04 Subcommittee on Research Safety  
 SOP 151-05 Conflict of Interest in Research Policy  
 SOP 151-16 Development, Approval and Maintenance of Policies & Procedures

### b. RESCISSIONS

R&D SOP 151-01, dated December 3, 2007.  
 R&D SOP 151-01, dated June 30, 2010  
 R&D SOP 151-01, dated March 12, 2012

### c. APPENDIX

- A. Research Reporting Structure
- B. Definitions

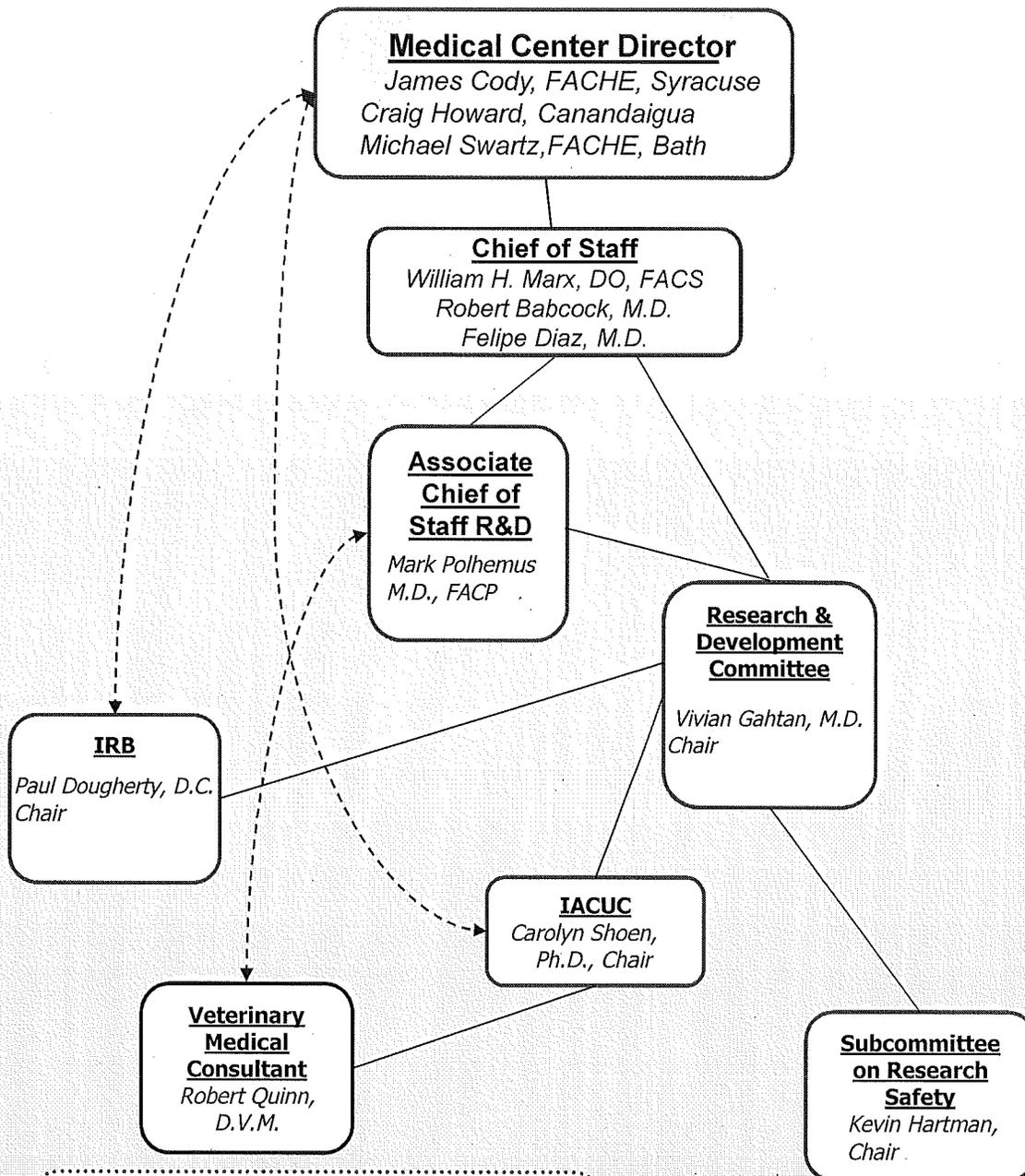


**MARK E. POLHEMUS, M.D., FACP**  
**ACOS/R**

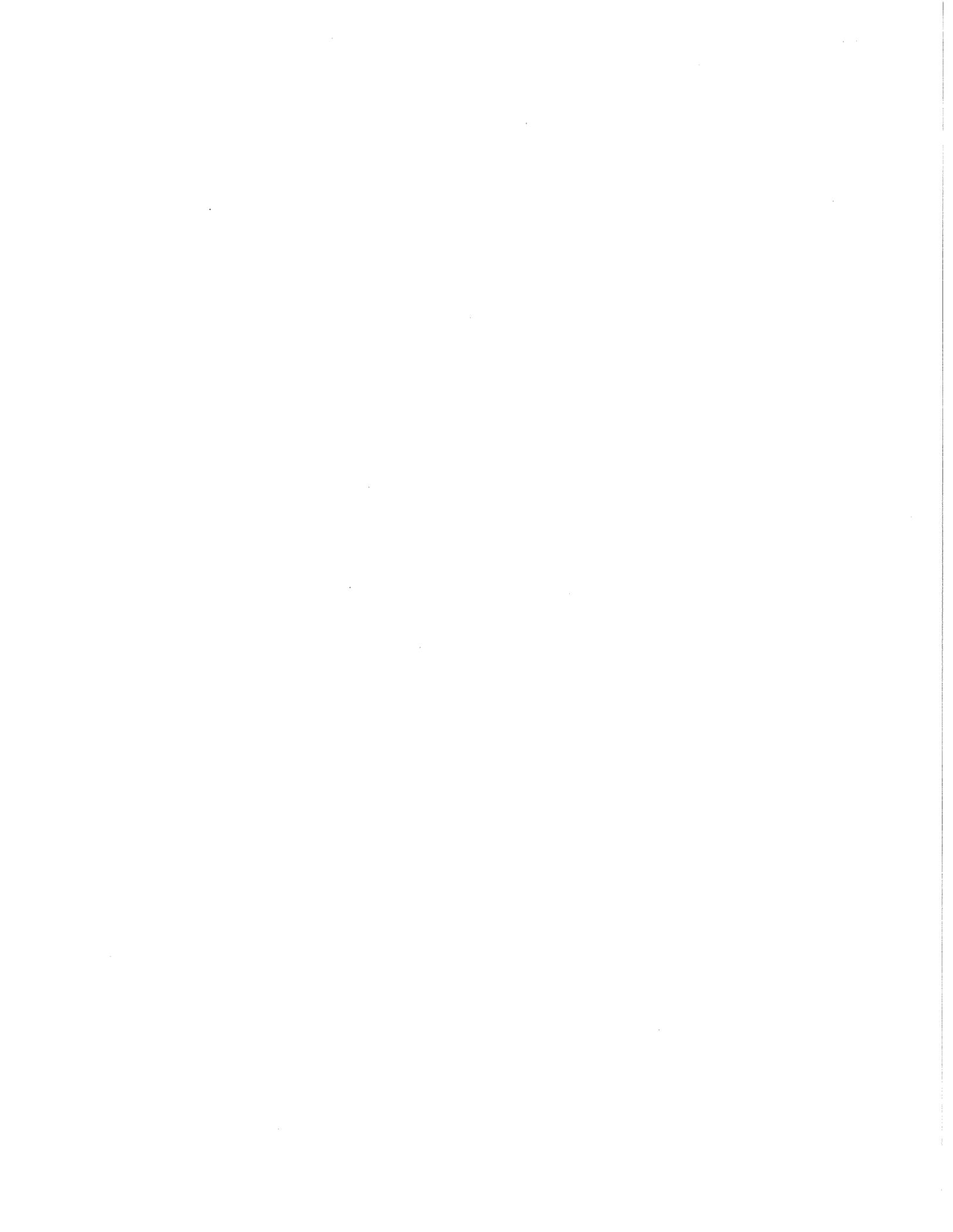
# Research Committee Reporting Structure

Syracuse VA Medical Center

February 2014



**Please Note:**  
Each Subcommittee Chair, members, the VMC, and investigators are aware they may directly communicate any concerns with the VAMC Director, COS, or ACOS/R.



## **Appendix B - Definitions**

**Adverse event:** An AE is any untoward physical or psychological occurrence in a human subject participating in research. An AE can be any unfavorable or unintended event, including an abnormal laboratory finding, symptom, or disease associated with the research or the use of a medical investigational test article. An AE does not necessarily have to have a causal relationship with the research, or any risk associated with the research or the research intervention, or assessment. A local AE is one occurring at a site for which the VA investigator's Institutional Review Board (IRB) of record is responsible. Please refer to SOP 151-17 "Adverse Event Reporting."

**Advertising:** Media intended to recruit prospective research participants. This does not include media (1) authored by someone other than the sponsor and VA employees or agents; (2) intended to be read solely by VA employees who are not intended to be participants and limited to study name, inclusion and exclusion criteria and contact information; or (3) documents intended for internal use by the study's research staff. Media include, but are not limited to newspaper, radio, TV, bulletin boards, posters, brochures, flyers, and web pages.

**Affiliate:** A university, medical or dental school, or foundation with a written VA affiliation agreement.

**Allegation.** An allegation is an assumption made by a party that must be proved or supported with evidence.

**Animal (Laboratory Animal).** A laboratory animal is a live (non-human) vertebrate used or intended for use in research, research training, experimentation, or biological testing, or for a related purpose.

**NOTE:** The term "animal" is further defined in VHA Handbook 1200.7.

**Animal Research:** Animal research, as used in VHA Handbook 1200.7, refers to any use of laboratory animals in research, testing, or training.

**Approval Date:** The date of the initial or most recent continuing approval of research by the IRB as documented on correspondence to the Principal Investigator.

**Assent:** An affirmative agreement to participate in research; this is not the same as informed consent. Failure to object should not be construed as assent. If there is impaired decision making capacity, the practitioner must explain the proposed research to the prospective research subject even when the surrogate gives consent. **Under no circumstances may a subject be forced or coerced to participate in a research study.** For additional information, please refer to SOP151-06 "Impaired Decision Making Capacity (IDMC)".

**Assurance (Assurance of Compliance):** An Assurance of Compliance is a written commitment to a Federal department or agency to ensure compliance with applicable requirements. For example, the participation of human subjects in VA research requires a Federal Wide Assurance (FWA) for the Protection of Human Subjects, and the participation of laboratory animals in VA research requires a Public Health Service (PHS) Animal Welfare Assurance.

**Attending Physician:** Physician directly responsible for clinical care of the participant.

**Banked Specimens:** Specimens that are put aside for future use under the existing approved protocol or new protocols yet to be approved. Banked human biological specimens do not include material used in an approved protocol that is destroyed when its intended approved use has been completed or at the termination of the study for which it was originally intended.

**Children:** Children are defined as persons who have not attained the majority legal age for consent to treatments or procedures involved in research. New York State law for majority legal age is 18.

**Coded Data:** Information stripped of any personal identifiers and randomly coded to provide a link by which identities can be accessed through a separately held key. *Coded data allows an investigator to update an individual's information.* Coding consists of labeling information that:

- Does **not** include any patient identifiers (*see a list of the 18 HIPAA identifiers below*)
- Is not derived from or related to the 18 HIPAA identifiers
- Cannot be translated so as to identify the individual. Thus initials, Social Security Numbers (SSNs) and other forms of identification may not be used as codes, even in partial or scrambled form.

For example, the code might be a barcode or a combination of random numbers and letters. If sensitive VA research data are coded, the key to linking the code with these identifiers must be stored and remain within the VA, but it should not be stored alongside the coded data.

*The 18 HIPAA identifiers are:*

- 1) Names
- 2) All geographic subdivisions smaller than a state, except for the initial three digits of the zip code if the geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people
- 3) All elements of dates except year and all ages over 89
- 4) Telephone numbers
- 5) Fax numbers
- 6) E-mail addresses
- 7) Social security numbers
- 8) Medical record numbers
- 9) Health plan beneficiary numbers
- 10) Account numbers
- 11) Certificate or license numbers
- 12) Vehicle identifiers and license plate numbers
- 13) Device identifiers and serial numbers
- 14) URLs
- 15) IP addresses
- 16) Biometric identifiers
- 17) Full-face photographs and any comparable images
- 18) Any other unique identifying number, characteristic or code, unless otherwise permitted by the Privacy

Rule for re-identification

- Scrambled SSNs
- Initials
- Last four digits of SSN
- Employee numbers

**Confidentiality:** The researcher's agreement with the participant about how the participant's identifiable private information will be handled, managed, and disseminated.

**Confirmed Report.** In the context of VA research, a confirmed report refers to non-compliance that is supported by incontrovertible factual information.

**Co-investigator:** Any other individual(s) who has involvement and directly aides the Principal Investigator(s) in the conduct of the study such as other clinical providers, research fellows, residents, associates, research pharmacist(s), and others who are authorized to prescribe study-related medications. For FDA regulated studies, these individuals are listed on FDA Form 1572, Box #6, as sub-investigators.

**Conflict of Interest (COI):** A conflict of interest occurs when any arrangement, situation or action, financial or otherwise, affects or is perceived to exert inappropriate influence on the design, review, conduct, results or reporting of research activities or findings. The impact of the conflict may occur in any phase of the research from the development of the study design, to the consenting of research participants, and to the management of the study. The conflict may also bias review of proposals, analysis of data and dissemination of research results through publications and presentations. Please refer to SOP 151-05 "Conflict of Interest."

**Financial Interest Related to the Research:** As part of the COI definition, IRB members and/or consultants will not participate in the review of protocols or plans in which they have a conflict of interest, except to provide information requested by the IRB. The IRB will request recusal of any member with such a financial interest (meaning financial interest in the sponsor, product or service being tested) based upon the following criteria:

- a) IRB member or family member (spouse and dependent children) serves as a PI or co-investigator or serves as a scientific/medical advisor to the research;
- b) IRB member or family member (spouse and dependent children) has received payments including salary, consulting fees, royalty or licensing payments from intellectual property, honoraria and/or gifts from the sponsor of the research (or from a direct competitor of the sponsor of the research), or their representative(s) during the past 12 months or anticipates receiving such payments during the next 12 months;
- c) IRB member or family member (spouse and dependent children) has equity interest in the entity sponsoring the research (or in a direct competitor of the entity sponsoring the research), excluding mutual funds;
- d) IRB member or family member (spouse and dependent children) holds a position as director, officer, partner, trustee, or any other significant position (e.g. scientific advisory board/consultants) with the entity sponsoring the

research (or a direct competitor of the entity sponsoring the research). This may exclude Data and Safety Monitoring Board membership;

- e) IRB member or a family member (spouse and dependent children) holds patent rights or royalties whose value may be affected by the outcome of the research, including royalties;
- f) The IRB member is a direct supervisor of individuals conducting the research or is directly supervised by individuals conducting the research.

**Continuing Non-compliance.** Continuing non-compliance is persistent or repeated failure, either in the past or extending into the present, to satisfy VA or other Federal research regulations and requirements. Continuing non-compliance may or may not involve harm to participants.

**De-Identified Data:** Information that does not identify an individual (or relative, employers, or household members of an individual) and with respect to which there is no reasonable basis to believe that the information can be used to identify an individual.

VHA would consider health information no longer protected health information (PHI) if it has been appropriately de-identified in accordance with the HIPAA Privacy Rule as outlined in VHA Handbook 1605.1, Appendix B. *Please note that de-identified data cannot be updated, since there is no way to ever correlate it back to an individual.*

**Deviation:** Any departure from the procedures stated in the approved research protocol or informed consent without prior review and approval of the modification.

**Significant Deviations:** Any departure from the procedures stated in the approved research protocol or informed consent that increases the risk to participants and is required to be reported to the IRB within 5 days of the incident. Examples include but are not limited to the following:

- Infractions involving dosing/distribution of study medications causing risk to the participant
- Infractions in following the guidelines for proper informed consent execution (e.g. using an expired informed consent)
- Infractions in which the sponsor (if applicable) requests notification to the IRB
- Infractions in which procedures were performed outside the approved research protocol

**Non-Significant Deviations:** Any departure from the procedures stated in the approved research protocol or informed consent that poses no increased risk to the participants and do not require reporting to the IRB. Examples include but are not limited to the following:

- Infractions involving expected concomitant medication deviations
- Infractions involving missed/late visits that pose no increased risk to the participant
- Infractions involving unintentional clerical errors on the informed consent (i.e. participant identifiers are not on all pages)

**DSMB (Data Safety Monitoring Board):** Responsible for data and safety monitoring of a clinical trial. The board should provide an IRB with safety information in a digestible format, at appropriate intervals that will allow the IRB, together with investigators, to perform a more reliable assessment of the significance of AE data in terms of protection of human participants. DSMBs also evaluate efficacy – e.g. if one treatment arm proves to be more effective than another, the DSMB may recommend study closure.

**Emergency Use:** The use of an investigational drug or biological product with a human participant in a life-threatening or severely debilitating situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval. Emergency use of an investigational drug or biologic is not considered research according to 45 CFR 46.116(f), however FDA regulations do consider emergency use research since it involves drug treatment (please see references under “**Human Research**”). For details on the process to obtain emergency use, please refer to SOP 151-02.

**Expected Adverse Event:** Adverse events that are not unanticipated problems involving risk (UPRs). For approved and marketed drugs or devices, those adverse events described in the approved package insert, and for investigational new drugs or devices, those adverse events described in the FDA Investigator’s Brochure. Refer to SOP 151-17 for further details.

**Exempt Research:** Exempt research is research determined by the Institutional Review Board (IRB) to involve human subjects only in one or more specific minimal risk categories (38 CFR 16.101(b)). Please refer to local SOP 151-08.

**FDA Regulated Test Article:** Any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to FDA regulation or under sections 351 or 354-360F of the Public Health Service Act.

**Good Clinical Practice (GCP):** A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

**Health Information:** Health information is any information created or received by a health care provider or health plan that relates to: the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or payment for the provision of health care to an individual. This encompasses information pertaining to examination, medical history, diagnosis, findings or treatment, including such information as: laboratory examinations, X-rays, microscopic slides, photographs and prescriptions.

**Human Biological Specimens:** Any material derived from humans, such as blood, urine, tissues, organs, hair, nail clippings, or any other cells or fluids, whether collected for research purposes or as residual specimens from diagnostic, therapeutic or surgical procedures.

**Human Research Protection Program (HRPP):** An HRPP is a comprehensive system to ensure the protection of human subjects participating in research. The HRPP consists of a variety of individuals and committees such as: the Medical Center Director, Associate Chief of Staff (ACOS) for Research and Development (R&D), the Administrative Officer (AO) for R&D, compliance officers, the R&D Committee, the IRB, other committees or subcommittees addressing human subjects protection (e.g., Biosafety, Radiation Safety, Radioactive Drug Research, Conflict of Interest), investigators, IRB staff, research staff, health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer) and research pharmacy staff. The objective of this system is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human subjects in research.

**Human Research:** According to VA regulations, is any research involving any of the following: (1) one or more human subject(s). (2) Data containing identifiable private information about one or more living individuals. (3) One or more human biological specimens.

According to FDA regulations, the research activity involves an FDA regulated test article because one or more of the following is true: 1) the activity involves the use of a drug, other than the use of a marketed drug in the course of medical practice; 2) the activity involves the use of a device to evaluate safety or effectiveness of that device; 3) data from the activity will be submitted to, or held for inspection by, the FDA in support of a marketing or research application for an FDA-regulated product. Per FDA regulations, this research activity involves human participants because one or more of the following is true: 1) the test article will be used on one or more humans; 2) data obtained from controls will be submitted to, or held for inspection by, the FDA in support of a marketing or research application for an FDA-regulated product; 3) data obtained from use of a device on tissue specimens will be submitted to, or held for inspection by, the FDA in support of a marketing or research application for an FDA-regulated product.

*For additional clarification on determining whether an activity is human research, please refer to the form "Determining Whether a Proposed Activity is Human Research According to VA or FDA Regulatory Definitions."*

**Human Subject:** A human subject is a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or through identifiable private information (38 CFR 16.102(f)). The definition provided in the Common Rule includes investigators, technicians, and others assisting investigators, when they serve in a "subject" role by being observed, manipulated, or sampled. As required by 38 CFR 16.102(f) an intervention includes all physical procedures by which data are gathered and all physical, psychological, or environmental manipulations that are performed for research purposes.

**NOTE:** *The FDA definition of human subject differs according to the applicable regulation; FDA regulations define human subject as an individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient. For research involving medical devices a human subject is also an individual on whose specimen an investigational device is used. See 21 CFR 812.3(p), 21 CFR 50.3(g), 312.3(b,) and 56.102(e).*

**Identifiable Private Information:** Private information in which the identity of the participant is associated or can be readily ascertained by the investigator.

**Imminent Threat of an AE in Research:** Any situation in which an AE in research has not yet occurred but is likely to occur, as determined by an IRB, research, or clinical team member, without preventive measures.

**Impartial Witness:** A person, independent of the research, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the participant or the participant's legally authorized representative cannot read, and who reads the informed consent document and any other written information supplied to the participant.

**Individually-identifiable Health Information:** Individually-identifiable health information (IIHI) is a subset of health information, including demographic information collected from an individual, that is: (1) created or received by a health care provider, health plan, or health care clearinghouse; (2) related to the past, present, or future condition of an individual and provision of, or payment for health care; and (3) identifies the individual or a reasonable basis exists to believe the information can be used to identify the individual.

**Institutional Conflict of Interest**

An institutional conflict of interest may occur when the institution, or any of its senior management or an affiliate foundation or organization, has an external relationship or financial interest in a company or organization that itself has a financial interest in a VA investigator's research project.

**Institutional Official:** The IO is the individual legally authorized as Signatory Official to commit an institution to an Assurance. The Facility Director or equivalent serves as IO for VA facilities that conduct research.

**Institutional Animal Care and Use Committee (IACUC):** An IACUC is a committee formally designated by an institution to ensure compliance with animal research regulations and guidelines and maintenance of an Animal Care and Use Program (ACUP). At VA medical centers, the IACUC is a subcommittee of the R&D Committee. The IACUC at the Syracuse VAMC is named "Subcommittee for Animal Studies" (SAS). *NOTE: The term "Institutional Animal Care and Use Committee" and related terms are further defined in VHA Handbook 1200.7.*

**Institutional Review Board (IRB):** An IRB is a board established in accordance with and for the purposes expressed in the Common Rule (38 CFR 16.102(g).) Within VHA, the IRB was *formerly* known as the Subcommittee on Human Studies. At VA medical centers, the IRB is a subcommittee of the R&D Committee.

**Intervention:** Physical procedures by which data are gathered (for example, venipuncture) and manipulations of the participant or the participant's environment that are performed for research purposes.

**Interventional studies:** Studies that include research designed to evaluate the safety, effectiveness, or usefulness of therapies (i.e. drugs, diet, exercise, behavioral interventions, surgical interventions, or medical devices), diagnostic procedures (i.e. CAT scans or prenatal diagnosis through amniocentesis, chorionic villi testing, and fetoscopy), or preventive measures (i.e. vaccines, diet, or fluoridated toothpaste).

**Investigational New Device (IDE):** A device, including a transitional device, that is the object of an investigation designed to evaluate its safety or effectiveness. An investigational device may be an approved device that is being studied for an unapproved use or efficacy.

**Investigational New Drug (IND):** A new drug, antibiotic drug, or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms "investigational drug" and "investigational new drug" are synonymous. An

investigational drug may be an approved drug that is being studied for an unapproved or approved use in a controlled, randomized, or blinded clinical trial.

**Investigator:** An investigator is any individual who conducts research, including, but not limited to: the Principal Investigator, co-investigator or local site investigator. A VA investigator must uphold professional and ethical standards and practices and adhere to all applicable VA and other Federal requirements, and to the applicable VA facility's policies and procedures.

**IRB Chair:** The person responsible for the oversight of the review functions of the IRB.

**IRB Chair designee:** An IRB member with one or more years of experience on the IRB.

**IRB Member:** A voting member or non-voting ex-officio member of the IRB.

**IRB Staff:** Members of the Research Office who support the functions of the IRB.

**Legally authorized representative:** An individual or body authorized under applicable law to provide permission on behalf of a prospective participant to the participant's participation in the procedure(s) involved in the research. As defined by VHA Handbook 1200.5, a legally authorized representative includes not only a person appointed as a health care agent under a Durable Power of Attorney for Health Care (DPAHC), a court appointed guardian of the person, but also next-of-kin in the following order of priority unless otherwise specified by applicable NY state law: Power of Attorney or legal guardian for the living and the executor of the estate for deceased, spouse, adult child (18 years of age or older), parent, adult sibling (18 years of age or older), grandparent, or adult grandchild (18 years of age or older).

**Life-Threatening:** Diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the participants must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

**Memorandum of Understanding (MOU):** An MOU is a written agreement entered into by two or more parties to set forth terms, conditions, and understandings of the parties with respect to specific activity. For example, an MOU may be developed to delineate each party's responsibilities, as allowable by law, in collaborations between two or more Federal agencies or between a Federal agency and a private entity.

**Minimal risk:** Risk in which the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

**Non-compliance.** In the context of the Human Research Protection Program (HRPP), non-compliance refers to failure to follow the regulations, the requirements, or the determinations of the Institutional Review Board (IRB) or the human research protection policies of the Syracuse VAMC. In the context of research utilizing animal subjects, non-compliance refers to failure to follow the regulations, the

requirements, or the determinations of the Subcommittee for Animal Studies or the animal research regulations of AAALAC, OLAW, USDA, and VA. In the context of research conducted in research laboratories, non-compliance refers to failure to follow the regulations, the requirements, or the determinations of the Subcommittee for Research Safety or the laboratory safety and security policies of the Syracuse VAMC, VA ORO, and CDC.

**Non-financial conflict of interest:** Could include concerns for promotions, tenure, publications and grants; token gifts (e.g. lunches or items with sponsor logos) goal oriented awards; or future participation incentives.

**Non-interventional studies:** Studies on normal human functioning and development that involve limited invasive or non-invasive procedures i.e. urine collection, moderate exercise, fasting, feeding, sleep, learning, responses to mild sensory stimulation, surveys or questionnaires, etc. are, for the purposes of this policy, considered non-interventional studies.

**Non-significant risk device:** a device that does not meet the definition for a significant risk device.

**Observational studies:** Studies include research that does NOT involve any intervention, alteration in standard clinical care or use in participants of any invasive or non-invasive procedure. Studies limited to the recording of data on individuals receiving standard medical care, the use of existing specimens or data, or the retrospective review of health information are considered observational studies.

**Office of Research and Development (ORD):** ORD is the office within VA Central Office responsible for the overall policy, planning, coordination, and direction of research activities within VHA. *NOTE: The Research Integrity Development and Education Program (PRIDE) is the program within ORD that is responsible for training, education, and policy development related to human subjects protection.*

**Office of Research Oversight (ORO):** ORO is the primary VHA office for advising the Under Secretary for Health on all matters regarding compliance and oversight of research in the protection of human subjects, animal welfare, and research safety. ORO oversees investigations of allegations of research misconduct and research impropriety.

**Off-site Event:** Any adverse event experienced by a human participant enrolled in research at a site other than the Syracuse/Canandaigua/Bath VAMC or its research entities (i.e. multisite research).

**On-site Event:** Any adverse event experienced by a human participant enrolled in research at the Syracuse/Canandaigua/Bath VAMC or its research entities (regardless of where the event occurs).

**Primary Reviewer:** Any member of the IRB, based on their area of expertise, who is assigned by the IRB staff with the concurrence of the IRB Chair or designee to review, and is not participating in the research.

**Principal Investigator (PI):** A PI is a qualified person designated by an applicant institution to direct a research project or program. The PI oversees scientific, technical, and the day-to-day management of the research. In the event of a research project conducted by a team of individuals, the PI is the responsible

leader of that team. The PI is ultimately responsible for the conduct of the research protocol on which they are named. A PI must be designated at the Syracuse/Canandaigua/Bath VAMC and must hold a paid VA appointment and may not be a Student, Clinical Resident, Clinical Fellow or a Research Post-Doctoral Fellow. A PI overseeing a protocol conducted with such a trainee (student, resident, or fellow) must have sufficient experience in the area of the trainee's research interest and is responsible for oversight of the research activities and the trainee. The trainee may hold the title of co-investigator only. It is the PI's responsibility to ensure that if the trainee does not complete all aspects of the research prior to leaving the VA, the protocol is completed or terminated in an orderly fashion, and in accordance with local, VA, and other Federal requirements. The PI must also ensure all research records are retained by VA.

**Prisoner:** Any individual involuntarily confined or detained in a penal institution, including individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

**Privacy:** A person's desire to control the access of others to themselves. "Access" includes physical, behavioral, and intellectual information about an individual available for scrutiny by others.

**Private information:** Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

**Progress Report:** The completed progress report form and submitted attachments.

**Progress Report Deadline:** The first of the month of the IRB meeting at which continuing review is scheduled to occur. The progress report deadline may be extended to accommodate those reports received after the deadline if there is adequate time for review by the IRB staff, IRB Chair, and members.

**Quorum:** Minimum number of voting members who must be present at the meeting for business to be legally transacted, and includes at least one member whose primary concern is in a non-scientific area. At meetings of the IRB, a quorum must be established and maintained for the deliberation and vote on all matters requiring a vote.

**Related:** An event is "related" if it is likely to have been caused by the research procedures.

**Research:** A systematic investigation (**defined as the testing of concepts by the scientific method of formulating a hypothesis or research question, systematically collecting and recording relevant data, and interpreting the results in terms of the hypothesis or question**), including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge or any experiment that involves an FDA regulated test article **and one or more human subjects...** **The definition of generalizable knowledge for IRB purposes means that (1) the conclusions are drawn from particular instances of a systematic investigation involving human participants, and (2) the information from the systematic investigation is to be disseminated.** VA Research is defined as

research conducted by VA investigators (serving on compensated, work without compensation (WOC), or Intergovernmental Personnel Agreement (IPA) appointments) while on VA time, utilizing VA resources (e.g. equipment), or on VA property including space leased to, or used by VA. The research may be funded by VA, by other sponsors, or be unfunded. **Clinical Research is defined as any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505 (i) or 520 (g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. (21 CFR 50.3(c), 21 CFR 56.102(c)).**

**Research & Development Committee (R&D):** The R&D Committee is responsible, through the Chief of Staff (COS) to the medical center Director for: Advising and assisting the medical center Director in providing oversight, planning, and execution of the local research Program; and assisting the medical center Director in maintaining high standards throughout the R&D Program. Those standards include ensuring the:

- (a) Scientific and ethical quality of VA research projects;
- (b) Protection of human subjects in research;
- (c) Safety of personnel engaged in research;
- (d) Welfare of laboratory animals;
- (e) Security of VA data; and
- (f) Security of VHA research laboratories.

**Research Compliance:** The person or organizational element, except the Principal Investigator, designated by management to perform the duties relating to quality assurance and compliance of research studies.

**Research Compliance Officer (RCO):** The RCO is an individual whose primary responsibility is compliance oversight of research projects. VA RCOs must conduct periodic audits of research activities in accordance with VA requirements. A VA research facility's RCO must report directly to the facility director.

**Research Impropriety:** The term "research impropriety" refers to noncompliance with the laws, regulations, or policies regarding human subject protections, laboratory animal welfare, research safety, research laboratory security, research information security, research misconduct, and other matters as the Under Secretary for Health may assign. Research impropriety does not encompass improper procedures or conduct in areas outside of the jurisdiction of ORO, such as: waste, fraud, abuse, or fiscal mismanagement.

**Research Misconduct:** Research misconduct is fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. **NOTE:** The terms "fabrication," "falsification," and "plagiarism" are further defined in VHA Handbook 1058.2. Please refer to local SOP 151-07 "Misconduct in Research."

**Research Records:** Research records consist of IRB records as well as case histories (also referred to as investigator's research records) or any data gathered for research purposes.

(1) **IRB Records.** IRB records include but are not limited to: all minutes of IRB meetings, a copy of all proposals reviewed including all amendments, investigator brochures, any supplemental information including recruitment and informational materials, consent forms, information submitted for continuing review, all correspondence, and IRB membership with a resume for each member.

(2) **Case History.** A case history is a record of all observations and other data pertinent to the investigation on each research subject. An investigator is required to prepare and maintain adequate and accurate case histories. Case histories include the case report forms and supporting data including signed and dated consent forms, any medical records including, but are not limited to: progress notes of the physician, the individual's hospital chart(s), and nurses' notes. The case history for each individual must document that informed consent was obtained prior to participation in the study.

**Serious Adverse Event (AE) or Serious Problem:**

- 1) An SAE in research is an AE that results in death, a life threatening experience, inpatient hospitalization, prolongation of hospitalization, persistent or significant disability or incapacity, congenital anomaly, or birth defect.
- 2) A serious problem in research that results in:
  - a. Substantive harm or damage (or risk of substantive harm or damage) to the safety, rights, or welfare of research subjects, research staff or others; or
  - b. Substantive harm or damage (or risk of substantive harm or damage) to the safety or welfare of laboratory animals.
- 3) An AE or problem in research is also considered serious when medical, surgical, behavioral, social, or other intervention is needed to prevent preceding subparagraphs 1 & 2. *For further details on SAEs see SOP 151-17.*

**Serious Non-Compliance:** Serious non-compliance is the failure to adhere to the laws, regulations, or policies governing VA research that:

- 1) Results in substantive harm or damage (or risk of substantive harm or damage) to the safety, rights, or welfare of human subjects, research staff, or others; or
- 2) Results in the substantive harm or damage (or risk of substantive harm or damage) to the safety or welfare of laboratory animals; or
- 3) Substantively compromises the integrity or effectiveness of research protections, whether systemically or relative to a particular protocol or project.

**Severely Debilitating:** Diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis, or stroke.

**Significant risk device:** an investigational device that presents a potential for serious risk to the health, safety or welfare of a participant and (a) is intended as an implant; (b) is purported or represented to be for use in supporting or sustaining human life; (c) is for a use of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise preventing impairment of human health; or (d) otherwise presents a potential for serious risk to the health, safety or welfare of a participant.

**Site Investigator or Site PI:** A Site investigator or Site PI is an investigator at a site participating in a multi-site project who serves as the PI at that site.

**Sponsored Research:** refers to research conducted in whole or in part under a contractual agreement with one or more industry sponsors/collaborators. It does not refer to research conducted under a contractual agreement with one or more sponsors that are governmental entities or that are subdivisions of governmental entities. The sponsor may be a pharmaceutical company, a private or academic organization or an individual.

**Standard Operating Procedure (SOP):** A procedure written in standardized format, giving detailed instructions, which describe a routine activity so that each person following the SOP will perform the activity in a consistent and repeatable manner. The SOP author is responsible for technical content of the SOP.

**Subcommittee for Research Safety (SRS):** SRS is the subcommittee of the R&D Committee that reviews and approves the use of hazardous substances in VA research.

**Suspension or Termination of Research:**

- 1) Suspension refers to a temporary interruption in the enrollment of new subjects or other research activities.
- 2) Termination refers to a permanent halt in the enrollment of new subjects or other research activities.
- 3) The terms “suspension” and “termination” apply to interruptions related to concerns regarding:
  - a. The safety, rights or welfare of human research subjects, research investigators, research staff, or others; or
  - b. The safety, rights or welfare of laboratory animals.
- 4) Suspension and termination do not include:
  - a. Interruptions in human research resulting solely from the expiration of the IRB approval period.
  - b. “*Administrative Holds*” or other actions initiated voluntarily by an appropriate facility official, research investigator, or sponsor for reasons other than those described in the preceding paragraphs (3 & 4a).

**Administrative Hold (From VHA Directive 1058.01, May 21, 2010)** An administrative hold is a voluntary interruption of research enrollments and ongoing research activities by an appropriate facility official, research investigator, or sponsor (including the VHA ORD when ORD is the sponsor).

(1) The term “administrative hold” does not apply to interruptions of VA research related to concerns regarding:

- (a) The safety, rights, or welfare of human research subjects, research investigators, research staff, or others; or
- (b) The safety, health, or welfare of laboratory animals.

(2) The terms “suspension” and “termination” (defined at subparagraph 4aa) apply to research interruptions related to the concerns described at subparagraphs 4a(1)(a) and 4a(1)(b) as noted within VHA Directive 1058.01, version May 21,2010.

(3) An administrative hold must not be used to avoid reporting deficiencies or circumstances otherwise covered by this Handbook, related Handbooks, or other Federal requirements governing research.

**Termination:** All research related activity has been completed or was never started.

**Unanticipated Adverse Device Effect:** Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of participants.

**Unexpected Adverse Event:** Any adverse event, the specificity or severity of which is not consistent with the risk information previously reviewed and approved by the IRB. All unanticipated adverse device events are considered to be unexpected adverse events. If the nature and severity of an adverse event are accurately reflected in the consent document, then the IRB considers the adverse event to be expected.

**Unexpected Death:** The death of a research participant in which a high risk of death is not projected, as indicated by the written protocol, informed consent form, or sponsor brochure. This definition does not include deaths associated with a terminal condition unless the research intervention clearly hastened the participant's death. A participant's death that is determined to be clearly not associated with the research is also not an "unexpected death."

**Unexpected Problem:** Synonymous with unexpected adverse event.

**Unexpected Problem Involving Risks to Participants or Others:** Unanticipated problems involving risks to participants or others include any adverse event that is (1) unexpected, (2) serious, and (3) related or possibly related to participation in the research. Unanticipated problems also include unexpected adverse events, regardless of severity, that the IRB determines represent risk to participants or others. Unanticipated problems also includes events that are not categorized as adverse events, are not directly related to an individual's participation in a study, but represent risk to participants or others.

**VA-Approved Research:** VA-approved research is research that has been approved by the VA R&D Committee.

**VA Approved Tissue Bank:** Located off-station and must have the approval of the Chief Research and Development Officer, comply with VA regulations and safeguards and house human biological specimens collected under VA approved research protocols that are under both VA ownership and VA control.

**VA Research Laboratories:** VA Research Laboratories are research laboratories under the control of VA. In the context of VHA Handbook 1200.06, the VA research laboratory director is the VA investigator responsible for a particular laboratory. VA research laboratories include:

- (1) VA research laboratories located within VA facilities and in leased space;
- (2) VA research laboratories located in approved off-site facilities such as affiliate universities;  
and
- (3) Laboratories within the VA medical center in space that is leased to a private entity.

**VA Sponsored Tissue Bank:** Repositories for human biological specimens housed at a VA facility or an approved off-station location.

**Veterinary Medical Unit (VMU):** The VMU consists of the animal research facility plus the husbandry and veterinary technical personnel assigned to care for animals.

**VHA Sensitive Data:** All VA data on any storage media or in any form or format, which requires protection due to the risk of harm that could result from inadvertent or deliberate disclosure, alteration, or destruction of the information. The term includes information whose improper use or disclosure could adversely affect the ability of an agency to accomplish its mission, proprietary information, and records about individuals requiring protection under various confidentiality provisions such as the Privacy Act or HIPAA.

**Vulnerable Participants:** Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students; subordinate hospital and laboratory personnel; employees of the pharmaceutical industry; members of the armed forces; and persons kept in detention. Other vulnerable participants include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.

