

COOPERATIVE STUDIES
PROGRAM

INVESTIGATOR
GUIDELINES

FOR THE PLANNING AND CONDUCT OF
VA COOPERATIVE STUDIES

OFFICE OF RESEARCH AND DEVELOPMENT
DEPARTMENT OF VETERANS AFFAIRS

2018

Effective Date: March 20, 2018

Approved by CSP Central Office



Veterans Health Administration
Research Development
Improving Veterans' Lives  www.research.va.gov

Table of Contents

I. INTRODUCTION	1
A. PURPOSE	1
B. COOPERATIVE STUDIES PROGRAM	1
C. CSP INVESTIGATORS	3
II. DEVELOPING A CSP STUDY.....	3
A. LETTER OF INTENT	3
B. LOI REVIEW	6
C. THE PLANNING COMMITTEE.....	6
D. PLANNING MEETINGS	7
E. CSSEC PROPOSAL	8
III. CSP SCIENTIFIC REVIEW.....	8
A. CSSEC WRITTEN REVIEWS.....	8
B. CSSEC REVIEW PROCESS.....	9
C. CSSEC RECOMMENDATIONS.....	9
IV. INITIATING A CSP STUDY.....	10
A. PARTICIPATING SITE SELECTION.....	10
<i>Participating VAMCs.....</i>	<i>11</i>
<i>Hiring and Training of Study Personnel.....</i>	<i>11</i>
B. CASE REPORT FORMS.....	12
C. STUDY OPERATIONS MANUAL AND TRAINING MATERIALS.....	12
D. INVESTIGATIONAL NEW DRUG APPLICATION AND INVESTIGATIONAL DEVICE EXEMPTION.....	12
E. ORGANIZATIONAL/TRAINING MEETING	13
F. RECRUITMENT PLANNING	13
V. CONDUCTING A CSP STUDY.....	13
A. CSP STUDY MANAGEMENT AND MONITORING.....	14
<i>Study Group.....</i>	<i>14</i>
<i>Executive Committee.....</i>	<i>14</i>
<i>Data Monitoring Committee</i>	<i>15</i>
<i>CSP Human Rights Committee.....</i>	<i>15</i>
<i>Site Monitoring, Auditing and Resource Team.....</i>	<i>16</i>
B. STUDY CHAIR RESPONSIBILITIES.....	16
C. MEETING/TRAVEL ARRANGEMENTS.....	16
D. PROTOCOL CHANGES, EXCEPTIONS, AND DEVIATIONS.....	16
E. CHANGE IN FUNDING SUPPORT	17
F. ETHICAL AND REGULATORY CONSIDERATIONS	17
G. STUDY DATA	19

H. REPORTING OF ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, AND UNANTICIPATED ADVERSE DEVICE EVENTS.....	19
I. BREAKING STUDY BLIND	20
J. DUAL ENROLLMENT	20
K. SUBPROTOCOLS / SUBSTUDIES	20
L. COMMUNICATIONS.....	20
M. SITE VISITS.....	21
N. REPLACING AN SI OR STUDY CHAIR	21
O. PUTTING A SITE ON PROBATION	22
P. EARLY TERMINATION OF A SITE	22
Q. CSP STUDY FILES	23
R. PERIODIC REPORTS	23
<i>Local</i>	23
<i>CSP</i>	23
VI. CONCLUDING A CSP STUDY.....	24
A. CLOSE OUT	24
<i>Participants</i>	24
<i>Study Data / Results</i>	24
<i>Regulatory</i>	25
B. FINAL STUDY MEETING.....	25
C. PUBLICATIONS	25
D. ADMINISTRATIVE REPERCUSSIONS	26
E. CUSTODIANSHIP OF DATA	26
F. RELEASE OF STUDY DATASETS	27
G. CONTINUING ANALYSIS ACTIVITIES.....	28
VII. CONCLUSION	28
APPENDIX A - GLOSSARY OF ABBREVIATIONS AND ACRONYMS	29
APPENDIX B - COOPERATIVE STUDIES PROGRAM AUTHORSHIP POLICY	31

I. INTRODUCTION

A. Purpose

Cooperative Studies Program (CSP) research serves Veterans and the nation. Success is dependent upon good communication, cooperation, and a willingness to pursue a common goal. To achieve these outcomes, it is critical to perform specific responsibilities in a quality-based manner. These CSP Investigator Guidelines provide responsibilities, procedures and expectations for the five key phases of a CSP study. This document is specifically intended for CSP Study Chairs and Site Investigators (SIs)—referred to herein collectively as CSP Investigators—to ensure consistent practices across all CSP studies within a quality management framework. These guidelines also fall under the overall purview of CSP’s policy authority and supplement other quality documents maintained by CSP. CSP Center Directors may approve requests for exceptions and/or seek CSP Central Office (CSPCO) concurrence when appropriate. Questions about any of these materials may be directed to a CSP Center and/or CSPCO.

B. Cooperative Studies Program

CSP, a division of the Veterans Health Administration (VHA) Office of Research and Development (ORD), is responsible for the planning, conduct and funding support of multicenter clinical and epidemiologic research studies. The CSP mission is to advance the health and care of Veterans through cooperative research studies that produce innovative and effective solutions to Veteran and national health care challenges.

CSP is a complete clinical research program that dates back to the 1940s during the earliest efforts in designing and conducting multisite clinical trials in the United States. This national program works with VA clinician-investigators and facilities to perform VA research that addresses key questions for transforming practice, and for developing innovations in how clinical trials and epidemiologic research are conducted, both within VA and nationally.

Organizationally, CSP reports to the Chief Research and Development Officer (CRADO) in ORD. CSPCO in Washington, DC, manages the infrastructure for and scientific portfolio of clinical trials, observational, and genetic research through its network of clinical trials, epidemiologic, and recruitment centers throughout the country.

CSP clinical trial expertise is comprised of professional experts located at five CSP Coordinating Centers (CSPCCs) at the VA medical centers (VAMCs) in Boston, MA; Hines, IL; Palo Alto, CA; Perry Point, MD; and West Haven, CT. CSPCC staff include individuals with backgrounds in biostatistics and clinical research methods, project, administrative and budgetary management, and quality management and assurance. These centers help direct and support all phases of the research project, including:

- Proposal development
- Study implementation
- Central coordination of study conduct
- Data collection and management

- Statistical analyses
- Study progress monitoring
- Compliance
- Study publication and dissemination

Unique to CSP is its Clinical Research Pharmacy Coordinating Center (CRPCC), affiliated with the VAMC in Albuquerque, NM. CRPCC was established to provide resources for all CSP studies, specifically ones involving drugs or devices. If needed, this center can manufacture, package, and distribute pharmaceuticals to studies. Additionally, responsibilities include the following:

- Study planning and monitoring
- Liaising with the US Food and Drug Administration (FDA) and the pharmaceutical or device industries
- Providing expertise regarding FDA regulations
- Reviewing and distributing reports of adverse events (AE) and serious adverse events (SAE) collected during the course of the study
- Centrally controlling and distributing study drugs and devices

CSP Site Monitoring, Auditing and Resource Team (SMART) resides at CRPCC and is responsible for the training and oversight of Good Clinical Practices (GCP) in CSP studies.

CSP serves as sponsor for all of its studies. For interventional clinical trials, CSP follows responsibilities outlined in ICH E6 Good Clinical Practice (GCP). Quality by Design principles are also applied to promote efficiencies and mitigate risks and important errors throughout the lifecycle of the trial.

There also are five CSP Epidemiology Centers (CSPECs) that conduct, coordinate, and support population and genetics research. They emphasize observational methods of large cohorts and approaches that do not require a randomized approach to addressing clinical questions. These centers are located at VAMCs in Boston, MA; Durham, NC; Palo Alto, CA; Seattle, WA; and West Haven, CT.

CSP Pharmacogenomics Analysis Laboratory (PAL) at the Little Rock VAMC in Arkansas is dedicated to helping CSP studies that have genetic and/or pharmacogenomic data or biospecimens. With technological and analytical resources for such activities, the PAL provides another dimension for CSP to address Veterans' health care needs.

CSP Network of Dedicated Enrollment Sites (NODES) is a core set of sites based at VAMCs to provide recruitment and other site-level insights for conducting clinical research. As part of the CSP infrastructure, NODES partner with CSP Centers and CSP Investigators to help overcome common barriers to conducting multisite research. Collectively, NODES form a group that helps provide study-specific and program-wide

solutions in study planning and subsequent execution by offering insights that have not traditionally been incorporated in such activities. Within a given VAMC, a NODES team also can help navigate local procedures and policies for conducting CSP research. NODES sites are located at VAMCs in Dallas, TX; Hines, IL; Houston, TX; Long Beach, CA; Minneapolis, MN; Palo Alto, CA; Portland, OR; Salt Lake City, UT; and San Diego, CA.

CSP also partners with the Health Services Research & Development Service (HSR&D) Health Economics Resource Center (HERC) at the VA Palo Alto Health Care System. HERC economists provide design and analytical support in the conduct of CSP studies where cost effectiveness, quality of life, or other economic questions are relevant.

C. CSP Investigators

CSP Investigators and study personnel play a critical role in the success of CSP studies. Together with CSP Centers, they help with conceptualizing the research question and carrying out the study protocol. They also directly interface with Veterans and other populations whom CSP research serves. While CSP centers provide many of the key functions for a successful study, CSP Investigators also must share a commitment to program values and processes. Key points are provided below to help them succeed in their efforts. Understanding these principles will help with achieving the standards expected in doing a CSP study.

Serving as a CSP Investigator implies a commitment to Veterans first. CSP Investigators are expected to actively engage in the ethical conduct of research, oversight of clinical, scientific, and administrative responsibilities, and maintenance of the quality and integrity of the study in cooperation with study team members.

Participating in a CSP study requires adherence to all applicable federal, VA, and CSP policies. CSP has Standard Operating Procedures for most key activities in designing and conducting its studies. Training and overviews are provided at various stages, and questions about responsibilities or roles on a study should be directed to the CSP Center.

Oversight and management responsibilities are delegated to CSP Centers and in accordance with VHA Directive 1205. CSP Investigators are responsible to their assigned CSP Center(s) and, in turn, CSP Centers report directly to CSPCO. CSP Centers will know how and when to engage others to seek additional guidance and/or obtain approvals. CSP Center Directors may also approve requests for exceptions and/or seek CSPCO concurrence when appropriate.

II. DEVELOPING A CSP STUDY

A. Letter of Intent

Conducting a CSP study is demanding but rewarding. The successful planning, organization, conduct, and conclusion require the active engagement and cooperation of many individuals who must be willing and able to devote time and energy to a study's success. Participation in a CSP study is voluntary and doing so implies a willingness to adhere to CSP policies in all respects. Prior to initiating a CSP study, one should consider the requirements, demands, and team-oriented approach involved. Interested individuals may contact CSPCO or other CSP Investigators for more details.

The submission of a Letter of Intent (LOI) by an eligible VA clinician-investigator to CSPCO is the first step in CSP study-development process. The individual submitting the LOI is designated as the Principal Proponent. The LOI is a detailed proposal that describes the research question, need for a cooperative study, and ideas for how a CSP study may potentially achieve study objectives. An LOI should be no longer than 10 pages and contain the following information:

- **Title & Principal Proponent Name(s).** A Co-Principal Proponent may be named when a clear and justifiable need exists. No more than two Co-Principal Proponents may be named without prior CSPCO approval.
- **Objectives** of the proposed research, including concise mention of patients/participants, records or biospecimens, any interventions or interactions, and outcomes.
- **Relevance and potential impact** of the study to VA and to Veterans and how the study will affect clinical practice. Statements on any clinical equipoise, expected implementation of findings, and/or incorporation into practice guidelines are strongly encouraged.
- **Feasibility and justification** for conducting a multisite or large-scale observational study within VA.
- **Summary of the preliminary** research that has been accomplished with data to support a large-scale investigation.
- **Proposed study design** that includes the following items as appropriate:
 - Study population, with specific inclusion and exclusion criteria
 - Interventions, interactions, or treatments and services to be compared
 - Outcomes or endpoints to be evaluated
 - Research design (randomized trial, observational cohort study) and rationale
 - Sampling strategy
 - Logical links among questions, data, and primary and secondary associations
 - Number of participants, records, or biospecimens, and number of participating VAMCs
 - Duration of study
 - Data sharing plan
 - Resources required (Full-Time Employees [FTEs], Full-Time Equivalent Employees [FTEEs], and estimated total costs)
 - Methods of data collection
 - Units of measurements, strategies for analyses
 - Other details, as needed
- **Acknowledgment** of VA policy to include women and minorities in research and adherence to CSP policies overall.
- If desired, include a statement on experience and/or qualifications for conducting a multisite or large-scale observational study.

The following documents also should be included in the submission, but do not count toward the 10-page limit:

- **Completed Form 10-1313-13** or equivalent. (See <https://www.va.gov/vaforms/medical/pdf/10-1313-13-fill.pdf>.)
- **Statement of disclosure.** A formal statement that confirms the absence of a financial or contractual relationship between the Principal Proponent and any proposed organization involved in the trial that may constitute a real or apparent conflict of interest. If such a relationship or contract does exist, or appears to exist, the Principal Proponent must provide full disclosure.
- **Statement of eligibility.** To be eligible for planning support, the Principal Proponent must either have at least a 5/8 VA appointment or have applied for and received a 5/8 appointment waiver from the Director, CSP, within the previous year approving an LOI submission. In the latter case, a copy of the waiver approval establishing eligibility to receive funds should be attached to the request. A Principal Proponent may not be a VA Central Office employee.
- **Cover letter** from the Principal Proponent's VAMC Director and the Associate Chief of Staff for Research and Development (ACOS/R&D) acknowledging and approving the submission and time to dedicate to required activities.
- **Curriculum Vitae (CV)** of the Principal Proponent(s) with VA address, email, telephone, and fax numbers (NIH Biosketch is acceptable if it provides sufficient expertise and experience information).
- **Potential Planning Committee members.** Names, addresses, telephone numbers, and email addresses of five to seven experts who would be appropriate for the study Planning Committee should the LOI be approved. The list should include potential VA SIs.
- **List of ongoing and submitted proposals** that are directly related (e.g., pilot study, single-site, and smaller clinical trial) to the study proposed in the LOI and the funding source.
- **Suggested subject matter experts (SMEs).** A list of names and affiliations of SMEs who could serve as potential reviewers, Data Monitoring Committee (DMC) members, or other roles not directly related to study planning or conduct may be included on a separate page.

If there is interest in submitting other relevant background materials, CSPCO should be consulted; however, supplemental material will be distributed to the reviewers at the discretion of CSPCO.

The Principal Proponent should submit seven hardcopies of the LOI and CVs, an electronic version in compact disc (CD) format, and all correspondence with applicable local signatures to:

ATTN: CSP LOI (Planning Request)
 Cooperative Studies Program (10P9CS)/VA Office of Research & Development
 810 Vermont Avenue, NW
 Washington, DC 20420

The VAMC may also email an electronic version of the LOI to csp@va.gov. Hardcopies must still be submitted via regular mail. CSP will not process incomplete submissions.

Note: Individuals interested in a novel approach to conducting comparative effectiveness research using VA's electronic health record through the Point of Care Research (POC-R) initiative should contact CSPCO for information on any additional LOI requirements.

B. LOI Review

CSPCO will initially review an LOI for program relevance. If accepted, CSP will send the LOI out for scientific peer-review. This review typically involves three or more SMEs who will evaluate the relevance, feasibility, and potential clinical impact of the proposal. The CRADO will then make a decision on an LOI based on reviewer recommendations, as well as program priorities, ongoing and planned activities, and available funds. An applicant will typically receive a response to a planning request within approximately 3 months, depending on whether CSP requires additional information to complete reviews or if there are extenuating circumstances. One of three actions is taken as part of the decision:

- Approved for study planning. The LOI is approved to proceed through the standard CSP planning process and is assigned to a CSP Center to prepare for a full proposal for submission.
- Approved for preliminary planning. The LOI is deemed of potential interest but requires further thought and/or development on proposed concepts. The LOI is assigned to a CSP Center for assistance with preliminary planning activities to address key limitations or concerns. This decision does not commit to an approval for developing into a full proposal.
- Disapproved. LOIs that are not approved will receive a copy of the reviewer comments.

The Principal Proponent and associated VAMC ACOS/R&D will receive a written notification of the planning request decision from CSPCO with reviewer comments. LOIs receiving an approval decision also receive information on the assigned CSP Center, CSP study number, and any further conditions or considerations of the approval.

C. The Planning Committee

Planning a CSP study requires close cooperation and critical thought among several groups and individuals. The Principal Proponent provides clinical and scientific leadership in the planning process in collaboration with CSP Center expertise and CSPCO input. The assigned CSP Center Director will identify the Study Biostatistician or Epidemiologist and Project Manager (PM) with whom the Principal Proponent will work as a team. CSP personnel will communicate the specific roles and responsibilities and guide the team through the planning process. Together, the Principal Proponent and CSP Center staff will provide the basis for a Planning Committee.

The Planning Committee is a multidisciplinary group consisting of roughly eight to ten individuals responsible for preparing the final study proposal. The committee typically includes the Principal Proponent, the Study Biostatistician or Epidemiologist, the PM, the Study Clinical Research Pharmacist (CRP), and SMEs in

clinical, logistical, and/or technological areas applicable to the study. CSPCO approves members through the assigned CSP Center Director. Approvals are based on, but not limited to, subject matter expertise, commitment to the planning process, ability to provide diverse perspectives in study design, having no conflicts of interest, and resource requirements.

- The Planning Committee's clinical expertise other than the specialty of the Principal Proponent and CSP staff should be considered for representation on the Planning Committee.
- If multiple disciplines are involved in the proposed study (e.g., medical and surgical), they should be reflected in the composition of the Committee.
- CSPCO leadership are ex officio members.
- Participation does not require VA affiliation. If industry and/or other federal agency support is planned, a representative from that organization may be invited to participate in the planning process with CSPCO approval and in accordance with other requirements stated in these Guidelines.

CSP planning process is intended to fully consider a number of factors. To assist, other groups may be involved in the planning stage including:

- CSP Human Rights Committee (HRC) whose charge is to be patient advocates and provide input into the burden and experience Veterans may have to undergo to participate.
- CSP NODES who can provide feasibility and other assessments of proposed methods from a site-level perspective.

D. Planning Meetings

Developing a full study proposal centers around in-person planning meetings and culminates in a final proposal for Cooperative Studies Scientific Evaluation Committee (CSSEC) review. CSP follows Quality by Design principles and expects planning activities to adhere to this approach. Typically, there are two planning meetings that last two days each with much preparatory activity preceding the event. Under special circumstances, CSPCO may approve additional planning meetings. The assigned CSP Center will communicate the specific tasks and timelines of the planning meetings.

If no activity toward planning the first meeting occurs within 3 months of LOI approval, CSP will discontinue further support. The assigned CSP Center Director is responsible for notifying CSCPO of any lack of progress and the need to discontinue planning support.

At the first in-person meeting, the Planning Committee goes through a structured agenda to establish the study question and determine the clinical impact, design, feasibility, and key elements of a proposal. In addition to an emphasis on Quality by Design principles, there should be discussion of potential participating VAMCs, and prerequisite participant, data, and/or biospecimen availability. Additional discussions may include collaborations with pharmaceutical or device companies, use of a contractor, use of a biorepository, site monitoring, and plan for publications. The outcome of the first in-person meeting is a written document

with details on the study question, design, feasibility, and plan for proposal completion. Staff from CSP and others in VA Central Office will attend this meeting to help ensure proposed directions are consistent with programmatic, scientific/clinical, budgetary, and other priorities.

The second planning meeting (and any subsequent meetings) refines the protocol and data collection instruments, assesses preliminary participant availability estimates, formulates the final budget, and, if applicable, receives input from the HRC and NODES. The Principal Proponent is responsible for circulating a near-complete protocol to Planning Committee members along with any additional assignments. This includes proposed data elements and instruments, and informed consent documents submitted to each member of the Planning Committee and, if applicable, the HRC several weeks prior to the meeting. CSP Center will develop a preliminary budget with input from the Planning Committee—including justification of equipment or unusual items, and brief but informative job descriptions. After the final planning meeting, the CSP Center will prepare the final proposal for submission to CSSEC, through CSPCO, by the required deadline.

E. CSSEC Proposal

Study proposals undergo rigorous scientific peer review. In collaboration with the CSP Center, the Principal Proponent is responsible for finalizing the draft of core scientific and clinical elements and study methodology. The assigned CSP Center will provide guidance on specific elements for proposals. Deficiencies in any important aspect can result in the proposal being returned for appropriate action. The CSP Center Director has authority to disapprove submission if the proposal does not meet CSP or CSSEC standards.

III. CSP SCIENTIFIC REVIEW

Scientific and clinical merit, study performance plans, and ethical considerations are evaluated by the Cooperative Studies Scientific Evaluation Committee (CSSEC). CSSEC is a scientific peer review body that is a chartered Federal Advisory Committee by authority of the Under Secretary for Health and managed by CSPCO. CSSEC members are accomplished clinical researchers representing various medical specialties and biostatistics/epidemiology. When needed, ad hoc reviews supplement the CSSEC to ensure an appropriate level of expertise in review activities. Study Teams come to the CSSEC meeting and the review process provides an ability to directly discuss all key aspects of the proposal and overarching considerations for impactful clinical research.

In addition to new CSP study proposals, CSSEC may review ongoing studies if there are major protocol changes, significant increases in the budget, if the study is not meeting initial projected recruitment goals, or at the request of CSPCO or the CSP Center.

CSSEC reviews generate recommendations to CSPCO that are incorporated in decisions regarding funding and subsequent action.

A. CSSEC Written Reviews

Prior to a CSSEC review meeting, CSSEC members and, if needed, ad hoc reviewers, provide written clinical and biostatistical critiques addressing:

- Clinical and overall importance of the project

- Feasibility, clarity, and achievability of objectives
- Adequacy of the plan of investigation
- Correctness of the technical details
- Adequacy of safeguards for the welfare of the participants
- Character and definition of response variables measurement
- Data collection and frequency of observations
- Sample size
- Plans for data processing, analysis, and data sharing

Overall, CSSEC looks at the importance of the question, methodological soundness, potential impact of findings and relevance to VA and CSP. In addition, CSSEC also considers whether study teams have thoroughly evaluated the key points that contribute to the study's ability to achieve the most critical scientific and clinical goals in the field and, more broadly, in clinical and epidemiologic research.

When written reviews are completed, de-identified versions are distributed to the respective Study Team (Principal Proponents, Study Biostatistician or Epidemiologist, and CSP Center Director) prior to the CSSEC meeting.

B. CSSEC Review Process

At the meeting, CSSEC first holds a closed session to summarize and discuss the key critiques from written reviews and other questions raised at the meeting. Afterwards, the Study Team is brought before CSSEC and presented with the main critiques as determined in the closed session. The Study Team is then given an opportunity to address critiques and further clarify points in the proposal. Follow up and/or discussions typically arise in an interactive discussion between CSSEC and the Study Team. When sufficient discussion has occurred as determined by the CSSEC Chair, the Study Team is excused, and CSSEC enters an Executive Session to consider the responses.

C. CSSEC Recommendations

CSSEC members vote whether or not to approve the proposal, which allows for a formal recommendation on and scoring of it. If disapproved, no further action is taken on the proposal. If approved, one of four actions is taken as part of the formal recommendation:

- CSSEC accepts the proposal without changes and recommends it for funding.
- CSSEC accepts the proposal with the understanding that the Principal Proponent, CSP Center Director, and the Study Biostatistician/Epidemiologist will make certain changes or additions to the proposal for CSPCO review.

- CSSEC finds the proposal worthwhile, but in need of major revisions, and recommends resubmission.
- CSSEC finds the proposal flawed to an extent that cannot be corrected without redoing a full planning process, if at all; therefore, resubmission is not recommended.

CSSEC then provides a numeric rating reflecting its recommendation on the scientific merit and priority of the proposal from 10 (best) to 50. The Principal Proponent, the CSP Center Director, and the Study Biostatistician/Epidemiologist are informed of the CSSEC score and recommendation following the close of the Executive Session (i.e., at the meeting).

It is important to note that CSSEC actions constitute recommendations to CSPCO. Any level of CSSEC approval or score does not ensure funding. Written notification from CSPCO provides the official decision on the proposed study. Studies approved but not funded are reviewed on a continuing basis and will be dropped from the funding waitlist if CSPCO determines that funding will not become available. CSP may advise the Study Team to explore other options for planning.

IV. INITIATING A CSP STUDY

Study startup or initiation is defined as the period from when the CSP Center is notified of funding approval to the point the first participant is enrolled. The timeframe is dependent on all who are involved and activities should begin as soon as possible. Typically, preparatory actions may be initiated after CSSEC review. All efforts should be focused on achieving efficiency and obtaining broad input into decisions.

Upon notice of funding, the Principal Proponent is referred to as the Study Chair and is responsible to CSP through the assigned CSP Center for the conduct of the study. S/he should not engage in other activities that will negatively impact an ability to be fully dedicated to the study or that may actually or potentially influence the integrity of the study. The appointment of a Co-Chair may be allowed (e.g., when a study involves two major disciplines). There must be a clear and justifiable need, however, and the request for a Co-Chair must be approved by CSP. A National Coordinator should also be hired by the Study Chair to help with study initiation.

There are a number of steps to be taken by the Study Chair and National Coordinator before participant intake/enrollment can begin. These should be done in a timely fashion to avoid delays in funding and/or participant intake. The following outlines several of the key responsibilities of the Study Chair (or National Study Coordinator). Neither the Study Chair nor the National Coordinator may hold additional simultaneous roles (i.e., at their site) within the study unless previously approved by CSP.

A. Participating Site Selection

Site selection is based on patient availability, SI commitment, and other factors that contribute to site success. Sites may be surveyed by the Chair's office and/or the CSP Center to ensure optimal selections are made. The Study Chair should pay particular attention to factors and considerations raised by NODES for selecting any site in a CSP study. When the sites are identified, the Study Chair sends the list of nominations to the CSP Center Director. CSP Center will ensure that all potential participating VAMCs have a Federal

Wide Assurance (FWA) from the Office for Human Research Protections (OHRP). Only VAMCs having an active FWA will be allowed to participate (international sites may have other considerations). If the VA Central Institutional Review Board (IRB) is used, participating sites must have a Memorandum of Understanding (MOU) allowing them to be an IRB of record.

VAMCs wishing to participate must identify an Investigator to serve as the SI who meets CSP requirements and is eligible to receive VA research funding (i.e., at least 5/8 VA time or approved by CSPCO). The identified SI will require active support from the SI's service and other services (e.g., Pharmacy, Clinical Laboratory). Potential SIs will be asked to provide current CVs, conflict of interest forms, and a copy of credentialing, if applicable. They will be expected to commit and work with their local facility to secure the applicable reviews and approvals, as well as hire expected support staff. SI nominations are approved by CSPCO to help ensure thoroughness in the selection process. There must be an Investigator who can serve as leader of the Study Group in the absence of the SI.

Participating VAMCs

After a local SI is informed of selection, s/he will be responsible for all site activities including those performed by study site staff. The SI will work with his or her ACOS/R&D to prepare a formal request for funds—signed by the VAMC Director—to the CSP Center Director. Accepting these funds implies agreement to comply with applicable VA research and CSP policies per VHA Directive 1205 in the conduct of the study. Any deviation from the approved budget requires the endorsement of the CSP Center Director and CSPCO approval.

The CSP Center will work with the Study Chair to develop a template of the Informed Consent Form. This document is to be used by every participating facility. Local IRB and/or R&D requirements to the document may be added, but no items may be removed from the template without CSP Center approval. SIs must provide the CSP Center with proof of local approvals and any local IRB stamped ICF. The Study Chair/National Coordinator working with the responsible CSP Center is responsible for any VA Central IRB (VA CIRB) filing/approvals. In addition, Study Chairs are expected to work closely with CSP Centers to ensure overall regulatory compliance with VA, CSP, and federal requirements.

If there has been a significant delay (e.g., more than 12 months) between approval by the local R&D Committee and the Subcommittee on Human Studies, IRB (local or VA CIRB), and the initiation of the study for any reason (e.g., delay in release of funding, hiring freeze), it may be necessary for these committees to review the proposal again or, at least, reaffirm their commitment to participate. These delays can also impact funding, whether in receipt or pending transmission. A site may also be dropped if delays are significant and deemed by the Study Chair and/or CSP Center to impact progress of the overall study.

Hiring and Training of Study Personnel

CSP study site personnel are generally hired on term appointments, and hiring processes may vary by site. Study personnel must satisfy training requirements before participant entry begins. SIs and study site personnel must meet VA-mandated training requirements for research to participate in CSP studies per VHA Handbook 1200.05. Additionally, CSP requires SIs and Study Coordinators of interventional studies to receive SMART GCP training before a site will be approved to begin study activity. SIs are responsible for determining if there are any local requirements to fulfill outside of what CSP requires.

B. Case Report Forms

The Study Chair shall work with the CSP Center on Case Report Form (CRF) development. CRFs should be finalized at least 3 months prior to study kick off, or as directed by the CSP Center. If time permits, prospective SIs, study Site Coordinators, and NODES should review form content and structure early in the study initiation phase, as it becomes more difficult to make changes later. Changes to final forms after the kick-off meeting may result in study delays. CSP Centers will follow standard operating procedures for obtaining any needed approvals for CRF use.

C. Study Operations Manual and Training Materials

The Study Chair, National Coordinator, and CSP teams prepare the Operations Manual. This manual supports the protocol and ensures that study procedures are followed consistently across all sites. It includes details of randomization procedures, administration of treatments, data collection, flow, recording, security and encoding, as well as procedures for reporting adverse medical events. A section on ethical conduct of the study is included as well as a section on complying with GCPs. In addition, the SI's responsibilities to their local Pharmacy Service concerning prescription writing or drug ordering, instructions for using investigational or study supplies, the Pharmacy Service's responsibility to the SI, and other items germane to the conduct of the study are clearly defined by the inclusion of the Drug/Device Treatment and Handling Procedures (DTHP) as a component of the Operations Manual. The manual is assembled and distributed by the CSP Center. This group may need to prepare other training materials for the Organizational Meeting (e.g., video or demonstrations).

D. Investigational New Drug Application and Investigational Device Exemption

CRPCC will determine if an Investigational New Drug (IND) or Investigational Device Exemption (IDE) is required and provide the necessary guidance regarding FDA approvals and submissions. In most instances, CSP is designated as the sponsor of the IND or IDE. In regulated studies, the Study Chair and every SI participating in the study must complete regulatory forms for the FDA through the Sponsor and meet other specific requirements, as needed. CRPCC will coordinate the preparation and submission of the IND or IDE application according to FDA requirements. The Study Clinical Research Pharmacist will be the CSP Sponsor's Representative to the FDA and will work closely with the Study Chair and CSPCC to resolve FDA-related issues regarding the study. All correspondence with the FDA from study personnel is directed through the Study CRP.

The FDA will notify the Sponsor's Representative in writing of the date it receives an IND or IDE application. Drug and significant risk device studies may begin 30 days after the FDA receives the application, unless the FDA notifies the Sponsor to the contrary. CSP will obtain a signed FDA Form 1572 (Statement of Investigator) or Investigator's Signed Agreement (for device studies) from the Study Chair and each SI as soon as the participating VAMCs are selected. Drugs or devices cannot be shipped until the signed documents have been received. CRPCC will coordinate routine updating of FDA Form 1572 on behalf of the Sponsor at required intervals.

A medical device procured by CSP is the property of CSP, not the medical facility, as it is purchased by the research appropriation. The medical device may not be included in a medical facility's inventory.

E. Organizational/Training Meeting

Prior to the recruitment of participants, CSP conducts an organizational/training meeting. Meeting attendees typically include any individual with a responsibility for properly conducting the study protocol including SIs, Site Study Coordinators, the Study Chair, National Coordinator, CSP Center staff, and Executive Committee members. The primary purposes of the meeting are that attendees:

- Know the protocol requirements
- Understand CSP and VA priorities, expectations and policies for conducting human subjects research
- Review the data collection forms for accuracy and know how to complete them
- Discuss what SIs and Site Study Coordinators need to do to comply with GCP and regulatory requirements
- If special medical techniques, data collection forms, or electronic systems are to be used, then relevant training will occur at this meeting

The Study Chair and CSP Center are responsible for developing the agenda for this meeting. In addition to achieving meeting objectives, they should emphasize how to best engage participants and promote an active learning environment.

F. Recruitment Planning

Achieving recruitment targets is a primary CSP study goal, particularly for SIs. All involved in recruitment should plan/prepare as much in advance including obtaining stakeholder (e.g., patients, clinicians) input on interest, proposed methods, site requirements, and communication strategies. Often, once a recruitment plan is initiated it is difficult to rethink or redo activities. Advertisements require R&D Committee and Human Subjects Subcommittee/IRB approval, and records of these approvals shall be maintained in the SI's files. The Study Chair and CSP Center Director also must review and approve any communication plan. If it is necessary to review medical records prior to obtaining a consent and Health Insurance Portability and Accountability Act (HIPAA) authorization, SIs will need a partial HIPAA waiver for recruitment purposes from the IRB of record. Advertising through local media has particular restrictions, and you will need to request guidance from CSPCO. NODES provides additional expertise on available effective recruitment practices.

V. CONDUCTING A CSP STUDY

Each individual must know his/her responsibilities when conducting a CSP study. The assigned CSP Center will work closely with all groups (Study Chair, participating sites, labs, CRPCC, HRC, Planning Committee, DMC, etc.) to enable effective and efficient collaboration within CSP, ORD, and VHA and to help with compliance with applicable policies. SIs are, however, ultimately responsible for knowing the requirements for conducting clinical research and including any local policies and regulations requiring further compliance.

If an individual has questions about study responsibilities and/or requirements, s/he should ask the assigned CSP Center responsible for the study.

A. CSP Study Management and Monitoring

CSPCO delegates responsibilities for each CSP study to the assigned CSP Center Director, who will, in turn, keep CSPCO fully informed and request any necessary CSPCO approvals. The CSP Center Director will routinely provide a detailed report of progress to CSPCO, paying special attention to participant accrual, quality and/or problems that might affect the successful completion of the study. Any study that does not reach acceptable recruitment goals will be at risk for termination. The decision to continue a study is at the discretion of the CSPCO, but may be informed by other groups tasked with oversight responsibilities.

Multiple groups have responsibilities for overseeing various aspects of the conduct and/or monitoring of a CSP Study—including the Study Group, Executive Committee, DMC, IRB, SMART, HRC, and CSSEC. After participant intake begins, the CSP Center will distribute appropriate progress reports to these committees before regularly scheduled meetings and provide interim updates between meetings. If a study has significant problems or requires substantial changes, the CSP Center will review as needed.

The standard schedule of meetings for the Study Group, Executive Committee, and DMC are outlined during planning, but may change as necessary throughout the study duration.

Study Group

The Study Group meets on a regular basis and performs review of recruitment and other study-specific issues. Led by the Study Chair, the Study Group also includes the following members:

- Study Biostatistician or Epidemiologist
- Study CRP
- Pharmaceutical Project Manager (PPM)
- CSP PM
- National Study Coordinator
- SIs
- Selected consultants, as needed

CSP and ORD Central Office staff also may be included.

Executive Committee

The Executive Committee acts as the management group and decision-making body for the scientific execution of the study and is responsible to CSPCO. It reviews and provides decisions for all proposed changes to the study protocol, any subprotocols or substudies, use of the study data, publications of study

results, and recommends actions related to medical centers whose performance is unsatisfactory. Any substantive changes in protocol design or operation of the study recommended by the Executive Committee must have the appropriate approvals. As with the Study Group, the interim results of blinded portions of the study will not be presented to this group.

- Led by the Study Chair, the Executive Committee includes an additional six to ten members:
- Study Biostatistician or Epidemiologist
- CSP PM
- Study Health Economist
- Study CRP
- PPM
- National Study Coordinator (from the Study Chair's office)
- SIs (2-3)
- Head of any special central support unit related to the study
- Selected consultants, as needed

The CSP Director, assigned CSP Center Director, and the CRPCC Center Director (if applicable) are ex officio members. If there are no more than five SIs for the entire study, they may all be members of the Committee.

Data Monitoring Committee

The Data Monitoring Committee (DMC) provides a continuing critical and unbiased evaluation of the study's progress and formulates operational policy consistent with the best current biomedical research practice. The DMC also reviews aggregate safety data reports. It does not initially evaluate the scientific merit or methodology of the study, nor does it subsequently participate in the study's conduct; these functions are performed by other committees. The DMC maintains the confidentiality of interim results that are presented at scheduled meetings. The DMC usually has five to eight members and includes study SMEs, one or two independent biostatisticians, and other appropriate technical or scientific specialists. Any study that involves a study intervention will have a DMC. The DMC usually first meets within 6 months of the first participant enrolled. The DMC must be prepared to make difficult decisions and recommendations, especially if poor performance appears to be placing the success of the study in jeopardy.

CSP Human Rights Committee

CSP Human Rights Committee (HRC) conducts site visits to participating VAMCs—accompanied by a member of the CSP Center—to evaluate the consent and other study processes from a human rights perspective. If possible, the committee will observe at least one informed consent being given and will talk

with research participants. Typically, at least one site visit is conducted in connection with each study at some point in its ongoing phase. The committee will submit a report of the visit to the CSP Center Director. The report will not identify the participant(s) by name.

Site Monitoring, Auditing and Resource Team

The Site Monitoring, Auditing and Resource Team (SMART) serves as the oversight quality assurance arm of CSP for Good Clinical Practice (GCP) compliance. As an independent arm of the study sponsor (CSP), SMART supports CSPCO, the Executive Committee, and clinical sites by providing the following functions:

- Monitoring and other GCP support needed for the study
- GCP orientation at kick off (if possible), annual meetings, and through online GCP training and tools
- Monitoring and auditing both centrally and through site visits
- Support for FDA site visits

SMART GCP training and site visits emphasize adherence to the protocol and Human Subject Protections.

B. Study Chair Responsibilities

The Study Chair and Study Biostatistician or Epidemiologist must monitor various aspects of performance closely throughout the study and routinely provide this information to the appropriate individuals or groups. The Study Chair will need to notify personnel at participating sites if their performance is less than satisfactory. The Study Chair must also work with the Executive Committee to discuss whether remedial action is necessary and take such action promptly. CSPCO may decide to terminate if the study is not achieving its objectives. Therefore, the Study Chair must take a proactive approach to managing sites and overseeing study quality. CSP Center will provide support and also help oversee activities. The Study Chair should, however, remain engaged with the CSP Centers regularly to ensure responsibilities are met.

C. Meeting/Travel Arrangements

Study-related meetings require significant planning and effort on the part of the Study Chair and/or the CSP Center. CSPCO will support any CSP study-related travel through a centrally managed travel fund and in accordance with a study budget. CSP Center will handle logistics, including any required approvals, for the meeting. All travelers are responsible for their own local approvals and personal travel arrangements. Travelers are required to book any CSP study-related travel using the VA travel system. If attendance is cancelled for any reason, the traveler must inform the CSP Center organizing the meeting.

D. Protocol Changes, Exceptions, and Deviations

Any changes or exceptions to a study protocol following CSSEC and IRB approval must be approved through a protocol amendment process. It may be helpful to seek interpretation and clarification on protocols from the Study Chair before considering any changes or exceptions. The Study Chair, Study Biostatistician or Epidemiologist, and Study CRP will discuss proposed study protocol changes before presenting them for

approval. The Executive Committee, DMC, CSP Center Director, and CSPCO must review and approve proposed study protocol changes.

CSPCO will make the decision whether the proposed study protocol changes require the additional approval of CSSEC. SIs will need to inform the ACOS/R&D at participating VAMCs once study protocol changes have been approved. This is because any changes may require resubmission to the local R&D and Human Subjects Subcommittee, IRB. CRPCC will submit approved changes to the FDA prior to implementation if the study is conducted under an IND or IDE.

In addition, deviations from protocol are not permitted, except to deal with immediate safety hazards for participants. Any deviation—intentional, unplanned, or inadvertent—must be reported per CSP requirements to the Study Chair, CSP Center, and IRB of record.

E. Change in Funding Support

CSPCO must approve changes in the study budget. If there are substantial changes, CSSEC may need to review to determine the scientific and/or clinical appropriateness. SIs must initiate requests for additional funding for participating VAMCs through the ACOS/R&D of the specific VAMC. The requestor will need to include the reasons for your request as well as a list of needs—including personnel (FTE, General Schedule [GS] grade, and costs), equipment, and operating costs—and then forward the request to the Study Chair for approval and the assigned CSP Center Director. The CSP Center Director and CSPCO will notify ACOS/R&D and the SI if budget changes are approved.

Funds and FTEs for a CSP study are limited to the needs of the study and are not to supplement other clinical or research activities. Inappropriate use of CSP funds may jeopardize all research funding at the VAMC. Unused funds will be withdrawn from the VAMC.

F. Ethical and Regulatory Considerations

CSP is grateful to Veterans who choose to participate in research and committed to their protection by upholding the highest standards in the ethical conduct of research. CSP Investigators and personnel must be familiar with VA research requirements including federal regulations, VA and CSP policies, and any additional requirements of local VAMCs. Maintaining the highest ethical standards is critical for the public mission of advancing scientific knowledge through quality research. CSP Investigators are, however, responsible for their conduct and those of their personnel. They should seek guidance whenever needed from CSP Centers.

Note: These Guidelines do not replace VA policies, but rather highlight certain requirements given their importance.

Human Subjects Protection

All CSP SIs and staff must adhere to the requirements for the protection of research participants set forth in VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research.

VHA 1200.05 incorporates the principles of the Belmont Report and is consistent with federal regulations for the protection of human subjects in research, while also containing requirements specific to research conducted at the VA. The full text of VHA 1200.05 can be found here:

http://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=3052.

Informed Consent and HIPAA Authorization

SIs must ensure that informed consent is obtained from every Veteran participant engaged in research via an IRB-approved informed consent form. CSP uses the CIRB template and recommendations for Informed Consent documentation. Similarly, SIs must obtain appropriate Health Insurance Portability and Accountability Act (HIPAA) authorization, per guidance in VHA 1200.05.

Specific VA consent requirements include:

- For information regarding who may consent to the participation of individuals with impaired decision-making capacity, refer to VHA Handbook 1200.05.
- For information regarding the documentation of consent of participants who are able to sign only with an “X,” refer to VHA Handbook 1004.0. (See also VHA Handbook 1200.05 for details regarding the requirement to place a dated progress note in the participant’s electronic medical record [EMR] in such circumstances.)

Failure to obtain informed consent and/or HIPAA authorization will result in disciplinary sanctions by CSPCO, possible referral to the ORO, and could result in the dismissal of the SI. Data from participants without a properly signed and dated informed consent form and HIPAA authorization will be excluded from all study reports. CSP Centers can provide specific policy requirements and/or guidance as needed.

Participant Confidentiality and Privacy

It is CSP policy to protect the confidentiality of participant study data to the fullest extent permitted by law. All CSP Investigators and personnel are responsible for protecting privacy and confidentiality of study participants. In order to protect participant confidentiality, study CRFs will not contain participant identifiers, such as names or social security numbers. A unique study-generated participant identifier number will be assigned to each participant and placed on study forms.

Participating VAMCs will maintain personally identifiable information (PII), including individually identifiable health information (IIHI). Per the study protocol of many studies, CSP may require participant PII and IIHI—such as addresses, social security numbers, or data from CRFs—for scientific and/or safety reasons. Examples include data from VA central databases, central study monitoring through EMR review, long-term follow up of participants, or letters/surveys that are mailed to participants from the CSP Center.

When CSP requires PII and IIHI, this information is provided on a separate form or recorded on VA Form 10-1086 (Informed Consent) and submitted to the CSP Center. SIs will need to provide this information to the CSP Center according to the protocol’s data security plan, and the local medical center’s data security policy, if the VAMC has additional requirements. The CSP Center will maintain PII—on paper and/or and

electronically—separately from the study’s case report form data to avoid unauthorized personnel to link participant identifiers to study data. CSP studies may require Certificates of Confidentiality on occasion, and the

CSP Center will provide information and guidance to the CSP Study Chair and SIs for the terms of these certificates and how to follow and adhere to their conditions.

Finally, when CSP representatives visit participating VAMCs for study-specific purposes, staff must provide access to participants’ EMRs for quality assurance purposes.

Initial and Annual Reviews

All CSP studies must be reviewed and approved by a VA IRB, either at the SIs local VAMC or by VA Central IRB, depending on which is chosen as the IRB of record. VA policy governs reviews of human subjects research, which are done at least annually by the IRB of record. In addition, local VAMC R&D Committee Reviews may be conducted more frequently as needed.

SIs are responsible for complying with requirements related to these reviews. SIs will receive notification of pending annual review requirements and must coordinate the IRB submission with the assigned CSP Coordinating Center. SIs must provide the CSP Center with proof of approval from the IRB of record. If the CSP Center does not receive written notification (minutes or Chair letter) of the review by the study’s anniversary date, VAMC participation may be placed on administrative hold.

Sites will need to care for participants already randomized to ensure safety until any holds are lifted. SIs should contact the IRB and Research Office at the participating VAMCs directly for information about the requirements of IRB and R&D review.

For studies using the VA Central IRB, SIs can access information directly at: <http://www.research.va.gov/vacentralirb/>. SIs also may contact the CSP Center for further resources and information.

G. Study Data

CSP retains ownership rights to all data collected in a CSP study. The assigned CSP Center will work closely with the participating sites to provide guidance as it relates to the collection, submission, clean up, and analysis of the applicable data. (See also section VI.E. Custodianship of Data.)

H. Reporting of Adverse Events, Serious Adverse Events, and Unanticipated Adverse Device Events

During planning and study initiation phases, procedures are established for collecting and reporting adverse events (AEs) and adverse device events (ADEs). Specific procedures for SIs and study site coordinators are included in the study protocol, and the Operations Manual will contain specific procedures. Studies using an Electronic Data Capture system (EDC) for AE reporting must use the minimum set of approved, standardized form content and data elements developed by the program. For studies with an IND or IDE, the FDA will receive annual reports of AEs, SAEs, ADEs, and unanticipated adverse device effects (UADEs)

from the Study CRP. The Study CRP is the sponsor's central point of contact and is responsible for coordinating safety collection, and managing and reporting for a study, including expedited safety reporting to the FDA.

SIs should know the procedures, requirements, and contacts for all safety reporting activities. Study Chairs will help oversee safety reporting activities with CSP Centers.

I. Breaking Study Blind

Many CSP studies involving drugs are blinded so that participants, SIs, and Study Chairs do not know which treatment is administered, and maintaining this blind is critical to the study's integrity. In an emergency situation, however, each study has procedures in place for breaking the blind. CSP Investigators should know procedures as detailed in the study protocol and/or Operations Manual.

J. Dual Enrollment

CSP policy requires that a participant be enrolled in only one, randomized drug or device intervention study at a time, though enrollment in other noninterventional studies while participating in a CSP study (e.g.: surveys; long-term, follow-up cohort studies) is permitted. Screening forms should solicit information about other studies in which participants may be participating. CSPCO would consider dual enrollment exemptions on a study-by-study basis with appropriate justification. CSPCO makes a final decision on exemptions, and approvals are determined by what is best for the participant and to protect the integrity of the involved studies. CSP Investigators should be vigilant about these requirements since noncompliance may result in a protocol deviation.

K. Subprotocols / Substudies

Subprotocols (or substudies) are generally discouraged since they add burden and costs to study personnel, study participants, and CSP. All policies that govern CSP projects also apply to approved subprotocols, including those related to manuscript review and approval.

In exceptional circumstances, subprotocols that are proposed after CSSEC review and that require the collection of additional data, tests, procedures, or biologic samples will be considered only when the entire study is meeting expected accrual and budget goals. CSPCO approval is required for any subprotocol regardless of the source of funding support.

CSP will not support unapproved substudies; if commitments related to substudies were made to other parties without CSP approval, CSP will inform those entities accordingly.

L. Communications

Communication activities intended for a broader audience typically require approvals to help ensure that they adhere to VA policies on public relations. Interested parties should contact the CSP Center for further guidance.

If study newsletters are prepared and issued regularly, it is done by the National Study Coordinator or designee in coordination with the CSP Center. The newsletter is a primary means of keeping study personnel informed between meetings. The newsletter should contain items of general interest to the site personnel, progress and performance reports, treatment-related issues, and discussion of any problems that arise. The newsletter should never include unblinded data or study results. The CSP Center and/or Study Chair may distribute the newsletter via email and/or post it on the study website (e.g., SharePoint).

Sites also will be expected to participate in routine conference calls and possible, face-to-face study group meetings.

M. Site Visits

Site visits by CSP staff as part of the program's study sponsor role can be a key part of oversight activities. Site visits can be routine or for cause and are determined by a number of factors that include a predetermined schedule of monitoring, risk-based management findings, and site responsiveness and participation. Site visits by the sponsor can be done by staff from the CSPCC, SMART, and Human Rights Committee members. In most cases, these efforts will be a collaboration with the local site.

On occasion, the FDA, as a part of its Biomedical Compliance Monitoring Program for Sponsor, Monitors, and Clinical Investigators, will visit a CSP Center, CRPCC, or participating facility/site. When the FDA

announces its impending visit, SMART is responsible for working closely with the Study Chair, the Study CRP, and other individuals to prepare them for the FDA visit. Occasionally, collaborating pharmaceutical companies, whether sponsoring the IND or IDE or not, may wish to conduct site visits to assure compliance with FDA regulations. Such visits must be approved by CSPCO, and coordinated by the CSP Center and respective VAMC Directors.

N. Replacing an SI or Study Chair

CSP studies frequently take several years to complete. During that time, an SI or Study Chair may find s/he cannot continue with the study. In such cases, suitable replacements should be found as quickly as possible in order to maintain the continuity of the study. Any CSP Investigator unable to continue in a study should help with transition activities to the fullest extent possible.

If an SI cannot conduct the study through its completion, s/he should give as much advance notice as possible to the Study Chair and, if possible, suggest an appropriate replacement. Approvals for the proposed replacement SI will follow standard CSP procedures. If no suitable or available replacement for the departing SI exists, the VAMC's participation in the study will be terminated.

If the Study Chair cannot continue to lead the study, s/he should inform the CSP Center Director as early as possible so that nominations can be made to CSPCO. The nominee does not necessarily have to be from the same VAMC as the original Study Chair. If the individual accepts the nomination, the VAMC will be contacted to obtain the approval and support of the VAMC and its R&D Committee. The local ACOS/R&D should initiate a letter endorsing the nominee as described previously. In cases of an "emergency," where there is little or no advance notice, the CSP Director may temporarily appoint someone as Study Chair until

the formal process is accomplished. If no suitable or available replacement Chair exists, CSPCO will determine the action to be taken, including study termination.

If an IND has been filed for the study, new SIs and/or new participating VAMCs will be required to sign FDA Form 1572 (Statement of Investigator) for submission to the FDA. If an IDE has been filed for the study, new SIs and/or new participating VAMCs will be required to sign an Investigator's Signed Agreement. In the case of either an IND or IDE, addition of new participants may not be instituted until approved by the Sponsor.

O. Putting a Site on Probation

Sometimes, a participating site is unable to perform at an optimum level. CSP Study Management Team continually monitors and responds to site performance. While CSP Centers and NODES will help provide best practices, SIs should contact the Study Chair, CSP Center and/or NODES also reach out to others to avoid challenges before they occur. If it happens, the Study Chair, local SI, and CSP Center meet to devise an improvement plan. If this does not help to enhance study site performance, the Study Team—endorsed by the Executive Committee and DMC, if necessary—may place the site on probation.

The SI will receive a probationary letter that states the reasons for probation and the specific steps s/he will need to take to return the study site to normal operation. During a period of probation, the Study Chair and CSP Center work with the local SI to help the site successfully meet expectations. NODES should be engaged to assist. If these efforts are not successful, the Study Chair, SI, and local ACOS/R&D may decide to remove the site from the study. The SI will still be responsible for any research participants enrolled in the study until an appropriate transition is completed.

P. Early Termination of a Site

It is sometimes necessary to drop sites from a study. This decision is made in the best interests of the study and is not necessarily a reflection of an individual or VAMC. This action should be approved by the CSP Center Director, who will then notify CSPCO. Early termination is usually based on recommendations from the Executive Committee and the DMC and, most often, reflects inadequate enrollment, a judgment that performance targets cannot be achieved for various reasons, and/or serious noncompliance with GCP and/or other policies.

For instances of serious or continuing GCP and/or regulatory noncompliance, CSP will make every effort to promptly bring the SI into compliance; if unable, CSP will terminate the SIs involvement. Termination for noncompliance will be reported to the local R&D Committee, local RCO, CSPCO, and FDA (if applicable).

VAMCs that lose an FWA during the course of a study may not continue in human subjects research. When considering research participants at these sites, the CSP Center will immediately do one of the following:

- Submit a request to CSPCO to enable participants to continue in the study at a participating VAMC. The VAMC must have a valid FWA, IRB approval, and an SI who has agreed to assume all study-related activities for these participants.

- Develop a plan to safely transition the participants out of the study. The transition plan may recommend no further contact with the research participants once informing them that their participation is stopped, or amend the protocol to allow the participants to transition out of the study while giving permission only for medical record review at the end of the study.

If another VAMC needs study equipment purchased for the terminated site, the CSP Center Director will notify ACOS/R&D at the terminated VAMC that CSP equipment is to be transferred. The CSP Center Director will accept requests for any necessary funding for shipment. If shipment to another VAMC is not imminent, the Study Chair, and Study Biostatistician or Epidemiologist may transfer the equipment to another location to be determined. If CSP does not need the equipment, it may be used for other purposes following CSPCO approval.

Some VAMCs are supported by a capitation plan instead of a set site budget. The Executive Committee may set the criteria for terminating a capitated VAMC. The CSP Center will typically manage any activities related to terminating sites that fail to meet these standards.

Q. CSP Study Files

Sponsor files for CSP studies are maintained by and at the assigned CSP Center. The Study Chair, SI, and laboratories should also maintain copies of all data forms and study-related correspondence at the direction of the CSP Center based on the VA Record Retention Policy. This applies in the case of hardcopy or electronic study files.

R. Periodic Reports

Local

Every site that conducts research is required to provide certain information regarding its activities on an annual basis (VHA Handbook 1200.5). For such reports, the local R&D office at each VAMC will be responsible for providing instructions to its SI and compiling the information. Study Chairs and SIs are responsible to their respective sites for providing any requested information in accordance to local processes.

CSP

CSP produces various reports during the course of a study. The Study CRP will coordinate activities related to required Annual Progress Report submissions to the FDA when CSP is the sponsor. The CSP Center will work with different groups to prepare DMC and other progress reports. Reports can be submitted to CSPCO or other offices and/or individuals as directed by CSPCO. Requests for information and/or reports that are not already required by VA or federal policy and/or are not considered part of standard practice for the conduct of clinical research must go through the Director, CSP Center to CSPCO.

VI. CONCLUDING A CSP STUDY

Once study participants have completed protocols and all data are collected, there are still several critical steps that must be taken to ensure proper close out of a CSP study. Study Teams will need to give particular attention to properly addressing matters related to research participants, study data, reports and publications, and any subsequent study-related responsibilities.

A. Close Out

Participants

In some instances, research participants will continue to require treatment after completing their participation in a CSP study. The SI/individual's treatment provider should transition from any study treatments to an appropriate treatment plan following CSP study participation. Final results of the CSP study are not typically immediately available for the physician's guidance.

If a participant has responded well to a medication that is still considered investigational based on the treatment provider's judgment, and the physician would like to continue its use before final results are available, the treating physician may contact the source of the medication (e.g., pharmaceutical manufacturer) for any compassionate care use. CSP will be unable to provide study medications once a study is completed. When final results are available following publication of the primary results manuscript, letters reporting study results are sent to all research participants through the SI with IRB approval.

Specific plans for handling the closeout phase, unblinding, and notifying SI and participants of study results are typically included in the study protocol. To help the SI notify the IRB of study closure, the CSP Center provides a letter outlining a planned schedule of closure events relevant to IRBs when terminating their review of research projects, including:

- Date of last participant visit
- Mechanisms used to assure care of participant officially returned to Primary Care Physician (PCP), including documenting this with a note in the Computerized Patient Record System (CPRS)
- Anticipated date of database closure at the CSP Center
- Anticipated end date of primary analysis activities

Study Data / Results

When follow up of all enrolled study participants has ended, the CSP Center is responsible for developing final data summaries and analyses, which are completed within a reasonable time after receipt of the last study data at the CSP Center. SIs are responsible for ensuring all data are submitted and queries from the CSP Center are addressed. The CSP Center is responsible for reporting status of all of these activities to CSPCO.

At the conclusion of the study, the assigned CSP Center should have all study data. The CSP Center will maintain readily accessible files regarding the study after its completion, and data will be evaluated for archiving based on the VA system of records. If it is not appropriate to archive data/records at that time, the data files should be reevaluated annually. Participating VAMCs should retain study files and records after the study is completed in accordance with National Archives and Records Administration (NARA) requirements as indicated in the VHA Records Control Schedule. The CSP Center is responsible for managing all study-related files that it maintains, including electronic files.

Regulatory

CRPCC, in cooperation with the Study Chair, the Study Biostatistician or Epidemiologist, and the participating VAMCs, direct the return of all surplus medications or investigational devices that were centrally distributed. CRPCC will provide a final accounting of medications or devices used by participants. The surplus medications or devices will be disposed of in a manner determined by CRPCC.

The sponsor of an IND or IDE is required to submit a Final Report to the FDA shortly after completion of the study. The Study CRP will coordinate this activity on behalf of CSP if it is the sponsor. Each SI is required to notify his or her respective R&D Committee and Human Studies Subcommittee or IRB that the study has ended.

Once the study is complete, the CSP Center will contact other CSP Centers to determine if equipment purchased specifically for the study can be used by other studies. If so, the CSP Center will arrange for its transfer through the appropriate mechanism. Otherwise, the CSP Center will provide guidance on proper handling of the equipment.

B. Final Study Meeting

The Study Group and the DMC, if possible, will have a combined final meeting once analyses and results of the study are available for distribution and discussion, provided funding is available. This meeting usually occurs after the manuscript writing meeting of the Executive Committee or its designated writing subcommittee. At this meeting, the Study Chair and the Executive Committee present the major study results and their interpretation to the SIs. The Study Group's discussion of the results may provide the manuscript writers with other useful interpretations and provide a forum for discussion among the SIs.

C. Publications

The importance of publications cannot be overstated given the commitment of time and resources by several individuals and groups (see Section II.D in these Guidelines). CSP considers scientific publications and proper dissemination of study findings to be of utmost importance.

CSP study publications should be produced in a timely fashion. The Study Chair, Study Biostatistician or Epidemiologist, and the CSP Center Director play key roles in ensuring timeliness and quality. If progress on the major results manuscript is not sufficient, the CSP Center Director and Director, CSP, may designate other individuals to write the manuscript. CSP authorship policy is provided in Appendix B. Generally, authorship on papers shall be in accordance to accepted criteria by the general scientific community. CSP

Center Directors are delegated responsibility for ensuring a manuscript meets CSP publication requirements prior to submission.

The presentation or publication of data collected by SIs is under the direct control of the study's Executive Committee, with all actions subject to CSPCO oversight to ensure compliance with policies. This control applies to whether the publication or presentation provides the results of the principal undertaking or the results of an ancillary analysis.

The Executive Committee is responsible for approving the publication and presentation of all data and results of the study. Specific CSP policies and policies related to CSP publications are further specified elsewhere and available upon request from CSPCO.

Materials for publication should generally be submitted within one year of receipt of all data at the CSP Center. The Executive Committee may be funded for one meeting during this year to prepare the manuscripts for final publication, provided funding is available.

When a major manuscript is submitted, the CSP Center should send a copy of the manuscript to CSPCO. When a manuscript has been accepted for publication, the Study Chair and the Study Biostatistician or Epidemiologist should provide lay summaries and relevant information to CSPCO to assist in public affairs and other communication activities. CSPCO will work with the appropriate offices to coordinate such efforts for major publications.

D. Administrative Repercussions

The CSP policies for data analysis and dissemination of results apply to all members of the Study Group (Study Chair, SIs, Study Biostatistician or Epidemiologist, etc.). If a Study Chair or SI misuses study data, submits unauthorized manuscripts for publication, or releases results prior to the lifting of any embargoes or agreed upon times, the following administrative actions may be taken (at the discretion of CSPCO):

- Removal as SI or Study Chair
- Forfeiture of research funding
- Prohibition from receiving VA research funding for a period to be determined by CSPCO (and possibly other ORD Service Directors) and commensurate with the seriousness of the infraction

Individuals also may be subject to civil or criminal penalties or fines based on the Trade Secrets Act.

E. Custodianship of Data

CSP is the custodian of all data collected from a study it supported. All SIs must send their data to the participating CSP Center at the appropriate time. While most data should be submitted to the CSP Center shortly after it is collected, there may be special circumstances when an SI or a central laboratory investigator may keep the data for longer periods of time. In these circumstances, the CSP Center Director will determine the appropriate time to submit the data to the CSP Center.

All analyses related to the objectives of the study and publication plan as specified in the study protocol will be performed by CSP. The designated health economist will perform any economic analyses. All raw study data will reside at the CSP Center and will not be released until objectives, as stated in the protocol and manuscripts in the protocol publication plan, are complete. CSP owns all data from its studies. CSPCO is responsible for the use, management, and retention of all CSP study data.

F. Release of Study Datasets

While CSP is the custodian of study data, the program does not seek to limit the use of the data; rather, to ensure that these data are used in scientifically and ethically sound ways while protecting the rights and welfare of research participants. After or near the completion of planned study manuscripts, SIs are encouraged to submit proposals to the Executive Committee for publications that will meet appropriate scientific and ethical standards. SIs should be aware, however, that the CSP Center's primary responsibility is to prepare the needed analyses for the primary results manuscript and secondary manuscripts as stated in the protocol or planned by the Executive Committee. Secondary analyses by the CSP Center may be delayed until the primary analyses and manuscripts are completed. As such, CSP resource uses follow these priorities. Alternatively, the CSP Center may provide SIs with appropriate data sets if they have the resources to use these data sets. Submission to journals of secondary manuscripts should wait until the primary manuscript has been accepted, but the CSP Center Director can request exemptions to CSPCO.

The Study Executive Committee may consider further uses of data, provided that these uses do not conflict with the study protocol, informed consent, CSP policies, VA policy, or other applicable regulations. Potential uses include analyses of the data, publication of the results of analyses, or distribution of copies of all or part of the study dataset. Raw data may be provided to other investigators after all planned objectives and manuscripts are complete and depending on what is indicated in the study informed consent form. Both VA and non-VA SIs who are not part of the Study Group, must request data through the Executive Committee (if still functioning), and CSPCO. If the Executive Committee no longer exists, the CSP Center Director manages any CSP study data requests. If, in the judgment of the CSP Center Director, the Study Chair and/or Executive Committee cease to exercise their responsibilities in an appropriate manner, CSP will take over the management of access to the study data. Any requests for CSP data by VA or other investigators will be reviewed by the CSP Center and require final approval by the CSPCO.

All recipients of CSP data—beyond what is stated in the original protocol—must authorize a Data Use Agreement (DUA) with specific terms that may be related to the following:

- Authority for releasing data, data use, data management and security
- Adherence to informed consent, privacy, and HIPAA requirements
- Any reporting requirements, human subjects protection, and responsibilities applicable to CSP

The CSP Center will provide the SI requesting the data with a de-identified database to prevent identification of research participants. HIPAA guidelines for de-identified datasets are used, when possible. SIs are typically provided with only limited datasets sufficient to complete the proposed research.

G. Continuing Analysis Activities

In general, the appropriate individual should use the ORD Merit Review mechanism (e.g., through CSR&D or HSR&D) to request funding for continuing analytic activities after the completion of the primary manuscript, or for ones not included in the original CSSEC submission and budget. CSP Investigators may request supplemental funds from CSP for analytic activities at the discretion of CSPCO. Typically, such requests undergo scientific peer review before a final decision is made.

VII. CONCLUSION

Multisite clinical research is a complex activity that involves solid coordination and commitment among all involved to achieve success. CSP is dedicated to Veterans and the nation to provide high-quality evidence that informs practice and enhances health. This mission requires that it help SIs understand their roles, responsibilities, and the overall framework for conducting clinical research. These Guidelines are intended to serve as a resource for successfully designing and completing a CSP study.

Suggestions for ways to enhance scientific, operational, and ethical aspects of conducting CSP studies that should be included in subsequent editions of this document are welcome. Comments should be directed to CSP at CSP@va.gov.

APPENDIX A - GLOSSARY OF ABBREVIATIONS AND ACRONYMS

ACOS	Associate Chief of Staff
ADE	Adverse Device Effect
AE	Adverse Event
CPRS	Computerized Patient Record System
CRADO	Chief Research & Development Officer
CRF	Case Report Form
CRP	Clinical Research Pharmacist
CSP	Cooperative Studies Program
CRPCC	CSP Clinical Research Pharmacy Coordinating Center
CSPCC	CSP Coordinating Center
CSPCO	CSP Central Office
CSPEC	CSP Epidemiology Center
CSR&D	Clinical Science Research & Development Service
CSSEC	Cooperative Studies Scientific Evaluation Committee
CV	Curriculum Vitae
DMC	Data Monitoring Committee
DTHP	Drug/Device Treatment and Handling Procedures
DUA	Data Use Agreement
FDA	Food & Drug Administration
FTE	Full Time Employee
FTEE	Full Time Equivalent Employee
FWA	Federal Wide Assurance
GCP	Good Clinical Practice
GS	General Schedule
HERC	Health Economics Resource Center
HIPAA	Health Insurance Portability and Accountability Act
HRC	Human Rights Committee
HSR&D	Health Services Research & Development Service
IDE	Investigational Device Exemption
IIHI	Individual Identifiable Health Information
IND	Investigational New Drug
IRB	Institutional Review Board
LOI	Letter of Intent
MOU	Memorandum of Understanding
NARA	National Archives and Records Administration
NIH	National Institutes of Health
NODES	Network of Dedicated Enrollment Sites
OGC	Office of General Counsel
OHRP	Office for Human Research Protections
ORD	Office of Research & Development
ORO	Office of Research Oversight
PAL	Pharmacogenomics Analysis Laboratory

PCP	Primary Care Physician
PII	Personally Identifiable Information
PM	Project Manager
POC-R	Point of Care Research
PPM	Pharmaceutical Project Manager
R&D	Research and Development
RCO	Research Compliance Officer
REQUIP	Research Equipment Quick Use Initiative Program
SAE	Serious Adverse Event
SI	Site Investigator
SMART	Site Monitoring, Auditing and Resource Team
SME	Subject Matter Expert
UADE	Unanticipated Adverse Device Effect
VA	Department of Veterans Affairs
VA CIRB	VA Central Institutional Review Board
VACO	VA Central Office
VAMC	Veterans Affairs Medical Center
VHA	Veterans Health Administration

APPENDIX B - COOPERATIVE STUDIES PROGRAM AUTHORSHIP POLICY

Sections:

- I. Purpose
- II. Abbreviations, Acronyms and Definitions
- III. Scope
- IV. Authorship Criteria
- V. Roles and Responsibilities
- VI. Ethical Considerations
- VII. Copyright
- VIII. References

I. Purpose

This section outlines the purpose of this policy.

- A. This policy provides standards and procedures to Cooperative Studies Program (CSP) staff members and SIs for their inclusion as authors on CSP publications. Outlined are authorship criteria, procedures for designating groups as authors, determining author order, and assigning appropriate credit in acknowledgments. The policy also outlines roles and responsibilities, summarizes ethical considerations of authorship and the copyright rule for federal employees.
- B. Several work products are generated from CSP studies. This policy is not intended to address all possible considerations in determining authorship, but should be given strong consideration in relevant discussions. While the main emphasis of this policy is on CSP publications, principles may be applied to other contexts not specifically addressed here based on community standards and/or reasonable judgment.

II. Abbreviations, Acronyms, and Definitions

- A. The following abbreviations, terms and acronyms apply to this policy. Further details may be obtained from the CSP Universal Glossary.
 - 1. CSP – Cooperative Studies Program
 - 2. CSP Centers – CSP research groups identified in VHA Directive 1205 that report to CSPCO, including: CSPCCs, CSP Clinical Research Pharmacy Coordinating Center, Epidemiology Research & Information Center, Clinical Epidemiology Research Center (CERC), and the Pharmacogenomics Analysis Laboratory
 - 3. CSP Staff Member – VA employee with primary job duties at a CSP Center or CSPCO
 - 4. EPGP – Epidemiology & Population Genomics Program
 - 5. Executive Committee – CSP study group as defined in the CSP Investigator Guidelines involved with making major CSP study decisions related to the protocol, operations, and/or policies and responsible to the Director, CSP
 - 6. ICMJE – International Committee of Medical Journal Editors

7. IRB – Institutional Review Board
 8. ORD – VA Office of Research & Development
 9. Study Chair (or Co-Chair) – individual as described in the CSP Guidelines who is the scientific/clinical lead of a CSP study
 10. VACO – VA Central Office
- B. For the purpose of this policy, the following definitions apply.
1. Author – An individual who makes substantial contributions (as determined by the Executive Committee) to the conception, design, and/ or acquisition of data or analysis and interpretation of data for a publication; has responsibility for drafting the publication or revising it critically for important intellectual content; also, an approver of the final version to be published.
 2. Coauthor – An author who is not the first author and who contributes to the development of an information product and who substantively participates in decisions and/or contributes to processes resulting in the publication; typically, this individual is involved early in the process.
 3. First Author – An author who receives primary credit for the publication and has overall responsibility for the integrity of the product; this individual often serves as the primary contact for all matters related to the publication.
 4. Plagiarism –The appropriation of another person’s ideas, processes, results, or words without giving appropriate credit (cf. VHA Handbook 1058.2).
 5. Publication – A scientific/scholarly work product resulting from CSP supported activities that are intended to disseminate information on findings, study activities, and/or thoughts and opinions to scientific communities and the public; it may refer to journal articles, editorials, commentaries, and letters published in scientific journals, book chapters and books, scientific conference abstracts, presentations, and technical reports.
 6. Study Group – All persons with key responsibilities in the conduct and completion of a CSP study, including the Study Chair, CSP Staff Members, Executive Committee members, SIs, and study coordinators at participating sites, and VACO/CSR&D personnel that contribute in an ongoing and substantial way to the development, execution and completion of the study. Since activities can span a lengthy period of time, individuals who are involved may change. Therefore, Study Group members are not necessarily only presently involved individuals.
 7. Writing Group – Authors who are Study Group members specifically responsible for writing a publication.

III. Scope

- A. This policy is applicable to instances when authorship is being considered for CSP Staff Members, CSP Study Group members, and/or VACO/ORD personnel for any CSP publication for which VA has primary responsibility. It covers publications that intend to: (1) list VA/CSP employees individually or by group name as authors; and (2) are prepared as a part of CSP Staff Members’ and investigators’ federal employment (including WOC and IPA employees). Publications include those written solely by VA employees or by VA employees in collaboration with partners, those published or disseminated by VA, and those written by VA employees but published or disseminated by other organizations. Since the main context considered is for CSP

supported activities, particular consideration is given to CSP study processes and roles when applicable.

IV. Authorship Criteria

- A. CSP generally encourages providing opportunities for authorship among a wide range of Study Group, CSP Staff Members, and external collaborators. Executive Committees on behalf of Study Groups should establish mechanisms for recognizing and rewarding not only authorship but the other numerous essential contributions to medical science/public health science and to the process of developing and disseminating publications. The Study Chair and Executive Committees are also recognized to be in the best position to know relative contributions of individuals (including Study Group, CSP Center Staff Members, and VACO/ORD personnel) whether for authorship purposes or otherwise. While not required, Writing Groups should also consider inviting individuals to be co-authors who may have particular expertise and/or insight to contribute to the public value of the publication. CSP also acknowledges, however, that authorship is an earned honor and not automatically conveyed simply by a role or position.
- B. CSP subscribes to the criteria for determining who qualifies for authorship based on the “Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals,” developed by ICMJE.
 1. Determining Who Qualifies for Authorship
 - a. Authorship credit should be based on three conditions, all of which must be met:
 - i. Substantial contributions to conception and design, acquisition of data, and/or analysis and interpretation of data
 - ii. Drafting the information product or revising it critically for important intellectual content
 - iii. Approval of the final version to be disseminated (e.g., published or presented).
 - b. Acquisition of funding, general supervision of researchers/authors, or review and approval of product publication, by themselves, do not justify authorship.
 - c. All persons designated as authors should qualify for authorship, and all those who qualify based on the above criteria should be listed. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.
 - d. At least one author, usually the first, should take responsibility for the integrity of the work as a whole, from inception to publication/distribution, subject to applicable CSP policies.
 - e. The CSP Center Director responsible for coordination of the study also has responsibility for the integrity of the work given his/her role as supervisor of CSP Center staff involved in the publication and duties per VHA Directive 1205.
 - f. CSP Executive Committees shall discuss these authorship criteria and document in the study protocol any other considerations prior to the start of the study and determine First Authorship on publications. Additional responsibilities are stated in the CSP Investigator Guidelines. Modifications may be made over the course of the study as conditions

warrant. Note that some journals may limit the number of authors on a manuscript and take this factor into consideration in their decision making.

2. Determining Author Order

- a. The order of authorship on the byline should be a joint decision of the coauthors. Author order should be discussed early and revised as needed. Authors should be prepared to explain the rationale for the order in which authors are listed.

3. Designating Groups as Authors

- a. Authorship is increasingly attributed to a group. All members of the group who are named as authors should fully meet the criteria for authorship. Group members who do not meet these criteria should be listed (with permission) elsewhere, such as in the acknowledgement section (see below). When the author list appears on the publication list with a term such as “for the study group,” or with the members of the study group listed as a “single author” together with members of the writing committee, and where the study group membership is shown as a footnote or appendix, it is not necessary for every member of the group to approve the manuscript.
- b. In general, the primary paper resulting from a CSP study should include the names of all significant group members from study sites, coordinating centers and, where applicable, from CSPCO. In general, these will be included under the “Study Group” designation and included as a footnote or appendix.
- c. For publications that will appear in journals or other publications, consult the publication for samples of how group authorship is attributed.
- d. The CSP Investigator Guidelines address group authorship formats. Options for designating a group as author include the following:
 - i. Identifying some individuals in the byline as authors who have written “on behalf of” or “for” the named group. The other members of the team may be listed elsewhere. (Sample byline: X, Y, and Z on behalf of the CSP Study # SIs.)
 - ii. Identifying the writing group in the byline, with authors in the writing group listed in a footnote. The other members of the team may also be listed elsewhere. (Sample byline: Writing Group* for the CSP Study # SIs.)
 - iii. Identifying the author group name only in the byline. Elsewhere in the publication, authors should be clearly identified. Other team members who do not qualify for authorship should be listed separately (Reference B). (Sample byline: The CSP Study # SIs.)

4. Assigning Appropriate Credit in the Acknowledgments Section

- a. CSP recognizes that publications often result from years of effort and contributions by many individuals and that individuals change their level of involvement over time. An acknowledgment section would be an appropriate method for providing credit to individuals who previously had a key role for making a publication possible but do not meet authorship criteria.
- b. In making acknowledgements, a more specific heading may be used, such as “members of the response team” or “participating investigators,” and the functions or contributions described—for example, “collected data” or “provided and cared for study participants.”

All persons acknowledged must give written permission to the lead author, because a reader may infer their endorsement of the data and conclusions. Financial and material support should be acknowledged.

5. Considerations for Authorship in Key CSP Publications

- a. CSP studies typically produce several types of publications. The following provides examples of common CSP publications and the individuals and/or groups who typically play a key role in the publication that may meet authorship the specific criteria above. These examples are strictly illustrative in nature and should not be viewed as proscribing who should or should not be an author nor seen as an exhaustive list.
 - i. Primary results paper – Typically, the most important product of a CSP study that present results on the primary objectives. Potential authors may include: Study Chair, Study Biostatistician or Epidemiologist, Study Pharmacist, Health Economist, Executive Committee members, national study coordinator, SIs, key collaborators, CSP Center Director/Staff Members, and ORD/CSPCO staff.
 - ii. Methods paper – Often the publication that describes key considerations, challenges, and/or innovations in the design of a CSP study. Potential authors may include: Study Chair, Study Biostatistician or Epidemiologist, Study Pharmacist, Planning Committee members, ORD/CSPCO staff.
 - iii. Secondary analysis papers – Given the amount of data collected in a CSP study, secondary analyses often result in important results to be disseminated. Potential authors may include: Secondary analysis proponent, Study Biostatistician or Epidemiologist, Study Chair, Executive Committee members, statistical programmers, and SIs. Other individuals may also be invited to collaborate on these publications.

V. Roles and Responsibilities

This section outlines author roles and responsibilities; specifically, roles and responsibilities pertaining to planning, research, writing/review/revision, and clearance phases of a publication.

A. Author Roles and Responsibilities

1. Authors employed by VA must list their VA in their affiliation first. If an author was employed by VA, but is no longer employed at the time of publication, then a statement to this effect should be included along with their current affiliation.
2. First Author. In addition to meeting the criteria for authorship, first authors have these additional responsibilities:
 - a. Provide leadership for the writing team in determining author order, establish writing assignments and deadlines for written contributions and coauthor reviews, and ensure an open forum for coauthors to share their concerns and suggestions.
 - b. Compile drafts, distribute them for review, and provide specific direction for reviews and revisions.
 - c. Ensure that all ethical considerations (e.g., IRB review, disclosure of conflicts of interest) have been addressed.

- d. Communicate and adhere to the requirements of this policy.
 - e. Ensure approval by the CSP Center Director.
 - f. Ensure that CSPCO and ORD Communications are notified.
3. Coauthors. Contributors to the development of publication should participate in initial decisions about authorship and other contributions as soon as possible (i.e., when the study begins, when a plan for data analysis is developed, and/or when an invitation to submit an article is received). Coauthors should participate in setting assignments and deadlines for written contributions and coauthor reviews. Each coauthor should provide assigned written sections and reviews in a timely manner. Coauthors also are involved in the selection of the journal for manuscript submissions. The writing team should revise author order as necessary to reflect evolving contributions of team members.

B. CSP Center Roles and Responsibilities

- 1. Implementation, Training, and Mentoring. Each CSP Center's Director should ensure that this policy is implemented and that appropriate staff receive sufficient training and mentoring in CSP's authorship policy and center-specific procedures.
- 2. Ensure compliance with applicable VHA and ORD publication policies including VHA Handbook 1200.19.
- 3. Ensure that all CSP staff (including CSPCO) has been thoroughly considered in discussions of authorship.
- 4. Dispute Resolution. The CSP Center Director should resolve disputes about author designation, author order, or serious delays in the writing/review/revision process if they cannot be resolved at Executive Committee or Writing Group levels. Disputes that cannot be resolved by CSPCO should be taken to the Director, CSP, for final arbitration and ruling.

VI. Ethical Considerations

To ensure public trust and the credibility of CSP and its staff, authors should avoid the following breaches of ethical principles.

A. Withholding Information

- 1. CSP authors are ethically obliged to release information immediately when required to protect public health. Concerns about future publication in journals should not preclude timely release of information. Such release must be approved by the Director, CSP.
- 2. CSP authors shall not withhold relevant information from a publication for the purpose of generating multiple publications from a research project or dataset.

B. Redundant Publication

- 1. In general, reports of scientific findings shall not be submitted to more than one journal at a time for review. Once findings are published, authors of subsequent related publications should make the prospective publisher aware of all directly related reports already published, in press, or submitted for publication. If information is republished, the readers should be made aware of the original report through a footnote or reference. Further

guidance on redundant publication has been issued by the ICMJE in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals.

C. Plagiarism

1. Careful attention to proper attribution is increasingly important in today's electronic document environment, where information or entire passages may be easily inserted—and left in without proper attribution.
2. Plagiarism is included in the federal definition of reportable scientific misconduct. The Director, CSP, has oversight responsibility for all CSP activities. Additionally, the Chief Officer, ORO, is the primary official responsible for all matters related to scientific misconduct for VA research. References may be obtained upon request.
3. Self-plagiarism – the reuse without attribution of portions of previously published manuscripts should be avoided.

D. Disclosing Conflicts of Interest

1. Objectivity is an important value in science and is the basis for public trust. To ensure the scientific integrity and objectivity of information products authored in whole or in part by CSP staff and Study Team members, it is important to avoid situations in which financial or other interests might compromise or give the appearance of compromising the work.
2. A conflict of interest exists when an author has financial or personal ties to activities that could inappropriately influence the design, conduct, or reporting of scientific work or could influence conclusions drawn from such work (Reference A, Reference C). Financial ties include compensation for services (e.g., consulting fees or honoraria), equity interests (e.g., stocks, stock options, bonds, or other ownership interests), and intellectual property rights (e.g., filed or pending patents, copyrights, and royalties from such rights). Financial relationships to industry can also be more indirect—for example, through spouses or dependent children or from previous employment with a commercial entity. The CSP Investigator Guidelines address scientific integrity and expectations for the ethical conduct of all CSP activities, including publications. Further guidance on financial conflict of interest may be obtained from CSPCO, the Office of General Counsel (OGC), and/or ethics officials based at VA regional counsel offices.
3. Although financial ties are among the most serious threats to scientific objectivity, other threats include pressures related to scientific advancement, professional competition, recognition from peers, and media attention.
4. Disclosure of financial or other conflicts does not eliminate the potential for bias, but rather provides additional information in which the objectivity of the science or information can be evaluated. These disclosures are typically obtained at CSP planning and/or the start of a CSP study.
5. For CSP publications, authors must comply with VA guidelines for disclosing conflicts of interest.
6. A statement indicating that views expressed are solely those of the authors do not represent those of the Department of VA must be included.

VII. Copyright

- A. Works created by federal employees as part of their official duties cannot be copyrighted in the United States. Upon acceptance of information for publication and receipt of a copyright transfer form from a publisher, federal authors should sign the form where it specifies that they were a federal employee when the work was prepared and thus that there is no copyright to transfer.

If the publisher does not provide such a form or there is no allowance on the form to sign as a federal employee, then the federal employee should submit the following notice in a signed letter:

I was an employee of the US Federal Government when this work was conducted and prepared for publication; therefore, it is not protected by the Copyright Act, and copyright ownership cannot be transferred.

- B. If there are multiple authors, some of whom are nonfederal, the federal employee should follow the procedures specified above.
- C. Although the content of a publication authored by federal employees may not be copyrighted, some publications (e.g., journals) may copyright the format in which the information is published. This copyright on format may inhibit VA's ability to freely copy the published information. If the publication is of such a nature that wide distribution is desirable (e.g., guidelines), the authors should seek a license from the publication to freely copy and distribute the information as it was published. This license should be negotiated prior to publication. VA's Office of the General Counsel is available to assist in this process.

VIII. References

- A. Uniform requirements for manuscripts submitted to biomedical journals [home page on the Internet]. Philadelphia: International Committee of Medical Journal Editors. Available from <http://www.icmje.org/recommendations>, accessed on November 7, 2016.
- B. Flanagin A, Fontanarosa PB, DeAngelis CD. Authorship for research groups [editorial]. JAMA. 2002; 288(24):3166-8.
- C. DeAngelis CD, Fontanarosa PB, Flanagin A. Reporting financial conflicts of interest and relationships between investigators and research sponsors. JAMA. 2001; 286(1):89-9.
- D. VHA Handbook 1200.19: Presentation of Research Results.
- E. CSP Investigator Guidelines
- F. CSP Staff Administrative Guide
- G. CSP Standard Operating Procedures