

**COOPERATIVE STUDIES PROGRAM (CSP) STUDY  
INITIATION AND MANAGEMENT PROCESSES**

- 1. REASON FOR ISSUE:** This Veterans Health Administration (VHA) Handbook provides guidance for Cooperative Studies Program (CSP) study initiation and management.
- 2. SUMMARY OF CHANGES:** This Handbook updates CSP program elements including the renaming of CSP epidemiology centers and the Network of Dedicated Enrollment sites (NODES) and discussions related to their activities.
- 3. RELATED ISSUES:** VHA Directive 1205.
- 4. RESPONSIBLE OFFICE:** The Office of Research and Development's Cooperative Studies Program (10P9CS) is responsible for the contents of this Handbook. Questions may be addressed to 202-443-5600.
- 5. RESCISSION:** VHA Handbook 1205.01 dated November 7, 2008, is rescinded.
- 6. RECERTIFICATION:** This Handbook is scheduled for recertification on or before the last working day of April, 2019.

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**CONTENTS**

<b>PARAGRAPH</b>	<b>PAGE</b>
<a href="#">1. Purpose</a> .....	1
<a href="#">2. Background</a> .....	1
<a href="#">3. Definitions</a> .....	1
<a href="#">4. Scope</a> .....	2
<a href="#">5. Letters of Intent and Planning Process</a> .....	3
<a href="#">6. Review of Proposals</a> .....	3
<a href="#">7. Study Initiation</a> .....	3
<a href="#">8. Study Management</a> .....	4
<a href="#">9. Study Publications</a> .....	5
<a href="#">10. References</a> .....	5

## COOPERATIVE STUDIES PROGRAM (CSP) STUDY INITIATION AND MANAGEMENT PROCESSES

**1. PURPOSE:** This Veterans Health Administration (VHA) Handbook provides guidance for the initiation and management of Cooperative Studies Program (CSP) activities.

**AUTHORITY:** Title 38 United States Code (U.S.C.) 7301(b) and 7303, 38 Code of Federal Regulations (CFR) 16.114.

### 2. BACKGROUND:

a. The CSP, a division of the Department of Veterans Affairs (VA) Office of Research and Development's (ORD) Clinical Science Research and Development Service (CSR&D), was established as a clinical research infrastructure to provide coordination for and enable cooperation on multi-center clinical trials and epidemiological studies that fall within the purview of VA. When appropriate, CSP may work with other divisions of VA and non-VA entities including the National Institutes of Health, Department of Defense, academic medical centers, private industry, and international research organizations.

b. A cooperative study is a research activity in which investigators from two or more VA facilities agree to carry out a common research protocol in a similar manner. In a cooperative study, there must be adequate mechanisms for planning, evaluation, study execution, human subjects protection, interim monitoring, final analysis, interpretation of results, and dissemination of findings.

c. Cooperative studies are particularly advantageous in the later stages of evaluating safety, efficacy, and effectiveness of health care interventions that have already had the necessary preliminary trials in humans. For most medical conditions, they can more rapidly pool observations made across several facilities. For rare medical diseases or disorders, they may be the only feasible approach to adequately address a clinical question. In certain instances, cooperative studies also may contribute to the early development and refinement of new therapeutic techniques. Cooperative studies that are clinical trials or that focus on epidemiological, health services, or rehabilitation research can benefit from a multi-center approach that facilitates the accumulation of participant samples that are:

(1) Sufficiently large in number to provide a definitive answer to the research questions.

(2) Sufficiently diverse in demographic factors to permit broad generalization of results.

### 3. DEFINITIONS:

a. **Letter of Intent.** A Letter of Intent (LOI) in the CSP is submitted to the Director, CSR&D and outlines the proposed research. A CSP LOI must include the following:

(1) Objectives of the proposed research;

(2) Importance of the study to VA, including any background data from relevant research, and its feasibility within VA;

- (3) A brief description of the study design including the patient population to be studied;
- (4) Treatments, interventions, exposures or outcomes to be compared;
- (5) Randomization or observational approach, type of data collection (retrospective or prospective), and endpoints to be evaluated;
- (6) Number of participants and medical facilities required to meet study endpoints;
- (7) Duration of the study in years; and
- (8) Curriculum vitae of Principal Proponent(s).

b. **Proposal.** A CSP proposal is a description of the rationale, objectives, and methods for a clinical research study aimed at answering an important clinical question that is submitted for approval and funding support. It is the result of planning activities involving a Principal Proponent and CSP personnel.

c. **Protocol.** A CSP protocol is an organized description of the research that is submitted for review and contains at least the following elements:

- (1) Background and significance of the proposed research, including its relevance to VA;
- (2) Study hypotheses and objectives;
- (3) Study population, including sample size, recruitment strategies, and inclusion or exclusion criteria;
- (4) Study design and methodological considerations, including, but not limited to, screening, randomization processes, sampling or bias as applicable;
- (5) Study interventions or treatments;
- (6) Study endpoints, including safety endpoints;
- (7) Study data collection, management, security, analyses, informed consent and privacy procedures, human subjects protection plan(s) and participant follow-up;
- (8) Safety monitoring plan, including the reporting of serious adverse events and adverse events, interim data analyses, study monitoring, and reports to oversight bodies;
- (9) Publication and data access/sharing plans; and
- (10) Any additional requirements specified by CSP Central Office (CSPCO).

**4. SCOPE:** This Handbook provides mandatory requirements and key procedures for researchers, review committees, and others to follow in developing, reviewing, funding, managing, and overseeing CSP research activities.

## **5. LETTERS OF INTENT AND PLANNING PROCESS:**

a. CSP studies can be initiated by the submission of a CSP LOI by an eligible VA researcher (Principal Proponent) (see VHA Handbook 1200.15), or as a service-directed project initiated by the Director, CSR&D.

b. CSP LOIs are submitted to the Director, CSR&D, through the Associate Chief of Staff (ACOS) for Research and Development (R&D) and the Director at the Principal Proponent's VA facility.

c. Following administrative and scientific review of a CSP LOI, meritorious proposals may be assigned by the Director, CSR&D, to one or more CSP Centers for planning. The CSP Center(s) (CSP Coordinating Center and/or CSP Epidemiology Center) and the Principal Proponent(s) work collaboratively to determine steps and carry out responsibilities for developing a full study protocol.

d. One important step is to identify a planning committee with appropriate expertise for designing the protocol. The primary objectives of planning are to identify the key clinical question(s) to be answered, determine the feasibility of a study, and develop a full protocol for scientific review by the Cooperative Studies Scientific Evaluation Committee (CSSEC).

e. In some instances, pre-planning meetings may be organized to evaluate merits of a potential study and identify critical elements for informing the full planning process that is specified in paragraph 5d.

## **6. REVIEW OF PROPOSALS:**

a. The scientific review of CSP proposals is conducted by the CSSEC. The peer review process requires an in-person meeting among CSSEC members, any ad hoc reviewers, and the study proponents to discuss the proposal. Activation of studies reviewed by CSSEC requires the recommendation of CSSEC and the approval of the Director, CSR&D.

b. Ad hoc reviews may be obtained by the Director, CSR&D, or designee, if a full committee meeting is not warranted given the scope or size of the project.

c. VA facilities must meet the requirements of VHA Handbook 1200.01, which describes the responsibilities of the facility Director; the R&D Committee; the ACOS for R&D or Research Coordinator; and the Administrative Officer for R&D, in relation to the review of all research proposals and programs, including CSP projects, at their facilities.

## **7. STUDY INITIATION:**

a. Upon funding approval, the Principal Proponent(s) becomes the Study Chair(s) and the study is administered by the CSP Center(s) designated by the Director, CSR&D. Conduct of the study is a cooperative effort of the Study Chair(s), CSP Center (including Center Director and Study Biostatistician(s) or Epidemiologist(s)), and their respective staffs. If drugs or devices are involved, the Director, CSP Clinical Research Pharmacy Coordinating Center and/or study pharmacist have responsibilities for administration of drugs and devices and any regulatory

requirements. Other components of CSP, including the Network of Dedicated Enrollment Sites (NODES), may be included as needed.

b. The CSP Center(s) and Study Chair(s) proceed with initiating the study. This process may include revising the protocol based on scientific review or Human Rights Committee (HRC) recommendations, developing data collection tools, identifying participating study sites, establishing a study Executive Committee, hiring study personnel, and drafting and producing study management and procedural documents, as necessary.

c. A study Executive Committee is constituted for all CSP studies and is responsible to the Director, CSR&D, through the assigned CSP Center Director(s) for study activities.

d. An independent Data Monitoring Committee (DMC) is constituted for each CSP clinical trial to monitor and review study progress and safety. A CSP HRC also provides independent ethical review and advocacy of participant considerations for studies. Each CSP study must undergo Institutional Review Board (IRB) review, obtain IRB approval, and obtain any other local approvals for conducting research.

e. CSP Center Directors or their designees will communicate relevant VA and CSP policies and procedures to appropriate groups to inform them on how the study will be conducted.

f. Any agreements with collaborators are established through CSPCO and can be developed with assistance from the CSP Center responsible for the study, if needed.

g. Any sites engaged in a CSP study must comply with requirements in the Common Rule (38 CFR Part 16), all other applicable Federal regulations, VA and VHA policies (see VHA Handbook 1200.05). In addition, the site must hold a Federal Wide Assurance (see VHA Handbook 1058.03) and have an IRB of record registered with the Department of Health and Human Services, Office for Human Research Protections.

**8. STUDY MANAGEMENT:** CSP study management is the responsibility of the CSP Study Chair(s), assigned CSP Center Director(s), and respective CSP center staff. The CSP Center Director(s) is responsible for fully informing the Director, CSR&D/CSPCO of all major study activities and for forwarding any actions or recommendations requiring Director, CSR&D approval.

a. CSP may perform site visits or audits of participating sites without prior notice to the site study personnel or VA facility.

b. CSP Center Director(s) or the Director, CSR&D may terminate a site's participation based on performance, safety, or ethical concerns.

c. The CSP Center Director(s) or the Director, CSR&D may direct for-cause audits at CSP study sites or suspend CSP study activities for potential performance, safety, or ethical concerns.

d. The Director, CSR&D, may require mid-term scientific or progress reviews of on-going CSP studies.

e. A cooperative study will be terminated when the objective has been attained or when it is not feasible or ethical to continue the study.

**9. STUDY PUBLICATIONS:** CSP study publications require review and approval of the study's Executive Committee and the respective CSP Center Director(s), in addition to complying with VHA Handbook 1200.19.

**10. REFERENCES:**

- a. VHA Directive 1200, Veterans Health Administration Research and Development Program.
- b. VHA Directive 1205, Veterans Health Administration Cooperative Studies Program.
- c. VHA Handbook 1058.03, Assurance of Protection for Human Subjects in Research.
- d. VHA Handbook 1200.01, Research and Development (R&D) Committee.
- e. VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research.
- f. VHA Handbook 1200.15, Eligibility for VA Research Support.
- g. VHA Handbook 1200.19, Presentation of Research Results Handbook.