Department of Veterans Affairs **VHA HANDBOOK 1205.01**
Veterans Health Administration **Transmittal Sheet**
Washington, DC 20420 **November 7, 2008**

COOPERATIVE STUDIES PROGRAM (CSP) STUDY INITIATION AND MANAGEMENT PROCESSES

1. REASON FOR ISSUE. This Veterans Health Administration (VHA) Handbook provides process and procedures for Cooperative Studies Program (CSP) activities.

2. SUMMARY OF MAJOR CHANGES. This is a new Handbook, which clarifies key CSP study-related processes.

3. RELATED DOCUMENTS. VHA Directive 1205.

4. RESPONSIBLE OFFICE. The Office of Research and Development's Cooperative Studies Program (125) is responsible for the contents of this Handbook. Questions may be addressed to 202-461-1676.

5. RESCISSION. VHA Manual M-3, Part II, Chapter 9, dated October 30, 1989, is rescinded.

6. RECERTIFICATION. This Handbook is scheduled for recertification on or before the last working day of October 2013.

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COOPERATIVE STUDIES PROGRAM (CSP) STUDY INITIATION AND MANAGEMENT PROCESSES

1. PURPOSE

This Veterans Health Administration (VHA) Handbook provides process and procedures for Cooperative Studies Program (CSP) activities.

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 collaboration 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, academic medical centers, private industry, and international agencies.

b. A cooperative study is a research activity in which two or more investigators from two or more different medical centers agree to carry out a common research protocol in an identical manner. In a cooperative study, there must be adequate mechanisms for planning, evaluation, execution, interim monitoring, final analysis, and interpretation.

c. Cooperative studies are particularly advantageous in the later stages of evaluating safety, efficacy, and cost effectiveness of health care interventions that have already had the necessary preliminary trials in humans. For more common 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 patient 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. COOPERATIVE STUDIES PROGRAM (CSP) LETTERS OF INTENT (LOIs)

CSP LOIs must include the following:

a. Objectives of the proposed research;

b. Importance of the study to VA and its feasibility within VA;

c. A brief description of the study design including the patient population to be studied;

d. Treatments to be compared;

e. Randomization or observational approach, type of data collection (retrospective or prospective), end points to be evaluated;

f. Number of patients and medical centers required;

g. Duration of the study in years; and

h. Curriculum vitae of Principal Proponent.

4. CSP LOI 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 Director at the originating VA medical center.

c. Following administrative and scientific review of a CSP LOI, meritorious proposals may be sent by the Director, CSR&D to a CSP Center(s) for planning. The CSP Center(s) and the Principal Proponent 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 objective of planning is to determine the feasibility of a study and develop a full protocol for scientific review by the Cooperative Studies Scientific Evaluation Committee (CSSEC).

5. CSP PROTOCOLS

Full CSP protocols need to contain the following elements:

a. Background and significance, including relevance to VA;

b. Study hypotheses and objectives;

c. Study population, including sample size, recruitment strategies and inclusion or exclusion criteria;

d. Study design, including any screening and randomization processes, study interventions, and patient follow-up;

e. Study endpoints, including safety endpoints;

f. Study processes, including data collection, management and analyses, and informed consent procedures;

g. Safety monitoring plan, including the reporting of serious adverse events and adverse events, interim data analyses, study monitoring, and reports to oversight bodies; and

h. Publication plans.

6. REVIEW OF CSP PROPOSALS

a. The scientific review of CSP proposals is conducted by the CSSEC. The review process requires an in-person meeting among CSSEC members and the study proponents to discuss the proposal. Ad hoc reviews may also be obtained by the Director, CSR&D, if a full committee meeting is not warranted given the scope or size of the project. Activation of CSSEC reviewed studies requires the recommendation of CSSEC and the approval of the Director, CSR&D.

b. VHA Handbook 1200.1 describes the responsibilities of the facility Directors, the R&D Committee, and the ACOS for R&D or Research Coordinator, and the Administrative Officer for R&D in relation to review of all research proposals and programs at their facilities, including CSP projects.

7. CSP STUDY INITIATION

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

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

c. The study Executive Committee is responsible to the Director, CSR&D through the CSP Center Director for study activities.

d. A Study Executive Committee is constituted for all CSP studies. Independent Data Monitoring Committees (DMCs) are constituted for all CSP clinical trials to monitor and review study progress and safety. CSP Human Rights Committees (HRCs) also provide independent ethical review of studies. All CSP studies must undergo Institutional Review Board (IRB) review and obtain IRB approval.

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 CSP Central Office 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 (Title 38 Code of Federal Regulations (CFR) 16) and all other applicable Federal regulations and VA and VHA policies. In addition, the site must hold a Federal Wide Assurance (see VHA Handbook 1058.3) and have an IRB of record registered with the Department of Health and Human Services, Office for Human Research Protections.

8. CSP STUDY MANAGEMENT

CSP study management is the responsibility of the CSP Study Chair, respective CSP Center Director(s), and assigned CSP center staff; the CSP Center Director(s) is responsible for fully informing the Director, CSR&D 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 Medical Center.

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

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

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

9. CSP 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. VA Directive 6500.

b. VHA Directive 1200.

c. VHA Handbook 1200.5.

d. VHA Handbook 1605.1.

e. VHA Handbook 1605.2.

f. VHA Directive 1205.