



**Health Care Compliance Association
CMS and the Clinical Research Policy**

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Introduction

- In response to a June 7, 2000 Executive Memorandum, issued by President Clinton, requiring Medicare to pay for routine care costs in clinical trials, the Health Care Financing Administration (HCFA)* implemented a Clinical Trial NCD on September 9, 2000.
- On July 10, 2006, CMS announced the first reconsideration of the Clinical Trial Policy NCD.
- On December 13, 2006, CMS organized a Medicare Coverage Advisory Committee (MCAC)** public meeting at their head office in Baltimore, Maryland to re-evaluate the current Clinical Trial Policy.
- On April 10, 2007, CMS released their proposed revisions to the Clinical Trial Policy NCD with a 30-day public comment period.
- CMS will publish the final NCD within sixty days after the end of the comment period. The revised policy will be effective with the publication of the final NCD.

*Now Centers of Medicare and Medicaid Services (CMS)

**Now Medicare Evidence Development & Coverage Advisory Committee (MedCAC)

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Introduction – Summary of Proposed Changes

- CMS is proposing the following revisions:
 - Rename the policy, the Clinical Research Policy (CRP).
 - Provide a definition of research.
 - Continue the seven highly desirable characteristics and rename them “general standards for a scientifically and technically sound clinical research study” and add an additional standard: “The research study must have a written protocol.”
 - Revise the requirements that qualify a clinical study for Medicare coverage by renaming them “Medicare-specific standards,” eliminating the first, and combining and modifying the second and third requirements for greater clarity. Add the following Medicare-specific requirements:
 - The research study must be registered on the ClinicalTrials.gov website prior to the enrollment of the first study subject.
 - The research study protocol must specify and fulfill method and timing of public release of results.
 - The research study must have explicitly discussed inclusion criteria and considered relevant subpopulations (as defined by age, gender, race/ethnicity, socioeconomic, or other factors) in the study protocol.
 - The protocol must contain a discussion of how the results will generalize to the Medicare population.

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Introduction – Summary of Proposed Changes (cont'd)

- The NCD process may establish additional standards through Coverage with Evidence Development (CED).
- Rename routine costs to “routine clinical services” and clarify the definition.
- Add a definition of administrative services required to carry out studies and clarify that Medicare will not cover administrative services.
- Add a definition for investigational clinical services and cover those services when the service is available to Medicare beneficiaries that are not participating in a study or when it is required through CED.

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Introduction – Summary of Proposed Changes (cont'd)

- Clarify those processes that ensure that both the Medicare-specific standards and the general standards for a scientifically and technically sound clinical research study are met.
 - General standards:
 - Studies approved by DHHS Agencies, the Veterans Administration or the Department of Defense.
 - Studies approved by research centers or cooperative groups funded by one of the above Federal Agencies who have approved their process.
 - Studies conducted under an Investigational New Drug (IND) where the protocol has been reviewed by the FDA.
 - Studies that FDA requires and approves as a post-approval commitment.
 - Studies required through CED.
 - Medicare specific standards:
 - CMS will use routine processes to ensure that the Medicare-specific standards are met.
- Remove the following options for “deeming” studies:
 - Self-certification process.
 - IND Exempt studies.

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CMS' Proposed Decision Memo and Draft Clinical Research Policy

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CMS Proposed Decision Memo

- The proposed revisions to the Clinical Trial Policy address the following categories of issues:
 - General issues
 - Appropriate *standards of a clinical trial* that, if met, would ensure that the study is conducted pursuant to section 1142 of the Act
 - Appropriate *processes that ensure that those standards are met*
 - *Items and services that are covered in studies meeting those standards*

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General Issues

- *Clinical Research Policy (CRP)* is the revised title to the “Clinical Trial” Policy contained in the Clinical Trials NCD.
- CMS defines clinical research as:

Clinical research is the observation of events in groups of individuals who share a particular characteristic, such as a symptom or illness; or who have the same treatment or diagnostic test provided for a symptom or illness. Inferences are made based on comparisons of predefined health outcomes among groups. Procedures are in place to assure that the rights, safety, and wellbeing of research study participants are protected. Research studies need to conform to all applicable Federal regulations concerning human subject protection and privacy including 45 C.F.R. Part 46 and Parts 160 and 164.

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General Issues (cont'd)

- Below are some examples of the types of clinical studies that might fall under the definition of research, but this list should not be considered an all-inclusive list:
 - *Randomized controlled trials and other comparative clinical studies of effectiveness and comparative effectiveness;*
 - *Observational clinical studies of outcomes of specific interventions, primary and secondary prevention strategies, or of implemented strategies related to delivery of care or testing of hypotheses regarding health services research; and*
 - *Clinical studies of diagnostic tests, including measurements of sensitivity and specificity, and impact on physician decision making and patient outcomes.*

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Research Studies that Qualify for Medicare Coverage under Draft Clinical Research Policy

- Under the draft CRP the following study would qualify for coverage (replaces the QCT analysis):
 1. Meets all 5 “Medicare-specific standards”
 2. Is one of 5 types of studies that are deemed to have all 8 “general standards”
 - and
 3. Additional requirements set by Medicare only if study is being reviewed under the coverage with evidence development process

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Standards of Clinical Trial Medicare Specific-Standards

Current Clinical Trials NCD

- The subject or purpose of the trial must be the evaluation of an item or service that falls within a Medicare benefit category (e.g., physicians' service, durable medical equipment, diagnostic test) and is not statutorily excluded from coverage (e.g., cosmetic surgery, hearing aids).
- It cannot be exclusively designed to test toxicity or disease pathophysiology.
- Trials of therapeutic interventions must enroll patients with diagnosed disease. In addition, they may enroll healthy patients in order to have a proper control group.

New Clinical Research Policy

- The clinical research study is not designed to exclusively test toxicity or disease pathophysiology. Research studies, including some Phase I trials, whose protocols commit to measuring therapeutic outcomes as one of the objectives, may meet this standard only if the disease being studied is chronic, life threatening, or debilitating.
- The research study is registered on the ClinicalTrials.gov website prior to the enrollment of the first study subject.
- The research study protocol specifies and fulfills method and timing of public release of all pre-specified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early.
- The research study protocol must have explicitly discussed inclusion criteria and considered relevant subpopulations (as defined by age, gender, race/ethnicity, socioeconomic or other factors).
- The research study protocol contains a discussion of how the results will generalize to the Medicare population to infer whether Medicare patients may benefit from the intervention. In particular, the protocol describes the potential impact of age-specific and other factors on outcomes and whether the research study is powered sufficiently to draw conclusions with respect to the Medicare population.

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Standards of Clinical Trial Medicare Specific-Standards -- Therapeutic Intent

Medicare clarifies its understanding of the trial needing to have therapeutic intent.

Current Clinical Trials NCD:

The wording is not clear on whether secondary objectives of therapeutic benefit will meet criteria. Comments by CMS and actions by Medicare medical directors have indicated that only studies with therapeutic intent as one of the primary objectives would meet requirement.

Revised Clinical Research Policy:

The clinical research study is not designed to exclusively test toxicity or disease pathophysiology. Research studies, including some Phase I trials, whose protocols commit to measuring therapeutic outcomes as one of the objectives, may meet this standard only if the disease being studied is chronic, life threatening, or debilitating.

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Standards of Clinical Trial General Standards – Seven Desirable Characteristics

Seven Desirable Characteristics have a new name: “General standards for a scientifically and technically sound clinical research study.”

Current Clinical Trials NCD

Current NCD lists seven highly desirable characteristics:

- The principal purpose of the **trial** is to test whether the intervention potentially improves the participants' health outcomes;
- The **trial** is well-supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use;
- The **trial** does not unjustifiably duplicate existing studies;
- The **trial** design is appropriate to answer the research question being asked in the trial;
- The **trial** is sponsored by a **credible** organization or individual capable of executing the proposed trial successfully;
- The **trial** is in compliance with Federal regulations relating to the protection of human subjects; and
- All aspects of the **trial** are conducted according to the appropriate standards of scientific integrity.

New Clinical Research Policy

General standards for a scientifically and technically sound clinical research study:

- The principal purpose of the **research study** is to test whether a particular intervention potentially improves the participants' health outcomes;
- The **research study** is well-supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use;
- The **research study** does not unjustifiably duplicate existing studies;
- The **research study** design is appropriate to answer the research question being asked in the study;
- The **research study** is sponsored by an organization or individual capable of executing the proposed **study** successfully;
- The **research study** is in compliance with **all** Federal regulations relating to the protection of human subjects **found at 45 C.F.R. Part 46. If the study is FDA-regulated, it also must be in compliance with 21 C.F.R. Parts 50 and 56;** and
- All aspects of the **research study** are conducted according to the appropriate standards of scientific integrity.
- All research studies have a written protocol.**

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Approval Processes (“Deemed Trials”) To Ensure All the General Standards are Met

Current Clinical Trials NCD

Trials “deemed” to have the 7 desirable characteristics:

- Trials funded by NIH, CDC, AHRQ, CMS, DOD, and VA.
- Trials supported by centers or cooperative groups that are funded by the NIH, CDC, AHRQ, CMS, DOD and VA.
- Trials conducted under an investigational new drug application (IND) reviewed by the FDA.
- Drug trials that are exempt from having an IND under 21 CFR 312.2(b)(1) will be deemed automatically qualified until the qualifying criteria are developed and the certification process is in place.

New Clinical Research Policy

Studies “deemed” to meet the general standards:

- Studies of health outcomes reviewed and funded by a program component of DHHS, the Veterans Administration or the Department of Defense.
- Studies reviewed and approved by health care research centers or cooperative health care research groups, funded by one of the above Federal Agencies, provided that the Federal Agency reviews and approves the applicant research centers’ or cooperative research groups’ subcontract and subgrant funding requirements, selection procedures and oversight methods, and determines that those processes provide the same level of protocol review as provided by the supporting Federal Agency.
- Studies conducted under an Investigational New Drug (IND) when the FDA has reviewed the study protocol and the IND application has not been put on hold.
- The study is required and approved by FDA as a post-approval study.
- The study is required as an outcome of the NCD process using CED.

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Coverage Covered Items and Services – Routine Clinical Services

CMS renamed routine costs to “routine clinical services” and clarified the definition.

Current Clinical Trial NCD

Definition of “Routine costs”:

- Items or services that are typically provided absent a clinical trial (e.g., **conventional care**);
- Items or services required solely for the provision of the investigational item or service (e.g., administration of a noncovered chemotherapeutic agent), the clinically appropriate monitoring of the effects of the item or service, or the prevention of complications; and
- Items or services needed for reasonable and necessary care arising from the provision of an investigational item or service—in particular, for the diagnosis or treatment of complications.

New Clinical Research Policy

Definition of “Routine clinical services”:

- Items and services that are available to Medicare beneficiaries outside of a clinical study, other than items or services that meet the definition of investigational clinical services;
- Only those items and services used for patient management within the study;
- Items or services required solely for the provision of the investigational item or service (e.g., administration of a non-covered chemotherapeutic agent);
- The clinically appropriate monitoring of the effects of the item or service (e.g., blood tests to measure tumor markers); and
- Items or services required for the prevention, diagnosis, or treatment of complications (e.g., blood levels of various parameters to measure kidney function).

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Standards of Clinical Trial NCD Coverage with Evidence Development (CED) Standard

Current Clinical Trials NCD:

Coverage with Evidence Development (CED) is not part of the current Clinical Trials NCD. CED runs parallel to the current Clinical Trials NCD.

Revised Clinical Research Policy:

CMS may require additional Medicare-specific standards for clinical research studies that have been identified through the NCD process using CED.

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Research Studies that Qualify for Medicare Coverage under Draft Clinical Research Policy

- Under the draft CRP the following study would qualify for coverage (replaces the QCT analysis):
 1. Meets all 5 “Medicare-specific standards”
 2. Is one of 5 types of studies that are deemed to have all 8 “general standards”
 - and
 3. Additional requirements set by Medicare only if study is being reviewed under the coverage with evidence development process

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Coverage
Covered Items and Services – Investigational Clinical Services

Current Clinical Trials NCD:

The current clinical trial policy does not define investigational clinical services.

Revised Clinical Research Policy:

Investigational clinical services are those items and services that are being investigated as an objective within the study.

CMS proposes circumstances under which these investigational clinical services would be covered:

- *The item or service in a clinical research study is an item or service that is currently available to the Medicare beneficiary outside the study (i.e., the item or service is covered under § 1861(a)(1)(A) of the Act).*
- *The item or service is required as a condition of coverage through the National Coverage Determination (NCD) process using Coverage with Evidence Development (CED).*

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Coverage
Non-covered Items and Services – Administrative Services

Current Clinical Trial NCD:

The current clinical trial policy does not define administrative services for carrying out trials.

Revised Clinical Research Policy:

Administrative services are defined as all nonclinical services, such as investigator salaries; protocol development; recruiting participants; data quality assurance activities, statistical analyses; dissemination of findings; and study management. Administrative services also include clinical services provided to solely satisfy data collection and analysis needs that are not used in the direct clinical management of the patient.

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Potential Implications for the Industry

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Potential Implications

- The Coverage for Evidence Development (CED) is a broader initiative from CMS to generate data on the utilization and impact of the item or service evaluated. This could mean potentially enhanced coverage for items and services in the future.
- The coverage of the investigational clinical services means increased access to items and services.
- Research sites may want to rethink their policies defining what is clinical research to ensure consistency with the CRP.
- Research sites and investigators will need to develop a process for registering studies on the ClinicalTrials.gov website.

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Implications for the Research Community

- Sponsors, Universities and research sites will need to educate the investigators and research coordinators regarding how to include “public release of results” in their protocols.
- Protocols will need to be specific as to how the study will generalize to the Medicare Population.
- Organizations will need to update their coverage review processes to include the requirements of the CRP.
- Organizations will need to perform a coverage review for IND exempt studies.
- Organizations will need to ensure that all studies include protocols (especially for Investigator Initiated Research).

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Questions You May Be Asking...

- What should we do with open studies?
- When do we anticipate guidance on MSP Issues?
- How quickly should research sites ramp up to begin to register studies on ClinicalTrials.gov and will this apply to open studies?
- How should research sites and investigators deal with Off-Label uses in light of the CRP?
- Should research sites provide written comment?
- Will the CRP limit reimbursement for HUDs?

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Questions & Answers

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References

- Current Clinical Trial NCD; Available at http://www.cms.hhs.gov/mcd/viewncd.asp?ncd_id=310.1&ncd_version=1&basket=ncd%3A310%2E1%3A1%3ARoutine+Costs+in+Clinical+Trials
- Draft CRP and Proposed Decision Memo; Available at <http://www.cms.hhs.gov/mcd/viewdraftdecisionmemo.asp?id=186>

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