

Proposed Clinical Research Policy Decision Memo

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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*

General Issues

- *Clinical Research Policy (CRP)* is the revised title to the “Clinical Trial” Policy
- CMS defines 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.

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.*

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 Trial NCD

Current Policy 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

Modified seven desirable characteristics:

- 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.**

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

Medicare's requirement of therapeutic intent as the primary objective has been removed in the proposed clinical research policy.

Current Clinical Trial NCD:

The trial must document therapeutic intent as the *primary* objective of the trial. It cannot be exclusively designed to test toxicity or disease pathophysiology.

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.

Standards of Clinical Trial Medicare Specific-Standards

Current Clinical Trial 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).
- The trial must document therapeutic intent as the primary objective of the trial. 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](https://www.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.

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

Current Clinical Trial NCD:

Coverage with Evidence Development (CED) is not part of the current clinical trial.

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.

Approval Processes To Ensure All the Standards Set by CMS are Met

Current Clinical Trial NCD

“Deemed” trials include:

- 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; and
- 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

As with all other items and services provided to Medicare beneficiaries, Medicare contractors will use routine processes to ensure that the Medicare-specific standards and NCD CED standards are met.

The following processes will assure that the general standards of scientifically and technically sound clinical research study are met and assure that the research is conducted with AHRQ support pursuant to section 1142 of the Act. Therefore, clinical research studies will be “deemed” to have met the standards in the policy.

- 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.**

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).**

Coverage

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.

Coverage

Covered Items and Services – Investigational Clinical Services

Current Clinical Trial 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 § 1862(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).*

TIMELINE

- Public comment period
 - April 10, 2007 through May 10, 2007
- Final National Coverage Determination
 - By July 9, 2007

MORE INFORMATION

- Proposed decision memorandum

<http://www.cms.hhs.gov/mcd/viewdraftdecisionmemo.asp?id=186>

- Coverage with Evidence Development guidance document

http://www.cms.hhs.gov/mcd/ncpc_view_document.asp?id=8