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CMS Issues Proposal to Revise Clinical Trial Policy National Coverage Determination

Recently, the Centers for Medicare & Medicaid Services (CMS) released a proposed National Coverage Determination (NCD) to revise the current Clinical Trial Policy and to rename it the Clinical Research Policy. The proposed NCD addresses a range of issues CMS has identified since the Clinical Trial Policy was implemented in 2000 and includes requirements for clinical research coverage as well as study approval processes. The proposed policy is intended to provide more detailed guidance in these areas while imposing additional requirements that must be met to qualify for Medicare coverage.

Comments on the proposed Clinical Research Policy are due to CMS by May 10, 2007, and the final NCD will be published no later than 60 days after the close of the comment period.

I. Clinical Research

CMS has indicated that the purpose of changing the policy's name is to signal CMS's "continued support of beneficiaries' participation in the full range of qualified, scientifically sound research projects" beyond "a very narrow definition of 'clinical trial.'" CMS proposes to define "clinical research" as follows:

> 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.

The proposed definition further provides examples (but not an exhaustive list) of activities that meet the definition:

- 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.
- Clinical studies of diagnostic tests, including measurements of sensitivity and specificity, and impact on physician decision making and patient outcomes.

II. Coverage Qualification Standards

CMS has restructured and revised the standards clinical research must satisfy in order to qualify for Medicare coverage. In order to obtain Medicare coverage, clinical research must satisfy the following standards: A) General standards for a scientifically and technically sound clinical research study; B) Medicare-specific standards of a clinical research study; and C) NCD Coverage with Evidence Development (CED) standards.

A. General Standards

Except as noted below, the proposed general standards are carried over from the existing Clinical Trial Policy. The general standards for a scientifically and technically sound clinical research study are:

1. The study's principal purpose is to determine whether an intervention improves a participants' health outcomes.

2. The study is well-supported by available scientific and medical information or is intended to clarify or establish the health outcomes of interventions already in common clinical use.

3. The study is not an unjustifiable duplication of existing studies.

4. The study is appropriately designed to answer the research question.

5. The study sponsor has the ability to execute the study successfully.

6. The study is in compliance with Federal regulations concerning protection of human subjects (at 45 C.F.R. Part 46) and, if applicable, FDA regulations at 21 C.F.R. Parts 50 and 56.

7. The study is conducted in accordance with appropriate standards of scientific integrity.

8. The study is conducted under a written protocol. (This is a new standard.)

B. Medicare-Specific Standards

Under the Medicare-specific standards, CMS proposes to provide further guidance with respect to the meaning of "therapeutic benefit" and to require greater public disclosure with respect to the existence of the research and research results. The Medicare-specific standards provide that:

1. The study must not be designed exclusively to test toxicity or disease pathophysiology. Some Phase I trials measuring therapeutic outcomes may meet this standard only if the disease being studied is chronic, life threatening, or debilitating.

2. The study must be registered on the ClinicalTrials.gov website prior to the enrollment of the first study subject.

3. The study protocol must specify and fulfill method and timing of public release of all pre-specified outcomes, even if outcomes are negative or study is terminated early.

4. The study protocol must explicitly set forth inclusion criteria and demonstrate consideration of relevant subpopulations (as defined by age, gender, race/ethnicity, socioeconomic or other factors).

5. The study protocol must discuss how the results will generalize to the Medicare population, particularly, 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.

C. National Coverage Determination (NCD) Coverage with Evidence Determination (CED) Standards

CMS proposes that it may require studies to meet additional standards for clinical research identified through the NCD process using CED.[1] CED standards are utilized when CMS is concerned that a research study will not allow the Agency to determine that the item was used as specified in the NCD or there is not sufficient evidence to determine that the item is reasonable and necessary. NCD CED standards are developed on a case-by-case basis and either require the collection of additional data or the provision of services in research settings with added safety measures, patient protections, monitoring, and clinical expertise. For example, CMS could require, under the CED standards, that certain data be collected and submitted to a registry.

III. Deemed Approval

CMS proposes that studies that fall within certain categories are "deemed" to have satisfied the coverage standards set out in the policy. Those categories are:

1. Studies reviewed and funded by a program component of the Department of Health and Human Services (HHS), the Veterans' Administration (VA), or the Department of Defense ("DOD").

2. Studies reviewed and approved by health care research centers or cooperative health care research groups that are funded by one of the above Federal agencies, if certain agency oversight requirements are met.

3. Trials conducted under an Investigational New Drug Application (IND) reviewed by the FDA (and not put on hold).

4. Studies that have been required and approved by FDA as post-approval studies.

5. Studies required by a CED NCD.

The proposed policy contains a narrower spectrum of categories of clinical trials that will be deemed to qualify for coverage than does the existing Clinical Trial Policy. While IND exempt trials enjoy "deemed" status under the existing policy, the proposal would require all IND-exempt trials to meet the criteria set out in the Clinical Research Policy. In addition, CMS proposes to eliminate a process for self-certification of deemed status that was never implemented under the existing policy.

[1] *See* Centers for Medicare and Medicaid Services, *National Coverage Determinations with Data Collection as a Condition of Coverage: Coverage with Evidence Development* (July 12, 2006), http://www.cms.hhs.gov/mcd/ncpc_view_document.asp?id=8.

IV. Covered Services

CMS proposes various definitions in an attempt to clarify which costs related to clinical research are covered.

A. Routine Clinical Services

CMS proposes to clarify the definition of items and services covered in clinical studies and rename "routine costs" "routine clinical services". As part of the revised definition, CMS explains that while items and services available to Medicare beneficiaries outside of the trial setting and used for patient management within the study are covered, the investigational item or service itself is excluded from coverage. CMS proposes the following 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. 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).

B. Investigational Clinical Services

CMS proposes adding a definition of "investigational clinical services" that provides that "[i]nvestigational clinical services are defined as those items and services that are being investigated as an objective within the study." Investigational clinical services would not be covered.

C. Administrative Services

CMS proposes that administrative services associated with carrying out a trial not be covered and proposes to define "administrative services" as follows:

> Administrative services are defined as all non-clinical 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.

D. Coverage with Evidence Determination (CED)

CMS proposes to clarify that investigational services required through the NCD process using CED would be covered by Medicare, even if the item is not routinely covered outside of the trial.

V. Loss of Coverage

CMS proposes to reserve discretionary authority to determine that a research study for which Medicare payments have been made does not meet (or no longer meets) the criteria for coverage or

that the study jeopardizes the safety or welfare of beneficiaries. If such a determination were made, participating beneficiaries would not be liable for costs. CMS further notes that, where appropriate, the billing providers would be held liable for the costs and fraud investigations of the billing providers and the study's principal investigator may be pursued.

VI. Issues Not Addressed

In the proposed NCD, CMS does not clarify the interface between Medicare Secondary Payor (MSP) provisions and clinical trial coverage, nor does CMS address trials employing devices that FDA has approved for marketing under the Humanitarian Device Exemption (HDE). CMS states that the appropriate means for determining coverage of FDA-required studies for HDEs is through the CED process as part of an NCD.

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