CMS Manual System	Department of Health & Human Services (DHHS)
Pub 100-03 Medicare National Coverage Determinations	Centers for Medicare & Medicaid Services (CMS)
Transmittal 74	Date: SEPTEMBER 7, 2007
	Change Request 5719

SUBJECT: Medicare Clinical Trial Policy (CTP)

I. SUMMARY OF CHANGES: Effective July 9, 2007, NCD 310.1, Routine Costs in Clinical Trials, is revised to clarify that the item or service under investigation in a clinical trial, if covered outside the trial, is covered in the context of the trial.

In addition, effective July 9, 2007, NCD 310.l, Routine Costs in Clinical Trials, is revised to add coverage with evidence development (CED). CED is determined through the NCD process, and conditional upon meeting standards of patient safety and clinical evidence, items and services not otherwise covered would be considered "reasonable and necessary" in the context of a clinical trial.

This revision of section 310.1 of Pub. 100-03 is a national coverage determination (NCD). NCDs are binding on all carriers, fiscal intermediaries, quality improvement organizations, qualified independent contractors, the Medicare Appeals Council, and administrative law judges (ALJs) (see 42 CFR section 405.1060(a)(4) (20

NEW / REVISED MATERIAL
EFFECTIVE DATE: July 9, 2007
IMPLEMENTATION DATE: October 9, 2007

Disclaimer for manual changes only: The revision date and transmittal number apply only to red italicized material. Any other material was previously published and remains unchanged. However, if this revision contains a table of contents, you will receive the new/revised information only, and not the entire table of contents.

II. CHANGES IN MANUAL INSTRUCTIONS: (N/A if manual is not updated)
R=REVISED, N=NEW, D=DELETED

R/N/D	CHAPTER / SECTION / SUBSECTION / TITLE
R	1/Table of Contents
R	1/310.1/Routine Costs in Clinical Trials (Effective July 9, 2007))

III. FUNDING:

No additional funding will be provided by CMS; contractor activities are to be carried out within their operating budgets.

IV. ATTACHMENTS:
Business Requirements
Manual Instruction

Unless otherwise specified, the effective date is the date of service.

Attachment - Business Requirements

Pub. 100-03	Transmittal: 74	Date: September 7, 2007	Change Request: 5719

SUBJECT: Medicare Clinical Trial Policy (CTP)

EFFECTIVE DATE: July 9, 2007

IMPLEMENTATION DATE: October 9, 2007

I. GENERAL INFORMATION

A. Background: On June 7, 2000, the President issued an executive memorandum directing the Secretary of Health and Human Services to "explicitly authorize [Medicare] payment for routine patient care costs and costs due to medical complications associated with participation in clinical trials." In keeping with the President's directive, the Centers for Medicare & Medicaid Services (CMS) engaged in defining the routine costs of clinical trials and in identifying the clinical trials for which payment for such routine costs should be made. On September 19, 2000, CMS implemented its initial Clinical Trial Policy through the National Coverage Determination (NCD) process.

On July 10, 2006, CMS opened a reconsideration of its NCD on clinical trials at Pub. 100-03, NCD Manual section 310.1. This Change Request (CR) communicates the findings resulting from that analysis.

B. Policy: Upon reconsideration, effective for items and services furnished on and after July 9, 2007, CMS has determined that routine costs of a clinical trial include all items and services that are otherwise generally available to Medicare beneficiaries (i.e., there exists a benefit category, it is not statutorily excluded, and there is not a national non-coverage decision) that are provided in either the experimental or the control arms of a clinical trial except the investigational item or service itself, unless otherwise covered outside of the clinical trial.

Additionally, CMS, through the NCD process, through an individualized assessment of benefits, risks, and research potential, may determine that certain items and services for which there is some evidence of significant medical benefit, but for which there is insufficient evidence to support a “reasonable and necessary” determination, are only reasonable and necessary when provided in a clinical trial that meets the requirements defined in that NCD. This modification adopts CMS’s proposed addition of coverage with evidence development.

The revised NCD can be found in section 310.1, of Pub.100-03, of the NCD Manual.

II. BUSINESS REQUIREMENTS TABLE

Use“Shall" to denote a mandatory requirement

Number	Requirement	Responsibility (place an “X” in each applicable column)								
		A / B	D M E	F I	C A R		R H H	E D C	Shared-System Maintainers	OTH ER

									FISS	MCS	VMS	CWF	
5719.1	Effective for claims for clinical trial services furnished on and after July 9, 2007, contractors shall be aware of the new clinical trial policy found in Pub 100-03 of the NCD Manual, section 310.1.	X	X	X	X		X	X					
5719.2	Effective for claims for clinical trial services furnished on and after July 9, 2007, contractors shall be aware that each additional Medicare national coverage policy approved under CED will be implemented under separate NCD manual instructions, business requirements, and an accompanying CR.	X	X	X	X		X	X					
5719.3	Effective for claims for clinical trial services furnished on and after July 9, 2007, through the implementation date of this CR, contractors shall not search for claims, but may go back and adjust claims brought to their attention.	X	X	X	X		X	X					

III. PROVIDER EDUCATION TABLE

Number	Requirement	Responsibility (place an "X" in each applicable column)											
		A/B MAC	DME MAC	FI	CARRIER		RHHI	EDC	Shared-System Maintainers				OTHER
									FISS	MCS	VMS	CMS	
5719.4	A provider education article related to this instruction will be available at http://www.cms.hhs.gov/MLNMattersArticles/ shortly after the CR is released. You will receive notification of the article release via the established "MLN Matters" listserv. Contractors shall post this article, or a direct link to this article, on their Web site and include information about it in a listserv message within one week of the availability of the provider education article. In addition, the provider education article shall be included in your next regularly scheduled bulletin. Contractors are free to supplement MLN Matters articles with localized information that would benefit their provider community in billing and administering the Medicare program correctly.	X	X	X	X		X	X					

Number	Requirement	Responsibility (place an "X" in each applicable column)											
		A/B MAC	DME MAC	FI	CARRIER		RHHI	EDC	Shared-System Maintainers				OTHER
									FISS	MCS	VMS	CMS	

IV. SUPPORTING INFORMATION

Use "Should" to denote a recommendation.

X-Ref Requirement Number	Recommendations or other supporting information:

V. CONTACTS

Pre-Implementation Contact(s):

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Post-Implementation Contact(s): Appropriate RO

VI. FUNDING

A. *For Fiscal Intermediaries, Carriers, and the Durable Medical Equipment Regional Carrier (DMERC)*:
No additional funding will be provided by CMS; contractor activities are to be carried out within their operating budgets.

B. *For Medicare Administrative Contractors (MAC)*:
The Medicare Administrative Contractor (MAC) is hereby advised that this constitutes technical direction as defined in your contract. CMS does not construe this as changes to the MAC Statement of Work (SOW). The contractor is not obligated to incur costs in excess of the amounts specified in your contract unless and until specifically authorized by the contracting officer. If the contractor considers anything provided, as described above, to be outside the current scope of work, the contractor shall withhold performance on the part(s) in question and immediately notify the contracting officer, in writing or by e-mail, and request formal directions regarding continued performance requirements.

Medicare National Coverage Determinations Manual

Chapter 1, Part 4 (Sections 200 – 310.1)
Coverage Determinations

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(Rev. 74, 09-07-07)

310.1 ROUTINE COSTS IN CLINICAL TRIALS *(Effective July 9, 2007)*

(Rev. 74, Issued: 09-07-07, Effective: 07-09-07, Implementation: 10-09-07)

Effective for items and services furnished on or after *July 9, 2007*, Medicare covers the routine costs of qualifying clinical trials, as such costs are defined below, as well as reasonable and necessary items and services used to diagnose and treat complications arising from participation in all clinical trials. All other Medicare rules apply.

Routine costs of a clinical trial include all items and services that are otherwise generally available to Medicare beneficiaries (i.e., there exists a benefit category, it is not statutorily excluded, and there is not a national non-coverage decision) that are provided in either the experimental or the control arms of a clinical trial except:

- The investigational item or service, itself *unless otherwise covered outside of the clinical trial;*
- Items and services provided solely to satisfy data collection and analysis needs and that are not used in the direct clinical management of the patient (e.g., monthly CT scans for a condition usually requiring only a single scan); and
- Items and services customarily provided by the research sponsors free of charge for any enrollee in the trial.

Routine costs in clinical trials include:

- 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 non-covered 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.

This policy does not withdraw Medicare coverage for items and services that may be covered according to local medical review policies *(LMRPs)* or the regulations on category B investigational device exemptions (IDE) found in 42 CFR 405.201-405.215, 411.15, and 411.406. For information about LMRPs, refer to www.lmrp.net, a searchable database of Medicare contractors' local policies.

For non-covered items and services, including items and services for which Medicare payment is statutorily prohibited, Medicare only covers the treatment of complications arising from the delivery of the non-covered item or service and unrelated reasonable and necessary care. However, if the item or service is not covered by virtue of a national non-coverage policy in *Pub. 100-03, NCD* Manual and is the focus of a qualifying clinical trial, the routine costs of the clinical trial (as defined above) will be covered by Medicare but the non-covered item or service, itself, will not.

A. Requirements for Medicare Coverage of Routine Costs

Any clinical trial receiving Medicare coverage of routine costs must meet the following three requirements:

- 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 not be designed exclusively to test toxicity or disease pathophysiology. It must have therapeutic intent.

- Trials of therapeutic interventions must enroll patients with diagnosed disease rather than healthy volunteers. Trials of diagnostic interventions may enroll healthy patients in order to have a proper control group.

The three requirements above are insufficient by themselves to qualify a clinical trial for Medicare coverage of routine costs. Clinical trials also should have the following desirable characteristics; however, some trials, as described below, are presumed to meet these characteristics and are automatically qualified to receive Medicare coverage:

1. The principal purpose of the trial is to test whether the intervention potentially improves the participants' health outcomes;

2. 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;

3. The trial does not unjustifiably duplicate existing studies;

4. The trial design is appropriate to answer the research question being asked in the trial;

5. The trial is sponsored by a credible organization or individual capable of executing the proposed trial successfully;

6. The trial is in compliance with Federal regulations relating to the protection of human subjects; and

7. All aspects of the trial are conducted according to the appropriate standards of scientific integrity.

B. Qualification Process for Clinical Trials

Using the authority found in §1142 of the Act (cross-referenced in §1862(a)(1)(E) of the Act), the Agency for Healthcare Research and Quality (AHRQ) will convene a multi-agency Federal panel (the "panel") composed of representatives of the Department of Health and Human Services research agencies (National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), AHRQ, and the Office of Human Research Protection), and the research arms of the Department of Defense (DOD) and the Department of Veterans Affairs (VA) to develop qualifying criteria that will indicate a strong probability that a trial exhibits the desirable characteristics listed above. These criteria will be easily verifiable, and where possible, dichotomous. Trials that meet these qualifying criteria will receive Medicare coverage of their associated routine costs. This panel is not reviewing or approving individual trials. The multi-agency panel will meet periodically to review and evaluate the program and recommend any necessary refinements to CMS.

Clinical trials that meet the qualifying criteria will receive Medicare coverage of routine costs after the trial's lead principal investigator certifies that the trial meets the criteria. This process

will require the principal investigator to enroll the trial in a Medicare clinical trials registry, currently under development.

Some clinical trials are automatically qualified to receive Medicare coverage of their routine costs because they have been deemed by AHRQ, in consultation with the other agencies represented on the multi-agency panel to be highly likely to have the above-listed seven desirable characteristics of clinical trials. The principal investigators of these automatically qualified trials do not need to certify that the trials meet the qualifying criteria, but must enroll the trials in the Medicare clinical trials registry for administrative purposes, once the registry is established.

Effective September 19, 2000, clinical trials that are deemed to be automatically qualified are:

1. Trials funded by NIH, CDC, AHRQ, CMS, DOD, and VA;

2. Trials supported by centers or cooperative groups that are funded by the NIH, CDC, AHRQ, CMS, DOD and VA;

3. Trials conducted under an investigational new drug application (IND) reviewed by the FDA; and

4. 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. At that time the principal investigators of these trials must certify that the trials meet the qualifying criteria in order to maintain Medicare coverage of routine costs. This certification process will only affect the future status of the trial and will not be used to retroactively change the earlier deemed status.

The CMS, through the national coverage determination (NCD) process, through an individualized assessment of benefits, risks, and research potential, may determine that certain items and services for which there is some evidence of significant medical benefit, but for which there is insufficient evidence to support a "reasonable and necessary" determination, are only reasonable and necessary when provided in a clinical trial that meets the requirements defined in that NCD.

Medicare will cover the routine costs of qualifying trials that either have been deemed to be automatically qualified, have certified that they meet the qualifying criteria*, or are required through the NCD process,* unless CMS's Chief Clinical Officer subsequently finds that a clinical trial does not meet the qualifying criteria or jeopardizes the safety or welfare of Medicare beneficiaries.

Should CMS find that a trial's principal investigator misrepresented that the trial met the necessary qualifying criteria in order to gain Medicare coverage of routine costs, Medicare coverage of the routine costs would be denied under §1862(a)(1)(E) of the Act. In the case of such a denial, the Medicare beneficiaries enrolled in the trial would not be held liable (i.e., would be held harmless from collection) for the costs consistent with the provisions of §§1879, 1842(l), or 1834(j)(4) of the Act, as applicable. Where appropriate, the billing providers would be held liable for the costs and fraud investigations of the billing providers and the trial's principal investigator may be pursued.

Medicare regulations require Medicare+Choice (M+C) organizations to follow CMS's national coverage decisions. This NCD raises special issues that require some modification of most M+C organizations' rules governing provision of items and services in and out of network. The items

and services covered under this NCD are inextricably linked to the clinical trials with which they are associated and cannot be covered outside of the context of those clinical trials. M+C organizations therefore must cover these services regardless of whether they are available through in-network providers. M+C organizations may have reporting requirements when enrollees participate in clinical trials, in order to track and coordinate their members' care, but cannot require prior authorization or approval.

(This NCD last reviewed July 2007.)