CMS Manual System	Department of Health & Human Services (DHHS)
Pub 100-04 Medicare Claims Processing	Centers for Medicare & Medicaid Services (CMS)
Transmittal 13551	**Date: December 19, 2025**
	Change Request 14268

SUBJECT: Updates to the Internet Only Manual (IOM) Publication 100-04, Chapter 32, Sections 69.1, 69.6 and 69.9 to Clarify Requirements for Clinical Trial Services

I. SUMMARY OF CHANGES: The purpose of this Change Request (CR) is to update Publication 100-04, Chapter 32, Sections 69.1, 69.6 and 69.9 of the Medicare Claims Processing Manual.

EFFECTIVE DATE: January 21, 2026
**Unless otherwise specified, the effective date is the date of service.*
IMPLEMENTATION DATE: January 21, 2026

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-*Only One Per Row.*

R/N/D	CHAPTER / SECTION / SUBSECTION / TITLE
R	32/69/69.1/General
R	32/69/69.6/Requirements for Billing Routine Costs of Clinical Trials
R	32/69/69.9/Billing and Processing Fee for Service Claims for Covered Clinical Trial Services Furnished to Managed Care Enrollees

III. FUNDING:
For Medicare Administrative Contractors (MACs):
The Medicare Administrative Contractor is hereby advised that this constitutes technical direction as defined in your contract. CMS does not construe this as a change to the MAC Statement of Work. The contractor is not obligated to incur costs in excess of the amounts allotted 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.

IV. ATTACHMENTS:

Business Requirements
Manual Instruction

Attachment - Business Requirements

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II. GENERAL INFORMATION

A. Background: This Change Request (CR) updates instructions to provide clarification of the requirements and to provide additional links regarding Clinical Trial Services.

B. Policy: N/A

III. BUSINESS REQUIREMENTS TABLE

"Shall" denotes a mandatory requirement, and "should" denotes an optional requirement.

Number	Requirement	Responsibility								
		A/B MAC			DME MAC	Shared-System Maintainers				Other
		A	B	HHH		FISS	MCS	VMS	CWF	
14268.1	The Medicare Contractor shall be aware of the manual updates in Publication 100-04, Chapter 32, Sections 69.1, 69.6 and 69.9.	X	X							

IV. PROVIDER EDUCATION

None

Impacted Contractors: None

V. SUPPORTING INFORMATION

Section A: Recommendations and supporting information associated with listed requirements: N/A

"Should" denotes a recommendation.

X-Ref Requirement Number	Recommendations or other supporting information:

Section B: All other recommendations and supporting information: N/A

VI. CONTACTS

Post-Implementation Contact(s): Contact your Contracting Officer's Representative (COR).

VII. FUNDING

Section A: For Medicare Administrative Contractors (MACs):
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ATTACHMENTS: 0

69.1 – General

(Rev.,13551,Issued: 12-19-2025:Effective: 01-21-2026:Implementation: 01-21-2026)

The CMS has issued a National Coverage Determination (NCD) which allows Medicare coverage for the routine costs of qualifying clinical trial services as well as reasonable, necessary items and services used to diagnose and treat complications arising from participation in all clinical trials. The coverage requirements for routine costs of qualifying clinical trial services are contained in the National Coverage Determinations Manual, Section 310.1, *www.cms.gov/regulations-and-guidance/guidance/manuals/downloads/ncd103c1_part4.pdf*

69.6 - Requirements for Billing Routine Costs of Clinical Trials

(Rev.,13551,Issued: 12-19-2025:Effective: 01-21-2026:Implementation: 01-21-2026)

Routine Costs Submitted by Practitioners/Suppliers

Claims with dates of service on or after January 1, 2008:

- HCPCS modifier 'Q1' (numeral 1 instead of the letter i); and,
- ICD-10 diagnosis code Z00.6 *(in either the primary or secondary positions)*

CMS covers *the* cost of healthy volunteers in a qualified clinical trial if it meets the following conditions:

- The trial is not designed exclusively to test toxicity or disease pathophysiology.
- The trial must have therapeutic intent.
- If the trial has therapeutic interventions, it must enroll patients with *a* diagnosed disease rather than healthy volunteers.
- If the trial is studying diagnostic interventions, it may enroll healthy patients to have a proper control group.

Claims submitted with modifier Q1 shall be returned as unprocessable if ICD-10-CM code Z00.6 is not submitted on the claim.

Contractors shall return the following messages:

Claims *Adjustment* Reason Code *(CARC)* 16: "Claim/service lacks information which is needed for adjudication. As least one Remark Code must be provided (may be comprised of either the Remittance Advice Code or NCPDP Reject Reason Code)."

Remittance Advice Remark Code *(RARC)* M76: "Missing/incomplete/invalid diagnosis or condition."

Effective for claims with dates of service on or after January 1, 2014, it is mandatory to report a clinical trial number on claims for items/services provided in clinical trials/studies/registries, or under *Coverage with Evidence Development (*CED.*)* Providers *must* report the 8-digit number on *clinical trial* number on the following claims locators:

- 837 professional claim format Loop 2300 REF02 (REF01=P4) (do not use 'CT' on the electronic claim); or
- CMS-1500 paper form place in Field 19 (preceded by 'CT').

In addition to the clinical trial number, claims should *also* include:

- ICD-10 diagnosis code Z00.6 (in either the primary *or* secondary positions)
- HCPCS modifier Q0 or Q1 as appropriate

Practitioner claims submitted without a clinical trial number shall be returned as unprocessable using the following messages:

CARC 16: "Claim/service lacks information which is needed for adjudication. At least one Remark Code must be provided (may be comprised of either NCPDP Reject Reason Code, or Remittance Advice Remark Code that is not an ALERT.)"

RARC MA50: "Missing/incomplete/invalid Investigational Device Exemption number for FDA-approved clinical trial services."

RARC MA130: "Your claim contains incomplete and/or invalid information, and no appeal rights are afforded because the claim is unprocessable. Please submit a new claim with the complete/correct information."

Group Code-Contractual Obligation (CO)

<u>Routine Costs Submitted by Institutional Providers</u>

All Institutional Clinical Trial Claims

Regardless of the date of service, clinical trial claims received after April 1, 2008, providers *must* report *the* 8-digit clinical trial number. To bill the 8-digit clinical trial number, institutional providers shall *use* value code 'D4'where the value code amount equals the 8-digit clinical trial number. Below are the claim locators in which to bill the 8-digit *clinical trial* number:

- 837 institutional claim format Loop 2300 REF02 (REF01=P4)

- Paper CMS-1450 value code ‘D4’

NOTE: Value code ‘D4’/amount data from the internal claims processing is mapped/populated to the 837 institutional claim formats for a coordination of benefits 837 institutional claim

NOTE: It is mandatory to report a clinical trial number on claims for items *or* services provided in clinical trials, studies *or* registries. Institutional claims submitted without a clinical trial number shall be *returned* to providers.

NOTE: *Modifier Q0 is used for services defined as an investigational clinical service provided in an approved clinical research study. Append this modifier on a Category B Investigational Device Exemption (IDE) code along with IDE number on the claim.*

The modifier *Q1* is a line item specific and must be used to identify items and services that constitute medically necessary routine patient care or treatment of complications arising from a Medicare beneficiary’s participation in a Medicare covered clinical trial. Items and services that are provided solely to:

- *Satisfy* data collection and analysis needs*;* and
- *That* are not used in the clinical management of the patient

are not covered and may not be billed using *modifier Q1*. Items and services that are not covered by Medicare by virtue of a statutory exclusion or lack of a benefit category also may not be billed using *modifier Q1*. When billed in conjunction with the Z00.6 diagnosis code, *modifier Q1* will serve as the provider’s attestation that the service meets the Medicare coverage criteria (i.e., was furnished to a beneficiary who is participating in a Medicare qualifying clinical trial and represents routine patient care, including complications associated with qualifying *clinical* trial participation).

Inpatient Clinical Trial Claims

Institutional providers billing clinical trial service(s) must report ICD-10 diagnosis code Z00.6 in either the primary or secondary position and condition code 30 regardless of whether all services are related to the clinical trial or not.

NOTE: HCPCS codes are not reported on inpatient claims. Therefore, the HCPCS modifier requirements (i.e., Q0/Q1) as outlined in the outpatient clinical trial section below, are not applicable to inpatient clinical trial claims.

Outpatient Clinical Trial Claims

On all outpatient clinical trial claims, providers *must* do the following:

- Report condition code 30,
- Report ICD-10 diagnosis code Z00.6, in the primary or secondary position; and
- *The 8-digit clinical trial identifier number in the 837I Loop 2300 REF02 (REF01=P4) or as* value code ‘D4’ on paper only CMS-1450.

- Identify all lines that contain an investigational item/service with HCPCS *modifier Q0 for dates of services on or after 01/01/08.*
- Identify all lines that contain a routine service with HCPCS *modifier Q1 for dates of service on or after 1/1/08.*

For clinical trial billing requirements for patients enrolled in a managed care plan*/MAO*, please refer to Section 69.9 of this chapter.

69.9 - Billing and Processing Fee for Service Claims for Covered Clinical Trial Services Furnished to Managed Care Enrollees

(Rev.,13551,Issued: 12-19-2025:Effective: 01-21-2026:Implementation: 01-21-2026)

Payment for Investigational Device Exemption (IDE) Studies

Medicare Advantage Organizations (MAOs) are responsible for payment of claims related to the enrollees' participation in both Category A and B IDE studies that are covered by the Medicare Administrative Contractor (MAC) with jurisdiction over the MA plan's service area. The MAO is responsible for payment of routine care items and services in Centers for Medicare & Medicaid (CMS) approved Category A and Category B IDE studies. The MAO is also responsible for CMS approved Category B devices. CMS will not approve Category A devices because they are statutorily excluded from coverage.

Payment for Clinical Studies Approved Under Coverage with Evidence Development (CED)

In National Coverage Determinations (NCDs) requiring CED, Medicare covers items and services in CMS approved CED studies. MAOs are responsible for payment of items and services in CMS approved CED studies unless CMS determines that the significant cost threshold is exceeded for that item or service (see 42 CFR 422.109).

Payment for Clinical Trial Services

Per Publication 100-16, Chapter 4, Section 10.7.1- 10.7.3, Medicare Advantage Organizations (MAOs) are responsible for payment of services. For additional information regarding MAO benefits refer to:
https://www.cms.gov/regulations-and-guidance/guidance/manuals/downloads/mc86c04.pdf

The clinical trial coding requirements for *MAO* claims are the same as those for regular Medicare fee for service claims. However, for beneficiaries enrolled in a *MAO* plan, institutional providers must not bill outpatient clinical trial services and non-clinical trial services on the same claim. If covered outpatient services unrelated to the clinical trial are rendered during the same day/stay, the provider must split bill *submitting only* the clinical trial services on a single claim and billed as fee-for-service. (*This* allows the Medicare claims processing system to not apply *the* deductible when the patient is found to be in a *MAO* plan). Any outpatient services unrelated to the clinical trial should be billed to the *MAO* plan