1 PURPOSE

1.1 This guidance describes the Coverage Analysis process which is defined as the systematic review of research related documents to determine the billing status of both the study itself and the medical items and services provided to the research subjects. Reimbursement coverage for medical items and services is determined based on thorough research, supported by published industry guidelines and compliance with Centers for Medicare and Medicaid Services (CMS) regulation including the Medicare Clinical Trial Policy, CMS Investigation Device Exemption (IDE) Guideline, CMS Coverage with Evidence Development Policy (CED), National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and the regulations on Category B investigational device exemptions found in 42 CFR 405.201-405.215, 411.15, and 411.406.

1.2 The guidance begins when the study documents outlined on the *CHECKLIST: Coverage Analysis Required Documents (HRP-449)* are submitted to the Coverage Analyst (CA) who completes the Coverage Analysis process for the study.

1.3 The guidance ends when the finalized Coverage Analysis is determined applicable and is applied by the principal investigator or designee.

1.4 Upon completion, the Coverage Analysis is a tool used in providing subjects with an accurate accounting of their financial liability before enrollment; an assessment of the true costs of the clinical trial; and demonstrates due diligence in complying with Federal Clinical Trial regulations.

1.5 The CMS Clinical Trial Policy (CTP) and related regulation is generally used in Coverage Analysis because CMS is the largest single payor, and many commercial plans have adopted CTP principles. Most state Medicaid plans generally follow CTP.

2 REVISIONS FROM PREVIOUS VERSION

2.1 If applicable, previous versions available in Human Research Protection Program Change Log.

3 POLICY STATEMENT

3.1 CMS coverage for reimbursement of medical items and services in a clinical trial is established according to the CMS Clinical Trial Policy–NCD 310.1; CMS Investigation Device Exemption (IDE) Guidelines, CMS Coverage with Evidence Development Policy (CED), National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and the regulations on Category B investigational device exemptions found in 42 CFR 405.201-405.215, 411.15, and 411.406.

3.2 The Coverage Analysis process is a formal, internally approved process applying to all clinical trials with protocol items and/or services that are to be billed by the hospital or professional billing system. A two-part process including (1) the determination if a study is a “qualified” clinical trial and (2) the determination of what medical items and services are routine costs of conventional care utilizing published industry guidelines while complying with CMS Clinical Trial Policy (CTP), Coverage with Evidence Development Policy (CED), National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs) regulation.

4 NATIONAL COVERAGE DETERMINATION (NCD) 310.1 for ROUTINE COSTS IN CLINICAL TRIALS

4.1 Per NCD 310.1 INDICATIONS AND LIMITATIONS OF COVERAGE:

4.1.1 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.

4.1.2 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:

4.1.2.1 The investigational item or service, itself unless otherwise covered outside of the clinical trial.

4.1.2.2 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

4.1.2.3 Items and services customarily provided by the research sponsors free-of-charge for any enrollee in the trial.

4.2 Routine costs in QUALIFYING clinical trials include:

4.2.1 Items or services that are typically provided absent a clinical trial (e.g., conventional care);

4.2.2 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

4.2.3 Items or services needed for reasonable and necessary care arising from the provision of an investigational item or service, for the diagnosis or treatment of complications.

4.3 This policy does not withdraw Medicare coverage for items and services that may be covered according to Local Coverage Determinations (LCDs) or the regulations on category B investigational device exemptions found in 42 CFR 405.201-405.215, 411.15, and 411.406. For information about LMRPs, refer to www.cms.hhs.gov , a searchable database of Medicare Administrative Contractor local policies.

4.4 For non-covered items and services, including items and services for which Medicare payment is statutorily prohibited, Medicare limits coverage to 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 Publication 100-03 National Coverage Determination (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.

5 PER NCD 310.1 REQUIREMENTS FOR MEDICARE COVERAGE OF ROUTINE COSTS

5.1 Any clinical trial receiving Medicare coverage for reimbursement of routine costs must meet the following three (3) requirements under 4.1 and 4.2 and 4.3 and must also be “DEEMED” as per 4.4.

5.2 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 following is a list of Medicare Benefit Categories (Table 1). This list is not all inclusive any may vary based on changing guidelines:

Table 1: Medicare Benefit Categories	
• Ambulance Services	• Inpatient psychiatric hospital services
• Ambulatory Surgical Center Facility Services	• Institutional Dialysis services and supplies
• Antigens	• Leg, arm, back, and neck braces
• Artificial Legs, Arms, and eyes	• Medical nutrition therapy services
• Aral antiemetic drugs	• Nurse practitioner services
• Audiology services	•
• Blood clotting factors for hemophilia patients	• Optometrist services
• Bone mass measurement	• Oral anticancer drugs
• Certified nurse-midwife services	• Orthotics and prosthetics
• Certified registered nurse anesthetist services	• Osteoporosis drug

Table 1: Medicare Benefit Categories	
• Chiropractor services	• Outpatient hospital services incident to a physician's service
• Clinical nurse specialist services	• Outpatient occupational therapy services
• Clinical social worker specialist services	• Outpatient speech language pathology services
• Colorectal cancer screening tests	• Partial hospitalization services
• Comprehensive outpatient rehab facility services	• Physician assistant services
• Critical access hospital services	• Physicians' services
• Dental services	• Pneumococcal vaccine and administration
• Diabetes outpatient self-management training	• Podiatrist services
• Diagnostic laboratory testing	• Post hospital extended care services
• Diagnostic services in outpatient hospital	• Post-institutional home health care services
• Diagnostic tests (other)	• Prostate cancer screening test
• Diagnostic X-Rays tests	• Prosthetic devices
• Drugs and biologicals	• Qualified Psychologist services
• Durable medical equipment	• Religious non-medical healthcare institution
• Erythropoietin for dialysis patients	• Rural health clinic services
• Extended care services	• Screening for glaucoma
• Eyeglasses after cataract surgery	• Screening for mammography
• Federally qualified health center services	• Screening for pap smear
• Hepatitis B vaccine and administration	• Screening for pelvic exam
• Home dialysis supplies and equipment	• Self-care home dialysis support services
• Home health services	• Shoes for patients with diabetes
• Hospice care	• Skilled nursing facility
• Immunosuppressive drugs	• Splints, casts. Other devices used for reduction of fractures and dislocations
• Incident to a physician's professional service	• Transplantation services for ESRD- entitled beneficiaries
• Influenza vaccine and administration	• X-ray, radium, and radioactive isotope therapy
• Inpatients hospital services	

5.2.1 Per CMS National Coverage Determination (NCD) 310.1, referred to as the Clinical Trial Policy "The trial must not be designed exclusively to test toxicity or disease pathophysiology. It must have therapeutic intent" (see *GUIDANCE: Definitions (HRP-001*).

5.2.2 Trials with therapeutic intent must have an objective/aim that assesses the effects of the intervention on patient outcome (i.e., prolongation of life, shrinkage of tumor or improvements in quality of life) and must not be exclusively designed to test toxicity or disease pathophysiology.

5.2.3 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:

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

5.2.5 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.

5.2.6 The trial does not unjustifiably duplicate existing studies.

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

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

5.2.9 The trial follows Federal regulations relating to the protection of human subjects; and

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

6 PER NCD 310.1 **QUALIFICATION DETERMINATION FOR CLINICAL TRIALS**

6.1 Using the authority found in §1142 of the Social Security Act (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) to develop qualifying criteria that will indicate a strong probability that a trial exhibits the desirable characteristics listed above.

6.1.1 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.

6.1.2 The multi-agency panel will meet periodically to review and evaluate the program and recommend any necessary refinements to the Centers for Medicare & Medicaid Services (CMS).

6.2 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.

6.3 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. Per National Coverage Determination (NCD) 310.1 and effective September 19, 2000, clinical trials that are deemed to be automatically qualified are:

6.3.1 Trials funded by National Institutes of Health (NIH), the Center for Disease Control (CDC), The Agency for Healthcare Research and Quality (AHRQ), and CMS.

6.3.2 Trials supported by centers or cooperative groups that are funded by the NIH, CDC, AHRQ, and CMS.

6.3.3 Trials conducted under an investigational new drug application (IND) reviewed by the Food and Drug Administration (FDA) and

6.3.4 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 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.

6.3.5 The 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.

6.4 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.

6.5 Should CMS find that a trial's principal investigator misrepresented that the trial met the necessary qualifying criteria 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.

6.6 Medicare regulations require Medicare + Choice (M+C) organizations to follow CMS NCDs. 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, to track and coordinate their members' care, but cannot require prior authorization or approval.

7 Coverage Related to Investigation Device Exemption (IDE) Studies

7.1 The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) allowed Medicare payment of the routine costs of care furnished to Medicare beneficiaries in certain categories of Investigational Device Exemption (IDE) studies.

7.2 CMS finalized changes to the IDE regulations (42 CFR § 405 Subpart B), effective January 1, 2015. CMS added criteria for coverage of IDE studies and changed from local Medicare Administrative Contractor (MAC) review and approval of IDE studies to a centralized review and approval of IDE studies.

7.3 An approval for a Category A (Experimental) IDE study will allow coverage of routine care items and services furnished in the study, but not of the Category A device, which is statutorily excluded from coverage. An approval for a Category B (Nonexperimental/investigational) IDE study will allow coverage of the Category B device and the routine care items and services in the trial.

8 RESPONSIBILITIES

8.1 The Principal Investigator or designee is responsible for ensuring the HRP-449 with required study documents is provided to the Coverage Analyst to initiate the Coverage Analysis process required for IRB approval.

8.2 The Principal Investigator or designee is responsible for ensuring the HRP-449 with required documents is submitted to the Coverage Analyst in the event of a revision to Protocol (affecting medical items services required), Investigators Brochure, Device Brochure, Informed Consent cost clauses, Clinical trial Agreement (revisions to Sponsor provided/covered medical services or items).

8.3 The principal investigator or designee is responsible for ensuring that all Medicare eligible beneficiaries are screened using the National Coverage Determination for routine costs that are incurred throughout the study.

9 PROCEDURE

9.1 PIs or their designees are to follow *PROCESS MAP: General Clinical Trials Billing Process Map (HRP-720), PROCESS MAP: Sharp System Oncology-Specific Clinical Trials Billing Process Map (HRP-721)* or *PROCESS MAP: Sharp Mesa Vista Research Center-Specific Clinical Trials Billing Process Map (HRP-722)* as appropriate.

9.1.1 PIs or their designees are to complete and submit with *FORM: Initial IRB Submission (HRP-211)*.

10 MATERIALS

10.1 GUIDANCE: Definitions (HRP-001)
10.2 FORM: Initial IRB Submission (HRP-211)
10.3 CHECKLIST: Coverage Analysis Required Documents (HRP-449)
10.4 PROCESS MAP: General Clinical Trials Billing Process (HRP-720)
10.5 PROCESS MAP: Sharp System Oncology-Specific Clinical Trials Billing Process Map (HRP-721)
10.6 PROCESS MAP: Sharp Mesa Vista Research Center-Specific Clinical Trials Billing Process Map (HRP-722)

11 REFERENCES

11.1 National Coverage Determination (NCD) for Routine Costs in Clinical Trials https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCAId=248&NcaName=Intensive+Behavioral+Therapy+for+Cardiovascular+Disease&ExpandComments=y&ver=2&NCDId=1&ncdver=2&bc=BEAAAAAAEEAAAA%3D%3D&

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