Clinical Trials Billing
Compliance from A to Z

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Disclaimer

This presentation reflects the opinions of the presenters and does not necessarily reflect the views of the University of Alabama at Birmingham. In addition, the examples set forth in this presentation are purely hypothetical.
Part I: Basic Overview of a Clinical Trial for Billing
Different Clinical Trial Perspectives

- Relationships – investigator, sponsor
- Agreements – awards, budgets, CDA’s, CTA’s
- Regulatory approvals: FDA, IRB, COI, etc.
- Scientific – conduct, analysis, reporting
- Financial – is study feasible
Definitions

- Clinical investigation – 21 CFR §§ 50.3(c), 56.102(c), 312.3(b), 812.3(h)
- NIH GPS – clinical research, clinical trials
- CDC, DoD, VA, CMS - ?
Clinical Investigation (FDA)

- Any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice. [21 CFR 312.3 (b)]

- Investigation means a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device. [21 CFR 812.3 (h)]

- Any experiment that involves a test article and one or more human subjects that either:
  - Is subject to investigational use or devices exemption under FDCA.
  - Is not subject to above but results intended for FDA submission
  - Non-clinical laboratory studies covered under different regulations [21 CFR 50.3 (c)].
  - Research, clinical research, clinical study, study, and clinical investigation synonymous for 21 CFR Part 56 [21 CFR 56.102 (c)].
Clinical Trials (NIH)

A biomedical or behavioral research study of human subjects that is designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices). Clinical trials are used to determine whether new biomedical or behavioral interventions are safe, efficacious, and effective. Clinical trials of an experimental drug, treatment, device or intervention may proceed through four phases:

• Phase I – testing in small groups (e.g. 20-8-) to determine efficacy and evaluate safety
• Phase II – Study in larger groups (e.g. 100’s) to determine efficacy and further evaluate safety
• Phase III – Study to determine efficacy in large groups (e.g. 1000’s) vs. standard/experimental/interventions
• Phase IV – post-marketing studies for effectiveness

NIHGPS, Definitions of Terms.
Phases of an Investigation (FDA)

- Clinical investigations usually divided into Phase 1, 2, and 3.

- Features of Phase I studies:
  - Initial introduction of new drug into humans
  - Closely monitored
  - Patients or normal volunteers
  - Metabolism and actions (pharmacokinetics)
  - Side effects with increasing dosage
  - Gain early evidence on effectiveness, if possible
  - Used to design Phase 2 studies

- Alternate reasons for Phase I studies:
  - Drug metabolism, structure-activity relationships, mechanism of action
  - Drugs as research tools
Phase 1 Trials (NCI)

- Division of Cancer Treatment and Diagnosis (DCTD) serves as IND sponsor
- Cancer Therapy and Evaluation Program designs and implements plans for new agents
- Phase 1 trials:
  - Determine safe dose for Phase 2 trials
  - Define acute effects on normal tissues
  - Examine agent’s pharmacology
  - Reveal evidence of anti-tumor activity
  - Therapeutic intent is always present in Phase 1 trials

NCI Investigator Handbook 2002, pg. 9
Clinical Trial Process I

IDEA/Hypothesis

Pre-Clinic Testing

Clinical Trial Protocol

Investigators

Institution

Commercial Manufacturers

Federal/Private Funding Agency
Who can be an investigator from the following?

- University Professor
- Practicing physician
- Academic institution
- Drug company
- Federal agency
Who can be a sponsor of a clinical trial?

- Investigator
- Hospital
- Academic Institution
- Funding Agency
- Drug Company
Clinical Trial Process III

Sponsor Contacts Investigator

Research Protocol
Investigator’s Brochure
Clinical Trial Agreement

Institutional Negotiation
CTA Signed

Institutional Reviews
IRB, COIC, etc. Approvals

Investigator Feasibility Study
+ Balance
Grant Awards/Clinical Trial Agreements

- Contractual in nature

- Spells out terms and conditions for performance of research project

- Includes consideration for performance
Elements in Clinical Trial Agreement

1. Performance criteria
2. Term of Agreement
3. Termination provisions
4. Financial consideration/payment schedule
5. Data ownership
6. Confidentiality
7. Publication
8. Patents/intellectual property
9. Reporting of data
10. Compliance with applicable law
Elements in Clinical Trial Agreement

11. Monitoring of study
12. Cost of investigational item
13. Publicity
15. Indemnification
16. Insurance
17. Modifications to Agreement
18. Notices
19. Survival
Criteria for IRB Approvals

- **Eight requirements for IRB approval (7+1)**
  - (1) Risks to subjects are minimized: by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risks, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes. [45 CFR 46.111 (1); 21 CFR 56.111 (a) (1)]
  - (4) Informed consent will be sought from each prospective subject...in accordance with and to the extent required by [45 CFR 46.116, 21 CFR 50.27]
Elements of Informed Consent

- Eight basic elements
  - Statement that study involves research
  - Foreseeable risks and discomforts
  - Benefits reasonably to be expected
  - Confidentiality
  - Voluntary participation

- Six additional elements
  - Presence of unforeseeable risks
  - Circumstances for termination
  - Additional costs to subjects for participation
    [45 CFR 46.116 (a), (b); 21 CFR 50.25 (a), (b)]
Financial Conflicts of Interests

- May bias research
  - Design
  - Conduct
  - Reporting
  - Analysis
- 21 CFR Part 54 (FDA)
- 42 CFR Part 50 (NIH)
FDA Financial Disclosure Requirements Between Sponsor & Investigators

- Absence of Financial Interests
- Compensation affected by the outcome of study
- Significant payments of other sorts (>\$25K)
- Proprietary interests in test products
- Significant equity interests (>\$50K)

21 CFR 54.4
Significant Payments to Other Sorts

Payments made by the sponsor of a covered study to the investigator or institution to support activities of the investigator that have a monetary value of more than $25K, exclusive of the costs of conducting the clinical study or other clinical studies (e.g. grant to fund ongoing research, compensation in the form of equipment or retainers for ongoing consultation or honoraria) during the time the clinical investigator is carrying out the study and for 1 year following completion of study.

21 CFR 54.2
Example

Investigator A agrees to conduct study for Sponsor S:

- S agrees to pay $9000 per patient
- A negotiates with Medical Center to pay $4000 for all study labs and radiology services
- If A enrolls 10 subjects, how much surplus is involved?
- Is surplus a significant payment of other sorts?
Investigator Feasibility Study

Investigator Perspective

- Develop comprehensive cost plan and budget
- Detail visits and services
- Negotiate best possible budget
- Up front payments
- Gain/(Loss)
Institutional Feasibility Study

Service Provider Perspective

- Reimbursement analysis
- Delineate whether items/services are standard care/research only
- Will supplies be purchased? Are they billable/reimbursable?
- Any potential non-covered service; ABN’s
- Does billing office have information for generating claims?
- How will the patient be identified at registration?
End of Clinical Trials
Part I

Questions/comments
Part II - Medicare Guidance for Clinical Trials Billing

- National Coverage Decision
- Other Medicare Coverage Principles
National Coverage Decision (NCD) History

**June 7, 2000.** Presidential executive order issued to CMS to “explicitly authorize [Medicare] payment for routine costs... and costs due to medical complications associated with participation in clinical trials.”

**Sep. 19, 2000.** CMS National Coverage Decision (NCD) for Clinical Trials became effective. Medicare covers:

1. the routine costs of qualifying clinical trials, and

2. reasonable and necessary costs to treat complications of any clinical trial
NCD What is qualifying trial?

Trial Requirements + Desirable Characteristics = Qualifying Trial
NCD - Qualifying Clinical Trials

**Trial Requirements**
- Does the subject or purpose of the trial fall into a Medicare benefit category?
- Does the study have a therapeutic intent?
- If therapeutic, does the study enroll diagnosed Medicare beneficiaries?
- Trials of diagnostic interventions may include healthy volunteers in a proper control group

**Desirable Characteristics**
1. Principal purpose is to improve health outcomes
2. Well supported by scientific and medical information
3. Doesn’t unjustifiably duplicate existing studies
4. Appropriate design to answer question
5. Sponsored by credible organization
6. Complies with Federal regulations relating to protection of human subjects.
7. Standards of scientific integrity apply to all aspects.
Some trials are deemed to have desirable characteristics:

- Trials funded by NIH, CDC, AHRQ, CMS, DOD, and VA
- Trials supported by centers or cooperative groups funded by above
- Trials performed under IND application
- IND exempt drug trials under 21 CFR 312.2(b)(1)
NCD - Proposed Qualification Process

- Trials not deemed must be certified by the Principal investigators that the criteria have been met and the trial should be enrolled in national registry before coverage initiated.

- AHRQ to develop criteria reflecting the desirable characteristics promulgated.

- In interim, only those trials have trial requirements and are deemed to meet criteria are afforded coverage under the NCD.

- Notification to CMS still required.
NCD – Notification Requirements

- Sponsors must identify themselves via e-mail to Clinicaltrials@cms.hhs.gov
- Trial sponsor’s name and contact info
- Info on the drug under study (name, route of administration etc)
- Disease being investigated
- Expected enrollment and length of trial
NCD - Routine Costs Defined

All items and services that are otherwise generally available to Medicare beneficiaries that are provided in either the experimental or control arms of a clinical trial.
Routine Costs DO NOT Include

- Items and Services Not Generally Available
  - Those lacking a Medicare benefit category
  - Those which are statutorily excluded
  - Those that fall under a national non-coverage policy

- Items/Services Not Covered
  - Investigational item or services itself
  - Those provided solely to satisfy data analysis and collection needs and are not used in direct clinical management of the patient
  - Those customarily provided free of charge by the sponsor to any participant
  - Those provided solely to determine trial eligibility
Routine Costs Include

- Those typically provided absent a clinical trial (conventional care)
- Those required solely for the provision of the investigational item or service
  - e.g. administration of non-covered chemotherapeutic agent
- Those required solely for the clinically appropriate monitoring of
  - Effects of investigational item, or
  - Prevention of complications
- Those needed for reasonable and necessary care arising from provision of investigational item or service
  - In particular, for diagnosis and treatment of complications
Misrepresentation of Trial As Qualifying

- Medicare coverage of routine costs denied
- Medicare trial enrollees would not be liable for the costs
- Billing providers would be liable for the costs where appropriate
- Billing providers and PI’s subject to fraud investigation
NCD
Billing and Coding Requirements

- **Professional Claims**
  - QV procedure code modifier for each line item representing routine costs
  - Diagnosis code V70.7 (only for healthy control group volunteers)

- **Hospital (Technical) Claims**
  - Diagnosis code V70.7 as secondary or tertiary diagnosis
  - Condition Code 30
  - Outpatient claims should also the QV modifier
  - G codes allow hospitals to report services furnished in outpatient departments
Billing provider must include in the beneficiary’s medical record:
- the trial name,
- sponsor’s name, and
- sponsor assigned protocol number

If medical review initiated, then a copy of the signed informed consent must be readily supplied upon request.

Copy of items and services billed as routine costs in clinical trial.
NCD – Are these routine costs?

- CT Scans to determine subject eligibility for a trial
- Administration of investigational drugs to an inpatient
- Lab tests to determine if an investigational drug has produced side effects
The standard care for a patient with uncomplicated diabetes is four physician visits per year. The patient enrolls in a related clinical trial involving a new drug that requires 8 physician visits for the year. The sponsor agrees to provide the drug and pay for any additional physician visits required by the protocol.

Can the physician continue to bill for the four visits identified as standard care?

Assuming this is a deemed trial under the NCD, what impact does that have on the claims submitted to insurance?

What if the sponsor agrees to fund all physician visits?
Other Medicare Coverage Principles

- Medical Device Rules
- Outside funding for clinical trials
- Traditional rules of coverage of routine costs
- Off-label drugs
Coverage of Medical Devices

Nov 1, 1995. Medicare coverage was expanded to certain medical devices being studied as part of a Food and Drug Administration (FDA) approved clinical trial. Under this new policy, the FDA and CMS established a more precise mechanism for classifying devices in clinical trials, making it possible for some of these devices to be eligible for Medicare coverage.

Section 731(b) MMA Act of 2003, expands ability of CMS to cover costs in device trials by authorizing coverage of “routine costs” in certain category A device trials, effective January 1, 2005.
Device Classifications

- **Category A**
  - Innovative devices for which the absolute risk has not been established; initial questions of safety and effectiveness have not been resolved.
  - CMS may cover routine costs (effective January 1, 2005), however the device costs remain excluded from coverage.

- **Category B**
  - Newer generations of proven technologies; evolutionary changes in proven technologies
  - CMS views as potentially reasonable and necessary, and therefore, **eligible** for coverage and payment.
Notification Requirements

- In order to submit claims for costs in any device trial, providers must notify the fiscal intermediary prior to enrolling patients.

- Must submit
  - IDE Device cover form
  - Signed copy of FDA approval letter
  - Copy of the sponsor’s protocol
  - Copy of the IRB approved consent form along with the IRB approval letter
Coverage Requirements

The following criteria will be applied when making coverage determinations on FDA approved IDE category B devices:

- Device must be used within context of an FDA-approved clinical trial
- Device must be used according to the clinical trial’s patient protocol
- Established national policy or local policy for similar FDA-approved devices
- Policy/position papers or recommendations made by pertinent national and/or local specialty societies
- Medically necessary and reasonable for the particular patient
- Furnished in a setting appropriate to the patient’s medical needs and condition.
Category B Device Trials
Coding and Reimbursement

- Professional claims should include the QA modifier (investigational device) and the investigational device exemption (IDE) number assigned by the FDA.

- Hospital claims should include the IDE and any charges associated with the device should be included in revenue code 624.

- Reimbursement for a device is limited to Medicare reimbursement for a comparable approved device.

- Deductible and coinsurance apply

Billing for an IDE means that the provider attests that the device was approved at the time the service was rendered.
Category A Device Trials

- Fiscal Intermediary shall determine if the Category A device as used in the trial is:
  - Intended for the diagnosis, monitoring or treatment of an immediately life-threatening disease or condition
  - Immediately life threatening requirement = “a stage of a disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.”

- Use NCD rules for defining routine costs
Professional claims should include the QV modifier (investigational device), ICD-9 diagnosis code V70.7 and the investigational device exemption (IDE) number assigned by the FDA.

Hospital inpatient claims
- IDE number
- Condition code 30
- ICD-9 diagnosis code V70.7
- Revenue code 624
- Outpatient claims should also include QV modifier

Deductible and coinsurance apply
How will Medicare reduce the DRG payment for a hospital admission to implant a category A device so that payment for the device is excluded?
Medicaid

- Coverage may vary state to state, but services provided must be medically necessary.
Commercial Payers

- Depends on participant’s contract with his/her insurance company. ... care provided must be medically necessary.
Other Medicare Coverage Principles

- **Outside funding**
  - Medicare Provider Reimbursement Manual 504.1 states that “where research is conducted in conjunction with or as part of the care of patients, the costs of usual patient care are reimbursable to the extent such costs are not met by research funds.”

- **Coverage of medically necessary services**

- **Off label drugs**
  - Medicare generally may cover FDA-approved drugs for indications other than those in the approved labeling, at the Fiscal Intermediary’s discretion.
  - Specific rules apply to anti-cancer drugs
Other Payment Related Issues

- **Informed Consent**
  - Cost section should accurately and effectively communicate any potential cost to the subject for participation in the clinical trial

- **Advance Beneficiary Notice**
  - Need in order to bill patient for denied standard care costs
End of Clinical Trials
Part II

Questions/comments
Part III – Clinical Trials
Billing Monitoring
Key Steps in Clinical Trials Monitoring

- Identify Clinical Trials for Review
- Data Collection
- Compile actual claims generated by service providers
- Billing Analysis
- Communicate results of audit to research and billing staff
Key Steps in Clinical Trials Monitoring

- Identify Clinical Trials for Review
  - Gather database of clinical trials
  - Choose selection criteria
    - Investigators
    - Trials
    - Patients
Key Steps in Clinical Trials Monitoring

- **Data Collection**
  - Participant names, medical record numbers, visit dates and service rendered
  - Budget identifying what services should have been paid by the study sponsor
  - Consent form (cost section)
  - Visit Schematic/Protocol
  - Clinical Trial Agreement
  - Financial Statements for the study account
Key Steps in Clinical Trials Monitoring

- Compile actual claims generated by service providers
- Billing Analysis
- Communicate results of audit to research and billing staff
  - Consider process improvements
Process Improvements to Prevent Billing Errors

- Reimbursement analysis for all protocol services
- Develop a billing grid delineating clinical billable items and services on a visit basis
- Develop a standardized research price list
- Identify contacts in service departments
- Coordinate consent form cost section language to billing grid results
- Consistent determination of NCD coverage or device trial coverage
- Develop deliverables for communicating to billing and coding departments
Process Improvements – Cont’d

- Identify clinical trial participants at registration
- Research specific order forms/charge tickets
- Develop registry of clinical trial participants with study visit dates for use in billing operations
- Include billing offices in the grant/study account close-out process
- Routine monitoring of clinical trials billing
The End – Zzzzzzzzzzzz

Questions/Comments