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Draft Guidance for the Public, Industry, and CMS Staff

Factors CMS Considers in Making a Determination of Coverage with Evidence Development

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Public Comment: Electronic comments may be submitted to CAGInquiries@cms.hhs.gov. Alternatively, written comments may be submitted to the Coverage and Analysis Group, Centers for Medicare and Medicaid Services, mailstop: C1-12-28, 7500 Security Blvd. Baltimore, Md. 21244. Please refer to this guidance document when submitting comments. In order to ensure consideration, comments must be received by June 6, 2005.

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I. Purpose of this Guidance Document

The purpose of this guidance document is to describe factors CMS may consider in a decision to extend national coverage for certain items and services with coverage linked to a requirement for prospective data collection. This approach is referred to as coverage with evidence development (CED). The primary purpose of obtaining additional evidence through CED is for the agency's use in making payment determinations, i.e., that a treatment is reasonable and necessary. This document focuses on why we are collecting this data for Medicare payment purposes.

CMS is issuing this draft guidance document with the recognition that the linkage of national coverage decisions with data collections requirements had not been done frequently by CMS or other major payers. It is our intention to work intensively and carefully with all affected stakeholders to ensure that this approach achieves its objectives of improving the health of beneficiaries by enhancing access to medical technologies and services that improve health outcomes. We do not anticipate a substantial number of new coverage decisions in the near future that apply the data collection requirement. However, for transparency and for the most effective use of this kind of coverage decision, we are seeking more extensive public comment beyond the context of specific coverage decisions to refine and clarify the initiative. We expect the initiative to continue to be applied in specific cases where better evidence to support decision making by patients and clinicians is an essential part of reaching a conclusion that a treatment is reasonable and necessary.

II. Background

A. The National Coverage Determination (NCD) process

The process for the development of NCDs is described in detail in a September 26, 2003 Federal Register Notice[1]. Briefly, after a request for national coverage is approved, internal and external experts, including clinicians and researchers, review the available scientific and clinical evidence to determine the effectiveness of the item or service in question. A judgment about the adequacy of evidence for making coverage decisions depends on the methodological quality of the available research and the magnitude of the effect of an item or service on specific clinical outcomes. Using the principles of evidence-based medicine, the aggregate evidence is used to draw conclusions about whether the item or service under review is "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member."[2] We intend to discuss in greater detail the interpretation of "reasonable and necessary" in the context of coverage determinations in future guidance documents. In general, the core consideration in determining when an item or service is "reasonable and necessary" is the quality of the evidence available to assess whether it improves net health outcomes.

The NCD process results in three broad types of possible coverage decisions:

- *Non-coverage.* The evidence is not adequate to conclude that the item or service improves net health outcomes for the patient.

- *Coverage with conditions.* The evidence is adequate to conclude that the item or service improves net health outcomes only under the following specific circumstances:

  - The service is delivered to patients with specific clinical or demographic characteristics. Coverage of an item or service may be limited to patients with certain diseases, severity levels, age, or other factors.

  - The service is delivered by providers and/or facilities that meet specific criteria. Coverage may be limited to facilities or providers that have documented the competencies necessary to safely and effectively provide the technology or service in question.

  - The service is delivered in the context of specific data being collected. Coverage may be limited to providers who participate in and beneficiaries who are enrolled into a defined prospective data collection activity, when this data collection activity constitutes part of the evidence required to ensure the item or service provided to that patient is reasonable and necessary.

- *Coverage without conditions.* The evidence is adequate to conclude that the item or service improves net health outcomes for all patients with a particular clinical condition.

[1] http://a257.g.akamaitech.net/7/257/2422/14mar20010800/edocket.access.gpo.gov/2003/pdf/03-24361.pdf
[2] Social Security Act § 1862(a)(1)(A).

There are a number of older national coverage decisions that do not provide any conditions for coverage. CMS does not anticipate issuing additional decisions of this type.

B. Purpose of linking coverage with a requirement for data collection

CMS is committed to ensuring that advances in medical technology are available for its Medicare beneficiaries while also ensuring the care they receive is reasonable and necessary—a necessary condition for payment. The coverage with evidence development initiative is intended to enable Medicare to provide payment for items and services under conditions that help assure significant net benefits of the treatment for beneficiaries, and to give rise to additional information. This evidence will also assist doctors and patients in better understanding the risks, benefits and costs of alternative diagnostic and treatment options. Consequently, the linkage of coverage to data collection will also help to ensure that individual patients are receiving care that is reasonable and necessary given their specific clinical situation.

CMS believes that systematic, protocol-driven data has the potential to increase the likelihood of improved health outcomes. Care provided under these protocols generally involves greater attention to appropriate patient evaluation and selection, as well as the appropriate application of the technology. These additional data may alter the course of patient treatment based on the best available evidence, and may lead a physician to reconsider the use of the item or service or otherwise alter a patient's management plan, potentially improving health outcomes.

There is growing recognition that the rapid adoption of promising new technologies that improve outcomes could be promoted by linking technology diffusion to timely demonstrations of the value of new technologies in actual practice involving Medicare beneficiaries. As the pace of the introduction of a broader range of diagnostic tools and therapeutic interventions quickens, the demand for better information about their effectiveness for particular types of patients becomes even more urgent. Better evidence will help doctors and patients get the most benefits at the lowest possible cost in our increasingly complex and individualized health care system.

It is often the case that the benefit of a technology or service will be demonstrated in a specific population of patients, sometimes broad and sometimes narrow. Additional studies may be useful to better targeting those patients who benefit most in a broad population, or to identify additional patients who benefit beyond a narrowly studied population. Such studies may also identify patient characteristics associated with higher than average risk for poor outcomes. These types of practical questions are difficult to answer in a pre-market setting; they are best addressed in actual medical practice, where actual conditions of use and patient characteristics may differ significantly from those in a pre-market formal clinical trial. Together, these factors highlight the value of a systematic expansion of practical clinical research efforts to address the information needs of health professionals and patients.

As patients make more of their own health care decisions and clinicians become increasingly accountable for the quality and efficiency of the care they provide, a greater supply of reliable information on the risks, benefits and costs of the various treatment alternatives becomes critical to the provision of health care. Data produced as a consequence of linking

coverage to evidence development is intended primarily to determine whether an item or service continues to be reasonable and necessary. In addition, it will provide useful information to doctors and patients faced with complicated clinical decisions and the need to personalize those decisions for individual patients. As data accumulates, it will become increasingly useful in managing each individual patient from whom the data is collected, as well as all other Medicare beneficiaries with similar clinical conditions. Such benefits are clearest for patients with chronic conditions who are on some form of ongoing treatment (e.g., an implanted device or a long-term therapy). These patients may be particularly well served by new information produced regarding side-effects or complications of treatments that they continue to use. Well designed studies may occasionally provide evidence compelling enough to revise coverage decisions to more accurately identify additional patients who may or may not benefit from the treatment, e.g., to support coverage expansions to other, similar patients.

The potential value of information generated through coverage linked to evidence development must be carefully considered in the context of the burden associated with the collection of this data. It is critical that appropriate study methods be applied that produce sufficiently reliable information for the targeted decision makers. Value of information analysis is a formal approach to assessing the burden versus benefits of doing additional studies, and CMS plans to carefully consider the features of this approach in applying coverage with evidence development. Data collection should only continue as long as important questions remain and it is determined that the effort and resources required to collect this data are justified by the potential value of the information that will be generated. In addition, data collection required through coverage decisions should be aligned with any clinical study requirements associated with FDA review. We also plan to carefully consider all ongoing publicly and privately funded clinical studies to ensure that there is a need for additional data collection that is linked to coverage. The availability of information from other studies, whether for FDA safety/effectiveness review or other purposes, is an important consideration in determining the value of information potentially generated in the context of NCDs. Conversely, support for post-coverage evidence development to achieve a reasonable and necessary determination may help address important questions of safety and effectiveness that otherwise would be very difficult to address in the premarket setting, or in the postmarket setting in the absence of CMS support.

As noted above, any evidence development requirements should not only assure that the expected benefits of the evidence outweigh the costs, but also assure that no unnecessary costs are imposed. To minimize the financial and other resources required, careful attention must be paid to collecting the minimum data necessary to answer specific questions. Collecting that data should use the least resource-intensive mechanisms possible. The use of routinely collected data from administrative sources represents an important potential efficiency in the conduct of evaluations linked to coverage decisions. Finally, greater adoption and use of health information technology by providers in all settings has the potential to significantly reduce the burden associated with observational and experimental data collection. This will significantly enhance our ability to simultaneously speed adoption while developing better, more individualized evidence about new medical technologies and services.

CMS has applied a limited number of determinations of coverage with evidence development with the intent of assisting CMS and its contractors in determining whether an item

or service is reasonable and necessary and achieving a further goal – faster and broader, more effective access to new medical technologies. Rather than waiting for definitive studies to be completed to address all key questions related to whether the use of a particular technology is reasonable and necessary, CMS can now provide coverage along with an assurance that appropriate data will be collected to ensure that the item or service is reasonable and necessary and to answer specific, important remaining questions. The ability of this approach to expedite access to technologies and services is further described in each of the cases of coverage decisions reviewed below.

It is not the intent of this approach to reduce the importance or frequency of local coverage determinations as a pathway by which new technologies are made available in the Medicare program. We also do not anticipate circumstances under which CED would represent a net reduction in coverage available under existing local coverage policies.

C. Legal authority for coverage with evidence development

The statutory authority for linking coverage decisions to the collection of additional data is derived from Sec 1862(a)(1)(A) of the Social Security Act, which states that Medicare may not provide payment for items and services unless they are "reasonable and necessary" for the treatment of illness or injury. In some cases, CMS will determine that an item or service is only reasonable and necessary when specific data collections accompany the provision of the service. In these cases, the collection of data is required to ensure that the care provided to individual patients is likely to improve health outcomes.

There are two general circumstances under which clinical care provided may only be considered reasonable and necessary in the context of protocol-driven data collection. First, a particular medical intervention may have been demonstrated to improve health outcomes in a broad population of patients, but the evidence would only be adequate, and the service therefore reasonable and necessary for the individual patient, when specific data is collected and reviewed by the provider at the time that the service is delivered. This additional evidence, in conjunction with published scientific evidence and other information available to the physician and patient, would be used to support appropriate treatment decisions for such patients. This is consistent with the general application of additional data in the evaluation and management of patients. Conclusions are reevaluated as additional data are obtained from other tests or results from therapeutic interventions. The additional data may alter the interpretation of the original conclusions. Likewise, the information collected may require the physician to reevaluate the original conclusions, alter the management plan, and potentially improve health outcomes. Data collected at the time of treatment may also be important in ensuring that a patient's care is reasonable and necessary over a period of months and years. This is particularly true for treatments, procedures and implantable devices provide to patients with chronic medical conditions. An example of the first general circumstance in which data collection is linked to coverage is the recent NCD on implantable cardioverter defibrillators.

- *Coverage of ICDs*[3] – Two major trials reported since 2002, the MADIT II trial and the SCD-HeFT trial, demonstrated the mortality benefits of ICD implantation in many patients with severe ischemic or non-ischemic cardiomyopathy. Even with these high quality randomized trials, many important questions remain about which patients are most likely to derive benefit from the device. For example, the benefit for patients with LVEF between 31 and 35 percent and with class IV heart failure has been less conclusively demonstrated, as is the optimal timing for ICD implantation with respect to an acute myocardial infarction. Rather than wait for additional trials to be completed to answer these questions, CMS decided on a broad expansion of coverage for prophylactic use of ICDs linked to a requirement for additional data collection that can help assure effective follow up of these patients over time, as experience accumulates. The collection and review of baseline data by the implanting physician will help ensure that individual patients are being provided with care that is appropriate to their clinical circumstances and delivered by skilled, informed providers. The data gathered in this way should also help provide additional information over time on the risks and benefits of the procedure in patient subgroups, more data on the performance of specific types of devices, and helpful insights into the role of provider training and experience in procedure-related complications.

  Submission of clinical data about patients receiving an ICD for primary prevention to a data collection process provides assurance of patient safety and protection, helps providers improve care and follow up for patients who receive implants, and helps physicians and patients make decisions that reflect a better understanding of the outcomes and natural history of devices in particular types of beneficiaries. CMS implemented this initial registry using an existing electronic data submission system present in all hospitals so that the incremental cost is quite low and participation is broadly available.

The second general circumstance is when a particular medical intervention has yet to conclusively demonstrate an improvement in health outcomes, but existing information clearly suggests the intervention may provide an important benefit. In this case, CMS may determine that the adequacy of the evidence demonstrating improved health outcomes can only be assured if additional data is collected, reviewed and submitted at the time of the service. Thus, CMS may decide that the service is reasonable and necessary only in the context of additional data collection, because the additional care in clinical decision making and monitoring of the patient offers greater assurance that the benefits of receiving the service will exceed the risks. This type of coverage decision will generally represent faster and broader access to medical technologies and services compared to the alternative of non-coverage. Following are two examples of recent NCDs in which this approach was applied by Medicare--the coverage of anti-cancer drugs approved for colorectal cancer in specific NCI-sponsored clinical trials and the coverage of FDG-PET scanning for specific cancer indications.

- *Coverage of off-label, unlisted uses of drugs approved for colorectal cancer*: Medicare contractors generally cover all off-label uses of anti-cancer drugs listed in specific pharmaceutical compendia. In general, uses not listed in these compendia may be covered or non-covered at contractor discretion. In another recent decision, CMS

[3] http://www.cms.hhs.gov/mcd/viewdecisionmemo.asp?id=148

determined that off-label, unlisted uses of four drugs approved for use in colorectal cancer would be covered by all contractors if the patients receiving these drugs were enrolled in one of nine NCI-sponsored clinical trials. Contractors continue to have the flexibility to cover the off-label, unlisted uses for patients not enrolled in the NCI trials. In this case, a sufficient inference of benefit could support provision of coverage for patients treated in accordance with the protocols developed for the nine NCI-sponsored clinical trials. We based this inference on the evidence of safety and effectiveness of the chemotherapy for the FDA-labeled use, the decision by NCI to conduct a trial for additional uses, and the additional patient protections provided to patients receiving protocol-driven care.

The NCI trials provide rigorous safeguards for patients, and ensure patient evaluation and selection and reasonable use of cancer chemotherapy. Trial designs include an adequate plan for data and safety monitoring and ensure individualized analysis and evaluation of patients' response to chemotherapy and their health status. We therefore concluded that coverage for off-label use of chemotherapy could provide clinical benefits to Medicare beneficiaries with cancer, and that the information generated by these trials would be of great value to assisting clinicians and patients in making more informed decisions about the studied off-label uses once the results became available. The national coverage linked to data collection again represents a net expansion of coverage because it ensured that all contractors would provide coverage for any patient enrolled in the NCI trials, while also leaving in place the current discretion available to contractors in coverage off-label, unlisted uses of anti-cancer drugs in other settings. The particular trials selected in concert with the NCI do not represent all trials of these drugs that may have value to Medicare beneficiaries and we are interested in some systematic way of obtaining input of current and planned clinical studies. We are also interested in ways to learn more from our local coverage decisions.

- *FDG-PET for use in cancer diagnosis, staging and monitoring:* We previously determined that the evidence was not adequate to *reach* a conclusion that FDG PET scanning is reasonable and necessary for diagnostic use in all cancer, but that coverage was justified for a substantial number of malignancies and specific clinical indications with certain data collection requirements. This conclusion reflected extensive input about the state of relevant medical evidence from cancer experts and the public.[4] Based on studies of FDG PET's usefulness as a cancer biomarker and for cancer staging and diagnosis, CMS now provides coverage if certain patient safeguards for patients are provided, including mandatory collection of clinical data. Under these circumstances, FDG-PET has the potential to improve health outcomes by influencing patient management; and by helping physicians appropriately evaluate the PET scan results in the context of critical relevant clinical information. Without the data collection requirement, CMS would have continued adding coverage for specific clinical use of FDG-PET in cancer as each of these potential uses was demonstrated through well-designed clinical trials to influence patient management and alter patient outcomes. This could be a time-consuming process, with the result that many Medicare beneficiaries with cancer would not have the benefit of more definitive evidence on the specific

[4] http://www.cms.hhs.gov/mcd/viewdecisionmemo.asp?id=92

circumstances in which PET scanning has clinical utility. With the evidence requirement, considerably broader coverage may be available much sooner, and the data collected in this process will support better clinical decision making as it becomes available. As stated earlier, CMS believes that systematic, protocol-driven data also has the potential to increase the likelihood of improved health outcomes. Care provided under these protocols generally involves greater attention to appropriate patient evaluation and selection, as well as the appropriate application of the technology.

III. Factors Considered in Applying CED

In general, CMS will consider requiring data collection as a condition of coverage when additional information is needed for CMS and its contractors to determine if an item or service is reasonable and necessary.

CMS intends to work consultatively and iteratively with external experts and stakeholders in developing the criteria and process for determining when to apply CED. In the short term, we are aiming to identify a small group of high priority pilot efforts on topics for which there is substantial agreement that better evidence would be valuable in expanding access to specific technologies and services while learning more about their risks and benefits to support shared decision making.

An initial list of circumstances in which coverage with data collection might be valuable includes:

- The item or service is likely to provide benefit, but there are substantial safety concerns or potential side effects that are inadequately described in the available clinical literature.

- The risks and benefits for off-label uses of an item or service have not been adequately addressed in the available clinical literature, particularly when risks are common or potentially common.

- The available clinical studies may not have adequately described risks and benefits in specific patient subgroups, or in patients with disease characteristics that exclude them from clinical trials, which make up significant segments of the Medicare beneficiary population likely to receive the treatment if covered.

- Assessment of important outcomes has not been evaluated in the available clinical studies. These outcomes may include, but are not restricted to, long-term risks and benefits, quality of life, utilization, costs, and other real-world outcomes.

- Risks and benefits of surgical procedures may not be extensively evaluated because limited information about benefits and risks has been developed for many categories of Medicare beneficiaries. For example, some non-invasive FDA-approved devices may be well characterized in terms of safety, but less well studied in terms of clinical effectiveness in a pre-market setting for certain Medicare beneficiaries under the FDA risk-based regulatory

framework. The nature of device development and evolution, in which clinical experience leads to further product modifications that are expected to improve outcomes, often highlights the importance of post-market evidence development.

- Comprehensive evidence of effectiveness of treatments for rare diseases is not always available or feasible to develop in a pre-market setting. It may be beneficial to evaluate interventions for rare conditions such as use of orphan drugs and humanitarian use devices.

- When the current evidence is not generalizable to providers/facilities or the Medicare population has not been included in the available clinical studies, new evidence development may help evaluate the safety and benefit of requested items and services for our beneficiaries.

- There may remain questions about the comparative effectiveness of new items and services compared to existing alternatives or to usual care.

- The evidence to date shows statistically significant benefits but the clinical significance of the outcomes may not be well understood.

***Questions for the public*:**

- What other circumstances would be appropriate for consideration of CED, and what other factors and criteria should be considered?

- Can these factors and criteria be put in order of importance? How could CMS or other best determine their relative importance?

- Are there situations listed above that would be unlikely to be constructively addressed through evidence collection linked to coverage decisions?

- How can formal 'value of information analyses' be applied to help decide when to require data collection following a coverage decision?

- Are there other ways the data may serve to improve available evidence of safety and benefit of an item or service or improve the decision making process?

- Are there existing approaches to priority setting for clinical studies that could serve as a model for identifying priorities for CED?

- Should the focus of these activities be only on new technologies and services, or the entire spectrum of technologies and services?

IV. Process for Deciding When and How to Apply CED

CMS intends to apply CED to issues with the greatest potential benefit for Medicare beneficiaries and the Medicare program. Establishing those priorities may be accomplished with input from a wide range of experts and stakeholders, including:

- Patient advocates, consumer representatives and citizens
- Clinical experts, scientists, and technical experts
- Product developers and manufacturers
- Federal and state policy makers
- Medical professional associations and practicing clinicians
- Health plans, physicians group practices, hospitals, purchasers and employers
- Experts and advisory groups affiliated with FDA, NIH, AHRQ, CDC, DoD, and other Federal agencies
- State Medicaid programs, the VA and other public and private health care delivery systems
- The Medicare Coverage Advisory Committee, the Practicing Physician Advisory Committee, and other FACA-compliant health-related advisory committees

***Questions for the public*:**

- Are there other stakeholder groups that should be included in discussions of priority setting?
- What procedures and forums would be most effective for obtaining public input in this decision making process?
- Are there existing mechanisms and processes that would serve as a useful model for obtaining public input to identify and prioritize topics for CED?
- Should there be a process for requesting national coverage decisions with evidence development, and how should such requests be prioritized?

V. Evidence Development Methods

Developing methods for conducting simple, inexpensive clinical studies is essential to optimizing CED. CMS will avoid stipulating the use of a particular design, recognizing that data

collection protocols will vary according to use of the item or service being provided, the purpose of the data collection, and the group of patients receiving the item or service.

We will encourage well thought out study designs for linking coverage to evidence development that adhere to scientific, medical, and ethical principles. In general, we would seek to use de-identified data for all analyses, and all necessary procedures will be followed to ensure full protection of patient confidentiality. We recommend that providers, scientists, and other stakeholders collaborate to develop innovative study designs.

The following is a list of study designs that may be used to develop an evidence base:

- *Databases* – Databases require entry of baseline data concomitant with provision of the item or service. Primarily, they are used to monitor patient safety and benefit and provide feedback to physicians. They are often a routine part of providing quality patient care. In these instances, patients are not exposed to new risks.

- *Longitudinal or cohort studies* – In this study design, patients are followed over time after baseline clinical information is collected. They do not have a formal, randomized comparison group. Prospective studies can provide long term evaluation of patient safety. They can develop evidence on the course of disease for treated patients for a longer period of time than can most clinical trials. As a secondary use of the data, the course of disease with use of an item or service can be evaluated among patient subgroups within the cohort. These studies are often a routine part of quality patient care, and do not expose patients to any new risks.

- *Prospective* comparative *studies* (also called 'practical clinical trials'[5]) – These studies require a formal comparison group, can include randomization, and can be used to evaluate a broad range of real-world outcomes such as quality of life or cost effectiveness in addition to monitoring patient safety and benefit and informing decision making. Types of prospective studies include head-to-head comparisons; studies that evaluate payment mechanisms; and observational studies that compare the new item or service to usual care. These studies may also involve FDA-approved treatments or may be parts of routine quality improvement initiatives in health care organizations; and do not remove any covered benefits for patients.

- *Randomized clinical trials (RCTs) – RCTs* require rigorous study design and oversight. They are costly and generally limited to small groups of patients with specific entry criteria. They provide the best evidence of effectiveness when they are well conducted. These studies involve the most intense safety monitoring, because they may involve cases (as noted above) where the evidence on the benefits and risks of a treatment is uncertain. However, RCTs often provide evidence limited to patients with specific characteristics, such as those with younger ages and fewer comorbidities, that has limited their applicability to the general Medicare population.

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[5] Tunis SR, Stryer DB, Clancy CM. Practical clinical trials: increasing the value of clinical research for decision making in clinical and health policy. JAMA. 2003 Sep 24;290(12):1624-32.

As a general matter, observational studies may be most helpful for describing the "natural history" of patient outcomes in a treated population, including development of better evidence on whether particular types of patients are likely to have important side effects. In contrast, studies involving some form of randomization may be required to provide more definitive evidence on effectiveness or comparative effectiveness in particular types of patients.

***Questions for the public*:**

- What other study designs should be considered?
- What type of questions is each study design best able to answer?
- What are the limitations of each study design?
- Under what circumstances should CMS require a database? A longitudinal data collection? A prospective study? A clinical trial?
- What process should CMS use to evaluate the quality of a proposed study design?
- How should CMS determine whether the evidence collected suggests patients are either harmed or not benefited by the item or service?

VI. Process for Study Design and Implementation

When CMS requires evidence development, we should be assured that there is appropriate oversight of data collection enterprises and an efficient operations system.

Issues important in oversight and operations of evidence development include:

- *Qualified scientific oversight* – Each evidence development enterprise should appoint an individual with appropriate clinical, scientific, and technical expertise to oversee all aspects of the data collection.
- *Hypotheses* – The data collected[6] should be based on hypotheses integral to the evaluation of clinical safety and benefit of the item or service to the patient and provide information for physician decision making.
- *Data collection methods* – Data collection methods should be pre-specified in a protocol. Data could be collected using questionnaires or other instruments, web based data collection systems, or medical record abstraction[7].

[6] Under the Privacy Act, all data collected under CED, will be announced in a System of Records Notice.
[7] Under the Paper work Reduction Act, data collection instruments, electronic or otherwise, will be submitted to OMB for approval.

- *Sample size* – The sample size should be large enough to make inferences about safety and benefit of the item or service and physician and patient decision making.

- *Patient safety and monitoring* – There should be adequate oversight of patient safety and monitoring during the life of the data collection enterprise. For clinical trials involving patient randomization, this should be a data safety and monitoring board.

- *Timeframe* – There should be a start and end date based on estimates of the time it would take to collect enough data to make inferences about safety and benefit of the item or service and physician decision making.

- *Training* providers *and others* – Providers involved in the evidence development enterprise must be educated about the reasons for the study, receive training about data collection, and be informed of all aspects of the study's purpose and design.

- *Patient* confidentiality *and protection* – All necessary measures should be taken to ensure patient privacy. When appropriate, there should institutional review and informed consent.

- *Data security and quality assurance* – There should be intrinsic measures taken to maintain patients' data security. There should be a data auditing system to ensure data integrity for continuous quality improvement.

- *Efficiency and data collection burden* – Data collection instruments should be designed to minimize any burden to providers and patients while providing critical information. Data elements should be disease and technology-appropriate. There should be no redundancies in the data collection system. Existing data systems should be used when available to avoid expending resources on creating new data systems. In addition, wherever possible, efforts should be made to use existing health information technology to support implementation of these studies. In many cases, it will be possible to link administrative data to data gathered for registries and practical trials, significantly expanding the value of the aggregate information collected and reducing the burden of data collection. Further progress in adoption and use of health IT will contribute substantially to the goal of getting better evidence in the process of delivering health care services.

Questions for the public:

- Who should participate in study oversight and implementation?

- How should CMS determine the qualifications of investigators involved with coverage evidence development?

- What are other important oversight and operational issues?

- What are the major oversight and implementation issues?

- What approaches to study design and implementation would be least costly and most efficient? What are some specific ideas for minimizing the resources required for conducting these studies, while generating the maximum amount of useful information?

- What parameters are needed to evaluate operational issues?

- What criteria should CMS use to assess the appropriateness of the above operational issues involved in evidence development?

- How should CMS determine when the data collection should end?

- Who should have access to the data and in what form?

- How will evidence collected through CED be disseminated?

- How should the costs of study design, data collection, analysis and other activities associated with these programs be fairly allocated to various stakeholders?

- How can CMS best ensure that these studies are implemented in a way that is compatible with current public and private efforts to promote effective and consistent adoption and use of health IT?