Supporting Statement Part A
Medicare Coverage of Items and Services for Coverage with Evidence Development
(CMS-10697; OMB 0938-NEW)

Background

CMS has several policy vehicles relating to evidence development activities including the investigational device exemption (IDE), the clinical trial policy (CTP), national coverage determinations (NCD) and local coverage determinations (LCD), and coverage with evidence development (CED) through the national coverage determination process.

The Medicare program has adopted coverage policies that relate to clinical studies before the formal articulation in 2006 of the CED paradigm. In 1995, CMS (then known as the Health Care Financing Administration (HCFA)) established coverage for certain items furnished in FDA-approved IDE trials (42 CFR 405 Subpart B). CMS updated the coverage criteria for certain items and services in IDE trials effective January 1, 2015 (78 FR 74429-74437). In response to a June 7, 2000 Executive Memorandum, CMS (then HCFA) issued an NCD for coverage under the authority of section 1862(a)(1)(E) of routine costs in clinical trials, commonly referred to as the Clinical Trial Policy (Section 310.1 of the NCD Manual). The Clinical Trial Policy was revised in 2007 through the NCD reconsideration process.

In 2005, CMS began to implement NCDs requiring study participation (for example: NCD Manual §50.3 Cochlear Implantation Moderate Hearing Loss; NCD Manual §220.6.13 FDG PET for Dementia and Neurodegenerative Diseases). Subsequently, CMS issued guidance on the CED paradigm in the 2006 guidance document entitled National Coverage Determinations with Data Collection as a Condition of Coverage: Coverage with Evidence Development.

While CMS has embraced an evidence-based medicine coverage paradigm, CMS is increasingly challenged to respond to requests for coverage of certain items and services when we find that the expectations of interested parties are disproportionate to the existing evidence base. At the same time, we believe that CMS should support evidence development for certain innovative technologies that are likely to show benefit for the Medicare population, but where the available evidence base does not provide a sufficiently persuasive basis for coverage outside the context of a clinical study, which may be the case for new technologies, or for existing technologies for which the evidence is incomplete.

Coverage in the context of ongoing clinical research protocols or with additional data collection can expedite earlier beneficiary access to innovative technology while ensuring that systematic patient safeguards, including assurance that the technology is provided to clinically appropriate patients, are in place to reduce the risks inherent to new technologies, or to new applications of older technologies.

CMS is requesting OMB approval for this new collection of information.

The PRA package currently under review is for coverage with evidence development (CED). The CED process had been in operation since 2005 under 1862(a)(1)(E) of the Act. Early on, we had only 2 CED National Coverage Determinations (NCDs) that required data collection in registries, both of which had publically available data collection forms. Currently, we have approved nearly 100 CED research studies that involve complex data collections, most of which are proprietary to the study sponsor.

There is no specific form associated with submission to set up a CED clinical study. However, to be approved for setting up a CED clinical study, any submission must satisfy each of the "A – M" provided in the online Guidance Document, "Guidance for the Public, Industry, and CMS Staff: Coverage with Evidence Development" (https://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?MCDId=27). Although the criteria set out in the Guidance Document are not written in statute, the authority that gives CMS the ability to approve applications to set up a CED, and require satisfaction of criteria (A) – (M) is a statue, viz., Section 1862(a)(1)(E) of the Social Security Act. Criteria (A) – (M) in the Guidance Document state:

A. The principal purpose of the study is to test whether the item or service meaningfully improves health outcomes of affected beneficiaries who are represented by the enrolled subjects.
B. The rationale for the study is well supported by available scientific and medical evidence.
C. The study results are not anticipated to unjustifiably duplicate existing knowledge.
D. The study design is methodologically appropriate and the anticipated number of enrolled subjects is sufficient to answer the research question(s) being asked in the National Coverage Determination.
E. The study is sponsored by an organization or individual capable of completing it successfully.
F. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found in the Code of Federal Regulations (CFR) at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it is also in compliance with 21 CFR Parts 50 and 56. In addition, to further enhance the protection of human subjects in studies conducted under CED, the study must provide and obtain meaningful informed consent from patients regarding the risks associated with the study items and/or services, and the use and eventual disposition of the collected data.
G. All aspects of the study are conducted according to appropriate standards of scientific integrity.
H. The study has a written protocol that clearly demonstrates adherence to the standards listed here as Medicare requirements.
I. The study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Such studies may meet this requirement only if the disease or condition being studied is life threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.
J. The clinical research studies and registries are registered on the www.ClinicalTrials.gov website by the principal sponsor/investigator prior to the

enrollment of the first study subject. Registries are also registered in the Agency for Healthcare Quality (AHRQ) Registry of Patient Registries (RoPR).

K. The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 12 months of the study's primary completion date, which is the date the final subject had final data collection for the primary endpoint, even if the trial does not achieve its primary aim. The results must include number started/completed, summary results for primary and secondary outcome measures, statistical analyses, and adverse events. Final results must be reported in a publicly accessibly manner; either in a peer-reviewed scientific journal (in print or on-line), in an on-line publicly accessible registry dedicated to the dissemination of clinical trial information such as ClinicalTrials.gov, or in journals willing to publish in abbreviated format (e.g., for studies with negative or incomplete results).

L. The study protocol must explicitly discuss beneficiary subpopulations affected by the item or service under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations in the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.

M. The study protocol explicitly discusses how the results are or are not expected to be generalizable to affected beneficiary subpopulations. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Our goal is to consolidate and simplify the process so that the CED data collection is directly and explicitly related to the 13 "A-M" standards identified above. This proposed PRA notice is to describe to the public the process used to request coverage for a CED project.

A. Justification

1. Need and Legal Basis

The legal basis of CED comes from Section1862(a)(1)(E) of the Social Security Act (42 U.S.C. 1395y), which states that "in the case of research conducted pursuant to section 1142, which is not reasonable and necessary to carry out the purposes of that section."

While the intent of these CED NCDs was to monitor the appropriateness of use of these items and services, we recognized that the data could also be used to generate useful clinical evidence. More recent NCDs have tended to rely on section 1862(a)(1)(E) of the Act, in which CED is used to support clinical research.

Section 1142 of the Act describes the authority of the Agency for Healthcare Research and Quality (AHRQ) to conduct and support research on outcomes, effectiveness, and

appropriateness of services and procedures to identify the most effective and appropriate means to prevent, diagnose, treat, and manage diseases, disorders, and other health conditions. That section includes a requirement that the Secretary assure that AHRQ research priorities under Section 1142 appropriately reflect the needs and priorities of the Medicare program.

2. Information Users

CMS uses the 13 criteria to determine the validity of the CED. It is important that the CED is of the highest quality because CMS uses the information generated from CED for the following:

- Results from studies required under CED inform medical decision-making and improve patient care.
- Data from CED studies that are published in the medical literature may be used by CMS to make evidence-based changes to the NCD.
- Data generated from CED required registries are used by researchers to advance the field specific to the NCD.

For example, criterion D ,"The study design is methodologically appropriate and the anticipated number of enrolled subjects is sufficient to answer the research question(s) being asked in the National Coverage Determination," minimizes the risk of confounding factors influencing study results, and thus contributes to informed decision-making and improved patient care. Moreover, results from methodologically appropriate studies optimizes the probability that CED studies are published in the medical literature and may be used by CMS to make evidence-based changes to NCDs.
Criterion M, "The study protocol explicitly discusses how the results are or are not expected to be generalizable to affected beneficiary subpopulations. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility," ensures that results from a CED study informs CMS what subpopulation will be benefit from this device and if it's generalizable to the Medicare population. This will assist CMS in making national coverage determinations and improve patient care.

3. Use of Information Technology

Electronic submissions (i.e. email with attachments to the NCD analysts) are preferable. CMS also accept hard-copy.

4. Duplication of Efforts

CEDs are not regulated by any other Federal agency. Therefore, there is no duplication of effort and similar information is unavailable.

CMS uses different evaluation criteria than FDA. FDA's concern is safety and effectiveness. CMS evaluates the efficacy and health outcomes. CMS cooperates with FDA and share information. We always ask sponsor submit FDA approval letter with FDA's recommendations if it's available.

5. Small Businesses

These regulations apply to all firms, institutions or individuals involved in conducting clinical studies of medical devices, regardless of the size of the organization. Some manufacturers and study sponsors may be small businesses.

6. Less Frequent Collection

In general, requesters send us one protocol. We often work interactively with CED requesters to revise the protocol. Once the submission to set up a CED has been approved, CMS reviews the evidence through various means. Occasionally, there are approved information collections for specific CEDs (TAVR and TMVR). In such cases, CMS may formally contract with investigators to purchase registry data. When the CED clinical study is complete, CMS may use claims data associated with the clinical study, the clinicaltrials.gov study report and/or peer-reviewed publications to evaluate whether the information provided by the clinical study supports approval of the National Coverage determination (NCD) with which the CED is associated.

7. Special Circumstances

There are no special circumstances that would require an information collection to be conducted in a manner that requires respondents to:

- Report information to the agency more often than quarterly;
- Prepare a written response to a collection of information in fewer than 30 days after receipt of it;
- Submit more than an original and two copies of any document;
- Retain records, other than health, medical, government contract, grant-in-aid, or tax records for more than three years;
- Collect data in connection with a statistical survey that is not designed to produce valid and reliable results that can be generalized to the universe of study,
- Use a statistical data classification that has not been reviewed and approved by OMB;
- Include a pledge of confidentiality that is not supported by authority established in statute or regulation that is not supported by disclosure and data security policies that are consistent with the pledge, or which unnecessarily impedes sharing of data with other agencies for compatible confidential use; or
- Submit proprietary trade secret, or other confidential information unless the agency can demonstrate that it has instituted procedures to protect the information's confidentiality to the extent permitted by law.

8. Federal Register/Outside Consultation

The 60-day Federal Register Notice was published 6/04/2019 to the Federal Register [84 FR 25810].
No comments were received during this public comment period.

The 30-day Federal Register Notice was published 08/27/2019 to the Federal Register [84 FR 44898].
No comments were received during this public comment period.

9. Payments/Gifts to Respondents

Although Medicare coverage of devices or services identified in a CED clinical trial is dependent upon approval of the submission, no payments or gifts will be given to respondents to encourage their submission.

10. Confidentiality

The documents required by CMS may contain proprietary and trade secret information. CMS will retain the protections in §405.215, Confidential Commercial and Trade Secret Information. We note that section 502(c) of the Act broadly prohibits the disclosure of trade secret and confidential commercial or financial information -- information exempt from public disclosure by the Freedom of Information Act (FOIA) 5 U.S.C. 552(b)(4) outside the Department. This prohibition is found in the devices and regulatory inspections provisions of the Social Security Act, and is not limited to device-related information. This disclosure prohibition also applies to information reported or otherwise obtained by the Department during inspection activities and other activities. This prohibition is interpreted to allow information sharing within the U.S. Department of Health and Human Services only.

11. Sensitive Questions

The information required does not include questions about sexual behavior, attitude, religious beliefs, or any other matters that are commonly considered private or sensitive in nature.

12. Burden Estimates (Hours & Wages)

Below is a chart of CMS's approved CEDs for 2014-2018. We do not have records of CEDs that were not approved, but estimate that non-approved CEDs constitute approximately 10% of studies. Therefore, we estimate the total number of applicants (approved and not approved) is 74.

Table 1. CED Applications from 2014 to 2018

Application Year	Count of Approved CEDs
2014	19
2015	11
2016	20
2017	11
2018	6

Total Number of Approved CED	***67***

CMS estimates the hour burden of this collection of information as follows:
Number of submissions: Since January 1, 2014, we have received approximately 75 CED studies, averaging about 15 studies per year.

Annual hour burden: We estimate that for 15 requests per year, that the total time to be expended by all potential study sponsors is estimated to be about 1,500 hours. 5 full-time equivalents (FTEs), average 20 hours to write and submit a protocol for each study. Resources required for writing a scientific protocol includes technical, scientific, and financial experts. The 5 FTEs may include, medical doctor, statistician, data manager, project manager, executive administrative assistant.

To derive average costs: We used data from the U.S. Bureau of Labor Statistics for all salary estimates (See Table 2). The burden associated with the requirements under § 405.211 is the time and effort it would take a study sponsor that is requesting Medicare coverage of CED to prepare the following electronic documents.

Table 2 Using May 2018 National Occupational Employment and Wage Estimates in US to Estimate the Cost Occupation title (Occupation code)	2018 Mean wage (per hour)	Hourly wage includes100% in fringe benefits	Hours	Estimate cost
Physicians and Surgeons (29-1069)	$98.02	$196.04	30	$5881.20
Statisticians (15-2041)	$44.52	$89.04	30	$2671.20
Database Administrators (15-1141)	$44.25	$88.50	20	$1770
General and Operations Managers (11-1021)	$59.56	$119.12	10	$1191.20
Executive administrative assistant (43-6011)	$29.59	$59.18	10	$591.80
Total Cost				$12,105.40

In deriving costs to the public, we used the Bureau of Labor Statistics May 2018 estimate of $98.02+ 100% in fringe benefits for estimated hourly wage of $196.04 for Physicians and Surgeons (occupation code 29-1069), $44.52 + 100% in fringe benefits for estimated hourly

wage of $89.04 for Statisticians (15-2041), $44.25 + 100% in fringe benefits for estimated hourly wage of $88.50 for Database Administrators (15-1141), $59.56 + 100% in fringe benefits for estimated hourly wage of $119.12 for General and Operations Managers (11-1021), $29.59 + 100% in fringe benefits for estimated hourly wage of $59.18 for an executive administrative assistant (occupation code 43-6011). We estimate the cost $12,105.40 per study, for 15 potential CED studies, the cost of sponsors will be $181,581 for one year.

13. Capital Costs

We do not anticipate additional capital costs.

14. Cost to Federal Government

Review Cost: CMS estimated that 5 FTEs, GS12-15 are required to process and review CED applications (including amendments). This amounts to a yearly total of $1,109,540 based on a cost of $ 221,908 per position which is the agency's projected average cost of an FTE including benefits*.

*https://www.federalpay.org/employees/centers-for-medicare-and-medicaid-services Centers for Medicare & Medicaid Services Salaries of 2017 AVERAGE SALARY is $110,954 plus 100% in fringe benefits

15. Changes to Burden

This collection is new and is not subject to any changes in burden as of yet.

16. Publication/Tabulation Dates

Upon CMS approval of a CED study, we will post that approval on the CMS Coverage website with limited information (study title, sponsor name, and National Clinical Trial number) supplied by the interested party as part of their Medicare coverage CED study review request, along with the CMS approval date. The link to the CMS website for Coverage with Evidence Development is https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development. Publications will be included to the NCD review.

17. Expiration Date

CMS will display the expiration date and OMB control number. In addition, the public will be able to access the expiration date on OMB's website by performing a search using the OMB control number.

18. Certification Statement

There are no exceptions to the certification statement.

B. Collections of Information Employing Statistical Methods

CMS does not intend to collect information employing statistical methods.