DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Medicare & Medicaid Services

42 CFR Parts 405, 410, 411, 414, 423, and 425

[CMS-1600-FC]

RIN 0938-AR56

Medicare Program; Revisions to Payment Policies under the Physician Fee Schedule, Clinical Laboratory Fee Schedule & Other Revisions to Part B for CY 2014.

AGENCY: Centers for Medicare & Medicaid Services (CMS), HHS.

ACTION: Final rule with comment period.

SUMMARY: This major final rule with comment period addresses changes to the physician fee schedule, clinical laboratory fee schedule, and other Medicare Part B payment policies to ensure that our payment systems are updated to reflect changes in medical practice and the relative value of services. This final rule with comment period also includes a discussion in the Supplementary Information regarding various programs. (See the Table of Contents for a listing of the specific issues addressed in the final rule with comment period.)

DATES: Effective date: The provisions of this final rule with comment period are effective on January 1, 2014, except for the amendments to §§405.350, 405.355, 405.405.2413, 405.2415, 405.2452, 410.19, 410.26, 410.37, 410.71, 410.74, 410.75, 410.76, 410.77, and 414.511, which are effective January 27, 2014, and the amendments to §§405.201, §405.203, §405.205, §405.207, §405.209, §405.211, §405.212, §405.213, §411.15, and 423.160, which are effective on January 1, 2015.

The incorporation by reference of certain publications listed in the rule is approved by the Director of the **Federal Register** as of January 1, 2014.

III. Other Provisions of the Proposed Regulations

A. Medicare Coverage of Items and Services in FDA-Approved Investigational Device Exemption Clinical Studies--Revisions of Medicare Coverage Requirements

1. Background and Statutory Authority

a. General

Section 1862(m) of the Act (established by section 731(b) of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) (Pub. L. 108-173, enacted on December 8, 2003)) allows for payment of the routine costs of care furnished to Medicare beneficiaries in a Category A investigational device exemption (IDE) trial and authorizes the Secretary to establish criteria to ensure that Category A IDE trials conform to appropriate scientific and ethical standards. By providing Medicare coverage of routine costs in Category A trials, the Congress removed a financial barrier that may have discouraged beneficiaries from participating in these trials. It also gives Medicare beneficiaries the opportunity to have earlier access to new medical devices. However, the statute does not require Medicare to cover the Category A device itself. We note that throughout this section of the preamble, the words study and trial are used interchangeably.

(1) Category A IDE devices

For Category A IDE devices, existing §405.201(b) defines an "experimental/investigational (Category A) device" as an innovative device believed to be in Class III for which "absolute risk" of the device type has not been established (that is, initial questions of safety and effectiveness have not been resolved and the FDA is unsure whether the device type can be safe and effective). Existing §405.207(b)(2) states that payment may be made for the routine care services related to Category A IDE devices if, among other things, the services are furnished in conjunction with an FDA-approved clinical trial, and that the trial is

required to meet criteria established through the Medicare national coverage determination process.

(2) Category B IDE devices

Existing §405.201(b) defines a "non-experimental/investigational (Category B) device" as a device believed to be in Class I or Class II, or a device believed to be in Class III for which the incremental risk is the primary risk in question (that is, underlying questions of safety and effectiveness of that device type have been resolved), or it is known that the device type can be safe and effective because, for example, other manufacturers have obtained FDA approval for that device type. Existing §405.211 allows Medicare contractors to make coverage decisions for non-experimental/investigational (Category B) devices if certain requirements are met. If a Medicare contractor determines that a Category B device is covered, Medicare also covers routine care services related to a non-experimental/investigational (Category B) device furnished in conjunction with an FDA-approved clinical trial, per §405.207(b)(3). Based on our rulemaking authority in section 1871 of the Act, we proposed to apply the same Medicare coverage requirements and scientific and ethical standards to Medicare coverage related to Category B IDE studies/trials that would be applicable to Category A IDE studies/trials.

b. Background

We sought and received input from stakeholders (for example: manufacturers, study sponsors, and hospitals) regarding the Medicare coverage approval process for Category B IDE devices. The majority of stakeholders told us that obtaining Medicare coverage of the Category B IDE device and the costs of routine items and services is inefficient since local Medicare contractors have differing processes for reviewing IDE studies for purposes of Medicare coverage, which result in inconsistent Medicare coverage of Category B IDE devices and associated routine care services across the Medicare contractor jurisdictions. Stakeholders also

suggested that these factors contribute to their reluctance to enroll Medicare beneficiaries in IDE trials and studies, and that Medicare coverage variability between Medicare contractors made it difficult to conduct national IDE trials.

We also requested input from local Medicare contractors regarding their existing processes for determining coverage of Category B IDE devices and associated routine care services. They reported that they review pertinent available evidence and the FDA-approved IDE trial protocol as factors in their decision-making process to ensure that the device is reasonable and necessary for Medicare beneficiaries and furnished in appropriate settings. Local Medicare contractors apply varying levels of scrutiny to these factors. While most Medicare contractors extensively review IDE study protocols, other contractors may review them less extensively. Although there is variability among contractors, in many cases the review processes are duplicative in that multiple Medicare contractors are reviewing the same materials in the same way.

2. Summary of Provisions of the Proposed Regulation

We proposed to modify our regulations related to Medicare coverage of routine care items and services in Category A IDE studies and trials, and Medicare coverage of Category B IDE devices and routine care items and services. We proposed to establish criteria for IDE studies so that Category A IDE trials conform to appropriate scientific and ethical standards for Medicare coverage consistent with our authority under section 1862(m)(2)(B) of the Act. We proposed to extend the same Medicare coverage requirements to Medicare coverage of Category B IDE device trials, using our general rulemaking authority under section 1871 of the Act. We proposed that Medicare coverage decisions related to coverage of items and services in Category A and B IDE trials and studies be made by CMS centrally.

a. Proposed Definitions

We proposed to replace the definitions in §405.201(b) with the following:

- Category A (Experimental) device: A device for which "absolute risk" of the device type has not been established (that is, initial questions of safety and effectiveness have not been resolved) and the FDA is unsure whether the device type can be safe and effective.

- Category B (Nonexperimental/investigational) device: A device for which the incremental risk is the primary risk in question (that is, initial questions of safety and effectiveness of that device type have been resolved) or it is known that the device type can be safe and effective because, for example, other manufacturers have obtained FDA approval for that device type.

- ClinicalTrials.gov: The National Institutes of Health's National Library of Medicine's online registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.

- Contractors: Medicare Administrative Contractors and other entities that contract with CMS to review and adjudicate claims for Medicare items and services.

- IDE stands for investigational device exemption: An FDA-approved IDE application permits a device, which would otherwise be subject to marketing approval or clearance, to be shipped lawfully for the purpose of conducting a clinical study in accordance with 21 U.S.C. 360j(g) and 21 CFR parts 812.

- Pivotal studies or trials: Clinical investigations designed to collect definitive evidence of the safety and effectiveness of a device for a specified intended use, typically in a statistically justified number of subjects. It may or may not be preceded by an early and/or a traditional feasibility study.

- Routine care items and services: Items and services that are otherwise generally available to Medicare beneficiaries (that is, a benefit category exists, it is not statutorily

excluded, and there is not a national noncoverage decision) that are furnished in either the experimental or the control arms of a clinical trial and that would be otherwise furnished even if the beneficiary were not enrolled in a clinical trial.

- Superiority studies or trials*:* Studies or trials that are intended to demonstrate at some prespecified level of confidence that the effect of an investigational treatment is superior to that of an active control by more than a prespecified margin.

b. Proposed Provisions for Medicare coverage of items and services in FDA-approved IDE studies.

To ensure that Medicare coverage of items and services in Category A and B IDE studies is more consistent across Medicare administrative regions, we proposed that IDE coverage decisions be made by CMS centrally. We proposed a centralized IDE coverage review process for Category A and Category B IDEs, by adding §405.201(a)(3) stating that CMS identifies criteria for coverage of items and services furnished in IDE studies. We proposed to replace existing §405.211 with the following Medicare coverage requirements for items and services in Category A and Category B FDA-approved IDE studies.

- CMS will review the following items and supporting materials as needed: (1) the FDA approval letter, (2) IDE study protocol, (3) IRB approval letter(s), (4) ClinicalTrials.gov identifier.

- Medicare may cover routine care items and services furnished in any FDA-approved Category A IDE study if the criteria in proposed new §405.212(a) and (b) are met.

- Medicare covers a Category B IDE device and routine care items and services furnished in any FDA-approved Category B IDE study if the criteria in proposed new §405.212(a) and (c) are met.

- If an IDE device is furnished in an FDA-approved IDE study that does not wholly fall

under proposed new §405.212(b) or (c), CMS considers whether the study's attainment of the criteria in proposed new §405.212(a) are sufficient to mitigate the failure to meet the criteria in proposed new §405.212(b) or (c).

We also proposed to notify the public of Medicare covered Category A and B IDE studies by posting the IDE study title and ClinicalTrials.gov identifier on the CMS coverage website and publishing a list of trials in the **Federal Register**. We stated that a centralized review process would be more efficient by reducing the burden for stakeholders interested in seeking Medicare coverage related to nationwide IDE studies or trials. Having a single entity making Medicare coverage decisions would enhance administrative efficiency by eliminating the need for duplicative submissions from stakeholders to different Medicare contractors and duplicative reviews by Medicare contractors. In the preamble to the proposed rule, we stated that we did not believe that the proposed coverage requirements would significantly change the number of items and services covered compared to coverage under existing requirements.

We stated in the preamble to the proposed rule that any interested party who seeks Medicare coverage related to a Category A or B IDE study may send us a request letter that describes the scope and nature of the Category A or B IDE study, discussing each of the criteria in the proposed policy. Requests would be submitted via email to clinicalstudynotification@cms.hhs.gov or via hard copy to the following address: Centers for Medicare & Medicaid Services; Center for Clinical Standards & Quality; Director, Coverage and Analysis Group; ATTN: Clinical Study Certification; Mailstop: S3-02-01; 7500 Security Blvd; Baltimore, MD 21244.

c. Proposed Medicare Coverage IDE Study Criteria:

We proposed to add a new §405.212 that describes the Medicare coverage criteria that Category A and B IDE studies or trials must meet in order for Medicare to cover routine care

items and services in Category A IDE studies or trials, and for Medicare to cover Category B IDE devices and routine care items and services (per proposed revised §405.207 and §405.211). We proposed the following Medicare coverage IDE study criteria.

(1) The principal purpose of the study is to test whether the item or service meaningfully improves health outcomes of patients who are represented by the Medicare-enrolled subjects.

(2) The rationale for the study 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.

(3) The study results are not anticipated to unjustifiably duplicate existing knowledge.

(4) The study design is methodologically appropriate and the anticipated number of enrolled subjects is adequate to answer the research question(s) being asked in the study.

(5) The study is sponsored by an organization or individual capable of completing it successfully.

(6) The study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 45 CFR part 46.

(7) All aspects of the study are conducted according to appropriate standards of scientific integrity set by the International Committee of Medical Journal Editors.

(8) The study has a written protocol that clearly demonstrates adherence to the standards listed here as Medicare requirements.

(9) Where appropriate, the clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives may be exempt from this standard 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.

(10) The study is registered on the ClinicalTrials.gov website and/or the Registry of Patient Registries (RoPR) by the principal sponsor/investigator prior to the enrollment of the first study subject.

(11) The study protocol specifies the method and timing of public release of results on all pre-specified outcomes, including release of negative outcomes. The release should be hastened if the study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors. However, a full report of the outcomes must be made public no later than 3 years after the end of data collection.

(12) The study protocol explicitly discusses subpopulations affected by the item or service under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria [a]ffect enrollment of these populations, and a plan for the retention and reporting of said populations in the study. 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.

(13) The study protocol explicitly discusses how the results are or are not expected to be generalizable to subsections of the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability, or Medicaid eligibility.

We stated in the preamble to the proposed rule that all IDE investigational device studies where Medicare coverage is sought should conform to rigorous scientific and ethical standards. We believe that these criteria are essential to protecting Medicare study participants in Category A and Category B trials. Studies that have high scientific and ethical standards lead to

generalizable and reliable knowledge for the Medicare program including, providers, practitioners, and beneficiaries.

We believe that additional Medicare coverage criteria are needed for Category A and B IDE studies where Medicare coverage for items and services is sought, to ensure that the study design is appropriate to answer questions of importance to the Medicare program and its beneficiaries. Although an item or service may be considered appropriate when used by a clinician for the benefit of an individual patient, it may not be reasonable and necessary when used in the context of an IDE study or trial for purposes of Medicare coverage. The use of such a device in an IDE study or trial may expose study participants to increased risks that must be balanced by other factors, including the likelihood that the study would add important information to the body of medical knowledge relevant to the Medicare program.

While most studies are undertaken only after a detailed protocol has been developed, some are not. The protocol is the primary source of knowledge on the proposed design and management of the study. Without this document, reviewers and funding entities are unable to ascertain the quality and validity of the study, and whether the study is appropriate to answer questions of importance to the Medicare program. The exercise of committing to paper all the aspects of the study is crucial to ensuring that all potential concerns have been addressed.

We proposed these 13 Medicare coverage IDE study criteria because we believe they must be integral to any study that is approved for purposes of Medicare coverage. The proposed first four criteria and the seventh criterion were developed because they embody ethical values. The fifth and sixth proposed criteria were developed in response to reports of egregious misconduct in the past in endeavors to conduct clinical research by placing individuals at the risk of harm for the good of others.

In §405.211, we proposed that if the following two characteristics are also met, in

addition to the IDE study criteria listed in proposed new §405.212(a)(1) through (a)(13), we would automatically cover the costs of routine items and services in the Category A study or trial, and the costs of the investigational device and the routine items and services in a Category B study or trial as follows:

- The study is a pivotal study.
- The study has a superiority study design.

Existing §405.207(b)(2) requires that for Medicare coverage of related routine care services, all Category A IDE studies and trials must meet the criteria established through the NCD process. We proposed to modify §405.207(b) to remove the NCD process requirement and state that payment may be made for routine care items and services related to experimental/investigational (Category A) devices as defined in §405.201(b), and furnished in conjunction with an FDA-approved clinical trial that meets the Medicare coverage IDE study criteria in proposed new §405.212. We proposed to modify §411.15(o)(2) to specify that the exclusions from Medicare coverage include experimental or investigational devices, except for certain devices furnished in accordance with the Medicare coverage requirements proposed in revised §405.211.

3. Summary of Public Comments

We received 48 comments from various entities including the medical device industry, academic medical centers, health care systems, consultants, and medical societies. Regarding centralization of the IDE review process, commenters' opinions were mixed with the majority requesting additional details about the centralized review process, clarification of the IDE study criteria, and delayed implementation of the rule. Commenters expressed concerns about the proposed IDE study criteria, believing that they were duplicative of FDA review activities and suggested that CMS allow for additional input from stakeholders before the rule is finalized. The

following is a summary of the comments we received and our responses.

a. Definitions

Comment: Commenters were concerned that our proposed definition of routine care items and services would limit Medicare coverage of routine care items and services related to Category A or Category B IDE studies. The comments suggested that we align this definition with section 310.1 of the Medicare NCD Manual (Clinical Trials).

Response: We appreciate the commenters' feedback. While we believe that this definition of routine care items and services is aligned with section 310.1 of the Medicare National Coverage Determinations Manual, for purposes of clarity, we are modifying this definition to refer to items and services that are otherwise generally available to Medicare beneficiaries (that is, a benefit category exists, it is not statutorily excluded, and there is no national noncoverage decision) that are furnished during a clinical study and that would be otherwise furnished even if the beneficiary were not enrolled in a clinical study.

b. Provisions for Medicare Coverage of Items and Services in FDA-approved Category A or B IDE studies or trials

Comment: Several commenters were generally supportive of the concept of a centralized Medicare review process for Category A and B IDE studies for purposes of Medicare coverage. However, the commenters requested additional information regarding submission format and review timeframes, with some commenters concerned about the availability of appropriate staff at CMS to complete reviews and issue approvals. Commenters also asked for clarification regarding appeals of Medicare coverage decisions related to Category A or B IDE studies and evaluation/oversight of the CMS Medicare coverage review process.

Response: Seeking Medicare coverage related to Category A or B IDE studies is voluntary. While we are finalizing this rule, we are delaying implementation of these changes

until January 1, 2015. Upon implementation of these changes, interested parties, such as the study sponsor, that wish to seek Medicare coverage in Category A or B IDE studies must submit their requests via email to clinicalstudynotification@cms.hhs.gov or via hard copy to the following address: Centers for Medicare and Medicaid Services; Center for Clinical Standards and Quality; Director, Coverage and Analysis Group; ATTN: Clinical Study Certification; Mail Stop S3-02-01; 7500 Security Blvd.; Baltimore, MD 21244.

Requests must include the following information:

- A request letter that describes the scope and nature of the IDE study, discussing how the interested party believes that the IDE study meets each Medicare Coverage IDE Study Criteria.
- FDA approval letter of the IDE.
- IDE study protocol.
- IRB approval letter.
- National Clinical Trial (NCT) number.
- Supporting materials, as appropriate.

We understand and appreciate commenters' concerns regarding review time and the availability of appropriate staff to complete the reviews. Once a complete request is received by CMS (or its designated entity), we expect that the review timeframe will be approximately 30 days. While we believe that we have sufficient resources to process Medicare coverage reviews of the IDE studies, we are modifying the provisions of section 405.211 to allow for reviews by a CMS-designated entity if future needs arise.

We anticipate that claims for routine care items and services related to Category A or B IDE studies and claims for Category B IDE devices will continue to be submitted to local Medicare contractors who will identify routine costs for which Medicare payment is made for

each related claim. We plan to issue appropriate manual instructions to Medicare contractors. Additional information regarding Medicare claim appeals is available on the CMS website at http://www.cms.gov/Medicare/Appeals-and-Grievances/OrgMedFFSAppeals/index.html.

Comment: A few commenters opposed a centralized Medicare coverage process for Category A or B IDE studies and believed that the current local Medicare contractor review process is sufficient, that centralization could increase approval time, and may not have the intended impact of eliminating inconsistencies in coverage. Several commenters suggested that CMS focus on streamlining claims processing for routine costs incurred by Medicare beneficiaries participating in clinical trials. One commenter was concerned that local Medicare contractors may impose additional coverage requirements.

Response: While some stakeholders may be satisfied with the current localized coverage review process, we believe that centralizing the submission, review and determination of Medicare coverage IDE study requests enhances administrative efficiency by eliminating the need for duplicative submission of requests by providers and duplicative reviews by local Medicare contractors. For example, under existing procedures, each provider that participates in an IDE trial and that anticipates filing Medicare claims must notify the Medicare contractor and furnish the contractor with certain information about the IDE trial. Once the contractor notifies the provider that all required information for the IDE study has been furnished, the provider may bill related Category A or B IDE claims.

Effective January 1, 2015, interested parties (such as study sponsors) that wish to seek Medicare coverage related to Category A or B IDE studies, will have a centralized point of contact for submission, review and determination of Medicare coverage IDE study requests. Providers will no longer need to notify individual contractors regarding IDE studies for which they plan to submit claims since CMS-approved Category A and B IDE studies will be listed on

the CMS website and in the **Federal Register**. We encourage providers to check the CMS website to see if an IDE study has been approved for coverage before submitting IDE related claims.

Comment: Some commenters believed that the Medicare coverage requirements duplicate the responsibilities of the FDA (such as review of scientific and ethical standards) with commenters suggesting that CMS deem coverage for Category A or B IDE studies that have received FDA and IRB approval.

Response: CMS and FDA operate under different statutory authorities and have distinct authorities and responsibilities. FDA approves IDE studies or trials when, among other things, the risks to the subjects are outweighed by the anticipated benefits and the importance of the knowledge to be gained. For purposes of Medicare coverage, we seek evidence that an item or service is reasonable and necessary. The disease burden borne by elderly individuals and the important health care interventions unique to the Medicare population are important areas of focus for the Medicare program; we would not expect the FDA review to include substantive consideration of these Medicare priorities. Thus, we believe that Medicare coverage standards are needed for IDE studies for which Medicare coverage is sought. We wish to ensure that Medicare beneficiaries who volunteer to participate in studies are protected, that the study design is appropriate to answer questions of importance to the Medicare program, and to ensure that the information gained from important clinical trials could be used to inform Medicare coverage decisions.

There are numerous studies that may be considered scientifically valid but are of little benefit to Medicare beneficiaries or to the Medicare program. We believe that this policy establishes Medicare coverage requirements that need to be met to best support a body of clinical knowledge that is relevant to the Medicare program and its beneficiaries. It is essential that IDE

studies where Medicare coverage is sought serve the best interests of the Medicare program and its beneficiaries; and that they be useful in improving healthcare delivery to Medicare beneficiaries, and informing Medicare coverage.

Comment: Commenters suggested that the proposed coverage requirements would increase burden and create access barriers for Medicare coverage of Category A IDE routine care items and services and Category B IDE devices and routine care items and services, particularly in small or localized studies or trials. Commenters suggested that these changes may decelerate medical device innovation and that many sponsors may choose not to seek Medicare coverage for IDE trials due to possible delays during the transition to these new coverage requirements. Other commenters suggested that we pilot a voluntary centralized coverage review process for at least a year, or establish separate review processes for small and large studies since commenters believed that the existing review process by local Medicare contractors is appropriate for small, single-site studies, and that centralized review should only be applied to large, national studies. Some commenters requested clarification regarding whether Medicare would automatically cover items and services related to Category A or B IDE studies, if the studies met the criteria in proposed new §405.212.

Response: Seeking Medicare coverage related to Category A or B IDE studies is voluntary under existing procedures and will continue to be voluntary under the provisions of this final rule. Study sponsors are not required to seek Medicare coverage in order to conduct their studies or trials. Establishing separate Medicare coverage for IDE study review processes for large and small studies would create unnecessary infrastructure. Similarly, piloting the centralized Medicare coverage IDE study review process would create more duplication and variation in reviews and coverage of items and services, in addition to the variation currently present under the existing local Medicare contractor review process.

In this final rule, we are revising §405.211(a) to specify that Medicare covers routine care items and services that are furnished in FDA-approved Category A IDE studies if CMS (or its designated entity) determines that the IDE study criteria in §405.212 are met. We are also revising §405.211(b) to specify that Medicare may make payment for Category B IDE devices and routine care items and services furnished in FDA-approved Category B IDE studies if CMS (or its designated entity) determines that the IDE study criteria in §405.212 are met.

Comment: One commenter expressed concern that beneficiaries could be at risk of losing Medicare coverage for medical emergencies and other health care items and services that would otherwise be available to Medicare beneficiaries outside of an IDE study or trial.

Response: We do not believe this policy will have an impact on coverage for treatment of an individual trial participant with a medical emergency because this policy does not address Medicare coverage provisions outside the context of a Category A or B IDE study or trial. We would not expect to make a separate review of the IDE study information submitted to CMS (or its designated entity) for each enrolled subject or each related claim submitted to Medicare contractors for adjudication. Additionally, we are unaware of any current paradigm by which an FDA approved IDE trial would be conceived, developed, reviewed and approved in such a short timeframe, that is, a few minutes or hours, to address a beneficiary's medical emergency.

Comment: Commenters requested information about what role, if any, the FDA would serve in the proposed centralized IDE review process for purposes of Medicare coverage of Category A IDE routine care items and services and Category B IDE devices and routine care items and services.

Response: We did not propose any changes to §405.203, which addresses FDA categorization of IDE devices and subsequent FDA notification to CMS regarding such categorization.

c. Medicare Coverage IDE Study Criteria

Comment: Many commenters believed that proposed criterion 1 (the principal purpose of the study is to test whether the item or service meaningfully improves health outcomes in patients who are represented by the Medicare-enrolled subjects), was too specific to the Medicare population and should more closely align with FDA requirements since IDE studies are designed to answer FDA regulatory questions, not Medicare or other insurer coverage questions. Some commenters suggested that we modify the standard to indicate that measuring meaningful outcomes in Medicare beneficiaries need not be the principal purpose, but only one of the purposes.

Response: As discussed in the preamble to the proposed rule, we believe that this criterion is necessary because it embodies important scientific and ethical considerations needed to ensure that the study design is appropriate to answer questions of importance to Medicare and its beneficiaries. We expect that the results of all approved studies will specifically benefit the Medicare population and, as such, covered studies or trials must address how the study will affect Medicare beneficiaries if it desires to receive Medicare payment for services provided to Medicare beneficiaries within that study. However, based on the comments received, we are modifying this criterion to state that the principal purpose of the study is to test whether the device improves health outcomes of appropriately selected patients, since a discussion of the potential benefit of the device being studied to the applicable Medicare population is implicit in other criteria.

Comment: Commenters suggested that we remove or modify the second proposed criterion (the rationale for the study 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). Commenters believed that there is already well established government

oversight, and self-governance through IRBs and scientific review committees. The commenters requested additional guidance regarding how this criterion would align with FDA requirements and oversight through the IRBs and scientific committees.

Response: Study protocols typically have a section that describes the scientific rationale for the research. We believe that this criterion reflects a fundamental principle of research and does not require something that would otherwise be absent from a *bona fide* clinical study protocol. We seek assurance of compliance with this criterion because it is needed to ensure that the study or trial focuses on health outcomes important to the Medicare program and its beneficiaries. Therefore, we are not making changes to this criterion.

Comment: Some commenters were concerned about how proposed criterion 3 (the study results are not anticipated to unjustifiably duplicate existing knowledge) would affect IDE device studies that are versions of devices already on the market. A commenter believed that this criterion should not be used to restrict Medicare coverage of IDE studies that build on an existing body of evidence or that provide confirmatory data on new devices.

Response: We realize that FDA reviews many new devices being tested in IDE trials that may be similar to devices already on the market, and that this process is a necessary part of competition and innovation. However, because we are not assured that all devices of a similar class will necessarily have identical benefits and harms, we do not believe, as a general principle, that IDE studies or trials addressing new device versions always duplicate prior knowledge. We expect that knowledge about new devices or significantly changed devices will add to, rather than duplicate, existing knowledge. We believe this criterion is necessary to ensure that the study focuses on health outcomes important to the Medicare program and its beneficiaries. Therefore, we are not making changes to this criterion.

Comment: Commenters stated that proposed criterion 4 (the study design is

methodologically appropriate and the anticipated number of enrolled subjects is adequate to answer the research question(s) being asked in the study) is duplicative of the FDA's role. One commenter asked how we would determine if a study design is methodologically appropriate.

Response: Fundamentally, bona fide clinical research depends on the use of study designs that are appropriate to address the study questions. Otherwise there is no real production of generalizable knowledge, which is the hallmark of research, and enrolled subjects encounter risk without a realistic expectation that their participation will result in personal or societal benefit relevant to the Medicare program. The use of such a device in an IDE study may expose the study participants to increased risks that must be balanced by other factors including the likelihood that the study would add important information to the body of medical knowledge relevant to the Medicare program. There are numerous studies that may be considered scientifically valid but are of little benefit to the Medicare program. We are sensitive to the unique needs of Medicare beneficiaries, particularly the elderly. A trial design that may be adequate for a generally younger population may be comparatively insensitive to clinical factors commonly found in the elderly that may adversely impact the potential benefit or tolerability of a device, which is of particular importance to the Medicare program.

Comment: A few commenters requested information on how proposed criterion 5 (the study is sponsored by an organization or individual capable of completing it successfully) will be used to determine that the sponsoring organization or individual is capable of completing a study successfully.

Response: Institutional capabilities and scientific expertise are typically described in study protocols, which will be reviewed by CMS. Robust clinical studies depend on a supporting infrastructure to assure protocol adherence and that intended patient protections are actually in place. Clinical trials that are not completed successfully expose enrolled subjects to

the risks of research participation without the benefit of producing generalizable knowledge applicable to the Medicare program. We believe that this criterion reflects a fundamental principle of research and does not require something that would otherwise be absent from a bona fide clinical study protocol. Therefore, we are finalizing this criterion as proposed.

Comment: One commenter suggested that for proposed criterion 6 (the study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 45 CFR part 46) that we also require compliance with FDA regulations at 21 CFR 50 (Informed Consent) and 21 CFR 56 (Institutional Review Board oversight) since 45 CFR 46 only refers to government funded research.

Response: We agree with the commenter's suggestions and are modifying this criterion in this final rule to require that the study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 21 CFR parts 50, 56, and 812, and 45 CFR part 46.

Comment: Commenters recommended that we delete the reference to the International Committee of Medical Journal Editors in proposed criterion 7 (all aspects of the study are conducted according to appropriate standards of scientific integrity set by the International Committee of Medical Journal Editors.

Response: In response to the comments received, we are removing proposed criterion 7. We believe that the intent of proposed criterion 7 can be largely accomplished by adherence to the remaining CMS IDE study criteria.

We are also removing proposed criterion 8 (the study has a written protocol that clearly demonstrates adherence to the standards listed here as Medicare requirements) because the intent of proposed criterion 8 is implicit in the CMS coverage criteria and requirements.

Comment: One commenter suggested that proposed criterion 9 (where appropriate, the

clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives may be exempt from this standard only if the disease or condition being studied is life threatening and the patient has no other viable treatment options), since the commenter believed that Medicare would only be furnishing coverage for "conventional" care.

Response: As discussed in the preamble to the proposed rule, the intent of this criterion is to limit Medicare coverage to IDE studies that do not exclusively test toxicity or disease pathophysiology in healthy individuals, but also have a therapeutic outcome. However, a study that exclusively tests toxicity or disease pathophysiology may still be covered if the disease or condition being studied is life-threatening or a severely-debilitating illness, and the patient has no other viable treatment options. We recognize that many research projects could be considered to have varying degrees of contributions towards understanding interventions that improve health outcomes for the Medicare program. While we agree that in some cases, safety and toxicity studies may assess the benefits of the interventions they examine, and in limited circumstances may be considered appropriate to inform the clinical knowledge base applicable to the Medicare program, we are maintaining this criterion without change.

Comment: Commenters expressed interest in the possible impact of the rule on ClinicalTrials.gov reporting, and suggested that we require that proposed criterion 10 (the study is registered on the ClinicalTrials.gov website and/or the Registry of Patient Registries (RoPR) by the principal sponsor/investigator prior to the enrollment of the first study subject) comply with section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Pub. L. 110-85, enacted on September 27, 2007), which requires registration on ClinicalTrials.gov within 21 days of enrollment of the first subject.

Response: As discussed in the preamble to the proposed rule, we believe that all studies

seeking Medicare coverage under this policy should be registered with ClinicalTrials.gov. Registrants at ClinicalTrials.gov must submit a standardized set of data elements to describe the study design, eligible populations, outcome measures, and other parameters and results. Registration, for some studies, serves as a vehicle for Medicare beneficiaries to learn about, and identify studies in which they may want to participate. When results reporting is required, it also offers an assurance of quality because, generally, public access to information enables a higher level of accountability in the accurate reporting of the clinical study protocol and results, and in the conduct of the trial itself. This accountability derives both from public access to information about studies and from the risk of penalty for submitting false or misleading clinical trial information. We recognize that, for some studies of unapproved devices, FDAAA prohibits the public display of information on registration and results until after the device is approved or cleared for marketing. We have revised our regulation to avoid indicating that Medicare coverage of such IDE studies would require public display of all information in ClinicalTrials.gov for these unapproved devices. However, we believe that delayed display for this subset of studies, should the device be cleared or approved for marketing, will not significantly undermine our goals. For some studies, we expect public access to ClinicalTrials.gov data will not be delayed and therefore our requirement will immediately lead to greater public transparency for many of the studies supported by Medicare. For those studies about which information cannot be displayed publicly prior to marketing approval, we believe that the possibility of future public access and the risk of liability for the submission of false or misleading clinical trial information to ClinicalTrials.gov remain valuable. Registration with ClinicalTrials.gov also assures that Medicare beneficiaries and their treating healthcare professionals will, for those devices ultimately approved or cleared by FDA, eventually have pertinent information about these IDE studies. We note that clinical trials of devices that register

for purposes of this regulation are subject to any applicable requirements under FDAAA. Finally, we have modified the criteria to simply require registration on ClinicalTrials.gov.

Comment: In summary, proposed criterion 11 stated that the study protocol must specify the method and timing of public release of results on all pre-specified outcomes, including release of negative outcomes. One commenter stated that time to publication may not be in the control of the sponsors and that some studies may not be published at all for various reasons. Commenters suggested that we modify this criterion to be consistent with section 801 of the FDAAA.

Response: Based on the comments received, we are modifying this criterion to state that the study protocol describes the method and timing of release of results on all pre-specified outcomes, including release of negative outcomes and that the release should be hastened if the study is terminated early.

Comment: In summary, proposed criteria 12 and 13 stated that the study protocol must explicitly discuss the subpopulations affected by the items or services under investigation and discuss how the study results would be expected to be generalizable to the Medicare population. Commenters believed that explicitly requiring this information in the study protocol was inappropriate, with other commenters indicating that this information could be provided in the request for coverage submission package versus explicitly requiring it in the study protocol. A commenter stated that generalizability to populations beyond those which are studied in the trial may be difficult to articulate, especially when the class of device is new. Commenters opined that if the device class is the subject of a Medicare national or local coverage decision, the criterion is redundant and may create undue burden on a trial being conducted in a least burdensome environment.

One commenter suggested that for devices that represent a device improvement, the

existing body of knowledge and other supporting documents will likely address sub- and special populations. The commenter also stated that for truly new devices, safety and efficacy at a baseline level are not yet established and that a mandate to include special populations and under-represented groups is likely to be prohibitive to completion of the trial.

Response: We want to support and encourage the conduct of research studies that add to the knowledge base about efficient, appropriate, and effective use of products and technologies in the Medicare population, thus improving the quality of care that Medicare beneficiaries receive. We understand the commenters' concerns; however, we expect that the results of studies or trials approved for purposes of Medicare coverage will specifically benefit the Medicare population.

It is not our intention to require enrollment of all subpopulations. It is, however, our intention that study protocols for which Medicare coverage is sought address all populations affected by the technology under investigation, specifically those of interest to the Medicare program (populations due to age, disability, or other eligibility status). We expect that protocols describe the potential for subgroup differences and discuss how the study will evaluate any differences found.

In this final rule, we are combining and modifying proposed criteria 11 and 12 to state that for purposes of Medicare coverage, Category A or Category B IDE study protocols must discuss how Medicare beneficiaries may be affected by the device under investigation, how the study results are or are not expected to be generalizable to the Medicare population, and must include separate discussions for populations eligible for Medicare due to age, disability, or other eligibility status.

Comment: Commenters suggested that we remove the proposed Medicare coverage requirements that a Category A or B IDE study must be a pivotal study and have a superiority

study design. Commenters expressed concern that noninferiority studies were not specifically discussed. One commenter recommended that IDE studies conducted as part of the FDA premarket approval (PMA) process be deemed as meeting the pivotal trial definition and be eligible for automatic coverage. Commenters stated that noninferiority studies and studies without an active comparator are designed to address important research questions and ultimately improve patient care, and cited the following concerns about including this requirement:

- Requiring that the study be either a superiority or pivotal study may undermine innovation.
- Not all clinical questions require superiority designs.
- Development of devices that are similar to devices already on the market may only require evidence of equivalence or noninferiority to a preexisting device while offering an expanded treatment option and lower healthcare costs through competition in the market.
- Medical device development may follow less well-defined paths of clinical study with individual studies not always easily characterized by a specific Phase, but still providing important evidence on a device's safety and effectiveness.
- In many cases, the protocol is not changed between the pilot and pivotal phases and including this requirement may make studies in the pilot phase ineligible for coverage.
- Investigator-initiated studies often evaluate novel approaches in small studies and are unlikely to be pivotal.

Response: We appreciate the commenters' concerns about the proposed pivotal study and superiority study design Medicare coverage criteria. We believe that noninferiority trial designs are recognized to have certain risks of bias that are mitigated in superiority trial designs. These criteria were intended as specific positive factors that could have streamlined the Medicare coverage review of IDE study protocols. We did not intend that these proposals would be

absolute requirements or that IDE studies that are not pivotal or studies with noninferiority designs could not be approved for Medicare coverage. Therefore, we are modifying the Medicare coverage IDE study criteria in new §405.212 by removing the proposed pivotal study and superiority study design coverage requirements and removing the proposed definitions of pivotal studies or trials and superiority studies or trials in revised §405.201(b).

d. Additional issues

Comment: Commenters stated that submitting IRB letters for every site involved in a multi-site clinical trial would create significant burden for stakeholders and is duplicative of the FDA's review process.

Response: We believe that Medicare beneficiaries should be enrolled in studies that have been vetted by IRBs. However, we recognize commenters' concerns regarding the potential burden of submitting IRB letters for every site involved in a multi-site clinical trial. Therefore, we are clarifying in this final rule that interested parties, such as the study sponsor, that wish to seek Medicare coverage related to Category A or B IDE studies need only submit one IRB approval letter with their request.

Comment: Commenters requested assurance that information provided by the study sponsor will be kept confidential.

Response: Seeking Medicare coverage for Category A or B IDE trials is voluntary. Medicare coverage is not a requirement for study sponsors to conduct research. Effective January 1, 2015, interested parties (such as the study sponsor) that wish to seek Medicare coverage in Category A or B IDE studies must submit a request to CMS for review and approval of a Category A or B IDE study in order to meet the Medicare coverage requirements for Category A or B IDE routine care items and services, and Category B devices.

Upon CMS approval of a Category A or B IDE study, we will post on the CMS website

and periodically in the **Federal Register** limited information supplied by the interested party as part of their Medicare coverage IDE study review request (study title, sponsor name, NCT number, and the IDE number), along with the CMS approval date. We note that the same type of information is currently posted on the CMS website for other clinical study approvals related to Medicare coverage under the coverage with evidence development (CED) paradigm. We note that we did not propose any changes to §405.215, which addresses confidential commercial and trade secret information by specifying that, to the extent that we rely on confidential commercial or trade secret information in any judicial proceeding, we will maintain confidentiality of the of the information in accordance with Federal law.

Comment: Commenters requested information about appropriate procedures for notification of trial revisions, protocol changes, and review of consent forms. One commenter requested that we align with the ClinicalTrials.gov registry, so that sponsors and researchers can provide updates to both systems. Other commenters suggested that instead of notifying the public of CMS-approved IDE studies in the **Federal Register**, that we post this information to the CMS website.

Response: We do not believe that the creation of a shared registry with the National Library of Medicine's ClinicalTrials.gov registry to include information regarding CMS approval of Category A or B IDE studies could be accomplished before the effective date of this regulation. As previously discussed, limited information regarding CMS-approved Category A and B IDE studies will be posted on the CMS website and in the **Federal Register**.

Comment: A few commenters asked how the proposed changes to the coverage requirements would impact or interact with the NCD process, including CED.

Response: Medicare coverage of Category A IDE routine care items and services, and Medicare coverage of Category B IDE devices and routine care items and services do not predict

nor directly lead to Medicare coverage outside of the context of an IDE study, nor does it necessarily lead to consideration under the Medicare national coverage determination (NCD) process. The NCD process is separate and distinct with its own statutory basis and requirements. Additional information regarding the Medicare national coverage determination process can be found on the CMS coverage website at http://www.cms.gov/Center/Special-Topic/Medicare-Coverage-Center.html?redirect=/center/coverage.asp.

Comment: Commenters requested clarification about Medicare coverage of Category A IDE related routine care items and services and Category B IDE devices and related routine care items and services, when the Medicare beneficiary is enrolled in a Medicare Advantage plan or Medicare health plan.

Response: Medicare Advantage plans must abide by the IDE study payment policy as instructed in the Medicare Managed Care Manual, Chapter 4, Section 10.7.2.

4. Summary of Changes to Proposed Provisions

As a result of the comments received, we are making the following changes in this final rule.

- For the purpose of clarity, we are modifying the following definitions to state:

++ Category B (Nonexperimental/investigational) device refers to a device for which the incremental risk is the primary risk in question (that is, initial questions of safety and effectiveness of that device type have been resolved), or it is known that the device type can be safe and effective because, for example, other manufacturers have obtaind FDA premarket approval or clearance for that device type.

++ Routine care items and services refers to items and services that are otherwise generally available to Medicare beneficiaries (that is, a beneficiary category exists, it is not statutorily excluded, and there is no national noncoverage decision) that are furnished during a clinical study and that would be otherwise furnished even if the beneficiary were not enrolled in

a clinical study.

● We are revising §405.207(b)(3) to state "Routine care items and services related to Category A (Experimental) devices as defined in §405.211."

● We are revising §405.207(b)(3) to state "Routine care items and services related to Category B (Nonexperimental/investigational) devices as defined in §405.201(b), and furnished in conjunction with FDA-approved clinical studies that meet the coverage requirements in §405.211."

● We are modifying §405.211 so that—

++ Medicare covers routine care items and services furnished in an FDA-approved Category A IDE study if CMS (or its designated entity) determines that the Medicare coverage IDE study criteria in §405.212 are met.

++ Medicare may make payment for a Category B (Nonexperimental/investigational) IDE device and routine care items and services furnished in an FDA-approved Category B (Nonexperimental/investigational) IDE study if CMS (or its designated entity) determines that the Medicare coverage IDE study criteria in §405.212 are met.

++ CMS (or its designated entity) must review the following to determine if the Medicare coverage IDE study criteria in §405.212 are met (that is, FDA approval letter of the IDE, IDE study protocol, IRB approval letter, NCT number, and supporting materials, if needed).

++ A listing of all CMS-approved Category A IDE studies and Category B IDE studies shall be posted on the CMS website and published in the **Federal Register.**

● We modified new §405.212 (IDE study criteria) to require that, for Medicare coverage of items and services described in §405.211, a Category A (Experimental) or Category B (Nonexperimental/investigational) IDE study must meet all of the following criteria.

++ The principal purpose of the study is to test whether the device improves health outcomes of appropriately selected patients.

++ The rationale for the study 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.

++ The study results are not anticipated to unjustifiably duplicate existing knowledge.

++ The study design is methodologically appropriate and the anticipated number of enrolled subjects is adequate to confidently answer the research question(s) being asked in the study.

++ The study is sponsored by an organization or individual capable of successfully completing the study.

++ The study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 21 CFR parts 50, 56, and 812, and 45 CFR part 46.

++ Where appropriate, the study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Studies of all medical technologies measuring therapeutic outcomes as one of the objectives may be exempt from this criterion only if the disease or condition being studied is life threatening and the patient has no other viable treatment options.

++ The study is registered with the National Institutes of Health's National Library of Medicine's ClinicalTrials.gov.

++ The study protocol describes the method and timing of release of results on all pre-specified outcomes, including release of negative outcomes and that the release should be hastened if the study is terminated early.

++ The study protocol must describe how Medicare beneficiaries may be affected by the

device under investigation, and how the study results are or are not expected to be generalizable to the Medicare beneficiary population. Generalizability to populations eligible for Medicare due to age, disability, or other eligibility status must be explicitly described.

We are also making the following conforming changes to 42 CFR 405 subpart B.

- To reflect changes in §405.201(b), we are making conforming changes to the following sections: §405.201(a)(2); §405.203(a)(1) and (a)(2); §405.203(b); §405.205(a)(1); §405.209; §405.213(a)(1); and §411.15(o)(1), by replacing the term experimental/investigational (Category A) device with Category A (Experimental) device, and the term Non-experimental/investigational (Category B) device with Category B (Nonexperimental/investigational) device, as applicable.

- In §405.201(b), we are changing the term IDE to investigational device exemption (IDE) for clarity purposes.

- In §405.207(b)(2), we are making conforming changes to reflect changes to the definitions in §405.201(b) and revised §405.211.

- In §411.15(o)(2), we are making conforming changes to reflect revised §405.211.