September 5, 2013

Marilyn B. Tavenner
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Attention: CMS–1600–P
Mail Stop C4–26–05
7500 Security Boulevard
Baltimore, MD 21244–1850

Dear Administrator. Tavenner

Re: Comments: Medicare Physician Fee Schedule Proposed Rule: Proposed Changes for the Process for Covering Items and Services in an Investigational Device Exemption, Centers for Medicare and Medicaid Services (CMS) 78 Fed. Reg. 43282, 43342-47, 43523-25 (July 19, 2013)

Currently, Medicare Contractors have discretion to determine whether or not to cover IDE clinical trials based on information provided by participating clinical trial sites.[i] CMS has proposed to shift the decision-making process to the national level and away from the contractor level. In addition, CMS is proposing minimum standard "scientific and ethical standards" beyond those currently stipulated in the 1995 Interagency Agreement that every IDE study would be required to meet to be eligible for coverage.

JR Associates (JRA) is a consultancy focused on providing strategic and tactical guidance specific to reimbursement and health policy to providers and to manufacturers of medical devices, diagnostics, pharmaceuticals, and biologics. JRA appreciates the opportunity to submit comments on this topic.

Comment Summary

- JRA disagrees with the CMS proposal as presented, and favors any proposed modification in concert with the U.S. Food and Drug Administration (FDA). We believe the involvement of the FDA is necessary to make certain that both agencies are aligned regarding the specific roles and responsibilities of each agency. This alignment will help to avoid conflicts and duplication of responsibilities. The CMS proposed changes overlap with and in some cases are likely to conflict directly with current FDA regulations. These include the agreement of a least burdensome process and guidance documents that describe the clinical trial process for some IDE devices. A change in the statistical and clinical goals of a trial could also alter the opportunity for FDA approval, in both process and outcome. It is important to preserve the process that devices continue to be fairly evaluated for approval or clearance for marketing, since FDA has responsibility for devices across all trial subjects, including both Medicare and non-Medicare beneficiaries.

- JRA believes any proposed and final changes to the coverage process should be submitted jointly for public comment as an independent proposal rather than captured within a payment rule, specifically the 2014 proposed Medicare Physician Fee Schedule. Use of the payment rule as a conduit for this topic limits awareness of more representative stakeholders to file comments than if separately issued as a stand-alone proposal.
- JRA disagrees with the proposed requirement for superiority clinical trials for coverage. Superiority trials may result in trials that are too large to be feasible to conduct in size, time, and cost. The CMS proposal suggests a preference for trials having a superiority study design, and has created thirteen stated criteria that otherwise must be met, but may not be sufficient to allow a trial to qualify for coverage. This means that even if the criteria are met, CMS may still deny coverage. These types of trials are not always possible, necessary, or appropriate due to ethical considerations, especially in the case of Category B devices and procedures that provide incremental improvements, but for which Medicare or other payers are unlikely to reimburse at a higher rate. Further, for Category A device trials and any trial where routine care is provided, it is prohibitive to add a requirement that would essentially threaten the Medicare beneficiary coverage and payment for routine services to which they would otherwise be entitled.
- JRA opposes the proposal for CMS central management of the IDE coverage process. CMS has previously indicated that it does not have the capacity to add novel devices to the FDA/CMS parallel review pilot program, and has noted staffing limitations as an influencing factor. This proposal creates changes that will require extensive collaboration with manufacturers, FDA, and others in order to implement central decision-making for IDE coverage. CMS has not proposed any timelines or delineation of the logistical process. Specifically, no information is provided as to how trial sponsors will be confidentially notified of decisions and how CMS will disseminate confidential information to contractors about site specific information, such as patient informed consents, IRB approvals, and acknowledgement of provider numbers. The lack of acknowledgement of statutory FDA timelines and delineation of processes to maintain Federal Trade Secrets for premarket devices and trials is a concern.

In summary, this proposal could limit the number of trials that will be eligible for coverage, and may dissuade trial sites and Medicare beneficiaries from participating in clinical trials. CMS should consider opportunities to improve the clinical trial approval process at the contractor level and work to assure this process is more efficient and consistent.

JRA recommends delaying a final decision and convening a task force of stakeholders, including applicable federal and local contractor agencies, large and small manufacturers who sponsor trials, and a mix of academic and non-academic institutions that participate as trial sites, which will allow for public participation to begin the process of reviewing the current system and potential modifications.

Detailed Comments:

Need for FDA Input and Transparency

JRA believes that any proposed change in regulations associated with pre-market trial design must detail the roles and responsibilities of each federal agency to provide clarity to sponsors and clinical sites and to avoid internal agency conflicts and delays.

CMS states (emphasis added):

> "It is essential that CMS-approved IDE studies or trials serve the best interests of Medicare beneficiaries. We believe, **in concert with other federal agencies**, that appropriate study design is critical to ensure that not only are participants in research studies exposed to the least risk possible, but also to ensure that the results from the study would be useful in improving healthcare delivery. Scientifically and ethically flawed studies will not produce valid results, exposing Medicare beneficiaries to unnecessary risk; and wasting time and resources for all involved."[ii]

While CMS specifies that the process of developing clinical studies and study design should happen "in concert with other federal agencies", this process and the responsibility of assuring that IDE studies are scientifically and ethically sound has always been the purview of the FDA. However, this proposal is created by CMS alone rather than with FDA.

In addition, this proposed change to the IDE coverage process is presented within the proposed 2014 Medicare Physician Fee Schedule. JRA believes that a stand-alone proposal has a higher likelihood of drawing attention to representative stakeholders who are more likely to be impacted and who will file comments. It is critical that all stakeholders have an explicit opportunity to comment on this proposal.

Potential Conflicts with FDA IDE[iii]

CMS states that "The principle purpose of the study is to test whether the item or service meaningfully improves health outcomes of patients who are represented by Medicare-enrolled subjects." IDE trials as they are usually conducted would probably not meet that standard.

Depending upon the product being tested and the characteristics of the patient population being studied, IDE trials aim to demonstrate that products are safe and effective. Few premarket trials are Medicare-beneficiary centric. These proposed standards essentially change the approval process from one in which CMS covers most IDE trials to one in which the nature and purpose of an IDE trial will need modification to qualify for coverage and gain FDA market approval or clearance. It requires the merging of potentially different trial goals to meet both pathways, and requires coordination with both the FDA and CMS prior to the approval of the trial. This proposal will add complexity, costs and time to the approval process. The FDA and CMS may not agree on the trial design, making it impossible to conduct and meet the requirement of both agencies. The product must satisfy FDA requirements to be approved for marketing. However, the ability for adequate study will be limited if potential trial subjects, who may be Medicare beneficiaries, are at risk of losing coverage for the routine care and services to which they are entitled.

In a PMA clinical trial, the FDA often stages the trial to first capture a pilot phase followed by a second, "pivotal" phase, where the trial is expanded in numbers of subjects and/or sites. Most often, the protocol is unchanged between the pilot and pivotal phases. This proposal potentially creates a situation where the first phase of the trial may not be eligible for coverage. This would be a burden for the clinical trial sites, as some trial subjects will be covered and others will not, potentially resulting in enrollment limitations. Academic centers and private IRBs require that all trial subjects enrolled be treated identically from an insurance perspective. If this proposal is finalized, routine care in the first phase of the trial may not be covered (i.e. care that would otherwise be covered were the patient not enrolled in a trial). This is counter to the tenet that clinical trial participation should not preclude a Medicare beneficiary from getting the routine care to which they are entitled.

Qualifying for Coverage: Superiority Trial Design and the Thirteen Criteria (Id. At 43345, 43525)

FDA responsibility and regulatory requirements must be obtained in a least burdensome environment. The proposed rules do not detail how CMS will determine that the trial is not a pivotal trial or a superiority design.

CMS has proposed that if the trial in question is not designed to support superiority, the thirteen criteria must be "sufficient to mitigate the failure" of the study, meaning that even if the criteria are met, CMS may still deny coverage. With regard to a superiority statistical design, it is important to recognize that not all devices are "truly new." Many devices may have a clear comparative treatment that would be considered standard of care. In some cases, performing such a trial may be in conflict with ethical trial standards. Importantly, requiring a device that is not novel to be superior to like devices is unnecessarily burdensome. In these cases, the existing devices in the class (i.e. stents, pacemakers, neuromodulation devices, etc.) will remain on the market, based on non-inferiority or similar statistical trial designs. This requirement would create an undue risk of non-coverage, even though the device may be only incrementally changed from the class of devices in which it falls.

In addition, even after such a product is approved, CMS will most likely not be paying more for the procedure and service associated with implanting or otherwise using the device. As such, it is unclear why the device must demonstrate superiority. The cost of a superiority trial is far greater because the size and duration will be longer. This means that devices with incremental improvements that may already be approved and deemed safe and effective would not qualify for clinical trial coverage. Depending upon the means of the company, the device may not reach the market. This creates an unfair market advantage to companies with like devices on the market and a financial burden on companies developing improved devices that will not further financially burden the system. Further, this potentially hampers the opportunity for incremental device improvements that may benefit patients if the risk of denied coverage negatively influences funding.

Routine care coverage associated with a Category A device being studied in an IDE should continue to be based on notification of the scope of routine care proposed in the trial. Subject inclusion and exclusion criteria and trial design should remain within the FDA scope of authority.

Central Decision-Making

The proposal does not describe how CMS will assure that the details of the trial design, statistical design and proprietary trade secrets remain confidential.

CMS is proposing to move decision-making for coverage of the IDE process to the Director of the Coverage and Analysis Group for the local Medicare Contractors. In the past, CMS has noted that the reason the process has been in the hands of the contractors is that they are required to maintain confidentiality, whereas at the federal level, CMS has no such requirement. In addition, a national coverage denial could eliminate opportunities for conducting the trial. For small companies, such a denial is likely to threaten the company's ability to gain sufficient funding for the trial. In the case of devices that are improvements on other like devices that are already covered by CMS, this will minimize competition serves to mitigate high prices. Only large companies that can afford to fully fund routine care to Medicare beneficiaries in a trial will be able to bring devices to market.

Timeframes for Decision-Making and Logistics

CMS does not specify details about the decision-making process, a timeframe for these reviews, or what materials must be submitted. Without any references to systematic infrastructure, this proposal does not provide the opportunity for an objective review.

Recently, CMS has indicated that it currently lacks the staff necessary to add products to the pilot dual FDA/CMS review program. Staffing constraints may impact timely review of clinical trial requests for coverage with the implementation of the proposed coverage standards. Delays within CMS will create delays for private payers who may be making coverage decisions related to the trial. These delays can be extremely costly, and the added uncertainty may have a negative influence on trial funding.

CMS has not addressed who will bear the responsibility of filing IRB approval letters. As proposed, the responsibility will presumably fall on the trial sponsor. This will require the sponsor to address the IRB process, approval letters, and informed consents specific to the trial site. With trials having multiple sites, (some have as many as 50), CMS will need to manage a great amount of disparate information from potentially hundreds of trials. In addition, central management would essentially remove (or in some cases, duplicate) the clinical site routine interactions and contacts with known local contractors.

Suggested Improvements to the Current Process:

JRA recommends that the trial sponsor be able to submit the package of information that is currently required to get a baseline approval for coverage of the trial.

- Individual sites could provide their site-specific information and provide numbers to notify the contractor that they are participants in the trial.

Criteria used to review approved products for CED or other post-market trials should not applicable to the premarket IDE clinical trial process.

- Products enter into this regulatory process to achieve market approvals for patients other than Medicare patients. Implementation of this proposal is likely to create tension between

regulatory and reimbursement goals. CMS has a mechanism in CED to address Medicare-specific questions for products that require this level of investigation.

JRA believes that any focus on improvement should be on correcting the inconsistencies in the current clinical trial coverage process at the local level before suggesting implementing a process at the national level that may be difficult to manage.

- Currently, local contractors sometimes have different coverage decisions for the same technology. Frequently, this is an issue related to timing of decisions. Current discrepancies that occur at the local level can be addressed by consolidating the information provided by the trial sponsor. This can be done in advance of full enrollment, and will leave time for the sponsor to address the contractor's questions. There should be no barrier for coverage of routine care; the sponsor can define "routine care" prospectively with the Medicare contractor. This may minimize the discrepancies and idiosyncrasies in the current process.

Detail Conclusion

JRA recommends delaying a final decision and convening a task force of stakeholders, including applicable federal agencies and allowing for public participation to begin the process of reviewing the current system and potential modifications.

CMS should review the clinical trials reimbursement process in concert with FDA and propose a joint solution outside of the payment rulemaking process to allow for all stakeholders to review and comment. In addition, system revisions should ensure that Medicare beneficiaries continue to have access to clinical trials, per the 1995 interagency agreement

The joint proposal should include logistical details that preserve the FDA regulatory process in a manner that assures that device market approvals are not at risk. The proposal should ensure that CMS is not interfering with the market process and the ability for products that fall into an existing category to compete. Finally, the joint proposal should ensure that trial sites are not dissuaded from including Medicare beneficiaries in clinical trials when coverage is being sought.

Individual Comments Specific to the Thirteen Trial Coverage Criteria (Id. At 43344-45, 43524-5)

Numbers 1-3: Comments noted for each item.

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.

   Clinical trials designed to gain FDA approval must be representative of the entire potential audience of patients who may be prescribed the device. The trials must be balanced to include a mix of patients. In a prospective design, it is impossible to determine the payer mix of trial subject, especially given the FDA requirements specific to safety and efficacy to the device. Often it is the disease process rather than the age of the patient that must dictate whether the trial is appropriate to capture the applicable patient population. It is the provider conducting the trial who ultimately determines subject eligibility.

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.

This responsibility appropriately falls within the purview of FDA.

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

   Not all devices are "truly new." New stents, pacemakers, neuromodulation devices, etc. are being developed with improvements over existing devices. Information regarding the device "class" is likely to be well understood, and therefore, duplicative, but the safety and efficacy must still be articulated for the improved version. Denying coverage for such a trial, would be inappropriate since the clinical need for Medicare beneficiaries to receive the device is already articulated.

Numbers 4-8: These items are / should be the responsibility of FDA rather than CMS.

4. The study design is methodologically appropriate and the anticipated number of enrolled subjects is appropriate 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.

Numbers 9-10: No Comment

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.

Numbers 11-13: Comments noted for each item.

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 (http://www.icmje.org). However, a full report of the outcomes must be made public no later than three years after the end of data collection.

    Full publication of data related to a device that is still subject to FDA approval must follow the process of submitting the IDE to FDA. A 24 month timeline cannot be appropriately applied to all devices in a pre-market environment.

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 effect 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.

For a device that is not "truly new", but rather one that represents a device improvement, the existing body of knowledge and other post-market trials for a class of devices is likely to address subpopulations and special populations. For "truly new" devices, safety and efficacy at a baseline level is not yet established; a mandate to include special populations and under-represented groups is likely to be prohibitive to completion of the trial.

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.

    For some premarket devices, generalizability to populations beyond that which is studied in the trial may be difficult to articulate, especially when the class of device is new. For a device that is a new version of an existing device, a body of evidence is available to assess. Further, if the device "class" is the subject of a Medicare National or Local Coverage Decision, this criterion is redundant. This will create undue burden on a trial being conducted in a "least burdensome" environment, and likely to have a negative influence on Medicare beneficiary enrollment.

CMS proposes that all IDE studies will have to meet these criteria for coverage but still may not be sufficient for coverage. CMS also proposes to automatically approve an IDE study where the study meets all of the above criteria and the following two *additional* criteria:

- the study is a pivotal study
- the study has a superiority study design

The addition of these criteria may threaten the opportunity to enroll Medicare beneficiaries.

Should you have any questions or if JRA can be of further assistance, please feel free to contact us at 818-344-4380 or jr@1jra.com. Thank you for your attention to this important matter.

Sincerely,

Judy Rosenbloom, President
Jo Ellen Slurzberg, Vice President Global Health Policy
Beth Bontemps, Senior Reimbursement and Clinical Consultant

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[i] Implementation of the FDA/HCFA Interagency Agreement Regarding Reimbursement Categorization of Investigational Devices September 15, 1995 (D95-2)

[ii] Id. 43344

[iii] List of references for Premarket Approvals

- SEC. 515. [21 USC §360e] Premarket Approval; General Requirement
- 21 CFR 814
- The Least Burdensome Provisions of the FDA Modernization Act of 1997: Concept and Principles; Final Guidance for FDA and Industry 1332
- PMA Guidance Documents
- CPG Sec. 300.750 Class III Devices Subject to 515(b) Requirements