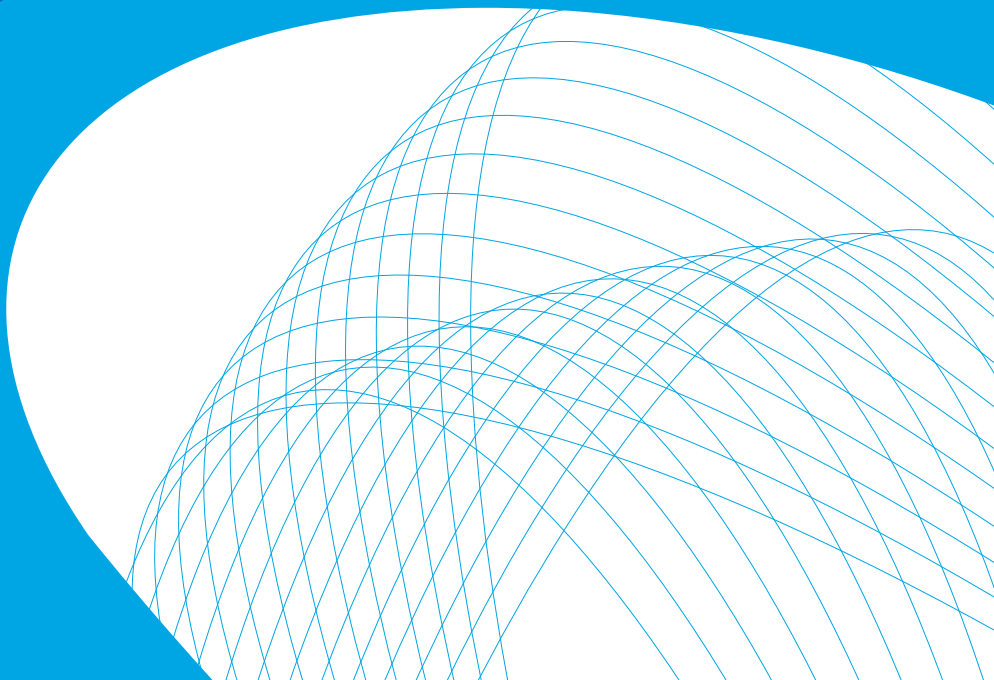
Implications of the FDASIA 2012 Investigational Device Exemption Provisions

March 2013

Prepared by:
Lakshman Ramamurthy
Jenifer Levinson
Elizabeth Guo
Tanisha Carino



Much of the media coverage on the 2012 Food and Drug Administration Safety and Innovation Act (FDASIA) has focused on whether the changes to user fees and approval pathways will lead to faster FDA review times and access to market. Yet changes to the Investigational Device Exemption (IDE) regulations that impact medical devices deserve a closer look. Listen to a podcast from Avalere experts and download this white paper on what FDASIA 2012's IDE provisions may mean for a device's path to market access and the nature of FDA-CMS relationships moving forward.

Key Implications from "Would Changes to FDASIA 2012 Impact CMS? Case Study: Investigational Device Exemptions":

- CMS and FDA policy making are increasingly intertwined and these changes demonstrate the need for formal parallel review efforts.
- The FDA's changes to the definition of "investigational device" may make it more difficult for manufacturers to receive CMS reimbursement during clinical trials.
- Successful manufacturers will strategically engage with CMS and FDA to obtain feedback on appropriate clinical trial design and ensure reimbursement for clinical trials.
- Manufacturers should monitor whether increased FDA-CMS engagement will alter the evidence requirements for market approval and patient access.

Executive Summary

FDA and CMS are increasingly working together to identify and review technologies in a similar fashion. This development leaves many FDA and CMS policies intertwined, and stakeholders searching for answers on how the new processes will function. For example, the FDA's redefining of the Investigational Device Exemption (IDE) has left many wondering how CMS will evaluate these technologies for reimbursement during clinical trials. While there are efforts underway to initiate formal parallel review, most manufacturers are likely to engage in more informal parallel review as was demonstrated by CMS' Coverage with Evidence Development (CED) decision on transcatheter aortic valve replacements (TAVR) before FDA approval. Avalere's analysis of these trends shows that manufacturers will need to engage FDA and CMS more often and more thoughtfully in order to decrease time to market and align data collection efforts. In addition, manufacturers should closely watch FDA and CMS policymaking as they will continue to impact one another.

Taking a Closer Look at FDA's Changing IDE Policy

Understanding IDEs

An investigational device exemption (IDE) permits a device that has not yet received market approval to be used in a clinical study designed to generate data on safety and/or effectiveness of the device. These clinical studies are often conducted to generate data that would support a FDA approval through either the pre-market approval (PMA) pathway or, in a few cases, the 510 (k) approval pathway. FDA could issue four types of decisions when green lighting IDEs: approval, conditional approval, staged approval, or disapproval. In conditional approval or staged approval, FDA approval of an IDE depends on a manufacturer's response to certain questions unaddressed in the initial application, or the requirement that some conditions are met before proceeding with the study.

Until now, FDA IDE approvals have been based on both safety and effectiveness of the device. In a November 2011 IDE guidance, FDA stipulated the following three factors for disapproval:[1]

1. The data cannot adequately characterize the safety profile of the device (e.g., mechanical durability, electrical safety) so that human clinical investigation is not considered reasonable.
2. The potential risks of the proposed study are not justified.
3. The proposed study design or analysis plan is inadequate.

FDA may evaluate elements of the proposed study design as bases for disapproval, including lack of primary safety and effectiveness endpoints, study design assumptions, enrollment criteria, and critical study assessment methodologies. The source of FDA's decision is Section 520(g)(7)(A) of the Food Drug and Cosmetic Act, which states that the sponsor demonstrate "…there is a reasonable assurance of effectiveness, and if available, information regarding the expected performance from the device."

FDASIA and the Future of IDEs

The 2012 passage of FDASIA targeted the third criteria for FDA's disapproval of an IDE. The law states that FDA "shall not disapprove" an IDE even if the study as designed is insufficient to support an approval decision and may require additional studies. This change raises the following three issues for product sponsors:

- IDE approvals may not predict as accurately the future pre-market approval for a product.

- The changes in legislation may create an environment where FDA is compelled to approve study designs that may not lead to FDA device approval.
- Patient groups and physicians may begin to question the usefulness and ethics of engaging in device clinical trials that are poorly designed and incapable of eventually resulting in market access.

In response to the legislative changes, FDA has decided to create a new "pre-decisional IDE process," which would allow for an informal review of the IDE so that sponsors can anticipate the agency's concerns about the study and whether it will satisfy FDA device approval requirements.[2]

Understanding Implications of FDA Actions on CMS

What does this mean for CMS?

- CMS' decision of "reasonable and necessary" for the clinical trial will have to be made in the context of FDA's changes to the approval of IDEs.
- Changes to IDE approval may trigger CMS to revisit its policy around coverage of Category B IDEs for Medicare coverage.
- CMS may have an interest to become more engaged earlier in the FDA's IDE protocol review and decision. Product sponsors will need to keep this in mind and monitor whether CMS should be engaged at earlier stages in discussions on the IDE protocol review and decision process.

Medicare's Category B IDE Reimbursement Policy

In 1995, to ensure the inclusion of more Medicare-aged beneficiaries in studies, FDA and CMS signed an agreement on reimbursement categorization of investigational devices to:[3]

- Assure Medicare beneficiaries greater access to advances in proven medical technology;
- Encourage clinical researchers to conduct high-quality studies; and
- Clarify Medicare coverage of reasonable and necessary medical services during clinical trials for investigational devices.

As part of this agreement, FDA categorizes devices into two categories: Category A or Category B. Category A devices are considered experimental and are NOT covered by Medicare under the IDE request process and are typically novel and first-of-their-kind

technologies. Medicare will only cover the routine costs of clinical trials in such cases. Category B, however, is reserved for newer generations of devices for which questions of safety and effectiveness have been proven. The device can only be considered for use if it is part of a FDA- and Institutional Review Board (IRB)- approved study. Medicare covers Category B devices under the IDE process if found "reasonable and necessary" and all other coverage requirements are met. CMS uses this categorization to help them determine whether the device under study in an IDE should receive Medicare coverage and reimbursement. This agreement has resulted in Medicare beneficiary access to the newest technologies with generally well-substantiated safety and efficacy profiles.

Currently, CMS reimbursement of routine care in the context of a clinical trial includes the costs of the investigational device as well as the cost of the services associated with carrying out the clinical trial when the trial is conducted under an FDA-approved IDE or a CED. For devices that qualify under the 1995 agreement, CMS regularly looks to FDA IDE approval to help it assess whether a device is "reasonable and necessary" for a patient. In that regard, a device that was not yet approved for market access in the United States, and therefore an "investigational" device, was deemed "experimental" and thus would not meet CMS' statutory requirement of "reasonable and necessary."

Future Medicare Coverage of Category B IDE Trials

Under FDASIA, if FDA is no longer using the IDE approval process to assess study design, how will the change in criteria for IDE disapproval translate into a local coverage contractor's evaluation of an investigational device for coverage and reimbursement? Will FDA's changed standards for IDE lead to a reciprocal change in how CMS evaluates categorization of these devices?

It may still be too early to know for certain what CMS' response will be, but initial reactions suggest that CMS coverage may be affected. Traditionally, it has been challenging for sponsors to receive IDE coverage from Medicare contractors, but the new change in FDA standards may compound the already difficult process, as some local contractors are beginning to request additional supporting information about trial design before determining coverage. CMS' Coverage and Analysis Group (CAG) is also closely monitoring how FDA handles the new legislative requirements. At an event in Washington, D.C., in December 2012, Louis Jacques, CAG director, noted CMS may reevaluate its IDE policy relative to the changes being implemented at FDA. Thus, if IDEs are approved despite study designs that would have been previously deemed by FDA as insufficient, CAG could revise its coverage of category B IDE and either create additional approval processes for CMS to approve the study design of these trials or begin denying Medicare coverage for these studies.

CMS-FDA Interactions - A Pilot or a Paradigm Shift

FDA and CMS decisions are no longer occurring in isolation, and the recent change in IDE policy illustrates that agency decisions may have cross-agency ramifications. These sorts of interactions can be seen in the FDA-CMS parallel review process. On Oct. 11, 2011, FDA and CMS launched a parallel review pilot program[4] for concurrent review of medical devices for up to five innovative devices per year. So far, Exact Sciences has announced that it is participating in the pilot initiative for parallel review, but no products have yet completed the entire pilot.[5] In March 2013, Medtronic also announced publicly that it is participating in the parallel review pilot for its Symplicity™ renal denervation program.[6]

Informally, CMS CED decisions are indicative of a trend in which FDA and CMS are increasingly collaborating on post-market evidence collection. The recent CMS decision on TAVR[7] reflects how this process might occur, from CMS initiating a national coverage decision before FDA approval of a new device to FDA and CMS utilizing the same registry for their data collection requirements. In addition, the final national coverage determination (NCD) for TAVR created a process for product sponsors to register their IDE studies with CMS. In the TAVR case, CMS has required coverage with evidence development for which each post-approval study will need to go through an FDA IDE review and CMS CED review process. CMS' TAVR decision provides insight into how CMS and FDA may align post-market approval and coverage requirements and how the two agencies may work together in its new parallel review pilot program for concurrent review of medical devices.

Increasingly, FDA and CMS are looking for new collaborative ways to gain efficiencies along the path from approval to coverage. While this may mean that products have the potential to see decreased times from development to market access, it also means that manufacturers may have to engage with FDA and CMS in novel ways, including considering how their interactions with one agency may affect the decisions of the other. The new way FDA is evaluating IDEs nicely illustrates how a change that seems to promote access early in product development can have different ramifications for patient access to new technologies down the road.

Notes

[1] U.S. Food and Drug Administration. "FDA Decisions for Investigational Device Exemption (IDE) Clinical Investigations: Draft Guidance." (November 2011)

[2] R Kern. "FDA To Re-Issue Draft Guidance On Investigational Device Exemption Standards." *The Gray Sheet* (4 March 2013)

[3] U.S. Food and Drug Administration. "Implementation of the FDA/HCFA Interagency Agreement Regarding Reimbursement Categorization of Investigational Devices" (September 1995) http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080302.htm

[4] *Federal Register* Vol. 76, No. 196. Friday, October 11, 2011. CMS and FDA. "Pilot Program for Parallel Review of Medical Products." [Docket No. FDA–2010–N–0308 8.] Available at: http://www.gpo.gov/fdsys/pkg/FR-2011-10-11/pdf/2011-25907.pdf

[5] Exact Sciences. "2010 Annual Report." Available at: http://investor.exactsciences.com/2010AR/pdf/exs_ar_2010.pdf

[6] Medtronic. "Symplicity™ Renal Denervation System One of First Devices Accepted to Participate in Concurrent Review for Joint FDA Premarket Approval and Medicare National Coverage Determination." Available at: http://wwwp.medtronic.com/Newsroom/NewsReleaseDetails.do?itemId=1362589417673&lang=en_US

[7] Centers for Medicare & Medicaid Services. "Decision Memo for Transcatheter Aortic Valve Replacement (TAVR)" (CAG-00430N) May 2012.

Avalere Health LLC
1350 Connecticut Ave. NW
Suite 900
Washington, DC 20036

www.avalerehealth.net

Avalere®