FDA-CMS Parallel Review

A Failed Attempt at Spurring Innovation

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Abstract

In 2010 the Food and Drug Administration and the Centers for Medicare & Medicaid Services (CMS) founded a pilot program for medical devices: simultaneous review of FDA premarket approval submissions and CMS national coverage determinations. By reducing the amount of time between obtaining marketing approval and securing Medicare coverage, the parallel-review program is supposed to facilitate the development of innovative medical devices and to shorten the time it takes to bring these devices to patients. After five years, however, the program's impact remains limited: so far, only one device has been approved through this process. Why are manufacturers not more interested in this opportunity? While parallel review might shorten time to national coverage determination, it is likely to delay marketing of the device. Moreover, while meant to promote innovation, parallel review does not address key obstacles manufacturers currently encounter in bringing their products to market.

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Keywords: pilot program for parallel review of medical products, Food and Drug Administration, Centers for Medicare and Medicaid Services, medical devices, premarket approval, national coverage determinations, local coverage determinations, innovation

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1. Introduction

In 2010 the Food and Drug Administration (FDA) and Centers for Medicare and Medicaid Services (CMS) announced the FDA-CMS Parallel Review pilot program for medical devices (FDA 2010). The program was launched in 2011. As stated in the notice in the Federal Register, its goal is to decrease the time between the FDA's premarket approval (PMA) of a new medical technology and a national coverage determination (NCD) by CMS (FDA 2011). This goal is to be accomplished by allowing both agencies to review clinical data at the same time and to save manufacturers from designing additional tests just for the CMS. As listed in the Federal Register, the appropriate candidates for the program are:

1) "New technologies for which the sponsor/requester has had sufficient pre-investigational device exemption (IDE) interaction with FDA or approved IDE application.
2) New technologies for which an original or supplemental application for premarket approval (PMA) or petition for de novo review would be required.
3) New technologies that fall within the scope of a Part A or Part B Medicare benefit category and are not subject to an NCD" (FDA 2011).

After five years, however, the program's impact remains limited: So far, only one device has successfully completed the program. In August 2014, Exact Sciences' Cologuard test obtained a PMA from the FDA and a draft NCD from CMS on the same day (FDA 2014a). The final NCD was issued in October of the same year (Exact Sciences 2014). Despite its limited

impact, the program remains open, and in February 2016, the FDA invited private insurance providers to participate in the expanded version of the program (Mezher 2016).[1]

Why are manufacturers not more interested in this opportunity to reduce the waiting period between the PMA and the NCD? First, few devices are eligible to participate. The program's focus on new technologies renders it irrelevant to those devices that can be cleared though the 510(k) process by being shown to be as safe and effective as—that is, substantially equivalent to—a legally marketed device. Second, the parallel review might shorten the wait time for a national coverage determination, it is likely to delay marketing of the device. Since NCD is not necessary for reimbursement, securing the FDA approval without the coverage decision in most cases allows the manufacturer to bring the device to market faster (Pavlovic and Halpern 2015). Third, the program does not address numerous obstacles that device sponsors currently encounter in bringing their products to market, such as obtaining a reimbursement code or dealing with the unpredictability of the FDA process (Makower, Meer, and Denend 2010; Pavlovic and Halpern 2015).

2. FDA Approval Process for Drugs and Medical Devices

A. Drugs

Before any new drug or medical device enters the market, FDA must first approve it.[2] The approval process for medical devices is quite different than that for drugs. Securing an approval for a new prescription medication often takes longer than a decade, with an estimated total cost per drug of $2,558 million (Tufts Center for the Study of Drug Development 2014). The FDA

[1] "Early input from payers regarding their evidentiary needs can streamline the process from FDA approval or clearance to payer coverage and improve public health by facilitating earlier access to innovative, safe, and effective medical devices" (FDA 2016e).

[2] The approval process summarized below is described in more detail at FDA (2016d).

drug approval process starts with preclinical testing, during which animal testing is used to determine whether the drug is safe for testing in humans (FDA 2014b). Preclinical tests take anywhere from one to three years. Subsequent clinical testing takes between five to ten years and comprises three key phases. In phase I, in order to determine its side-effect profile, relative safety, and the route of metabolism, the drug is administered to a small number of healthy patients; usually about 20 to 80 participants are involved. If the safety profile is determined to be acceptable, then phase II starts, and the drug is administered to a small number of patients suffering from the targeted condition. Phase II is meant to determine whether the drug is effective and what is the optimal dosage. If phase II is successful, the FDA and the drug development company jointly design phase III, during which the effectiveness and safety of the drug are compared against alternatives or standard-of-care therapies.

The phases of clinical trials were designed to ensure that dangerous drugs are identified in the early stages of development, before they can affect large numbers of patients. Only those drugs that successfully navigate the phases with satisfactory effectiveness and safety profiles qualify for the new drug application. If approved, manufacturers are also required to conduct postmarketing surveillance that takes on average two years and costs an additional $312 million (Tufts Center for the Study of Drug Development 2014). Furthermore, the FDA sometimes attaches postapproval trials as a condition of the approval. In sum, while the length of the process and its costs vary on a case-by-case basis, research indicates that bringing a new drug to market can cost as much as $3 billion and can take as long as a decade.

B. Medical Devices

For the great majority of medical devices, the approval process is shorter and less expensive than that for pharmaceuticals. Duration and cost vary depending on the class of the device. Higher-risk devices, those on the premarket approval (PMA) pathway, require an average of 54 months from the first communication with the FDA to approval to market the device. The average total cost from concept to approval for the PMA devices is approximately $94 million, with $75 million spent on stages linked to the FDA—almost 80 percent of the total cost of bringing these devices to market (Makower, Meer, and Denend 2010).

The first step in submitting a medical device for approval is identifying its classification (FDA 2015). The FDA categorizes medical devices into three groups, based on the level of control necessary to assure their safety and effectiveness (FDA 2014c). Class I is for the lowest-risk devices that are subject to general controls. FDA lists enema kits and elastic bandages as examples of class I devices. Class II is for moderate-risk devices that are subject to both general controls and special controls. Examples include powered wheelchairs and pregnancy test kits. Finally, class III is for the highest-risk devices. Implantable pacemakers and breast implants are examples of class III devices.

Ninety-five percent of class I devices are exempt from the regulatory process (FDA 2014c). Class II devices that can be shown to be as safe and effective as a legally marketed device are cleared through the 510(k) pathway. But class III devices must undergo the premarket approval process (FDA 2016d). FDA-CMS parallel review is focused on new technologies, and therefore it is relevant only to the devices on the PMA route, not to those on the 510(k) pathway. The 510(k) pathway is significantly simpler because it does not require any scientific testing; clearance requires only that the device be “substantially equivalent” to a previously legally

marketed device in terms of intended use, technological characteristics, and performance testing. Ninety percent of all medical devices enter the market through the 510(k) pathway (Pilot 2011). In contrast, the PMA process is similar to the new-drug-approval process and typically requires clinical trials. Before the FDA approves a PMA, the sponsor must provide valid scientific evidence demonstrating reasonable assurance of safety and effectiveness for the device's intended use (FDA 2016d).

3. CMS Approval Process

Medicare coverage is determined through national coverage determinations or, in the absence of a national coverage policy, through local coverage determinations (LCDs).[3] Both NCDs and LCDs are sets of instructions that describe conditions required for the Medicare coverage of a medical service procedure or device. They are meant to help providers submit correct claims. NCDs are developed by CMS, while LCDs are developed by Medicare administrative contractors (MACs). Since the beginning of Medicare, CMS has contracted with private insurance companies to operate as intermediaries between the government and private medical providers. Contracted processes include claims and payment processing, call-center services, clinician enrollment, and fraud investigation. These intermediaries play a significant role in determining Medicare coverage.

MACs issue LCDs when there are no appropriate NCDs or when there is a need to further define NCD conditions. MACs are multistate, regional contractors responsible for administering Medicare Part A and Part B claims. Since NCDs are mandated at the national level, their guidelines are binding for all fiscal intermediaries, carriers, and MACs. In contrast, the MACs

[3] Details about the NCD and LCD processes can be found at CMS (2015).

mandate LCDs, and their guidelines are only applicable at the local level. Each MAC is responsible for developing coverage policies within its jurisdiction. LCDs apply within the multistate area managed by a specific regional Medicare Part B contractor.

It is worth noting that qualifying for Medicare reimbursement is of paramount importance to manufacturers. In fact, there are many consulting companies that help manufacturers navigate this cumbersome process. One of consulting reports captures the importance of reimbursements vividly:

> Reimbursement is the primary driver to profitability of a new technology in that it assures the all-important revenue stream that keeps a company viable. . . . Because of [Medicare's] size and influence, private payers will usually adopt the same or similar coverage, coding and payment policies. (Stark and Jaeger 2011)

4. FDA-CMS Parallel Review and Innovation

The stated goal for the FDA-CMS Parallel Review program is to facilitate the development of innovative devices and shorten the time it takes to bring these important products to patients (FDA 2011). But does this program actually spur innovation? The policymakers who created the program initially had a very positive outlook on the potential of this reform. They expected that the policy would allow patients to access innovative medical devices sooner, ease intergovernmental communication, and streamline decision-making.

> The efficiencies gained by parallel review are expected to benefit all interested parties. Patients are expected to gain quicker access to innovative medical technologies if they are covered. The sponsor/requester gains timely insight to the information needs of CMS with respect to pursuing a positive NCD as well as a potentially shortened time to payment due to a streamlined multi-review process. The Agencies gain enhanced channels of communication. Specifically with regard to CMS, its early involvement will streamline the decision making process. It will also focus attention on health outcomes of importance to Medicare, and provide early awareness of any remaining evidence gaps. (FDA 2011)

However, upon closer examination, it becomes clear that these predictions were overly optimistic.

A. Limited Impact

After five years, the program's impact remains limited; so far, only one device—Exact Sciences' Cologuard test—has been approved through the process (Exact Sciences 2014). Cologuard is a multitarget stool DNA test developed for noninvasive screening for colorectal cancer. From the PMA submission to the final NCD, the process lasted 489 days, compared to the average of 612 days for other NCDs issued in 2013 (Ridge and Statz 2015). However, while the parallel-review process shortened the expected interval from FDA approval to coverage determination for Cologuard, this experience has not been replicated for other devices. The only other known parallel-review participant was Medtronic's Symplicity renal denervation system (Medtronic 2013). The device's phase III trial did not meet its primary efficacy endpoint, so it was unable to complete the parallel-review process (Gaffney 2014).

Why are manufacturers not more interested in the parallel-review program (Weixel 2013)? One culprit is restricted eligibility. The program is only relevant to class III devices, and only 10 percent of all medical devices fall into this category (FDA 2014c). Class III devices require premarket approval, but in 2015 the FDA issued just 43 original PMAs.[4] This number appears especially low when compared to the 3,015 devices cleared through the premarket notification process (510(k)) in the same year.[5]

Second, obtaining an NCDis not the only path to securing Medicare reimbursement. In fact, to date, CMS has issued just 340 NCDs (CMS 2016). To be more specific, between 1999 and 2011, CMS issued an average of just six NCDs per year for a medical technology that had been previously approved by the FDA (Chambers, May, and Neumann 2013). Instead of relying on NCDs, manufacturers prefer to seek coverage through LCDs (Pavlovic and Halpern 2015).

[4] Calculated by adding premarket approvals from each month (FDA 2016b).
[5] Calculated by adding 510(k) clearances from each month (FDA 2016c).

This allows them to avoid the risk of adverse coverage determination at the national level, which would be binding on all Medicare contractors.

B. Longer Time to Market

When reviewing a device, the FDA seeks to establish whether a device is "safe and effective" for its particular intended use.[6] In contrast, CMS seeks to determine whether an item or service is "reasonable and necessary" (Neumann and Chambers 2012). This means that the two agencies are guided by two different evidentiary standards and seek to answer different questions.

In a 2013 study, researchers evaluated NCDs issued between 1999 and 2011. They found that CMS is generally more restrictive compared with FDA approval, particularly for the coverage of medical devices (Chambers, May, and Neumann 2013). This finding strongly suggests that FDA's "safe and effective" standard is less stringent than CMS's "reasonable and necessary" standard. This being the case, it is unsurprising that manufacturers are not too interested in participating in the parallel review. Manufacturers likely believe that in most cases, it would take more time and resources to obtain an NCD along with the PMA than just to get permission to market the device. This is because obtaining an NCD requires additional evidence beyond what is needed for the PMA. For example, the device might be shown to be safe and effective enough for the general population to secure a PMA. But the CMS also requires that the device be shown to provide health benefits to the Medicare population. Adding an NCD to the FDA process means that devices undergoing parallel review will take longer before being available for patients than devices that only undergo the FDA approval process.

[6] "Unlike premarket notification, PMA approval is to be based on a determination by FDA that the PMA contains sufficient valid scientific evidence that provides reasonable assurance that the device is safe and effective for its intended use or uses" (FDA 2016a).

The longer time to market is especially troublesome given that the FDA's PMA process is already longer than its European equivalent. In a recent study, researchers surveyed 204 companies—about 20 percent of all public and venture-backed medical device manufacturers—about their experience working with the FDA versus comparable European regulatory authorities (Makower, Meer, and Denend 2010). For the devices seeking PMA, respondents said that it took an average of 54 months to work with the FDA, compared to 11 months for similar processes in Europe. Moreover, 85 percent of respondents considered EU authorities to be highly or mostly predictable, while only 22 percent gave the FDA the same predictability ratings. As a result of regulatory hurdles, devices are available to US citizens an average of two full years later than to patients in Europe, and in some cases the lag is nearly six years long. These delays cause manufactures to invest elsewhere and are a main reason why many Americans need to seek treatment abroad (Pollack 2011).

C. Unresolved Obstacles

Although the FDA-CMS Parallel Review program was intended to promote innovation, the program does not address some key obstacles that device sponsors currently encounter in bringing their products to market. Securing FDA approval and Medicare reimbursements is not the only obstacle manufacturers need to overcome to successfully market a medical device in the United States. For example, manufacturers also need to be identified in the Healthcare Common Procedure Coding System (HCPCS). To obtain a code, the new technology must be shown to be sufficiently different from existing technology and used by enough providers. Parallel review does nothing to shorten or ease the process of acquiring a new code (Pavlovic and Halpern 2015).

Another problem is the unpredictability of the approval process:

> In general, survey respondents viewed current U.S. regulatory processes for making products available to patients (the premarket process) as unpredictable and characterized by disruptions and delays. For example, 44 percent of participants indicated that part-way through the premarket regulatory process they experienced untimely changes in key personnel, including the lead reviewer and/or branch chief responsible for the product's evaluation. A total of 34 percent of respondents also reported that appropriate FDA staff and/or physician advisors to the FDA were not present at key meetings between the FDA and the company. Factors such as these make the U.S. premarket regulatory process inefficient and resource intensive. (Makower, Meer, and Denend 2010)

Finally, obtaining an NCD does not necessarily lead to private reimbursement. For example, the US Preventive Services Task Force identified Cologuard as an "alternative" screening method despite its success in the Parallel Review program and left it out of a group of recommended tests. The news cut Exact Sciences' stock price in half (Engel 2015).

5. Conclusion

While well intentioned, the FDA-CMS Parallel Review program falls short of its intended goals. Reducing the duration of the approval and reimbursement process with appropriate levels of safeguards is in everybody's interest: policymakers', manufacturers', and patients'. Yet, as evidenced by manufacturers' limited interest in the program, this particular reform does not contribute to the resolution of regulatory hurdles, at least not enough to make it worthwhile for manufacturers. Despite the evidence that the program is ineffective, regulators are moving ahead and opening the program to private payers. It's possible that being able to secure private reimbursement along with Medicare coverage will make the program marginally more attractive to device sponsors. So far, however, the CMS-FDA Parallel Review program has failed to deliver on its promises, and it is unlikely that opening the program to private payers will make much of a difference.

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