Innovative Governance Models for Emerging Technologies
10. Innovative governance schemes for molecular diagnostics

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10.1 INTRODUCTION

Molecular diagnostics are expected to shepherd in a new paradigm in health care delivery known alternatively as personalized, individualized or precision medicine. The key distinction of this new approach is that health care decisions will be based on a patient’s individual molecular profile rather than on population or group characteristics or averages. Thus, for example, the selection and dose of a drug will be based on the particular set of variants present in the patient’s genome that affect drug metabolism. Diseases will be detected much earlier based on the presence or concentration of a protein biomarker in the patient’s blood, rather than waiting for the disease to manifest in clinical symptoms. The prognosis and best treatment option for a cancer patient will be determined by the changes in gene expression patterns in the patient’s tumor.

These new molecular-based strategies for predicting, diagnosing, and treating disease are all dependent on sophisticated new molecular diagnostic tests. These molecular diagnostic tests will be the quarterbacks of the new personalized medicine paradigm. Just as a quarterback in football surveys the situation on the field, selects the appropriate play, and then sets that play in motion, molecular diagnostics will play a central role in assessing a patient’s health status and risks, selecting an appropriate intervention strategy, and then targeting the treatment based on the patient’s molecular profile. As is the case with quarterbacks, molecular diagnostics will therefore be critical to the outcome, and at least when successful, will be high profile, sophisticated, and high value.

The challenge for personalized medicine is that this model for molecular diagnostics is inconsistent with traditional economic and regulatory assumptions about diagnostic products. Extending the football metaphor another step, diagnostic tests have until recently been more analogous to offensive linemen in football. They have been relatively low cost, are...
called upon to perform tasks that are relatively straightforward and simple, and are generally fungible. The question facing the regulatory system therefore is how to transform diagnostics from being the linemen to the quarterbacks of medicine.

The frameworks for the regulation and reimbursement of diagnostics, combined with outdated business models and provider practices, stand as barriers to the successful development and commercialization of sophisticated molecular diagnostics that are critical to personalized medicine. In this chapter, we first expand on how path dependence has resulted in outdated frameworks for molecular diagnostics, and how this is slowing the uptake of personalized medicine. We then describe two innovative new programs – coverage with evidence (CED) and parallel review – that may expedite the commercial development of molecular diagnostics. The chapter concludes with some comments on the implications of these governance innovations for the “pacing problem.”

10.2 REGULATORY AND REIMBURSEMENT CHALLENGES FOR MOLECULAR DIAGNOSTICS

The sophisticated new molecular diagnostic tests that are the foundation of personalized medicine are encountering significant challenges and uncertainties with regard to both regulation and reimbursement. These problems are summarized below.

10.2.1 Regulation of Molecular Diagnostic Tests

There are two potential regulatory pathways for molecular diagnostics: one through the Food and Drug Administration (FDA), and the other pursuant to the Clinical Laboratory Improvement Act (CLIA) administered by the Centers for Medicare and Medicaid Services (CMS). The limitations and uncertainties about the application of both of these existing pathways to new molecular diagnostic technologies have generated much confusion among product sponsors. These uncertainties make it difficult for researchers and developers to successfully bring new products to market and threaten to slow or block the implementation of personalized medicine.

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10.2.1.1 FDA regulation

Molecular diagnostics are regulated by the FDA as medical devices. Among the wide range of medical devices evaluated by the FDA, molecular diagnostics fall into a category known as “in vitro diagnostics” (IVDs). These devices, which rely on measurements at the molecular level of samples removed from an individual’s body, are distinguished from in vivo devices such as blood pressure cuffs and thermometers, which rely on measurements taken directly from an individual. Since 1976, the FDA has been charged with ensuring that all medical devices it evaluates, including IVDs, provide a “reasonable assurance of safety and effectiveness.” Because the FDA evaluates devices before they enter regular clinical use, the agency relies almost exclusively on pre-market data supplied by the products’ sponsors to evaluate safety and effectiveness.

In order to devote more resources to products that pose the greatest risks and uncertainty without slowing market entry for less risky products, the FDA groups new devices into one of three categories based on their level of risk and subjects those categories to corresponding levels of scrutiny. Class I and II devices are considered low enough risk that compliance with general controls (for example, good manufacturing practices, product labeling) or special controls (for example, post-market surveillance, patient registries) is sufficient to provide a reasonable assurance of safety and effectiveness, generally without the need for clinical data. Class III devices are higher-risk and warrant additional investigation to ensure their safety and effectiveness, traditionally through a pre-market approval (PMA) process requiring clinical trials.

For devices that would otherwise fall within Class III, the FDA seeks to limit its reliance on the resource-intensive PMA process by allowing a new device to be marketed without a PMA if the product’s sponsor is able to demonstrate that its product is “substantially equivalent” to existing devices. This is known as a “pre-market notification” or 510(k) clearance. Pursuant to this pathway, devices can be legally marketed simply by demonstrating that they are “substantially equivalent” to existing devices.

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3 21 CFR 860.3(c)(1–2).
4 21 CFR 860.3(c)(3).
5 Jeffrey Gibbs, “Regulatory Pathways for Clearance or Approvals of IVDs,” in FOOD AND DRUG LAW REGULATION 43, 45 (FDLI, eds, 2008). The existing device may include products that were already on the market prior to 1976 and were never subjected to FDA regulation, or those that were cleared after 1976 through a 510(k) process.
existing devices that also were not required to go through the more rigorous PMA process. In contrast to the PMA process, which generally requires submission of high quality clinical data, only 10–15 percent of products cleared through the 510(k) process are required to submit clinical data of any type, making this a much faster and less expensive pathway to market.

For developers of new molecular diagnostics that will be evaluated by the FDA, the agency’s decision about which pathway the devices must follow – 510(k) or PMA – has major consequences. While the majority of existing IVD products on the market today have been cleared through the 510(k) pathway rather than through a PMA, the novelty of advanced molecular diagnostics increases the chances that they will be sent through the PMA process as there are less likely to be existing devices to serve as comparators within the 510(k) clearance process, at least initially. Given the substantial time and cost differences inherent to the two different pathways, the lack of predictability creates major problems for molecular diagnostic developers, who are unable to plan their long-term budgets, trials, and other logistics involved with bringing their products to market.

In addition to these challenges, the evidentiary requirements for devices to achieve clearance through the 510(k) process are less than clear. Currently, product sponsors rely on related 510(k) submissions and previously published guidance documents to inform their applications. However, there is a common perception that the FDA’s 510(k) requirements are growing more stringent, especially for molecular diagnostic tests, thereby casting doubt on the reliability of these sources. Specifically, 510(k) submissions for molecular diagnostic tests are more likely to require the submission of clinical data and face greater statistical scrutiny than submission for other types of devices. Whether required in the

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8 Institute of Medicine, SYSTEMS FOR RESEARCH AND EVALUATION FOR TRANSLATING GENOME-BASED DISCOVERIES FOR HEALTH 49 (2009).
10 Gibbs, supra note 5, at 48.
context of a 510(k) submission or a PMA application, there is a lack of consensus about how to conduct studies that will demonstrate the clinical utility of diagnostic tests. In contrast to clinical trials for therapeutics, in which the effect of a new product can be directly measured by patient outcomes, trials for diagnostics are less straightforward. For example, a diagnostic test that helps physicians tailor the dose of a given drug may be only one factor affecting the outcome of a patient taking that drug, which may also be influenced by other medication use, physician interpretation of the test, patient adherence, and other factors. While it is possible to design large trials to account for these variables, such trials would have to be on the scale of those conducted for pharmaceuticals and are likely prohibitively costly for most device companies.

Another major uncertainty for the developers of molecular diagnostics is potential changes in the FDA’s evaluation of IVDs. While the FDA claims to have the authority to regulate all types of IVDs, it has historically distinguished between those that are developed and offered within a single laboratory – referred to as “home brew” or laboratory developed tests (LDTs) – and those that are commercially marketed to multiple laboratories – referred to as IVD “test kits.” For the first two decades of the FDA’s oversight of medical devices, the agency chose not to evaluate LDTs at all, while requiring all test kits to go through the usual device regulation pathways. This choice was based on the fact that tests offered by single laboratories were historically less complex and lower risk than test kits that were widely marketed.

LDTs have traditionally only been required to comply with requirements contained within the Clinical Laboratory Improvement Amendments of 1988 (CLIA), which are enforced by CMS. These requirements include such things as laboratory certification, proficiency

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11 IOM, supra note 8, at 14.
testing, quality control measures, and laboratory inspections.\textsuperscript{15} CLIA regulations were written prior to the widespread use of molecular diagnostic testing, so their quality control measures, proficiency testing, and other requirements were not designed for the complex diagnostic tests being used today. The vast majority of genetic tests marketed today are approved through the CLIA LDT pathway rather than the FDA IVD route.\textsuperscript{16} In the past few years, the FDA has started to shift towards regulating LDTs, recognizing a need for providing more oversight for the advanced molecular diagnostics that are increasingly escaping FDA oversight through the LDT pathway. While the agency has not provided a specific timeline for implementing its new regulatory approach, the agency’s slow expansion of LDT oversight suggest that it is a question of when, not if, LDTs will be subject to FDA approval requirements.

The possibility that molecular diagnostic tests could face greater oversight in the future has prompted many to claim that such a change would quash future development of the molecular diagnostics field. As discussed above, the cost of bringing a test to market through the FDA is significantly greater than the cost of bringing it to market subject only to CLIA oversight. Because the reimbursement for molecular diagnostic tests is so poor (discussed below), the added costs of FDA regulation are difficult to recoup, even assuming that the tests work well. The lower likelihood of profitability, many argue, would make investors less likely to invest in these technologies.

\subsection{10.2.2 Reimbursement for Molecular Diagnostic Tests}

Just as is occurring with FDA regulation, the traditional reimbursement schemes for laboratory tests are struggling to keep pace with innovation in the molecular diagnostics field. While private payers have the ability to set their own payments for new tests, most payers follow the decisions made by CMS, making the agency’s policies especially influential in the success of these tests.\textsuperscript{17} Unfortunately, the lack of flexibility in CMS’ current reimbursement system has created major obstacles to the clinical

\begin{itemize}
  \item \textsuperscript{15} Centers for Disease Control and Prevention, “Good Laboratory Practices for Molecular Genetic Testing for Heritable Diseases and Conditions,” 58 No. RR-6 MORBID. MORTAL. WEEKLY REP. 1, 7-25 (2009).
  \item \textsuperscript{17} Parker, supra note 12, at 2.
\end{itemize}
adoption and commercial viability of molecular diagnostics. CMS influences the development and adoption of new technologies through three separate activities—coverage, coding, and payment.

First, in terms of coverage, CMS or its local Medicare administrative contractors (MACs) must make a coverage determination about the new product, in which they review the product and decide whether Medicare will pay for its use when furnished to Medicare beneficiaries. CMS makes just 15–20 national coverage determinations (NCDs) each year through a statutorily prescribed 6- to 9-month process requiring systematic evidence evaluation, publication of a proposed decision, response to public comments, and issuance of a final decision. Most commonly, CMS issues an NCD that provides coverage only in limited circumstances, as supported by the available evidence. In some cases, the agency may also decide to either cover the item or service in all cases, to deny coverage in all cases, or to formally leave coverage at the discretion of local contractors.

By statute, the program is prohibited from covering items and services that do not fall within at least one statutorily defined benefit category and those that are not “reasonable and necessary” for the diagnosis and treatment of Medicare beneficiaries.18 Notably, these criteria differ from FDA’s “safe and effective” criteria for product approval, creating a significant disconnect between the evidentiary requirements of the two agencies. Though the phrase “reasonable and necessary” remains undefined for CMS and local contractors, it has been informally interpreted to require a showing that an item or service improves health outcomes in Medicare beneficiaries.19 For molecular diagnostic tests, payers such as CMS have increasingly called for demonstrations of clinical utility to make this showing.20 Similar to the FDA, CMS has provided little specific guidance about how to demonstrate clinical utility for molecular diagnostics. In the absence of such guidance, test developers must either meet with CMS and local contractors individually or use CMS’ past reviews of molecular diagnostic tests to generate a rough prediction about what types of evidence will be required for their tests. This results in much variability in the quality of evidence provided by test developers.

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18 Social Security Act § 1862(a)(1)(A).
and inconsistent coverage decisions that delay patient access to important new technologies.  

A major concern voiced by the molecular diagnostics industry is that payers are requiring unrealistic levels of clinical data about new tests but have not provided the necessary guidance for test developers to understand how to generate those data, or how they differ from the data provided to the FDA. In the past, laboratory tests were almost uniformly inexpensive and were therefore reimbursed with little scrutiny from payers, even when they lacked strong supportive data. As a result, there is little precedent for test developers to follow when designing studies to demonstrate the value of their new, higher-cost diagnostics. From the payers’ perspective, the fact that there is often no way to clinically verify the accuracy of a molecular diagnostic test creates the need for more rigorous validation of these tests compared to, for example, a diagnostic test of hemoglobin for anemia, which can be verified by checking various clinical signs in the patient. The potential consequences of unreliable test results suggests the need for trials that are more similar to those required for pharmaceuticals than the data-sparse 510(k) applications typical of medical devices.

The greater need for data on clinical utility for coverage decisions on molecular diagnostics ties in with the coding and payment determinations for such products, which are determined independent of the coverage decision. In the coding process, a new product is assigned an identifying code, usually one that is shared by other products that are similar in terms of both their clinical function and the resources required to use them. Within the payment process, the agency sets the amount it will reimburse hospitals or providers who use the product in clinical care, generally paying the same amount for all products within a given code. The traditional method in which these reimbursement decisions are made has hindered the efforts of diagnostic test developers to secure product codes and payment amounts that reflect the value of their products – all of which have impeded progress in the development of those technologies and personalized medicine in general.

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22 See, for example, , Parker, supra note 12, at 9–10.
24 Parker, supra note 12, at 18.
The vast majority of molecular diagnostic tests are performed by clinical laboratories and thus are coded within the clinical laboratory fee schedule, which is a list of amounts that Medicare will reimburse for over 1,100 laboratory tests, organized by codes. The fee schedule, which established prospective pricing for clinical laboratory tests, used charge data from laboratories in 1983 to set prices for the hundreds of distinct laboratory services provided across the country. Notably, most if not all laboratory tests in use in 1983 reflected well-known science that had been used for years. As a result, they were priced as commodities with very low marginal costs rather than products of significant research and development as a growing number of molecular diagnostic tests require today. The original legislation apparently did not foresee this evolution and thus contains no mechanism to pay for novel, high-value tests outside of the fee schedule. The inability to provide value-based reimbursement for laboratory tests creates a significant disincentive for anybody to invest the time and money needed to develop complex molecular diagnostics, no matter how valuable they are for clinical care.

Not only does the fee schedule fail to account for research and development costs, but it also consistently underestimates the bare cost of performing complex tests and therefore provides less reimbursement than necessary for laboratories to simply recoup their costs. For example, Fragile X testing cost $266 to perform in 2004, but was reimbursed at only $62 by Medicare. The discrepancies between fee schedule estimated costs and actual costs is at least partially attributable to the fact that the fee schedule has not been regularly updated to account for inflation since 1984. Thus, payment for most diagnostic tests is based on a fee schedule that is widely perceived to under-reimburse for the costs and value of the test. Funders of personalized medicine research point to these and other uncertainties and problems in the reimbursement system as the key reason for declining investment in the diagnostics industry in recent years.

25 Secretary’s Advisory Committee on Genetics, Health, & Society (SACGHS), DEPARTMENT OF HEALTH AND HUMAN SERVICES, COVERAGE AND REIMBURSEMENT OF GENETIC TESTS AND SERVICES 46 (2006).
26 Id. at 43.
27 Olson & Berger, supra note 21, at 12.
10.3 TWO INNOVATIVE GOVERNANCE SOLUTIONS

The significant regulatory and reimbursement challenges facing molecular diagnostics present a serious impediment to realizing the promise of personalized medicine. While molecular diagnostics will play a central and indispensable role in the new paradigm of personalized medicine, the pre-existing regulatory and reimbursement frameworks for diagnostic tests stand as obstacles to the development and implementation of the new generation of sophisticated molecular diagnostics. The existing frameworks are too slow, low-paying and uncertain to provide the assurances needed by the developers of molecular diagnostics. Molecular diagnostics therefore are trapped by path dependency, where the pre-existing regulatory frameworks have embedded economic, scientific, power, and institutional assumptions that were well-adapted to the older technology but not the new technology.28

A long-term, comprehensive solution to the regulatory and reimbursement challenges facing molecular diagnostics will likely require major statutory changes. Such a process is likely to take many years, exemplifying the “pacing problem.”29 In the meantime, though, there are some innovative strategies that are being considered and applied to try to address some of the obstacles facing molecular diagnostics, specifically the delay in getting products to the market and the uncertainty about evidentiary requirements for both regulatory approval and reimbursement. Specifically, two innovations are Coverage with Evidence Development (CED) and parallel review. Although neither of these initiatives is limited to molecular diagnostics, they are both particularly salient and potentially beneficial for molecular diagnostics.30 In addition to the support of the agencies pursuing these initiatives, the two programs were both endorsed recently by, for example, the 2012 Presidential National Bioeconomy Blueprint31 and a recent Institute of Medicine workshop.32

29 Marchant et al., supra note 1.
32 Institute of Medicine, GENOME-BASED DIAGNOSTICS: CLARIFYING PATHWAYS TO CLINICAL USE; WORKSHOP SUMMARY (2012).
10.3.1 Coverage with Evidence Development

Coverage with evidence development enables CMS to temporarily cover new products that are not yet supported by sufficient evidence to meet CMS’ “reasonable and necessary” coverage threshold while additional data are generated to inform CMS’ long-term coverage decision. CMS first formally identified CED as an additional option for making coverage decisions in 2005, whereby it agrees to provide temporary payment for promising new technologies while clinical data are generated to better inform the agency’s longer-term coverage decision. In order to receive reimbursement for their use of the product, providers would be required to participate in a clinical trial or input specific clinical data into a registry, creating a body of clinical evidence that CMS will eventually use when making its long-term coverage decision. Research performed in the context of CED differs from research performed for most new products in that the cost of the product being evaluated (but not the administrative cost) is paid for by CMS, rather than by the product sponsor or private researchers. This cost-sharing mechanism not only helps product sponsors but also gives providers and patients faster access to promising products while reducing the chances that CMS will end up paying for ineffective products.

CMS actually used a CED-style policy (without calling it that) for the first time in 1995 to study the effect of lung volume reduction surgery in the treatment of emphysema. In response to the growing popularity of the reduction surgery and limited data on its effectiveness, CMS collaborated with the National Heart, Lung, and Blood Institute and the Agency for Healthcare Research and Quality (AHRQ) to run a multi-center randomized controlled trial. CMS limited coverage to patients treated at one of 17 clinical sites following the clinical trial protocol established by the National Institutes of Health. The results of the study, published in 2003, revealed that the procedure benefitted only a small subset of patients and actually increased the mortality rate for others. Using these data, CMS issued a national coverage determination restricting coverage only to the patient subset identified by the study that benefitted from the

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procedure. It has been estimated that this trial, which required a one-time $35 million outlay for research costs, saves CMS $150 million annually by preventing it from paying for ineffective treatments.\textsuperscript{35}

CMS also used data collected through CED to inform its coverage of PET scans in the management of various cancers.\textsuperscript{36} Prior to the 2005 decision to use CED, CMS had a non-coverage policy for the use of PET in managing most forms of cancer but received a number of requests for reconsideration in the context of specific cancers. In response to these requests, CMS commissioned AHRQ to perform a formal technology assessment. The inconclusive results of the technology assessment highlighted the need for additional information and led CMS to propose the use of CED, carried out through a registry. By 2009, enough data had been collected to conclude that PET scans did improve at least the initial treatment strategy for certain cancers, though the data remained inconclusive for the later stages of management. Using these data, CMS revised its policies to provide broad coverage for the initial treatment stages of the cancers being evaluated, while maintaining the CED policy for later stages.\textsuperscript{37}

In total, CMS has used its innovative CED mechanism less than 20 times since officially launching the CED program in 2005. To date, data from CED have only been used to revise two national coverage determinations, while the other applications have not yet started or are ongoing, including one molecular diagnostic CED study currently evaluating the efficacy genotype-guided dosing of warfarin.\textsuperscript{38} The success of some of the initial efforts demonstrated the potential of CED to promote more rational spending within CMS and spurred interest in its continued use. However, more recent applications have failed to lead to coverage changes and have pushed CMS to reconsider its implementation of CED.\textsuperscript{39}

In the fall of 2011, CMS removed the guidance document governing the application of CED, announced its intention to revise the policy to make it more relevant and useful, and solicited public comments through January 2012.\textsuperscript{40} Comments were specifically requested regarding: (a) the

\textsuperscript{35} Tunis and Pearson, supra note 33, at 1220–21.
\textsuperscript{36} Id. at 1222–23.
\textsuperscript{37} Id; see also Lindor, supra note 33, at 227–28.
\textsuperscript{38} CMS, NATIONAL COVERAGE DETERMINATION (NCD) FOR PHARMACOGENOMIC TESTING FOR WARFARIN RESPONSE (90.1) (April 25, 2010).
\textsuperscript{39} See Lindor, supra note 33, at 234–37.
\textsuperscript{40} CMS, CED Public Solicitation (Nov. 7, 2011).
use of CED outside of the national coverage determination process; (b) the impact of CED on the Medicare program; and (c) suggestion for ways to apply CED to maximize its benefit to Medicare beneficiaries.41 

In November 2012, CMS released a new draft CED guidance and requested additional public comments, with the goal of finalizing the guidance in the near future. The overall goal of this revision is to enable CMS to make better informed coverage decisions, in a way that improves the health of Medicare beneficiaries while also reducing barriers to further innovation in health care. Given the impediments to the development and commercialization of molecular diagnostics, an expanded CED program would have particular salience and potential for molecular diagnostics.42

10.3.2 Parallel Review

Both the FDA and CMS play key roles in the approval of new medical technologies. In the case of diagnostic devices, the FDA ensures that new devices provide a “reasonable assurance of safety and effectiveness,” while CMS determines whether those products are “reasonable and necessary” for the care of Medicare beneficiaries. Though these statutory mandates appear to overlap, they have been interpreted much differently in practice, with the FDA focusing predominantly on safety and effectiveness in the context of controlled clinical trials and CMS focusing primarily on patient outcomes in the real-world settings of clinical care.

As a result of these discrepancies, the information requirements of FDA and CMS have traditionally represented separate hurdles for the sponsors of new products. Because products must be cleared or approved by the FDA before they are covered by CMS, many product sponsors seek to satisfy the evidentiary needs of the FDA before even considering the needs of CMS. This process often results in a significant delay between FDA approval and CMS coverage while product sponsors are generating the additional data needed by CMS. The frequent reliance of third party payers on CMS coverage decisions means this delay can significantly affect the rate of adoption and overall success of new technologies. Moreover, FDA and CMS have created much uncertainty about the type and strength of clinical evidence needed to meet the agencies’ respective expectations for approval and reimbursement as a result of the shifting evidentiary expectations discussed above.

41 Id.
42 Lindor et al., supra note 30.
To help address these bottlenecks, the FDA and CMS have recently undertaken a new pilot project initiative for a process innovation called parallel review. Parallel review enables product developers to meet with both CMS and FDA simultaneously early in a product’s review process, with the goal of clarifying the agencies’ evidentiary expectations and reducing the inefficiencies that often result from addressing the agencies’ data needs separately. Initiated by FDA and CMS in the fall of 2011, the parallel review pilot program provides a mechanism for the two agencies to concurrently evaluate certain medical devices for approval and coverage, respectively. Specifically, the program allows CMS to begin its national coverage determination (NCD) process earlier, while the product is still being evaluated by FDA. This voluntary program does not change the review standards of either agency but rather seeks to reduce the inefficiencies that often arise when product sponsors address and fulfill the FDA’s evidentiary needs without simultaneously considering whether the same data collection process could be used to address CMS’s needs as well. By bringing both agencies to the table with the product sponsor earlier in a product’s development, the parallel review process is designed to highlight the similarities and differences between the agencies’ data needs and help sponsors avoid performing duplicative and inefficient studies, thereby reducing the time and costs of bringing new products to patients.

In response to concerns expressed by product developers during the public comment period on the proposed parallel review pilot program, the agencies amended the parallel review process in a number of ways to make it more flexible and attractive to the product developers. For example, it gave manufacturers whose products had been accepted into the parallel review pilot project the chance to opt out at any time before a final determination had been made by CMS on coverage. The agencies also assured product developers that they would maintain the confidentiality of data shared between the two agencies. In response to concerns about possible delays and additional red tape in the process, the agencies committed to review applications for the program within 30 days of submission, after which time products would follow the normal FDA review process and timeframes.

The parallel review pilot program is planned to run for two years, although the agencies reserved the right to shorten or lengthen the

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program duration as appropriate. At the end of the two year pilot project (November 2013), the agencies are expected to review the results of the pilot project and consider making the parallel review process permanent, with any modifications suggested by the results of the pilot project. The parallel review program is not specific to molecular diagnostics, and several different products have been accepted into the pilot program and are currently under review. One product currently taking part in the pilot is Exact Science’s Cologuard, a molecular diagnostic assay for stool markers of colorectal cancer.45

10.4 CONCLUSION

Molecular diagnostics present a classic case of the “pacing problem.”46 These products are a rapidly emerging new technology, differing in key ways (for example, cost, value, evidentiary requirements) from the earlier technology of relatively simple diagnostic tests. Molecular diagnostics are the sophisticated and high-profile quarterbacks directing the play of personalized medicine, not the fungible commodity linemen plodding along doing their relatively straightforward assignment without a lot of fanfare or recognition. Yet, the existing regulatory infrastructure is designed for the simple diagnostics of yesteryear, not today’s high-technology tests that require different regulatory and reimbursement models. The result is a governance bottleneck that is too slow, low-paying and uncertain to provide the framework and incentives needed to usher in the new era of personalized medicine based on molecular diagnostics.

The most common approaches to addressing such pacing problems with other technologies include restructuring of statutory or regulatory frameworks, or creating alternative governance mechanisms, usually outside the scope of government, such as a voluntary or partnership program. For molecular diagnostics, neither of those approaches seems feasible, at least in the foreseeable future. While the optimal solutions to the regulatory dilemmas facing molecular diagnostics may involve sweeping statutory or regulatory changes, these are less likely to be successful in the current political and economic climate – and certainly not in the short term. Instead, two innovative new approaches within the

46 Marchant et al., supra note 1.
existing regulatory framework have been created and are being implemented by the relevant government agencies (FDA and CMS). Both parallel review and CED are currently open to agency review and modification at this time, creating a window of opportunity to propose changes that have the potential to strengthen the utility of these policies and promote the development and use of high value molecular diagnostic technologies.

While neither CED nor parallel review will apply to all or even most molecular diagnostics, they can speed, coordinate and clarify the paths to market for selected products. These examples of creative innovations within an existing and outdated regulatory framework demonstrate another strategy for addressing the pacing problem. Both CED and parallel review have faced opposition both within and outside government, so their implementation has not been easy or uncontroversial. Nor is it obvious to identify and design such innovations. But the CED and parallel case studies demonstrate that it may be possible to expedite and better align regulatory frameworks to new technologies with creative innovation and leadership within government. It is important that we learn from, support and incentivize this type of innovative governance.

10.5 ACKNOWLEDGMENT

The research and writing of this chapter was supported by National Science Foundation grant (Award SES-0921806).