Hearing on "21st Century Cures: The President's Council of Advisors on Science and Technology (PCAST) Report on Drug Innovation"

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Testimony of:

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Introduction

Chairman Pitts, Vice-Chairman Burgess, Representative Pallone, and members of the committee - thank you for the invitation to appear before this committee today. As you are aware, the PCAST report on Innovation in Drug Development contains a number of thoughtful, well-crafted and potentially impactful recommendations for more rapidly translating decades of basic science discoveries into new therapies for high priority health needs. In addition to the important public health benefits of innovation, there are tremendous potential economic benefits to promoting the health of the life sciences industry, further highlighting the importance of the work that PCAST has done.

I served as one of the invited experts that worked with the PCAST Council members and staff in developing this report. Because of my former role as chief medical officer at the Centers for Medicare & Medicaid services, my input during working meetings and draft reviews generally reflected a payer/health system perspective. Throughout the discussions, it was clear that the main focus of the report was on innovation and clinical development activities that took place prior to or during regulatory review. For that reason, I thought it would be most useful for this hearing to reflect on the report's recommendations from the vantage point of "post-regulatory decision makers", including public and private payers, health delivery systems, providers, clinicians and patients. It is clear to most innovators and investors that reimbursement and other post-regulatory market dynamics are increasing significant with respect to the early stages of innovation in drug development. The goal of this testimony is to explore the implications of the PCAST recommendations in this broader context.

Of the various "post-regulatory decision makers" listed above, my focus will be mostly on the impact of payer and health systems decision making on innovation in drug development, followed by several recommendations related to these groups that could help to facilitate successful implementation of the recommendations in the PCAST report.

PCAST recommendations on improving drug evaluation

Several of the key recommendations in the PCAST report (recommendations 3,4, and 5) focus on policy mechanism to speed up the evaluation of new drugs. These include the proposal to expand use of FDA's

existing authorities for accelerated approval, a directive that was also reinforced in the FDA Safety and Innovation Act of 2012. Under accelerated approval, the FDA may approve products based on their impact on a surrogate or intermediate endpoint (such as a laboratory test result) that is reasonably likely to predict clinical benefit (outcomes that patients experience directly). Another mechanism recommended to speed the approval of important new drugs is the proposal to approve new drugs more quickly by identifying specific patient subgroups for which the benefit-risk balance is particularly favorable. Use of the drug in these patients is referred to as a "special medical use". Surrogate or intermediate outcomes may also be adequate for approval in this context. The patient subgroups targeted in this approach are those with serious manifestations of a disease, or at high risk of developing severe disease. Finally, the report suggests that the FDA conduct pilots of new "adaptive approval pathways" which would also provide a mechanism for new drugs to be approved in iteratively expanded patient populations as additional evidence from clinical studies is collected. As with special medical use, the intent of this mechanism is to speed the approval of drugs for patients with severe disease by focusing initially on patient subgroups expected to experience the greatest benefit.

Taken together, these recommendations have the potential to considerably reduce the time and expense required to complete pre-market trials and obtain regulatory approval for pharmaceutical and biotech products targeted to important unmet health needs. They also create a new challenge from the perspective of payers, health systems and other post-regulatory decision makers. Clinical and policy decisions on coverage and payment of new drugs have generally assumed that pre-approval studies have demonstrated with a fairly high level of confidence that the drug offers a net improvement in clinical outcomes (not intermediate outcomes). Furthermore, the historically high evidentiary bar for regulatory approval has offered some level of reassurance that some degree of off-label use may benefit patients without exposing them to significant or unknown risks.

It is unclear at this point, and was not discussed in detail in the PCAST deliberations, how the payers, health systems and other post-regulatory decision makers might react to the proposed mechanisms for more rapid regulatory approval. In order for this group of recommendations to have the desired impact on innovation, as well as patient benefit, it is important to develop a clear understanding of this post-regulatory landscape of decision makers, most importantly the health plans and delivery systems. There is no point in creating a regulatory superhighway for innovation that ends in White Oak (FDA) that simply turns into a reimbursement gravel road all the way from there to Security Blvd (CMS).

Payers, Health Delivery Systems and Innovation

As a result of health spending trends and resulting payment reforms, health systems, payers and providers are under increasing pressure to improve health care outcomes while lowering overall health care costs. Most health care policy discussions emphasize the urgency of maximizing value and efficiency of care, and this has inevitably become an increasing consdiration in coverage and payment decisions regarding new drugs, devices, procedures, diagnostics and all other health technologies.

Increasingly, what payers and health systems are looking for with respect to drugs and other technologies is a high level of confidence that the technology will produce meaningful improvements in health outcomes that matter to patients, and at a reasonable incremental cost. Even more desirable would be new products that produce greater clinical benefit with a net reduction in health care spending. Many post-regulatory decision makers recognize the value of innovation, but given the increasing pressures to increase value and efficiency, they are particularly focused on high value innovations – technologies which, if projected benefits and risks are demonstrated, have the potential to significantly improve health outcomes at the same or lower aggregate costs to the health system.

In this context, it becomes clear why the PCAST recommendations for improving drug evaluations could magnify the gap between the evidence that is acceptable for regulatory approval, and the type of evidence that payers and health systems require to assess the effectiveness and value of new drugs. To state it as simply as possible, from a payer perspective it is not particularly reassuring to consider the prospect of increasing numbers of new drugs being approved more rapidly by the FDA with less extensive data on safety and efficacy, as these decision makers come under increasing pressure to provide care that is higher quality, safer and less expensive.

Recommendations

There are a number of strategies that can be explored to minimize the potential headwind to innovation generated by quality/cost/efficiency pressures that characterize the post-regulatory environment. The recommendations below were adapted from a white paper developed in the context of a national gathering of industry and academic leaders hosted by Stanford's Clinical Excellence Research Center to identify private and public policy changes most likely to encourage healthcare innovations that would both improve health and lower US health care spending. A copy of the complete white paper is attached to this testimony.

Consistent and explicit standards of evidence for effectiveness and value

For many years, regulators put sustained effort into defining requirements for safety and efficacy, generally and for specific therapeutic domains and classes of technologies. Payers looking for evidence of effectiveness and value have done relatively little to define the evidentiary requirements, making it difficult for innovators to clearly understand what studies would be adequate to demonstrate effectiveness and value.

There is a need for greater transparency, predictability and consistency in how effectiveness and value of new biomedical technologies is evaluated and paid for by public and private sector payers. Increased transparency and consistency in the evidence requirements for payment across a wide range of public and private payers would significantly reduce payment uncertainty for investors and innovators, decreasing the risk, cost and duration of clinical development programs. Perceived risk within the investment community today is very high, causing a shift of venture funding out of health care. A predictable path to payment could substantially expand the willingness to invest, thereby increasing the development of cost-saving technologies. Simultaneously, clear evidence requirements would strengthen the data available for payers to make payment decisions and provide clearer information to patients and clinicians to make clinical decisions. In addition, the use of standards for inclusion of diverse and/or vulnerable populations in clinical studies would increase knowledge about possible benefits and harms of treatments in these subgroups and subpopulations.

Relevant DHHS agencies should actively seek out and participate in public-private sector initiatives to standardize the evidentiary requirements for demonstrating the effectiveness and value of new biomedical technologies. While general standards are helpful, product developers, investors, and decision makers would benefit most from standards that are developed for major categories of technologies and clinical conditions. The Secretary's Advisory Committee on Genetics, Health and Society had recommended the creation of such a public-private process to develop evidentiary standards for the clinical utility of genetic testing. The logic provided for this recommendation applies equally to other domains of biomedical technology. These standards could be developed by a national and voluntary private sector standard setting body, similar to the Institute of Medicine or the National Quality Forum for example, which serves as a standard-setting body for health care quality measures.

An example of such an activity, in relatively early stages, is the Green Park Collaborative – USA, managed by the Center for Medical Technology Policy. A more detailed overview is attached to this testimony.

Payers can provide coverage contingent on collection of additional data

To generate additional data on longer term clinical outcomes as well as costs and value, public and private payers could expand use of conditional payment mechanisms that link reimbursement to the collection of additional data. With the increased use of accelerated regulatory approval, there will be increasing need for payers to provide coverage while the remaining questions about clinical benefit, safety and target population are addressed. This approach could be deployed more consistently to enable earlier payment for technologies that have substantial potential for reducing costs and improving outcomes. In some cases, late phase and post-approval studies conducted to meet regulatory requirements may also be more efficiently conducted through this approach. A recent White House report on the National Bioeconomy Blueprint recommended increased use of this mechanism to promote the early adoption of potentially high value technologies, and similar recommendations have been advanced by other advisory groups and committees. In May 2012 Medicare held a public advisory committee to explore this approach, and issued updated draft guidance on such an approach - Coverage with Evidence Development (CED) - several months later.

A number of elements are critical to the success of conditional payment programs, most importantly the application of clear criteria for selection of eligible technologies that aim to improve outcomes and lower costs. It is also important to develop a streamlined process to approve study protocols, identify funding sources for research costs, and establish well-defined and reasonable study timelines. Furthermore, there are serious political challenges of withdrawing coverage once it has been provided, though the likelihood of this outcome might be moderated by having clearly defined agreements up front and clear pre-defined outcome and cost targets for retaining coverage. For this reason, it would be particularly important to establish clear benchmarks for outcomes and costs at a defined time period following approval, with a decision made at that point about approving unconditional coverage, retaining the conditional policy, or terminating coverage.

Some work has been done exploring how coverage linked to data collection could be deployed more broadly among private payers. Interest in this approach among private payers would increase if it was clearly designed to promote cost-reducing innovations, and as successful use by Medicare increases. It would be valuable to convene further discussions including Medicare, private payers and other key

stakeholders to explore how the confidence of private payers in this approach could be enhanced. To achieve an acceptable level of efficiency and study sample size, these studies and policies would need to be coordinated across multiple private payers. Should more consistent use of this approach be deployed, it would ideally be coordinated with efforts to expand research infrastructure (as discussed in next recommendation) in order to decrease the cost and increase the efficiency of the studies.

Improve Clinical Research Infrastructure within the Delivery System

A more detailed version of this recommendation is well developed in the PCAST report, though that discussion is targeted to expanding the type of research capacity that is capable of supporting regulatory-quality studies. In order to generate the type of evidence that will inform decisions by payers, health systems, patients and clinicians, it will become increasingly essential to leverage the delivery system itself as a platform for research and other forms of learning. Continued investments in improving research infrastructure, with greater opportunity for life sciences companies to contribute to this development and use this infrastructure to improve the efficiency of conducting clinical studies during the late phases of product development.

While improvements in clinical research infrastructure may require incremental resources, the emphasis of this recommendation is to allow for greater allocation of private sector funds to improve publicly funded research infrastructure. The incentive for such investment would be an understanding that this infrastructure would be made available for private sector funding, subject to well-defined criteria for public health and scientific importance. Several public sector initiatives to expand research infrastructure are already underway, and there should be greater attention leveraging these federal investments with supplemental funding from the life sciences industry. The National Institutes of Health, for example, funded a Health Care System Collaboratory that is supporting partnerships with integrated delivery systems "…to strengthen the national capacity to implement cost-effective large-scale research studies that engage health care delivery organizations as research partners". While the seven initial Collaboratory demonstration projects are federally funded and do not involve partnerships with product developers, the model could readily be expanded to support private sector clinical studies. Similarly, the Patient-Centered Outcomes Research Institute has recently launched a national patient-centered clinical research network call PCORnet, which is being formed out of what are currently 29 separate research networks. This initiative has great potential to provide the sort of practice-based research infrastructure to support the efficient generation of evidence of effectiveness and value for both

An important benefit of expanding the capacity to conduct clinical research within the health care delivery system is the ability to increase the representation of diverse populations in clinical trials (age, racial, ethnic, socioeconomic, genetic, etc.), in part to have better evidence about effectiveness of treatments in various subpopulations.

Conclusion

The PCAST report on Innovation in Drug Development contains a number of thoughtful, well-crafted and potentially impactful recommendations for translating several decades of basic science discoveries into new therapies for high priority health needs. Several of the key recommendations in the PCAST report (recs 3,4,5) focus on policy mechanism to speed up the evaluation of new drugs. These recommendations have the potential to considerably reduce the time and cost required to complete trials and obtain regulatory approval for pharmaceutical and biotech products targeted to important unmet health needs. They also create a new challenge from the perspective of post-regulatory decision makers: payers, health systems, clinicians, patients and others. It is unclear at this point, and was not discussed in detail by PCAST, how the payers, health systems and other post-regulatory decision makers might react to the proposed mechanisms for more rapid regulatory approval. From a payer perspective it is not particularly reassuring to consider the prospect of increasing numbers of new drugs being approved more rapidly by the FDA with less extensive data on safety and efficacy, as they come under increasing pressure to provide care that is higher quality, safer and less expensive. There are a number of approaches that can be taken to minimize the potential headwind to innovation generated by the post-regulatory environment:

- Consistent and explicit standards of evidence for effectiveness and value
- Payers can provide coverage contingent on collection of additional data
- Improve Clinical Research Infrastructure within the Delivery System

It would be useful to bring together the PCAST members and external experts that helped to develop this innovation report with a broader range of experts and stakeholders, particularly drawing from the universe of post-regulatory decision makers, to discuss the pros and cons of these and other strategies to ensure that the dynamics of biomedical innovation and health systems reformed are aligned to the greatest extent possible.

Thank you again for the opportunity to testify today. I would like to submit for the record the white paper on biomedical innovation and information on the Green Park Collaborative mentioned above.