ENGELBERG CENTER for Health Care Reform at BROOKINGS

June 27, 2012

Discussion Guide

State of Biomedical Innovation Conference

Introduction

As advancements in genomics and other emerging sciences provide new opportunities to develop better treatments for a broad range of diseases, working to improve the productivity of the U.S. biomedical innovation enterprise is paramount. Significant progress has been made in biomedical sciences in recent decades, but the rate at which new products are entering the market has remained relatively constant while the cost of developing products has increased. In the context of rising health care costs, assessing the policies and practices affecting the current state of U.S. biomedical innovation and how best to move the discovery and development of promising medical products forward efficiently is an increasingly urgent health and economic issue. This assessment should involve reviewing current policy initiatives and past experiences for lessons learned facilitated by clear and objective measures to evaluate the biomedical enterprise and identify where to concentrate future efforts. The Engelberg Center for Health Care Reform at Brookings is convening the State of Biomedical Innovation Conference with the goal of promoting dialogue around these issues. The primary objectives are to identify policies that could be used to jumpstart biomedical innovation and the key metrics that could be tracked to assess the impact of these initiatives.

Identifying Policies to Spur Biomedical Innovation

Continuing to build and improve the nation's biomedical enterprise will require a thorough pursuit and application of practical, effective policies and strategies. A discussion on the impact of policies is especially timely as 2012 marks the anniversary of the U.S. Food and Drug Administration's (FDA's) Kefauver-Harris Amendments of 1962, which established the modern safety and efficacy standards for new product approvals, and the Prescription Drug User Fee Act of 1992, which instituted an agreement between industry and FDA that would improve regulatory review processes.

Building upon the foundation established by these and other important policies, reforming the biomedical environment is critical to reinvigorating innovation. Beneficial reforms can be achieved by identifying roadblocks that exist throughout the innovation pathway and developing and implementing policies that align incentives of key stakeholders. Many efforts to address challenges in innovation have understandably focused on FDA regulatory policies and resources, and new legislation holds out the hope of significant progress. While regulatory issues are important, there are many other hurdles throughout the long development pathway. As such, discussion on the impact of policies must explore all phases of a product's lifespan. This includes considering initiatives to address misaligned incentives that result in the advancement of fewer innovative products, improve target validation in the preclinical stage, reduce the size and duration of clinical trials, minimize the number of late-stage failures, and take advantage of existing electronic health data to continue to assess safety and effectiveness once products are approved. Economic incentives necessary to encourage investment in the enterprise, as well as specific initiatives at the National Institutes of Health and FDA, are also vitally important to consider.

The potential positive impact that public-private partnerships can have as a means of bringing together scientists, legislators, manufacturers, regulators, and patient advocates is reflected in a number of innovation policy initiatives. Recent endeavors by groups such as the Coalition Against Major Diseases and the Institute for Applied Cancer Science at MD Anderson Cancer Center are helping to develop a new paradigm in which stakeholders are able to think and act collaboratively to improve the health of biomedical innovation. Whether built around improving clinical trial methodology, data sharing practices, target and biomarker validation, or patient engagement, these partnerships are helping to move the state of the industry forward.

Elucidating Key Metrics to Assess Policy and Innovation

Efforts to enhance biomedical innovation can only be evaluated objectively if reliable tools and metrics are established to identify and better understand their successes or failures. These metrics should span the innovation pathway, and the data sources used to measure them should be readily available, accessible, and well-understood. In addition, these metrics should be linked to an assessment of treatment outcomes and outcomes meaningful to patients. Without rigorous analysis that assesses whether products being developed are actually making a difference in patients' lives, the biomedical enterprise runs the risk of producing new products that fail to improve patient health.

Building upon this idea, the creation of an "innovation dashboard" capable of providing an overview of how well innovation is progressing could constitute an important step toward better tracking of innovation and supporting more efficient development of beneficial medical products. Ideally, the innovation dashboard would include metrics for the enterprise as a whole and by disease areas. The Engelberg Center is beginning to lay the foundation for such a dashboard by identifying a list of potential metrics and data sources that could be used. These metrics have been classified into four key phases of development as described below.

In the preclinical phase, the emphasis is largely on tracking inputs into the development process. Metrics could include the level of public and private investment in basic research, the number of precompetitive public-private collaborations in any given therapeutic area, the number of patents filed with the U.S. Patent Office and Trademark Office (USPTO), the number of products under development whose purpose is to treat the disease versus alleviate symptoms associated with the disease, and the number of products under development that are targeting a mechanism of action for which there are no competing approved products.

Metrics in the clinical phase help to demonstrate how efficiently the innovation enterprise is taking preclinical inputs and transitioning them into treatments. Here, the metrics might include the number of Investigational New Drug applications or Investigational Device Exemptions filed with the FDA, the level of public and private investment in clinical research, clinical trial burden (average number of patients required for approval per product, average clinical trial length reported overall and by development phase, and the average cost of trials and data collection), average lifespan of failed products, and average length of time needed to collect data for each endpoint or surrogate marker used for investigation. These metrics, especially those around surrogate markers and endpoints, could help point the way toward faster, more adaptive, more effective clinical trial design and practice.

Regulatory-phase metrics, which have been a significant part of the focus of recent FDA legislation, could help to flesh out the efficiency and effectiveness of product review as well as the success of the preclinical and clinical phases in developing innovative treatments. Tracking the number of products approved under Standard Review, Priority Review, and Accelerated Approval, for example, could approximate the number of products that are indicated for serious or life-threatening diseases or areas with little to no treatment options, functioning as a surrogate for how truly innovative the products are.

Measuring how long it takes to guide a product from its initial regulatory filings to approval is also important, as it offers a snapshot view of internal practices within FDA and the strength of collaboration and information exchange between FDA and industry scientists.

Finally, many post-market metrics will be crucial to accurately evaluating the downstream effects of innovation. Changes in patient survival rates, quality of life, or other outcomes that matter to patients, for instance, will be key in demonstrating that new products are having real-world impacts on patient lives. In an age of numerous health care reform initiatives, the average costs of a treatment or illness and the prevalence of outcomes-based reimbursement agreements will also be important for linking innovative products with better outcomes and reduction in costs.

Today's Innovation Landscape

Assessing the state of biomedical innovation is challenging and interpretation of the enterprise's health can vary considerably depending upon the stage of development that is evaluated. For example, analysis of some of today's early stage financing figures may paint a bleak picture of the preclinical development phase. According to a recent report, the number of new life sciences companies (both biotechnology and medical device) receiving first-time venture capital financing in 2011 was the lowest in 15 years. This decrease in new venture capital investment has continued into 2012, with the number of new companies receiving first-time financing in the first quarter of 2012 hitting the lowest quarterly level in 13 years.[1] In addition, recent reports have demonstrated concerning clinical development trends across disease areas, with average development times having increased between 1980 and 2009.[2]

At the same time, recent trends in product approvals and regulatory review may suggest more positive developments in the later stages of innovation. Thirty-four new molecular entities were approved in 2011—the most in the last 10 years. Of those, nearly two-thirds were either approved with new mechanisms of action in their therapeutic areas or to treat rare diseases for which few therapeutic options are available.[3] Independent analyses of new product approvals have shown that from 2000 to 2009, the number of products given priority review status grew as a percentage of total approvals, approaching 50 percent.[4] These numbers are important as new mechanisms of action, orphan products, and priority status are all indicative of innovation. As some studies have noted, it is important to view all of these components of the innovation process comprehensively; for example, reductions in regulatory review time may be offset by increases in clinical development time and other changes in development activities.[5]

These examples demonstrate that gathering real data to measure progress, as well as interpreting those metrics, poses many challenges. To better understand the impact that polices have had or are having on the innovation enterprise, more comprehensive historical data and trend analysis data will be required. Establishing an innovation dashboard of a valid set of measures, which could be updated regularly, could support more efficient and systematic evaluation of policies. Overcoming these challenges is important, given what is at stake for public health and the significant costs, time, and uncertainty of product development.

References

1. Pricewaterhouse Coopers and NVCA. (2012). *MoneyTree Report, Q1 2012.* Retrieved June 25, 2012, from https://www.pwcmoneytree.com/MTPublic/ns/moneytree/filesource/exhibits/12Q1MTPressRelease_FINAL.pdf.
2. Kaitin, KI and DiMasi, JA. (2010). Pharmaceutical Innovation in the 21st Century: New Drug Approvals in the First Decade, 2000–2009. *State of the Art*. 89:2, 183–188.
3. IMS Institute for Healthcare Informatics. (April 2012). *The Use of Medicines in the United States: Review of 2011*. Retrieved June 25, 2012, from http://www.imshealth.com/imshealth/Global/Content/IMS%20Institute/Documents/IHII_UseOfMed_report%20.pdf
4. Kaitin, KI and DiMasi, JA. (2010).
5. Ibid.