
# 21st Century Cures: A Call to Action

## Overview

For decades, our nation's commitment to the discovery, development, and delivery of new treatments and cures has made the U.S. the biomedical innovation capital of the world, bringing life-saving drugs and devices to patients and well over a million high-paying jobs to local communities.[1] This success has not gone unnoticed in the rest of the world, and other nations are now actively working to gain a competitive edge in various elements, whether through a focus on basic research or a streamlined approval process to bring new treatments to market more quickly.

It is clear that the discovery, development, and delivery process is a cycle, meaning that even data captured and analyzed at what some might consider the "end" of the process - the delivery phase - actively infuses new discovery and development of better treatments. The country that fully embraces the entirety of this cycle will be the innovation leader for the 21st Century. Thus, a key goal of the 21st Century Cures initiative is to help ensure it is the United States that charts this course.

As part of the 21st Century Cures initiative, the committee will issue a series of white papers seeking input and soliciting ideas on how Congress can help accelerate the discovery, development, and delivery of promising new treatments to patients. To accomplish our objectives, we must ensure that this cycle is fostered—not hindered—by the regulatory policies we have in place.

We know our goal is shared by the National Institutes of Health (NIH), Food and Drug Administration (FDA), and other agencies, as well as by our nation's patients and scientific pioneers in academia and industry. We also recognize that much work remains to be done. According to the President's Council of Advisors on Science and Technology (PCAST), "the pace of new therapeutic development has not kept up with the explosion of scientific knowledge."[2]

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[1] *See* MILKEN INSTITUTE, ACCELERATING INNOVATION IN THE BIOSCIENCE REVOLUTION: REPORT FROM THE 2011 LAKE TAHOE RETREAT 3 (Apr. 2012) [hereinafter "MILKEN REPORT"].

[2] PRESIDENT'S COUNCIL OF ADVISORS ON SCIENCE AND TECHNOLOGY, EXECUTIVE OFFICE OF THE PRESIDENT, REPORT TO THE PRESIDENT ON PROPELLING INNOVATION IN DRUG DISCOVERY, DEVELOPMENT, AND EVALUATION iii (Sept. 2012) [hereinafter " PCAST REPORT"].

Biomedical research and innovation, particularly at the molecular level, is happening at lightning speed alongside of, and supported by, equally breathtaking advancements in digital and personalized medicine, including the use of sensors, genomics, health information, and other technologies.[3] Congress must proactively ensure that our nation's laws and regulations keep pace. We want to solicit ideas on how Congress can effectively and responsibly do so, and thus, as detailed below, seek input, answers, and feedback on the discovery, development, and delivery cycle.

**Discovery**

The first part of the innovation cycle is discovery. Thanks to the leadership of NIH, academic medical centers, and industry, the U.S. has led the way in early discovery. However, our leadership role is being threatened as other countries contribute more to basic research from both public and private sources. For instance, while the Human Genome Project was completed over a decade ago in the U.S., the Beijing Genomics Institute is now the world's largest genetic research center and, with the support of a number of American researchers, produces at least a quarter of the world's genomic data.[4] While global research and discovery is a positive development, the U.S. must maintain its leadership role. How can we make sure that is the case? How much of the contributions should come from public and private sources? How can public-private partnerships further the discovery process?

While our nation's leadership has yielded important treatments for some patients, others still wait because the state of biomedical research and innovation in certain diseases is not as advanced. For example, although more than five million Americans are currently living with Alzheimer's disease, and despite the fact that the economic burden of the disease ultimately may exceed $1 trillion per year without effective therapies, we still lack a basic understanding of the disease's underlying causes.[5] How can we harness our nation's desire, human capital, and technological know-how to get to the bottom of what may cause Alzheimer's and other deadly diseases or conditions? How can we incentivize, coordinate, and accelerate research for diseases or conditions we know relatively little about?

In other areas, we have a better understanding at the molecular level about what biological mechanisms trigger the onset or proliferation of a particular condition or disease. Efforts are already underway to improve the tools scientists can employ to translate this information into potential therapies, including the work being done at the National Center for Advancing Translational Sciences (NCATS) and now through the Accelerating Medicines Partnership (AMP) at NIH. How can we best leverage advances in translational research, health information technology, and communications so that we can collectively "connect the dots" more quickly and start developing potential therapies and cures?

**Development**

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[3] *See* PETER HUBER, THE DIGITAL FUTURE OF MOLECULAR MEDICINE: RETHINKING FDA REGULATION, PROJECT FDA REPORT (May 2013) [hereinafter "HUBER, PROJECT FDA REPORT"]; *See also* ERIC TOPOL, THE CREATIVE DESTRUCTION OF MEDICINE (Jan 2012).
[4] Michael Specter, *The Gene Factory*, NEW YORKER, Jan. 6, 2014, at 34.
[5] *See* PCAST REPORT, *supra* note 2, at 5.

Development may be the most vital part of the innovation cycle. At its core, it is the process of translating ideas into reality with the goal of bringing treatments to patients and being rewarded for the pursuit. Other countries realize the importance of development and are establishing policies and incentives to attract companies and investors. The United States must take notice as well. For example, until recently, an average of 40 biotechnology companies a year were formed—in Cambridge, Massachusetts, alone—with the goal of translating basic research into the development of potential therapies for commercialization. Over the past several years, that number decreased to 15. In 2010, more biotechnology companies were formed in China than in the U.S.[6] How are other countries attracting companies and investment? Should we adopt some of those policies, too? What else can we do to lead the way?

After years of hard work, investment, and collaboration, the aspiration is that the scientific understanding of a disease will reach a level justifying further investment in the development of potential drugs or devices. When such concepts reveal early promise, clinical trials may be conducted with the ultimate goal of producing safety and efficacy data sufficient for FDA approval of a product for marketing. Traditionally, clinical trials have been designed to demonstrate how an experimental treatment affects the symptoms of a condition or disease over time in a large, representative patient population compared to a placebo or other alternative. But based on the advances that have been made in personalized medicine and health information technology, including the use of real world data, is the randomized, double-blinded, placebo-controlled model the best approach in all cases? The timelines, size, failure rates, and costs of conducting trials are at all-time highs,[7] with administrative and regulatory burdens often contributing to such increases. What can be done to help reverse these trends?

FDA's active participation in partnerships like the Biomarkers Consortium, the Critical Path Initiative, and the Clinical Trials Transformation Initiative is critically important. What has the agency learned from these partnerships, and have officials taken necessary steps to implement new data as broadly and consistently as possible? Much progress remains until efficient trials with flexible designs aided by innovative technologies are no longer the exception to the rule.[8] How can these types of trials become the norm? Is there a better way to validate biomarkers and surrogate endpoints? What roles can NIH and other outside experts play in the process? What cultural or organizational issues must be addressed in order to effectuate these broader changes?

Based in large part on our bipartisan efforts in the Energy and Commerce Committee over the years, FDA has ample authority to evaluate new drug and device applications on an expedited basis using alternative trial designs in conjunction with a wide array of innovative biomedical, technological, and statistical tools. Recently, the Food and Drug Administration Safety and Innovation Act (FDASIA) significantly expanded the Accelerated Approval pathway and authorized a new Breakthrough Therapy designation that FDA already has utilized in connection with recent product approvals. In authorizing these new authorities, the committee was clear that:

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[6] *See* MILKEN REPORT, *supra* note 1, at 3-4.
[7] *See* Malorye Allison, *Reinventing Clinical Trials*, NATURE BIOTECH. 41 (Jan. 2012).
[8] *See* HUBER, PROJECT FDA REPORT, *supra* note 3, at 7-15.

> A new generation of modern, targeted medicines is under development to treat serious and life-threatening diseases, some applying drug development strategies based on biomarkers or pharmacogenomics, predictive toxicity, clinical trial enrichment techniques, and novel clinical trial designs, such as adaptive clinical trials. As a result of these remarkable scientific and medical advances, the FDA should be encouraged to implement more broadly, effective processes for the expedited development and review of innovative new medicines intended to address unmet medical needs for serious or life-threatening diseases or conditions, including those for rare diseases or conditions, using a broad range of surrogate or clinical endpoints and modern scientific tools earlier in the drug development cycle when appropriate. This may result in shorter clinical trials for the intended patient population or targeted subpopulation without compromising or altering the high standards of the FDA for approval of drugs.[9]

The committee understands that FDA can only take full advantage of these broad authorities if the data presented to the agency justifies their utilization. But are there areas or opportunities where the agency is not using these authorities to their maximum potential where it should be? Is FDA structured and managed to enable the agency to rapidly incorporate innovative new approaches and technologies into its review processes? How can Congress ensure that the regulatory science keeps pace with advances in personalized medicine, including diagnostics?

Finally, recent analyses have shown that the cost of developing a new drug now exceeds $1 billion—double the costs in the early 1980s—and that it takes upwards of 15 years from initial molecular targeting to bring a drug to market.[10] Are the economic incentives and policies currently in place sufficient to encourage robust investment and promote innovation? How can we make sure that biomedical research and product development continues and attracts venture capital?

**Delivery**

Learning about the benefits and risks of a drug or device does not end when a clinical trial is completed or when FDA initially approves the product. In many ways, it is just beginning. Different uses for the drug or device are constantly being discovered, many times for treatment of different conditions and diseases. These conditions and diseases are often moving targets that will respond in a number of ways to various combinations of therapies in different patients with specific genetic characteristics. What else can be done to foster continued learning and investment in research after a drug or device, or combination thereof, has initial FDA approval? How can electronic health records and other health information technologies play a

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[9] Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144, § 901(a)(1)(B)-(C).
[10] *See* Allison, *supra* note 8, at 42. *See* also WENDY H. SCHACHT AND JOHN R. THOMAS, CONG. RESEARCH SERV., R41114, THE HATCH-WAXMAN ACT: A QUARTER CENTURY LATER, at 7 (Mar. 13, 2012).

role? What uncertainties or barriers currently exist in post-market, real world delivery settings—legal, regulatory, commercial, or otherwise—and how should they be addressed? There are reports that diagnostic testing breakthroughs sit unrealized due to regulatory uncertainty and other market forces that deter translating such innovation into patient-centered solutions. What are the current barriers to bringing new testing discoveries to market, and how might we overcome them?

Communication about how certain treatments are working in certain patients is happening through a multitude of media around the globe. These conversations between and among doctors, patients, researchers, and scientists in academia and industry should be facilitated. This includes the free flow of data, research, and results related to what a therapy or combination of therapies does or does not do well and in what types of patients. We need to harness the power of the Internet and social networks.

Further, FDA's review of supplemental applications for new uses or changes to a product are governed by pathways established at a time when computers could not identify trends in statistical or clinical data anywhere close to the degree they can today, let alone what they will be capable of doing tomorrow. Considering these ongoing developments, should we be rethinking the supplemental approval processes and how real world data can be leveraged?

Overall, the policies we have in place must allow for delivery to serve as a platform for new discovery and development. Any legal or regulatory framework that slows this cycle is not only ignoring reality, but also discouraging hope.

**Conclusion**

To ensure that the U.S. owns the discovery, development, and delivery cycle and thus, remains the world leader in innovation, we need input, answers, and feedback. No idea is too small. No idea is too big. This is a cycle that ultimately touches every single American – whether they are a patient, loved one, caregiver, researcher, advocate, innovator, or government official. Advances in science and technology, as well as personalized medicine, present us with an enormous opportunity, but it's going to take time and collaboration. We are interested in both how the individual pieces of the cycle can improve and modernize, but also how all the pieces of this cures cycle can work together more efficiently and effectively. To that end, we welcome any input or feedback on the questions raised in this white paper to cures@mail.house.gov by June 1, 2014. Our pursuit of 21st Century Cures is now underway.