

Deloitte.

Deloitte's Path to
21st Century Cures —
A Call to Action

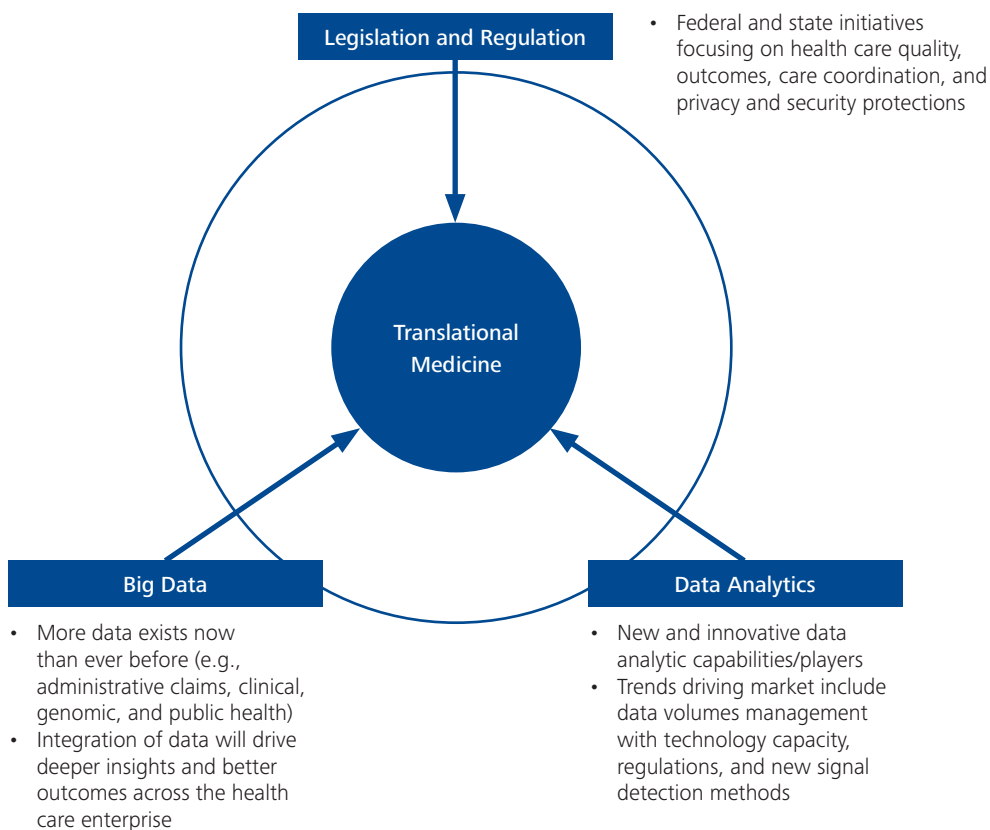


Introduction

Our country has had a strong commitment to life sciences research and development (R&D) for new treatments and cures. For the past two decades, the U.S. was the world's leading funder and life sciences innovator — providing up to 70 to 80 percent of global life sciences R&D funding.¹ In recent years, the U.S. has had a major decline in its global R&D competitiveness.² Other nations, especially those in the Asia–Oceania region, are more actively competing and investing in various elements of the value chain.

The U.S. life sciences industry faces unprecedented challenges with expiry of blockbuster patents, slowing pipelines, soaring R&D costs, increasing pricing pressure from payers, growing market share for generic pharmaceuticals, and tightened scrutiny by regulators over drug safety. Health care reform and our country's focus on curbing medical spending and its push to value-based care are also impacting life sciences R&D.

Traditionally, the R&D processes within the three elements of the life sciences value chain — discovery, development, and delivery — have occurred in silos with a limited flow of data and effective practices among them. However, forces within the current health care landscape are making life sciences innovators look differently at how they approach the value chain. These forces are 1) legislation and regulation, 2) data analytics, and 3) big data.

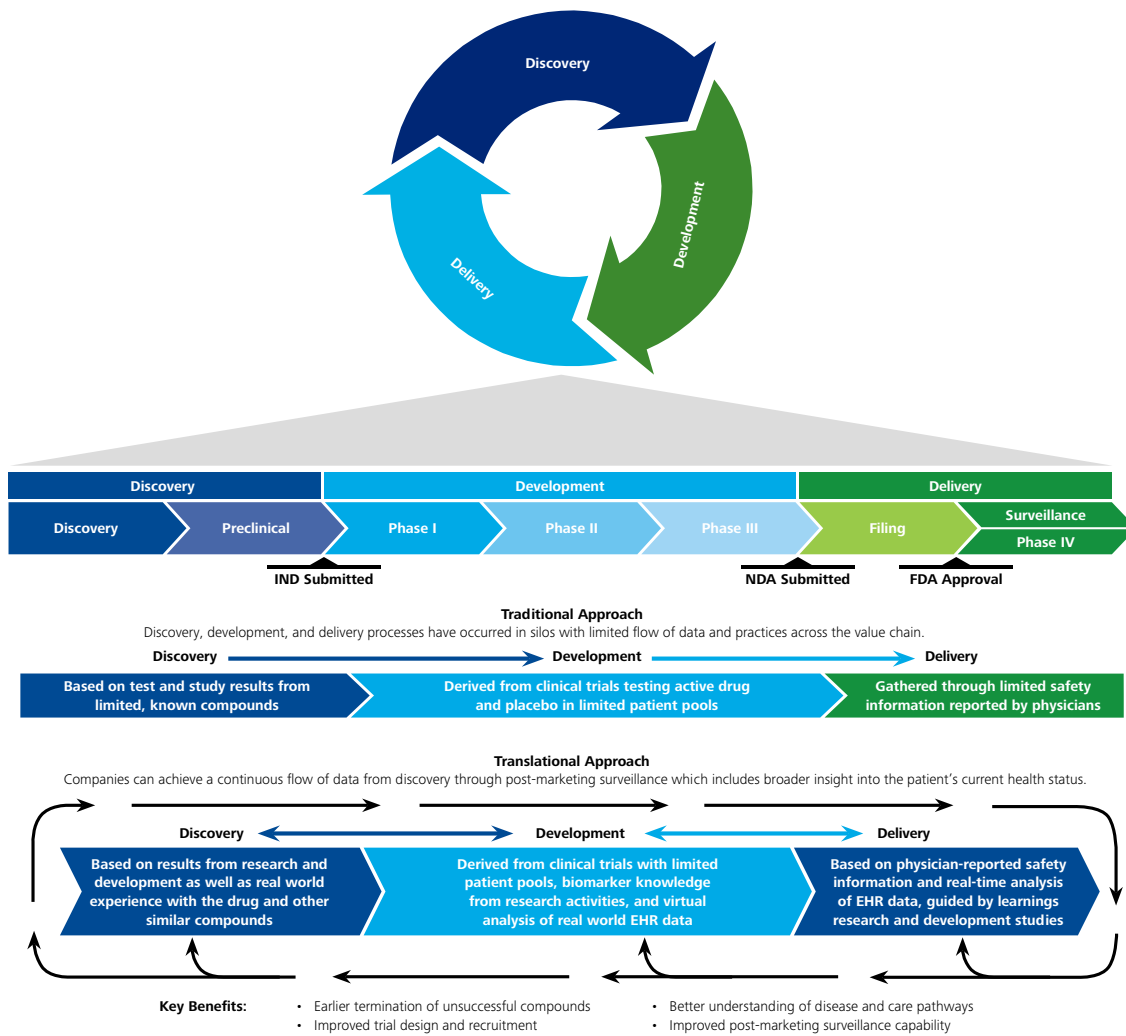


¹ Chakma, J., et al., Asia's Ascent — Global Trends in Biomedical R&D Expenditures. New England Journal of Medicine, 2014. 370(1): p. 3-6.

² IBID.

A translational approach to the R&D value chain removes discrete steps and connects the discovery, development, and delivery processes. New learnings inform this value chain, and additional discoveries and developments lead to a continuous process improvement cycle. This could accelerate U.S. life sciences R&D and bolster global competitiveness. In the following pages, we present ideas for achieving a translational approach to the value chain. We identify the “accelerators” for incentivizing more raw input of basic science into translational research, increasing development speed so that more therapies are patient-ready, and decreasing barriers to market entry.

Figure 1. Traditional Versus Translational Approaches



Discovery

Traditionally, stakeholders have had different approaches and goals to the discovery cycle. The goal for life science companies is to identify effective and unsuccessful compounds early in their development (attrition risk) to make R&D cost-effective. This requires systematic access to and application of patient-level data. For provider organizations, the goal is to aid in the development of novel therapeutics/diagnostics by improving the speed of knowledge transfer between research laboratories and patient care environments. This requires multiple integration points for process and information flows between scientific knowledge and clinical care. Incentivizing research output, bridging stakeholder differences, and connecting the discovery process to development and delivery is a challenge. It requires maintaining funding levels, continuing recognized academic research, and leveraging health technology.

The role of stakeholders

Government funding

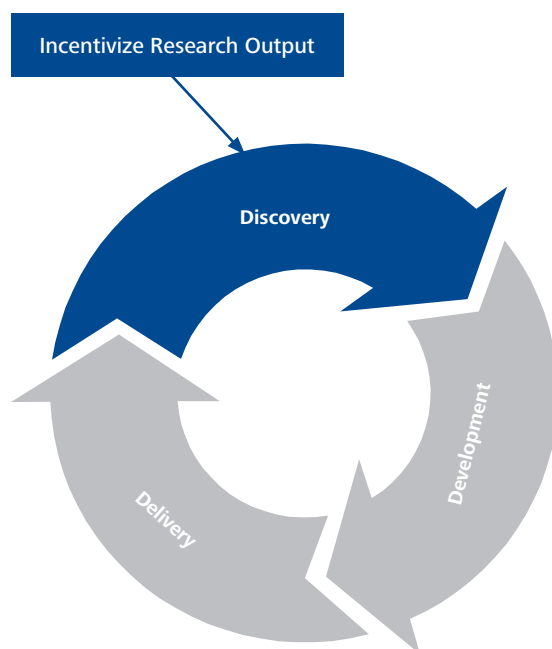
The federal government has long been an important source and catalyst for advances in medical research. Through funding primary research, the government spurs the discovery of novel life sciences products. Strong government funding coupled with new industry funding is important to taking leadership in R&D. Some governments or governmental institutions are taking novel steps to fund life sciences R&D innovation. Recently, the European Union's (EU), European Investment Bank (EIB), owned by and representing the interests of the EU Member States, agreed to provide about \$100 million to a large life sciences company to develop various drugs in return for milestone payments if the candidates progress.³ The EIB could lose money if the projects it backs are unsuccessful. This represents the first deal for the recently-launched InnovFin funding initiative set up by the European Commission and the bank.

Legal and regulatory framework

The passage of the Orphan Drug Act in 1983 developed a legal and regulatory framework for the development of products to treat rare and neglected diseases.⁴ The incentives spurred R&D with more than 400 medicines approved to treat rare diseases in the last 30 years, and one-third of new medicines in the last five years have been designated as "orphan drugs."^{5,6} The government is currently exploring other regulation that will encourage life sciences companies to explore new areas. The FDA recently published a draft guidance — New Chemical Entity Exclusivity Determinations for Certain Fixed-Combination Drug Products — intended to grant five years of marketing exclusivity for fixed-dose combination drugs containing a new drug substance.

Collaborations

Universities have become a willing partner in the efforts by life sciences companies to decrease the risks associated with early phase product



development. According to a Tufts Center study, many large life sciences companies have established at least one academic medical center (AMC) collaboration. Research in academic institutions is "particularly good for the basic underlying scientific development that should later translate into effective molecules in clinical trials." This enables the training of a steady pipeline of scientists who can take on the big challenges present in healthcare. Regional innovation clusters, often found around major research universities, are also important to innovation.

Funding research that is directly leading to product development is essential for pipeline growth and identifying new treatment targets. A new center committed to this effort is the National Center for Advancing Translational Sciences (NCATS), established to focus on translational innovation as both a scientific and organizational issue.⁷ NCATS seeks to foster teaming across the spectrum of research and reduce, remove or bypass bottlenecks in the development of new treatments and tests that will ultimately improve human health.⁸ The Center aims to make translational science more efficient, less expensive and less risky. NCATS, NIH, and others can advance research and trials in novel ways by increasing collaboration efficiencies, providing additional resources for small businesses and by making technologies widely accessible to the larger scientific community.

National Center for Advancing Translational Sciences (NCATS)

- Established to respond to the pressure to improve the translation of research from the bench to the bedside
- Represents an embrace of translational science and a revolutionary approach to diagnosis, treatment, and prevention
- Administers the Clinical and Translational Science Awards (CTSA) to promote clinical research at academic medical centers

3 http://www.pmlive.com/pharma_news/ucb_taps_eu_for_75m_in_r_and_d_funding_578891

4 <http://www.ncbi.nlm.nih.gov/books/NBK50974/>

5 <http://www.fda.gov/forindustry/DevelopingProductsforRareDiseasesConditions/default.htm>

6 Orphan Drugs "medicines that treat rare diseases affecting fewer than 200,000 patients in the United States"

7 http://www.ncats.nih.gov/files/NCATS_2012-2013_Report.pdf

8 <http://www.ncats.nih.gov/research/cts/ctsa/about/iom/iom.html> NCATS

Additionally, outside practitioners can facilitate translational research activities supported by federal agencies and capitalize on the research being conducted in the private sector. In order to facilitate accelerated progress, standard agreements and collaboration models are adopted. This understanding is critical to initiate collaborative approaches, avoid protracted negotiation and to allow important research to be conducted efficiently. These agreements help facilitate the exchange of research materials and confidential information,⁹ and enable clinical studies to determine the safety and effectiveness of new agents being developed or in clinical trials.

Deloitte Experience with Collaboration

- Deloitte has helped small single disease-focused non-profits build their technology infrastructure for better patient tracking and outcomes reporting in order to use the data to drive development of new therapies.
- Deloitte team has teamed with the National Heart Lung and Blood Institute (NHLBI) to create a group of the Centers for Innovation, which function to bring together publicly funded researchers with private life sciences companies and venture firms looking to invest in novel innovative technologies, devices, and therapeutics.
- Deloitte also has vast experience working with and establishing PPPs outside the healthcare sector as well.¹⁰

New teaming models

It is important to look at new ways to provide guidance for basic research and discovery in light of the current funding climate. The Accelerating Medicines Partnership (AMP) is a new \$230 million venture between the National Institutes of Health (NIH), 10 biopharmaceutical companies, and several non-profit organizations to transform diagnostics and treatments development by jointly identifying and comparing biological targets of disease. The desired goal is to increase the number of new diagnostics and therapies for patients and reduce the time and cost of developing them. This is an example of a consortium focusing on the research and creating teams to work together. This is a very similar approach to mapping of the human genome in 2000 which collected and shared research knowledge among the consortia to further accelerate research.

Consideration should also be given to alternative private funding sources, especially public private partnerships (PPPs). A clear framework and policy to enable PPPs was established by The National Council for Public-Private Partnerships (NCPPI). Between 1982 and 2006, one-third of drugs and nearly 60 percent of new molecular entities accepted by the FDA cited either an NIH-funded publication or an NIH patent.¹¹ Government funding can help attract private investors to a particular venture. The government

9 <http://onlinelibrary.wiley.com/doi/10.1002/meet.2011.14504801026/abstract> Data sharing

10 [http://www.deloitte.com/assets/Dcom-UnitedStates/Local%20Assets/Documents/us_ps_PPPUS_final\(1\).pdf](http://www.deloitte.com/assets/Dcom-UnitedStates/Local%20Assets/Documents/us_ps_PPPUS_final(1).pdf)

11 <https://www.aamc.org/research/adhocgp/081011.pdf>

granting process is a rigorous funds acquisition process. Governments traditionally realize cost savings of 20 to 50 percent when the private-sector is involved in providing services.¹² PPPs within health R&D can unlock research potential in particular disease areas by leveraging the better parts of both enterprises.

Recommendations

Summary

Drive research discovery by maintaining primary research funding levels, increasing funding for translational research, and tracking the impact of research dollars awarded

Pursue teaming with multiple stakeholders in the biopharmaceutical R&D value chain to increase the effective dissemination of information and increase the number of products in the pipeline

Source: Deloitte.

New areas of opportunity

Patient-centered care advocacy

These organizations can help coordinate and accelerate research through patient focused research initiatives, patient education, or through their patient reach via social networks. These groups can help promote education on relatively unknown diseases with patients demanding research based on personal experiences and can disseminate new information on clinical trials, products, adverse effects, and symptoms. This fosters an earlier diagnosis of symptoms, increased coordination of care, and lower healthcare costs in the long-term. Patients can help determine research projects and emphasize areas which have not been addressed in the past through collaborations and information/data sharing.

Focus on orphan diseases

Additional research for products approved for orphan status could lead to new indications and associated revenue streams. To foster new products for orphan diseases or to explore diseases not well studied, there are a variety of incentives that could be leveraged including:

- Tax credits
- Grants
- Waive FDA fees
- Expedite regulatory review (e.g., 60 day FDA review for breakthrough designation requests to treat a serious or life threatening disease or condition),
- Tax repatriation
- Product exclusivity
- Patent buyouts
- Provide government investment to reduce companies' discovery risk

Focus on digital health

Digital technology — wearable and implantable technology, web and email, mobile technology, and social networking — is transforming health care delivery, but it can also transform life sciences R&D. Consumers and

12 <http://www.ncppp.org/ppp-basics/top-ten-facts-about-ppps/>

payers are demanding a new generation of digital, connected health care. The confluence of scientific, medical, engineering, and wireless technology hubs is providing the needed environment for entrepreneurs and venture capitalists to exchange information, and start and grow effective companies. Benefits can be seen in the changing nature of the relationship and communication between patients and their health care providers especially for those that are geographically remote or living with chronic conditions.

Consumers have a growing interest in mobile health (mHealth) from simple to complex (Figure 2). In Deloitte’s 2013 Survey of U.S. Health Care Consumers, 15 percent have used technologies to monitor and manage health issues such as blood sugar or breathing function; 46 percent could be interested in doing so in the future. The future of mHealth and other digital technology is likely to have a transformation impact in the discovery process, such as monitoring patients and collecting data in clinical research.

National Alzheimer’s Project Act (NAPA)

- Created a national plan to promote research coordination, reduce duplicative efforts, and accelerate Alzheimer’s research efforts
- The Alzheimer’s Disease Neuroimaging Initiative (ADNI), provided access to ADNI data at no cost to more than 400 investigators worldwide resulting in improved understanding of how to conduct clinical trials
- Deloitte has helped small single disease-focused non-profits build their technology infrastructure for better patient tracking and outcomes reporting in order to use the data to drive development of new therapies

Figure 2. mHealth: From Simple to Complex

Single use mHealth	Social mHealth	Integrated mHealth	Complex mHealth
<p>Focuses on single purpose for a single user, typically consumer initiated</p> <ul style="list-style-type: none"> • Smartphone apps and wearable tech products (wrist bands, jewelry, clothing, glasses and embedded devices) that record data, support and encourage the wearer, encourage the user, who may decide to communicate the data others. • Consumer driven, use of commercially available apps with a popular focus on wellness, diet, and exercise. • Example: Fitness trackers and weight loss apps that provide tips and users to set goals and track weight, exercise, and calories. 	<p>Draws upon the social capabilities of mobile technology including support, encouragement, or a sense of competition sourced through peer and social networks</p> <ul style="list-style-type: none"> • Gamification and competition based apps; incentivization programs via financial cash-equivalent or rewards-based incentives to encourage users to meet their goals. • Consumers likely to pursue these activities on their own or via such vehicles as employment-based team challenges. • Example: A fitness app that tracks an individual’s running statistics and shares results via a social network driven, goal-achievement challenge. 	<p>Links apps and devices with the formal health care system, typically via an electronic health record (EHR). Exchanges data between a consumer and health care provider with real-time monitoring and care coordination</p> <ul style="list-style-type: none"> • Mobile technology linking physician and patient (e.g., personalized and interactive administrative reminders such as appointments and prescriptions refills). • Interfaces with organizations tailored to multiple end users — Consumers, clinicians, and administrators. • Example: Information from multiple apps that a patient uses is incorporated into the patient’s overall health record, giving a physician a more complete view of the patient 	<p>Leverages advanced integrated analytics and provides decision support capabilities at the point of care.</p> <ul style="list-style-type: none"> • Deep and complex data generated through mHealth facilitates analysis and predictive analytics at the population level — whether focused on optimal management of a specific chronic condition through to risk-analysis and epidemic predicting or monitoring. • Example: Data mining using algorithms to analyze data collected via mobile devices to deliver insights on an individual’s patterns of behavior for individual health management purposes. Data analysis oriented towards improving public health responses through analysis of sub-populations with different risk profiles and appropriate targeting of public health interventions.

Recommendations

Summary

Evaluate investment decisions to make sure the research is creating value, leading to accelerated research, and investing efficiently in the desirable type of products and technologies. Select research program metrics should track the achievements or failures of the proposed research efforts

Design Digital Health programs to be operable via multiple communication platforms and channels (such as phones, tablets, laptops, and social media) and provide privacy and security of personal information. Better, faster, and more widespread networks are required

Leverage patient-level data to drive discovery of a new drug, utilize electronic medical records to establish the safety signal of a questionable drug, and use electronic medical record data to increase clinical trial recruitment efficiency

Source: Deloitte.

<http://aspe.hhs.gov/daltcp/napa/NatlPlan2014.shtml>

<http://www.fda.gov/regulatoryinformation/legislation/federalfooddrugandcosmetictfdact/significantamendmentstothefdcact/fdasia/ucm329491.htm>

<http://img.en25.com/Web/ThomsonReutersScience/1001450.pdf>

<http://seekingalpha.com/article/1757582-roche-impact-of-rituxan-patent-expiration-in-europe>

<http://www.healthline.com/health-news/policy-investment-and-incentives-drive-rare-disease-research-051413>

<http://www.pcori.org/about-us/how-were-funded/>

<http://www.patientslikeme.com/>

Development

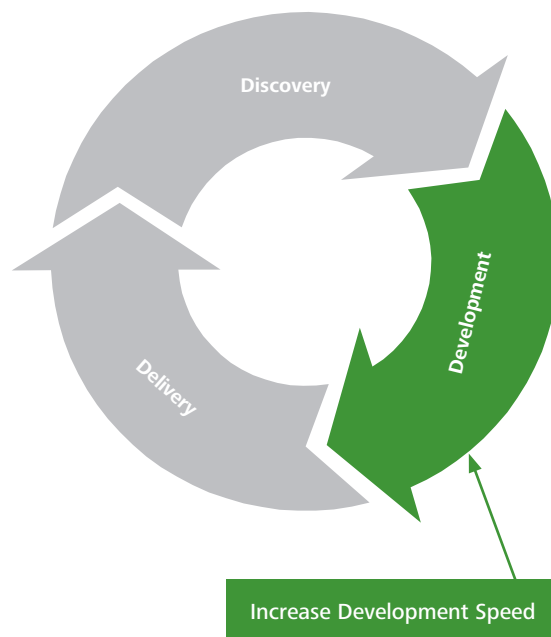
The development process is usually hindered by complex and resource-intensive regulatory requirements and practices. The current system encourages and rewards siloed product development and does not support the sharing of information among life sciences companies.¹³ The development process could benefit from the reduction of administrative hurdles and uncertainties so that translational research pursuits can proceed in a timely fashion toward safety and efficacy in clinical trials. Many regulatory policies and procedures could incentivize and encourage effective clinical trials and meaningful R&D. Measures to encourage collaboration and data sharing,¹⁴ as well as practical administration through cooperative and innovative policymaking, could increase the regulatory value proposition to consumers and life sciences companies.

Regulations and policies to foster cooperation

Effectiveness strategies

In order to encourage investors to fund life sciences research, regulatory frameworks and teaming among agencies and industry should be cooperative and reasonable to pursue. The European Union (EU), Japan, Mexico, and India are prioritizing regulatory frameworks and reimbursement policies that incentivize innovations in their “cures” space.^{15,16,17} And the life sciences industry avoids pursuing likely unsuccessful treatments in terms of compliance and safety. Likewise, countries like India are increasing their human capital capacity and increase the speed of R&D. Aside from making critical government investments in regulatory strategy, India has also invested in foreign markets, like Mexico, to competitively position their market for effectiveness. A benefit of this practice is maintaining critical regulatory requirements that facilitate safety by counterbalancing the supply of required personnel to increase the rate of reviews and capitalizing on other nation’s need to develop drugs at lower costs.¹⁵⁻¹⁸ Lastly, countries like Mexico are regarded as environments conducive for “cures” spaces to thrive due to creative economic policies like Free Trade Agreements that facilitate the supply of established and emerging market teaming around the world. In a similar move, Japan¹⁹ has started to consider policies to modernize and reform its approval process to increase innovation.

Research shows that “companies that seek the scientific advice of regulation authorities during the development process are more effective in



the EU’s Marketing Authorization Application (MAA) procedure.”^{20,21,22} This translates into more cooperative and transparent operational environments in which the life sciences industry has to directly engage with regulators early on in the process so they can more promptly adapt their therapies to meet approval and traverse the R&D cycle.

Build a learning healthcare system

Validate biomarkers and surrogate endpoints

In 2008, the U.S. Food and Drug Administration (FDA) sought to improve their accelerated drug approval processes by asking the Institute of Medicine (IOM) to conduct an evaluation focused on biomarkers and surrogate endpoints in chronic disease. IOM’s findings suggested that the FDA should create a consistent process and framework for biomarker evaluation to increase the rigor of the process to include analytical validation of biomarker tests, qualification and evaluation, and utilization.²³ Further, the plausibility of the biomarker in producing the desired clinical outcomes requires improvements in the evaluation of clinical evidence that surrogate endpoints correspond to clinical outcomes.²⁴

13 <http://www.ideaslaboratory.com/2012/07/27/assessing-u-s-international-competitiveness-in-biomedical-research/>
<http://www.iom.edu/Reports/2010/Transforming-Clinical-Research-in-the-United-States.aspx>

14 <http://www.iom.edu/Reports/2013/Sharing-Clinical-Research-Data.aspx>

15 The Impact of Regulatory Stringency on the Foreign Direct Investment of Global Pharmaceutical Firms, University of Cambridge Working Paper, 2004

16 The Effect of Regulation on Pharmaceutical Revenues: Experience in Nineteen Countries, Sood et al. (Health Affairs), 2009

17 Mexico: Shaking Up the System, 2010 <http://www.pharmaboardroom.com/article/country-report-mexico-shaking-up-the-system>

18 Mexico: Growing South America’s Pharmaceutical Industry, 2013 <http://www.pharmaceutical-technology.com/features/featuremexico-drugs-pharmaceutical-brazil-south-america/>

19 Japan has had stringent laws about using foreign data for safety and efficacy of drugs approved in other countries for Japanese importation. And the duration of clinical trials in Japan was 4 years compared to 18 months in the U.S. and UK and 30 months in France.

20 The Impact of Regulatory Stringency on the Foreign Direct Investment of Global Pharmaceutical Firms, University of Cambridge Working Paper, 2004

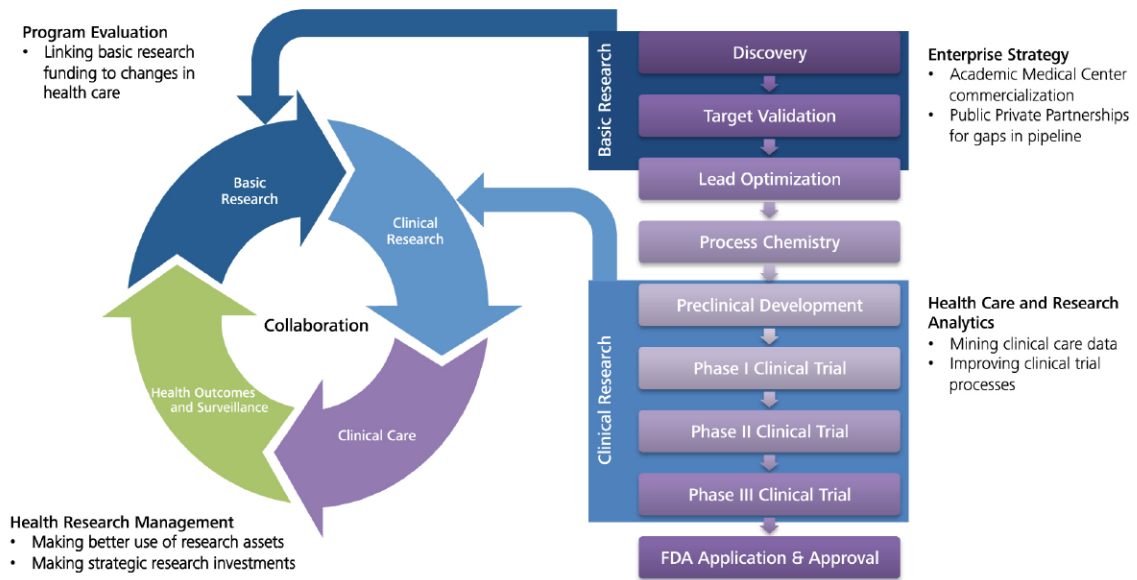
21 Potential Benefit(s) of Proposed Solutions to FDA, NIH and Others. The Sustainability of the Current Drug Development Process: Barriers and New Orientations, The Dutch Top Institute Pharm Escher Workshop, 2010

22 Demythologizing the High Costs of Pharmaceutical Research, Donald W. Light & Rebecca Warburton, London School of Economics Biosocieties Journal, 2011

23 Institute of Medicine. Evaluation of Biomarkers and Surrogate Endpoints in Chronic Disease. REPORT BRIEF MAY 2010

24 Buyse M, Sargent DJ, Grothey A et al. Biomarkers and Surrogate End Points—the Challenge of Statistical Validation. *Nat Rev Clin Oncol* 2010; 7: 309–317

Figure 3. Learning Healthcare System



Leverage insights and knowledge from PPPs

The FDA has gained several insights with regard to the advances of the PPPs pertaining to the modernization of drug development. However, societal expectations about drug safety and efficacy are rising while productivity in the life sciences industry is falling. In 2004, the FDA introduced the Critical Path Initiative with the intent of modernizing drug development by incorporating recent scientific advances, such as genomics and advanced imaging technologies, into the process. An important part of the initiative is the use of PPPs and consortia to accomplish the needed research²⁵. Poor quality and inefficiency in clinical research can seriously limit the number of questions that the field can answer about the appropriate uses of recommended or licensed medical products and significantly delay access to new therapeutic innovations. One of the lessons learned by the FDA is that the collaboration of stakeholders—federal agencies, patient groups, academic researchers, industry, healthcare practitioners, and others be established early on in the process; and that the partners be committed to the adoption and implementation of the agreed upon decisions. FDA is uniquely positioned to forge such collaborations and to establish regulations that will foster a high degree of compliance. The agency provides a forum for the identification of scientific hurdles that delay or prevent the development of new treatments and cures for today’s chronic diseases. They have made significant strides with regard to coordinating collaborations, providing informatics platform exchanges and instituting data standards. The results of their approach depends on dependable procedures and controls for reliability of the source data. In sum, FDA guidance will be an important step in the facilitation and adoption of electronic data gathering across the medical product industry.

Improve upon the randomized, double-blind, placebo-controlled model

Randomized controlled trials (RCTs) are considered the gold standard of evidence-based medicine in determining the efficacy of drug, devices, and treatments.²⁶ RCTs allow inferences about causation while non-randomized observational and experimental studies do not. However, RCTs are not without their weaknesses.

Investigators are moving towards the use of innovative study designs and the use of existing data collection platforms that allow for development of efficient interventional studies. Such study designs include pragmatic clinical trials (PCTs) or adaptive designs. PCTs can address a number of the disadvantages inherent in RCTs.²⁷ PCTs compare interventions that are relevant to clinicians and patients while focusing more on a heterogeneous patient population. Adaptive clinical trials allow investigators to identify subgroups of patients who are responding well to an interventional treatment and allow for mid-course corrections during the trial where needed. While approval for products will likely continue to require clinical trials that are randomized and controlled, there are considerations for allowing other study designs, including observational and quasi-experimental studies that use real-world data collected for purposes other than research, for supplemental applications.

Advances in statistical methods can facilitate research leveraging clinical trial and real world data to bring innovative medical products to patients more efficiently. Innovative statistical methods include sampling strategies, estimating values for missing data, analysis of multiple endpoints and pooling of data from different trials or other sources. These innovations

25 Annual Review of Medicine, Vol. 59, DOI: 10.1146/annurev.med.59.09056.155819, Woodcock, Janet, Woosley, Raymond, Feb, 2008

26 Devereaux PJ, Yusuf S. The evolution of the randomized controlled trial and its role in evidence-based decision making. *J Intern Med.* 2003;22:151-85

27 Tunis SR, Stryer DB, Clancy CM. Practical clinical trials: increasing the values of clinical research for decision making in clinical and health policy. *JAMA* 2003;290(12):1624-32.

and modeling techniques can enable broad study designs are the crux of the discussion about whether efforts to streamline study design and product approval processes will jeopardize precision and ability to infer causation.

Figure 4. Selected examples of innovative trial designs options

Seamless Phase II/III — operational combination of objectives from two phases into a single one	Adaptive Seamless Phase II/III — inferentially seamless design using data from patients enrolled before and after the adaptation	N-of-One Trials — form of prospective study where different treatments are evaluated in a single patient over time
Improvements in the use of historical controls in clinical trials	Phase III open label randomized trials	Use of patients as own controls in clinical studies

As new trial designs gain traction, opportunities have emerged to incorporate them into routine practice, maintaining the rigorous standards required to affirm a drug or device for market with a more efficient allocation of time and resources. Increasingly, study designs other than the traditional RCT are being used in the Learning and Exploratory Phases of clinical trials, in part by directly addressing the regulatory, logistical, and methodological barriers currently challenging uptake. Regulatory bodies, such as the FDA and European Medicines Agency (EMA), have begun to clarify issues associated with the new trial methods while research organizations have begun to dedicate resources solely to the designing, testing, and implementing of more complex trial designs; further, software developers have established a solid technological infrastructure to keep data clean and facilitate its security. In order to create new standards in clinical trials, ongoing efforts should continue with a focused effort on improving stakeholder education on various types and methods of alternate trial designs. This, coupled with greater evidence-based research supporting new designs and guidance from regulatory bodies, could be the start of a new norm.^{28,29} Further, massive and disparate data sets could provide the opportunity for adaptive and pragmatic clinical trial designs to assess real time safety and effectiveness during the course of routine patient care and facilitate innovations in statistical and data analytic methods.

Opportunities for HIT

Advances in health information technology (HIT) including the development of electronic health records, administrative claims, and interoperable research networks are helping to improve investigators capacity to efficiently conduct comparative effectiveness trials while providing new opportunities in personalized medicine.^{30,31} For example, The Patient-

Centered Outcomes Research Institute (PCORI) is developing a National Patient Centered Clinical Research Network that includes Clinical Data Research Networks (CDRN) and Patient-Powered Research Networks (PPRN) that will help to create a national research infrastructure that includes patients, clinicians, and healthcare systems.³² These programs will help to strengthen the U.S. capacity to conduct large and efficient CER trials through shared data resources.

Keep the regulatory science updated with advances in precision medicine, including diagnostics

Update human capital

Top talent must be retained for continuity and continued progress. The FDA has begun to create incentives and programs to encourage the retention of individuals with the desired skill set.³³

Research

Another important approach to incorporating innovative technologies into the FDA regulatory review process is through research. Research has been an important part of modernizing the FDA and is intended to promote innovation and to provide an environment where review and research scientist can develop insights to FDA's particular regulatory challenges.³⁴ CDER and CBER, two centers within FDA that are responsible for review and approval of new drugs and biologics, both have research labs and research staff that focus on cutting edge technologies (e.g., nanotechnology-based products) or complicated issues (e.g., excipient effects of the certain dosage forms) involved in regulated products. Center leaders have emphasized the important role of FDA's scientific community in keeping up with innovative technologies for the regulatory review process. CDER's Science and Prioritization and Review Committee identified science and research requirements by interviewing science and research staff, and the results are categorized and published in "Identifying CDER's Science and Research Needs Report" in July, 2011.³⁵ "Improve clinical trial design, analysis, and conduct" and "enhance individualization of patient treatment" are among the seven major categories of science and research requirements. This report is an essential first step to formulating priorities which will guide strategic planning of FDA's science and research efforts. FDA also has an Advancing Regulatory Science Initiative launched in February 2010 that is built on the achievements of existing Agency programs, like the Critical Path Initiative. The goal of the initiative is to develop new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of FDA-regulated products.

28 Kairalla, J. A., Coffey, C. S., Thomann, M. A., & Muller, K. E. (2012). Adaptive trial designs: a review of barriers and opportunities. *Trials*, 13(1), 145-145.

29 Barton, C., Coleman, K. (2013). Adaptive Clinical Trials. *Datamonitor*

30 Eapen, Z, Lauer M. The imperative of Overcoming Barriers to the Conduct of Large, Simple Trials. *JAMA* 2014; 311(14):1397-1398

31 Pearson J, Brownstein C, Brownstein J. Potential for Electronic Health Records and

Online Social Networking to Redefine Medical Research. *Clinical Chemistry* 2011; 57(2): 196-204

32 PCORI website: <http://www.pcori.org/2013/national-patient-centered-research-network/>

33 <http://www.fda.gov/ScienceResearch/ScienceCareerOpportunities/ucm379703.htm>

34 <http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/RegulatoryScience/UCM268225.pdf>

35 <http://www.fda.gov/downloads/Drugs/ScienceResearch/UCM264594.pdf>

FDA's priority areas for innovation in regulatory science

In its strategic plan, the FDA has identified several priority areas for innovation in regulatory science. These priority areas cut across product types and address the use of innovative computational methods and data sources as components of the implementation of several regulatory science priority areas. The FDA's regulatory science initiative is welcomed and supported by the pharmaceutical industry who agrees to pay a user fee to FDA to help fund an improved, more transparent and timely regulatory process. Under Prescription Drug User Fee Act V (PDUFA V), reauthorized in July 2012, FDA will have increased resources and staffing to consider the use of new scientific tools, such as pharmacogenomics and biomarkers, that can help demonstrate therapeutic benefits more rapidly.³⁶ In Generic Drug User Fee Amendment (GDUFA) Commitment Letter, FDA agreed to begin work on the FY 2013 Regulatory Science Plan in the letter and to consult with industry and the public to create an annual list of regulatory science initiatives specific to research on generic drugs.³⁷ GDUFA is the first user fee to directly fund regulatory science research activities. The research studies conducted under these initiatives will advance the public health by providing access to safe and effective generic drugs.

Recommendations

Summary

Encourage collaboration among stakeholders early and throughout the lifecycle of diagnostic and therapeutic development (e.g., through cross agency strategy development to provide guidance to the life sciences industry while encouraging open communication channels between them and regulatory agencies)

Continue innovation in trial design and statistical methods to address missing data, multiple endpoints, patient enrichment and adaptive designs, and the use of simulation and modeling to improve the effectiveness of clinical studies

Leverage clinical trial data (e.g., from existing data sets) to create large pooled data sets to understand differences in sub-populations of interest and accelerate biomarker validation

Source: Deloitte.

³⁶ <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/default.htm>

³⁷ <http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm337385.htm>

Delivery

Delivery, which feeds from Discovery and Development, provides a greater wealth of information to foster new Discovery and start the cycle all over again. Health information technology (HIT) provides the ability to improve analysis and gain better insight of the available information to make effective and timely decisions. A wealth of information, whether scientific or market-derived, will continue to expand and be available in order to understand diseases, providers, and patients at the granular level. The ability to collect information from anywhere and anytime has created a complex world where data are coming from many different sources. New tools, new markets, and new science will provide a greater wealth of information for iterative life sciences innovation fostering an environment where stakeholders are able to leverage new technology, and invest, generate, and reinvest capital impacts throughout the R&D value chain.

New data sources

Creating new value for life sciences shareholders will increasingly hinge on companies' readiness and competency in accessing and using massive and disparate data sets to drive new paradigms in research, development, marketing and surveillance. Below are examples of data initiatives that are critical to facilitating innovative results.

Systems approach

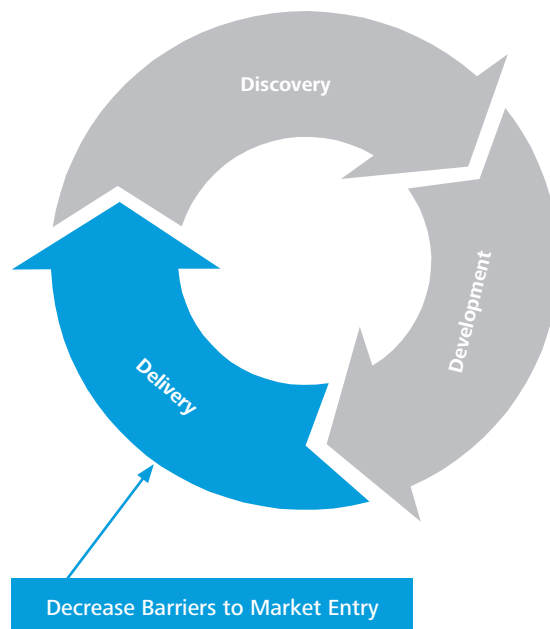
A systems approach that includes collecting health data (e.g., molecular, clinical, chemistries, cellular, organ phenotypic, imaging, social networking, EMR data, administrative claims data, etc.) and merging these data with new measurement and visualization technologies, and new computational and mathematical tools will foster effective post-approval research. This convergence of data and technology will allow researchers to simplify overwhelming amounts of data into models that can help drive life sciences Development and Discovery. These efforts can provide a better understanding of disease (etiology, pathology, prevalence, incidence, etc.), identifying signals (i.e., events) in the population, and potentially predicting disease and identifying opportunities for improving patient care.

Electronic health records

Electronic health record (EHR) data, because of its capture of patient-level clinical detail (e.g., lab results, diagnoses, family history) and a detailed picture of the care provided, presents a compelling and innovative opportunity for performing post-approval research and informing the Discovery and Delivery elements of the life sciences value chain. Recently, this data source has become more compelling since current market forces are driving up current U.S. EHR utilization rates. EHR usage in the U.S. rose from approximately 30% of physician offices and hospitals in 2005 to more than 50% of physician offices and 75% of hospitals by the end of 2011. Thus, EHR provide the potential for a clinically rich longitudinal data set for a large patient cohort.

Internet and social media networks

The Internet and social media networks have evolved into powerful tools to disseminate and collect patient health information. According to the IOM, 94 percent of social network users with a medical condition believe it is important to share their health data with other patients and improve care for future patients. Leveraging these tools can greatly expand the



reach of researchers and enable the collection of data from these large general populations, and as applicable, target subpopulations (e.g., children, elderly) to understand "real" user experiences and, potentially, avoid the "white coat" effect.

Deloitte's Hi2 — a portal for exchange and analysis of life science and healthcare data

- Deloitte has made a significant investment in health reform and analytics. A portion of this investment is devoted to the development of a subscription-based "Insights as a Service" capability we call Deloitte Health Informatics and Insights (Hi2).
- Hi2 was developed to work directly with large health systems to provide commercial subscription-based insights, enabling collaboration to effectively address market circumstances. The Hi2 approach to addressing the market circumstances involves deploying local analytics insights behind health system collaborators' firewalls, protecting patient data, and enhancing the valuable assets health systems have worked so hard to create

Strengthen adverse event reporting

Although several FDA-sponsored post-approval medication safety reporting initiatives currently exist, gaps in adverse event (AE) reporting remain. A more broad systems approach could bring detection of AEs to a new level and further strengthen patient safety. For example, a systems approach to developing a data resource could allow researchers to use a variety of detections methods, including new and existing biomarkers, to proactively identify an AE caused by currently marketed medications. Use of biomarkers may allow the detection of AEs at earlier time points and, perhaps, the predictions of AEs, especially if combined with structure-activity-relationship (SAR) models.

Other ongoing efforts to address these gaps focus on capturing the voice of the consumer (i.e., patient), intending that their voice, as a critical stakeholder, is part of the longitudinal medication safety data. These efforts have begun to use web-based data collection methods. Proper design of these instruments can be used to increase the size of population being monitored (thus increasing the likelihood of identifying rare events) and for tailoring the population being evaluated that were not well studied during the trials needed for FDA approval.

FDA's Sentinel Initiative

Leverage and exploit new data sources for post-approval surveillance

- In the Fall of 2007, Congress passed the FDA Amendments Act (FDAAA), mandating FDA to establish an active surveillance system for monitoring drugs, using electronic data from healthcare information holders.
- Launched in May 2008, the Sentinel Initiative aims to develop a proactive system to track reports of adverse events linked to the use of its regulated products.
- In the past FDA has used administrative and insurance claims data to investigate safety questions about Agency-regulated products, but generally it has only worked with one particular healthcare system at a time to evaluate a given safety issue. The Sentinel Initiative's goal is to create a distributed research network that will draw on existing automated healthcare data from multiple sources to actively monitor the safety of medical products continuously and in real-time. With pre-established privacy and security safeguards, these data holders would evaluate their information and send summary results to FDA.

Identify better patient treatment and new patient populations

These data sources could help also help develop and improve treatment for patients. Aggregated EHR data enable the tracking and analysis of patterns and outcomes of patient care after a product has been approved by FDA. This provides an understanding of the comparative (i.e., relative) benefits of a new product versus the standard of care, and produces evidence of the harms and benefits of the new product as used in the community, e.g., an evidence base on the real world net benefit of the product and the patients that it helps. By adding additional data, patients could be stratified by shared "biological" characteristics using molecular, biochemical and imaging diagnostics to more precisely select high-quality treatments. Conversely, these stratifications can be used to identify new populations and indications for drugs currently on the market.

Improve randomized control trials

These data can be used to expedite RCTs by providing more correct epidemiological estimates of disease prevalence and incidence of adverse events, care patterns, and the magnitude of unmet medical need. In turn, this streamlines trial design including patient inclusion and exclusion criteria, site selection, duration of follow up, and endpoint selection.

Enable Comparative Effectiveness Research

These data can also enable the tracking and analysis of patterns and outcomes of care after a product has been approved by FDA. This provides an understanding of the comparative (i.e., relative) benefits of a new product versus the standard of care, and produces evidence of the harms and benefits of the new product as used in the community, e.g., an evidence base on the real world net benefit of the product and the patients that it helps. Supplementing these clinical data with patient data shared using internet and social media resources helps refine the evaluating of how treatments are behaving in the post market real world.

Real world data in the supplemental approval process

The goal of the innovations in statistical methods coupled with new sources of data is to enable a more efficient process for developing products and opportunities to develop products for rare conditions that do not lend themselves to the RCT model because of feasibility constraints. FDA and EMA are not looking to replace RCTs but rather to augment them with real world data and new research methods. Many of the new designs may include post approval surveillance commitments that are longer in duration than had been the norm historically.

Internet and social media networks

As the pace of life sciences innovation quickens, effectively disseminating information to providers and patients will become critical for a product's effectiveness. Although traditional pathways of communication will continue to play a role in disseminating information, the role of internet and social media networks will have a more prominent role.

The Internet and social media networks have evolved into powerful tools to communicate health information and disseminate information on the efficacy of treatments to patients. Social media offers a more personal and open dialogue compared to traditional marketing channels like commercials or advertisements. These networks allow patients and life sciences companies to interact in new ways, including collecting and sharing information on the efficacy of treatments. Life sciences companies can share relevant health information with engaged users to indicate the efficacy of certain treatments. Furthermore, they will identify how to frame the clinical information for specific population groups and disease conditions. Patients have been a driving force for sharing and disseminating information regarding treatments and patient experiences through sites such as PatientsLikeMe, DiabetesMine.com, and TheCancerForums. The content is created within the blogs, online support groups, and resource tools for effective disease management and to indicate accomplishments and failures of treatment options. This allows patients to connect and interact with other patients to discuss treatment options and real user experiences.

Uncertainties in post-approval, real world delivery settings

Currently, there are regulatory uncertainties and other barriers that may inhibit delivery of life sciences products into the market. Regulatory

uncertainty about social media as a communication tool, even with the release of FDA guidelines, is a challenge. One barrier inhibiting delivery of life sciences products are laboratory developed tests (LDTs) — they hinder marketing diagnostic testing breakthroughs. Further, many insurers, including CMS, follow a cost plus payment model for diagnostics where payments reflect the process used to perform a test rather than the value it creates in diagnosis, treatment selection, and patient outcomes.

To encourage innovation in diagnostics, the FDA could adopt a progressive approval process for diagnostics. This process allows for a lower level of evidence for FDA approval of a new diagnostic while depending on post-marketing studies to gather additional evidence of clinical validity and utility. Second, the FDA could update its 2005 draft guidance on the approval process for companion diagnostics to reduce regulatory uncertainty around LDTs. Third, CMS could change the Medicare payment basis for diagnostics from cost plus to value-based payments to encourage innovation. Although this change may not affect certain private payers, Medicare could lead the way in valuing diagnostics. Finally, if FDA and CMS should collaborate, decisions about the accuracy and clinical utility of tests could be coordinated leading to more efficient coverage and payment decisions for diagnostics.

Intellectual property laws

Intellectual property laws often offer less protection or are under-enforced, even in markets that are considered relatively mature, such as India and China. Careful consideration should be given to the value proposition of patent protection, considering that protection may be limited and violation of rights may occur relatively promptly (e.g., months, not years), after product launch.

Emerging and developing countries

Emerging markets pose additional challenges when formulating the go-to market strategy. These challenges include significantly different economic, political, legal, and regulatory approval pathways that often are not well understood, are immature, and/or are in a state of rapid change. Further, the health care infrastructure may be much less developed and/or extensive, requiring different delivery options. Business strategies that include these markets should, therefore, also be dynamic and adaptable in order to achieve results on a global scale for product commercialization after obtaining product approval in mature markets (e.g., U.S., EU 5, Japan, etc.). Likewise, entities further down the supply chain, such as transportation carriers and distributors, may not have the systems in place to effectively provide the required post-marketing surveillance and actions (e.g., recall) that may be mandated by regulation. Vendor risk management is a critical element of an effective business strategy in these markets. Integration of the value proposition message of the product needs to be tailored to different stakeholders, including regulators, payers, physicians and patients, facilitating alignment of the value proposition message across

this value chain and across varying local markets. Moreover, this value proposition will be significantly influenced by comparative effectiveness and additional insights gained from various data sources (e.g., Big Data). Many regions have diseases which are not fully understood and may have different medical circumstances, due to differences in genotype and phenotype factors, which are particular to the region. In addition, the standard of care and primary treatment mechanisms may be significantly different in emerging markets. Recognizing the need to invest in additional clinical trials and other regulatory and legal region-specific requirements proactively is imperative, before attempting to introduce the product to the region, even after gaining approval in mature markets.

The legal (e.g., IP protection), regulatory and compliance (e.g., pharmacovigilance requirements, supply chain integrity) burden to gain approval should not outweigh the potential commercial opportunity. Commercial opportunity may need to be significantly greater in these markets in order to outweigh these uncertainties/barriers as well as the overall infrastructure investments. Moreover, strategic, financial, compliance, and operational risk factors associated with new and emerging markets should be effectively identified and carefully considered. These decision factors should be integrated into the company's business model to effectively invest in regions where there are opportunities to address the patient circumstances as well as broaden the company's commercial operations.

Recommendations

Summary

Leverage and exploit new data sources for post-approval surveillance

- Adopt a systems approach
- Leverage EHR data
- Leverage the power of the internet and social media networks

Strengthen adverse event reporting

Identify better patient treatment and new patient populations

Improve randomized control trials

Enable comparative effectiveness research

Rethink the supplemental approval processes

Leverage the power of social media networks to communicate treatment efficacy to patients

Address uncertainties and other barriers that exist in post-market, delivery settings

Enforce intellectual property laws

Conduct business in emerging and developing countries

Source: Deloitte.

Conclusion

In his 2011 State of the Union Address, the President invoked “our Sputnik moment.” Recalling U.S. investments in research and education after Russia launched the first space satellite 50 years ago, President Obama called for renewed efforts to meet international competition with investments in education and research, renewable energy, life sciences, and information technologies. Obama’s call to action still matters.

The U.S. has had a major decline in life sciences R&D global competitiveness with its industry facing unprecedented challenges. Its value chain is siloed, limiting the flow of data and effective practices among the discovery, development, and delivery processes. However, forces within the current health care landscape are making life sciences innovators look differently at the value chain.

We have presented ideas for achieving a translational approach to the value chain — connecting the processes and eliminating the discrete steps. We have identified “accelerators” along the chain to help bring life sciences discoveries to market faster and at a pace that keeps up with the explosion of new science knowledge. This could also help bolster life sciences R&D global competitiveness. America had achievements during its last Sputnik moment, and there’s no reason why this can’t be our rallying call for a Sputnik moment 2.0.

Advisors, Authors, and Contributors

Advisors

Terri Cooper, PhD
Principal
Deloitte Consulting LLP

Tom Breuer, MBA
Principal
Deloitte Consulting LLP

Homi Kapadia, MBA, MS
Principal
Deloitte Consulting LLP

Authors

Howard Underwood, MD, MBA, MS, FSA, MAAA, FCA
Specialist Leader
Deloitte Consulting LLP

Parag Aggarwal, PhD
Specialist Master
Deloitte Consulting LLP

Charles Anamelechi, MS/PhD
Senior Consultant
Deloitte Consulting LLP

LeeAnn Bailey, MD, PhD
Specialist Master
Deloitte Consulting LLP

Cindy Bo, MBA
Senior Manager
Deloitte Consulting LLP

Nakia Brown, PhD
Specialist Master
Deloitte Consulting LLP

Marianne Laouri, PhD
Specialist Leader
Deloitte Consulting LLP

John Phillips, MBA
Director
Deloitte Transactions and Business Analytics LLP

Contributors

Stacey Adam, PhD, CLS MT
Senior Consultant
Deloitte Consulting, LLP

David Ali, MBA
Consultant
Deloitte Consulting LLP

Catherine Carle, MSc
Consultant
Deloitte Consulting LLP

Xuan Chi, MD, PhD
Senior Consultant
Deloitte Consulting, LLP

Matthew Hefner, MS/MBA
Senior Manager
Deloitte Consulting, LLP

Matthew Hudes
Principal
Deloitte Consulting, LLP

Layla Lavasani, PhD, MHS
Senior Consultant
Deloitte Consulting, LLP

Sanjay Modi, MBA
Manager
Deloitte Consulting, LLP

Lynn Martin, PhD, RPh
Specialist Master
Deloitte Consulting, LLP

Simeon Niles, JD, MPH
Consultant
Deloitte Consulting, LLP

Rachael Nosin, MPH
Consultant
Deloitte Consulting, LLP

Elizabeth Stanley, MPH
Research Manager
Deloitte Services LP



601 E Street, NW | Washington, DC 20049
202-434-2277 | 1-888-OUR-AARP | 1-888-687-2277 | TTY: 1-877-434-7598
www.aarp.org | twitter: @aarp | facebook.com/aarp | youtube.com/aarp

July 11, 2014

The Honorable Fred Upton, Chairman
U.S. House of Representatives
Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Diana DeGette
U.S. House of Representatives
Committee on Energy and Commerce
2322A Rayburn House Office Building
Washington, D.C. 20515

Dear Chairman Upton and Representative DeGette:

AARP appreciates your efforts on the 21st Century Cures Initiative. AARP has taken a strong interest in this Initiative and looks forward to engaging in this bipartisan discussion as you continue to examine how the U.S. can promote greater innovation in the drug and medical device development arenas while maintaining high standards of safety and effectiveness. We are encouraged that as part of this effort you are seeking broad input from a number of relevant federal agencies, innovators in the private sector, academia, the provider community, and consumers.

AARP is a nonprofit, nonpartisan organization, with a membership of nearly 38 million, that helps people turn their goals and dreams into real possibilities, strengthens communities and fights for the issues that matter most to families such as healthcare, employment and income security, retirement planning, affordable utilities and protection from financial abuse. We welcome the opportunity to share our comments in response to the Initiative's "Call to Action" and the recent series of roundtables and hearings including the June 11 hearing on "Examining the Role of Incentives in Advancing Treatments and Cures for Patients".

Need to Balance New Drug Innovation with Affordability

Prescription drug innovation plays a vital role in the health and financial security of the older population. For older adults, prescription drugs are critical in managing their chronic conditions, curing diseases, keeping them healthy and improving their quality of life. Drug innovation is important to AARP and all older Americans, who tend to use more prescription drugs than any other segment of the population. However, AARP strongly believes that incentives for innovation need to be appropriately balanced with ensuring that new treatments are safe and effective, and are affordable to consumers.

Success of the Current System

The Drug Price Competition and Patent Term Restoration Act of 1984—more commonly known as the Hatch-Waxman Act—made significant changes to the patent laws in an attempt to balance the need for innovative new drugs with the availability of less expensive generic drugs. The law is now widely regarded as a success, saving U.S. consumers and the health care system more than \$1.2 trillion over the past decade.¹

Real Possibilities

The current system has also continued to drive innovation, with more than 3,400 medicines in development in the United States alone, an increase of 40 percent since 2005. Globally, there are more than 5,000 medicines in the pipeline, 70 percent of which are potential first-in-class medicines.² The pharmaceutical industry is clearly thriving, and has been one of the most profitable industrial sectors for many years.³

There is also evidence that FDA's existing incentives and approval processes are working well. For example, economic incentives like tax credits, smaller and shorter clinical trials, and longer market exclusivity have been helping to drive a steady increase in the number of orphan drugs. In 2013, the FDA granted orphan-drug designations to a record 260 drug applications, a 38 percent increase from 2012,⁴ and there are more than 450 rare disease medicines in development.⁵

In addition, researchers have found that FDA's approval times are consistently faster than its regulatory counterparts in other countries. Between 2004 and 2013, the overall median approval time for new drugs in the United States was 304 days, compared to 459 days in Europe and 487 days in Japan. Furthermore, of the 21 new drugs approved by all three agencies between 2009 and 2013, 76 percent were approved first by FDA.⁶

AARP also notes that FDA already has four tools at its disposal to help expedite the development and review of drug products: fast-track designation, accelerated approval, priority review, and breakthrough therapy designation, all of which have been generally successful.

Proceed with Caution in Expanding Incentives

AARP believes that proposals to expand market exclusivity should only be used in extremely limited circumstances and only to reward drug companies for innovations that substantially improve upon existing therapies. Companies should not be rewarded for simply meeting Food and Drug Administration (FDA) standards and delivering medicines that are safe and effective.

There is also no evidence that increasing market exclusivity would result in an increase in innovation. In fact, there are indications that current incentives may instead favor market potential and profit: many of the drugs approved in the past decade are mostly minor variations on existing drugs, and most new drugs are not superior on clinical measures.^{7, 8} Consequently, any efforts to build on these existing incentives should be undertaken with an overabundance of caution to ensure that they have the intended effect.

Similarly, AARP also believes that accelerated approvals should only be granted under limited circumstances, particularly given evidence that products approved under some form of priority review are more likely to cause severe adverse reactions or be withdrawn from the market.⁹ While the existing expedited development and approval avenues have been generally successful, there are lingering questions about their long-term implications. For example, some of the products approved using expedited processes have entered the market with extremely high prices, raising concerns about patient access and the overall burden on the health care system. Additional concerns stem from the fact that a shorter approval process raises the possibility that important safety risks will not be detected until

after approval.^{10, 11} Therefore, it is critical these accelerated pathways do not compromise efforts to ensure safety and effectiveness. With this paramount in mind, we encourage the committee to work with the FDA to carefully consider ways to make improvements to clinical trials where appropriate.

AARP is also greatly concerned about the prices of many of the drug products that have recently entered the market. For example, the new hepatitis C treatment Sovaldi represents a remarkable advance with an equally remarkable price: \$1,000 per pill, or \$84,000 for a typical course of treatment.¹² While the price of this drug for private plans and Medicaid has drawn a lot of attention, its implications on the Medicare Part D prescription drug program are only now starting to become apparent.¹³ There are also indications that other hepatitis C therapies expected on the market soon will not compete on cost.¹⁴ This trend is particularly evident in the area of oncology drugs, where twelve of the 13 new cancer therapies approved last year were priced above \$100,000 annually.¹⁵ These expensive products will increase spending under taxpayer-funded programs like Medicare and also lead to increased premiums and cost-sharing for program beneficiaries. As long as drug manufacturers continue to charge excessively high prices, Congress should ensure that measures to extend drug manufacturers' monopolies and increase the financial burden on taxpayers and government programs are extremely limited.

Importance of Funding the NIH and FDA

The U.S. leads the world in biomedical research. We must continue our national commitment to investing in the National Institutes of Health (NIH) -- the country's premier research agency -- if the U.S. is to remain at the forefront of medical breakthroughs for illnesses and disabilities that affect Americans of all ages and backgrounds. We must also provide adequate funding to the FDA to allow it to effectively carry out accelerated drug reviews and new drug approvals for innovative cures and treatments without compromising safety and effectiveness.

Cost as a Barrier to New Medicines

As you look to enhance access to new treatments, we encourage you to consider how the high cost of prescription drugs can limit the availability of life-saving medications to those who are most in need of them. The growth in specialty drugs with remarkably high prices and correspondingly high out-of-pocket costs in particular has spurred debate about whether the costs associated with these products are sustainable. While Congress should look at appropriate ways to promote greater innovation, it must also take a serious look at policies that are driving the high cost of prescription drugs.

Similarly, we must consider how costs impact access to new treatments under the Medicare Part D prescription drug program. A number of ideas have been put forward to expand access to medicines by making them more affordable for Medicare beneficiaries. For example, AARP has supported giving the HHS Secretary the ability to negotiate drug prices, which is particularly important where there is no price competition in the market. For example, even more limited authority -- such as allowing the HHS Secretary to negotiate drug prices when an innovative new drug therapy addressing a great need does

not have an alternative on the market – would help to reduce the high cost of unaffordable new drugs.

Congress could also examine legislative solutions such as the Medicare Drug Savings Act, which would require manufacturers to provide Part D drugs to low-income people at the same prices they provide under Medicaid. In addition, Congress could consider medical shared savings approaches for high cost drug therapies, where a portion of the payment for the drug would be withheld to see if savings are gained to the Medicare program.

Use New Levers to Spur Innovation and Competition

As more high cost drug therapies come on the market, it is clear that we must increase transparency in the marketplace to empower consumers with more price information to place downward pressure on prices. Additionally, AARP believes there must be greater transparency of drug manufacturers' actual development costs than currently exists. Since the pharmaceutical industry routinely uses R&D costs to explain their high prices, increased transparency could provide much-needed clarity and a better understanding of the industry's pricing methods.

As noted during your recent hearing, there is also a need for greater transparency and quantitative analysis to determine where innovation is lacking and the reasons why. It is unclear what areas of R&D are not responding under the set of incentives already in place and the degree to which innovative new projects are not being pursued by drug makers and how they make these assessments.

AARP also believes the application of scientific evidence, or comparative effectiveness research, would inform clinical and patient decision making as well as the development of evidence-based guidelines and, in general, clinical practice and service delivery. Comparative effectiveness research would provide an objective basis for selecting appropriate procedures and interventions including prescription drugs and other new technologies. Countries that base their treatment and coverage decisions on clinical studies that compare new drugs to available alternatives have found that these efforts can help contain costs while promoting positive health outcomes.¹⁶ AARP is also generally supportive of efforts to utilize new technologies and data to enhance the health care delivery experience for consumers by it making it more person-centered in nature.

Thank you for the opportunity to comment on these important issues. If you have any questions, please do not hesitate to contact me or Ariel Gonzalez on our Government Affairs staff at [REDACTED] or KJ Hertz at [REDACTED] or 202-434-3770.

Sincerely,

[REDACTED]

Joyce A. Rogers
Senior Vice President, Government Affairs, AARP

cc: The Honorable Henry Waxman, the Honorable Joe Pitts, and the Honorable Frank Pallone

¹ GPhA, *Generic Drug Savings in the U.S.: Fifth Annual Edition: 2013*, December 2013.

² PhRMA, *Explore the Drug Discovery Pipeline*. Available online at: <http://www.phrma.org/pipeline>.

³ E. Torreele, "Should Patents on Pharmaceuticals Be Extended to Encourage Innovation?" *Wall Street Journal*, January 23, 2012.

⁴ S. Reardon, "Regulators Adopt More Orphan Drugs," *Nature*, April 1, 2014.

⁵ PhRMA, *Rare Diseases: A Report on Orphan Drugs in the Pipeline*, 2013.

⁶ M.A. Hamburg, "Strong Review Performance Brings Innovative Medical Products to Patients," FDA Voice, May 8, 2014. Available online at: <http://blogs.fda.gov/fdavoiced/index.php/2014/05/strong-review-performance-brings-innovative-medical-products-to-patients-2/>

⁷ D.W. Light and J.R. Lexchin, "Pharmaceutical research and development: what do we get for all that money?" *BMJ*, 2012 Aug 7;345.

⁸ M. Lanthier, K.L. Miller, C.Nardinelli and J. Woodcock, "An Improved Approach To Measuring Drug Innovation Finds Steady Rates Of First-In-Class Pharmaceuticals, 1987 -2011," *Health Affairs* 32(8): 1433-1439.

⁹ D.W. Light, J. Lexchin, and J.J. Darrow, "Institutional Corruption of Pharmaceuticals and the Myth of Safe and Effective Drugs," *Journal of Law, Medicine, and Ethics*, Fall 2013.

¹⁰ "Health Policy Brief: Breakthrough Therapy Designation," *Health Affairs*, May 15, 2014.

¹¹ T. Moore and C. Furberg, "Development Times, Clinical Testing, Postmarket Follow-up, and Safety Risks for the New Drugs Approved by the US Food and Drug Administration: The Class of 2008," *JAMA Intern Med.* 2014; 174(1):90-95.

¹² L. Purvis and D. Whitman, "Expensive New Hepatitis C Drug Raises Alarms," *Huffington Post*, May 28, 2014.

¹³ T. Neuman, J. Hoadley, and J. Cubanski, "The Cost of A Cure: Medicare's Role in Treating Hepatitis C," *Health Affairs*, June 5, 2014. <http://healthaffairs.org/blog/2014/06/05/the-cost-of-a-cure-medicare-role-in-treating-hepatitis-c/>

¹⁴ A. Wang, "AbbVie's \$84,000 question," *Crain's Chicago Business*, May 12, 2014.

¹⁵ Light D.W., Kantarjian H., "Market spiral pricing of cancer drugs," *Cancer*. 2013 Nov 15;119(22):3900-2. doi: 10.1002/cncr.28321. Epub 2013 Sep 3.

¹⁶ D. Bahr and T.Huelskoetter, Comparing the Effectiveness of Prescription Drugs: The German Experience, Center for American Progress, May 21, 2014.



July 21, 2014

Chairman Fred Upton
2125 Rayburn House Office Building
Washington, DC 20515

Ranking Member Henry Waxman
2322A Rayburn House Office Building
Washington, DC 20515

Dear Chairman Upton and Ranking Member Waxman,

The American Society for Radiation Oncology (ASTRO), representing more than 10,000 radiation oncology medical professionals treating more than 1 million Americans with cancer each year, is encouraged by the Committee's comprehensive approach to identifying methods to accelerate the pace of curing diseases in America. ASTRO is working to improve cancer care and pinpoint practices that bring us closer to a cure for cancer, including providing funding for radiation oncology research, incident learning systems and practice accreditation.

Radiation oncology research funding

ASTRO commends Congress for demonstrating an understanding of the importance of sufficient and reliable funding for the National Institutes of Health (NIH). Radiation oncology is a crucial part of cancer treatment and a focus of NIH's research programs. As a part of Congress' oversight duties and to ensure that funding levels are appropriate, it is vital for Congress to know precisely how NIH research funds are allocated. Therefore, we urge the Committee to get a clearer understanding of NIH's funding of research projects related to radiation oncology and ultimately gain more insight into NIH's priorities.

Major advances in cancer diagnosis and treatment, including radiation oncology, are happening at a faster pace than ever. As you know, Congress has demonstrated longstanding support for NIH and cancer research, and we are committed to accelerating recent advances. Our hope is that by fulfilling this request, Congress can have a better understanding of which types of research are being funded by NIH. In a 2013 report to Congress, NIH acknowledged that less than one percent of its total budget was spent on radiation oncology specific research and just over four percent of the NCI's budget on radiation oncology research. With more than two-thirds of cancer patients receiving radiation therapy as a part of their cancer treatment, the funding for radiation oncology research is not adequate to achieve new discoveries in the field. We urge you to explore this disparity in funding. With federal funding diminishing, particularly in radiation oncology, promising young researchers are leaving the field.

Each year, ASTRO awards nearly \$1 million to fund research as part of the organization's overall effort to prevent, treat, and cure cancer. Specifically, ASTRO-supported research awards and grants supporting

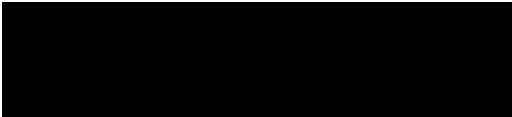
work in radiation and cancer biology, radiation physics, comparative effectiveness research, translational research and outcomes/health services research. While this is a significant part of our budget, we cannot make up for needed federal funding.

Ensuring patient safety

In June 2014, ASTRO launched RO-ILS: Radiation Oncology Incident Learning System, a new, national patient safety initiative to facilitate safer and higher quality radiation oncology care. RO-ILS allows radiation oncology centers to provide non-patient-specific data about near-misses and safety incidents that have occurred at their facilities in a secure, non-punitive environment as outlined in the Patient Safety and Quality Improvement Act of 2005. The data collected in RO-ILS will educate the radiation oncology community about how to improve safety and patient care. This data will be analyzed to inform radiation oncology safety procedures and processes, best practices, practice guidelines and/or recommendations. RO-ILS is a key milestone in ASTRO's Target Safety Campaign, a patient protection plan to improve safety for radiation oncology. Learning from near-misses and safety incidents is a critical piece to improving patient care.

ASTRO is committed to ensuring that patients receive the best possible care by encouraging radiation oncology practices to report incidents so that we can learn from errors and improve processes of care, identify education gaps and develop needed clinical guidelines for the field. To guarantee that there is accountability in radiation therapy practices, ASTRO will launch the Accreditation Program for Excellence or APEx in early 2015. This program will hold practices accountable to meet a broad range of practice standards and highlight any variances in the delivery of radiation oncology care. We urge the Committee to investigate how to incentivize the use of such incident learning systems and practice accreditation programs to ensure that patients receive safe, high-quality care.

Thank you in advance for your work on behalf of the health of Americans. Please feel free to contact Shandi Barney at 703-839-7382 if you have any questions.



Laura I. Thevenot
Chief Executive Officer