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.

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
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. 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. 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.” 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 health care. 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. 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. 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

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, 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 or 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 health care sector as well.
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.13

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 (NCPPP). 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.14 Government funding can help attract private investors to a particular venture. The government 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.15 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 health care 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 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.

Figure 2. mHealth: From Simple to Complex

Simple mHealth
Focuses on a single purpose for a single user, typically consumer initiated.

- Smartphone apps and wearable tech products (wrist bands, jewelry, clothing, glasses, and embedded devices) that record data, support and encourage the wearer, and encourage the user, who may decide to communicate the data to 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 enable users to set goals and track weight, exercise, and calories.

Social mHealth
Draws upon the social capabilities of mobile technology including support, encouragement, or a sense of competition sourced through peer and social networks.

- 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.

Integrated mHealth
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.

- Mobile technology linking physician and patient (e.g., personalized and interactive administrative reminders such as appointments and prescriptions via mobile devices).
- 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.

Complex mHealth
Leverages advanced integrated analytics and provides decision support capabilities at the point of care.

- 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 prediction 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.

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Recom
mendations

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

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
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. 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, 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. 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. 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, Japan 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.” 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 health care 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. 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.

Figure 3. Learning Health Care 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. 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 research. 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, health care 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. 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. 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 in statistical methods and modeling techniques can streamline study design and accelerate product approval processes by enabling quality data collection and analysis.

**Figure 4. Selected examples of innovative trial designs options**

<table>
<thead>
<tr>
<th>Seamless Phase II/III — operational combination of objectives from two phases into a single one</th>
<th>Adaptive Seamless Phase II/III — inferentially seamless design using data from patients enrolled before and after the adaptation</th>
<th>N-of-One Trials — form of prospective study where different treatments are evaluated in a single patient over time</th>
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<tbody>
<tr>
<td>Improvements in the use of historical controls in clinical trials</td>
<td>Phase III open label randomized trials</td>
<td>Use of patients as own controls in clinical studies</td>
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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. 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 health information technology (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. 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 health care systems. 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.37

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.38 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, 2011.39 “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.

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.40 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.41 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
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 initiates 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 offices42 and hospitals in 2005 to more than 78% of physician offices43 and 94% of hospitals44 by 2013. 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 Institute of Medicine (IOM), 94 percent of social network users with a medical condition believe it is important to share their health data with physicians and other patients to improve care. 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 health 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 health care 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 health care 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 health care 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. 46

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 may 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 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, 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., pharma-<covigilance 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.
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