Improving Drug Development and Patient Access With the Right People, Processes, and Culture: What Needs to Happen Right Now to Bring Better Medicines to the Patients Who Need Them

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Abstract

In a global environment where health care costs are soaring, R&D efforts are flatlining. Meanwhile, payers are demanding more value for their money. In this environment, the traditional siloed drug development model is not sustainable. Yet innovations such as adaptive trial designs, real-world data collection, precision medicine, and patient-centric trials that have been proven to streamline clinical trials, enrich the data they produce, and facilitate reimbursement have not been widely adopted. Why? Because the medicines ecosystem currently lacks 3 key prerequisites for innovative and sustainable change: (1) a highly trained workforce that can handle and interpret high volumes of fragmented data; (2) a dependable process for judging what constitutes value in medical innovation; and (3) corporate cultures that learn fast from failure and mine the competitive riches offered by a diverse workforce. Cultivating the right people, processes, and culture will require a concerted effort by industry, academia, governments, and nongovernmental organizations (NGOs) to devise efficient, effective solutions.

Keywords

workforce training, diversity, virtual global organization, innovation, clinical trials, payers

Healthcare systems worldwide are demanding increased efficiency, innovation, and affordability from the pharmaceutical industry. In a global environment where health care costs are soaring, R&D productivity is flatlining. At the same time, payers are demanding more value for their money. In this environment, the traditional siloed drug development model is not delivering affordable innovation. A more efficient, sustainable development model is imperative for the long-term health of the pharmaceutical industry.

Yet innovations such as adaptive trial designs, real-world data trials, precision medicine, and patient-centric trial designs that have been proven to streamline the conduct of clinical studies, enrich the data they produce, and increase the likelihood of launch and reimbursement have not been widely adopted.¹ Why? Because the industry currently lacks certain key prerequisites for innovation.

Pharmaceutical innovation can be sustainable and affordable only if the following elements are in place: a highly trained workforce, effective processes for communicating the value of innovation, and a corporate culture that leverages workforce diversity and adopts new tools flexibly and intelligently. In other words, the elements critical to successful innovation in drug development are the right people, the right processes, and the right culture.

Data, Data, Data . . . and the Workforce Skills Gap

Highly trained knowledge workers have always been essential to drug development, but that's truer today than ever. With rapid scientific advances (precision medicine, gene editing, chimeric antigen receptor T cell therapies, and more), the digitization of patient care with electronic health records (EHRs), electronic medical records (EMRs) and wearable digital devices, old ideas about data collection, transfer, visualization, and reporting—and how they should be conducted—are being overturned.

While applications of artificial intelligence, big data, and other fruits of data sciences are proliferating and spreading, relatively few people have the expertise to use these tools to guide development decisions, increase market access, or improve patient care. For example, cancer researchers

Therapeutic Innovation
& Regulatory Science
2019, Vol. 53(3) 398-402
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DOI: 10.1177/2168479018814224
tirs.sagepub.com

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Submitted 09-Oct-2018; accepted 19-Oct-2018

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understand that they could target treatments by linking the genetic sequences of patients' tumors with the huge existing stores of data on the specific gene mutations that seem to drive tumor growth but they have been thwarted to a great degree by a simple glitch: medical records are gathered in a dizzying array of nonstandard, noninteroperable formats² and are not linked to genetic profiling. Health data sciences and analytics are necessary if we are to mine EHR/EMR data productively and extract valuable real-world evidence (RWE).

Consequently, organizations need to invest in a workforce that can manage and interpret data, especially the new kinds of data generated as drug development shifts from a monolithic reliance on randomized controlled trials.¹ The explosion in data-rich trials, hybrid trials, virtual trials, genomics, and wearables makes sophisticated, technology-assisted data analysis a key competitive advantage because data from successful trials, failed trials, and failed preclinical projects could be transformative in reducing expensive and time-consuming rework.³

Organizations such as Duke Forge, Duke University's Center for Actionable Health Data Science⁴ (led by former FDA Commissioner Robert M. Califf), and Verily Life Sciences⁵ are addressing this gap deliberately by developing tools to collect and organize health data using data science to produce useful insights and improve health outcomes, with a workforce that is up to the challenge.

Workforce competency is a global opportunity that can likely only be achieved with a coordinated effort engaging multiple sectors. A recent World Economic Forum report concluded that businesses must collaborate with industry partners to get a clear view on future skills and employment needs, pool resources, and work more closely with governments to map out a roadmap of skill demand versus supply.⁶

Regional collaborations between industry and academia, supported by government funding, could create a talent pipeline to meet the demand for necessary clinical development skills and expertise. For example:

- ✓ In recent years, the Kyoto Pharmaceutical University (Kyoto) and the Meiji Pharmaceutical University (Tokyo) both initiated academic partnerships with a global clinical research organization (CRO) to introduce courses in clinical development in their graduate and undergraduate curricula. Their objective is to generate a talent pipeline of qualified pharmacist-scientists to participate in global clinical development work.^{7,8}
- ✓ In the early 2000s in Europe, PAREXEL faced a shortage of clinical research associates (CRAs). As a result, in 2002 the PAREXEL Academy was launched as a training institute to prepare professionals for careers in the biopharmaceutical industry. The program has since been certified by the German Agency for Employment for training clinical research associates. German citizens can apply for government funding through the use of a training voucher.⁹ To date, 5000 students have graduated. Students can also receive government

funding to participate in a postgraduate program in clinical monitoring and clinical trial management.¹⁰

While academic institutions can provide a strong foundation in the life sciences, graduates often lack practical knowledge of drug development, including knowledge of regulatory policies and standards, data governance, project management, and proficiency in the soft skills needed to communicate effectively with diverse stakeholders. Academia-industry partnerships can help close this knowledge gap.

The computing industry faced a similar skills and knowledge gap in the 1980s and 1990s. There were plenty of graduates with electrical and mechanical engineering skills, but not enough with software engineering skills. This was critical because systems needed to be made more interoperable to benefit from newly developed tools. Computing firms tackled this problem by partnering with universities to set up paid internships for students and by advocating for new programs and curricula in software programming and applications. And to help managers who oversee technical staff to be effective business leaders, universities began to offer MBA programs designed for technical professionals, preparing them to be business-savvy in managing people in technical systems development.

There also are ongoing partnerships among professional associations, hospitals, academia, and industry. For example, the Harmonized Core Competency Framework was developed and published by the Joint Task Force for Clinical Trial Competency.¹¹ The goal was to identify a universally applicable and globally relevant set of "knowledge, skills and attitudes" essential to the clinical research enterprise.

Play Together: Improving Communications Among Drug Developers, HTAs, Regulators, and Payers

The odds of obtaining reimbursement for new drugs are getting longer. For example, while the number of health technology assessment (HTA) bodies has doubled in the past 5 years across 20 countries, less than half the assessments for new cancer drugs resulted in a positive recommendation in 2017, and those recommendations were inconsistent among countries.¹² From March 2000 to March 2018, after examining the clinical effectiveness and cost-effectiveness of newly approved medicines, the UK's National Institute for Health and Care Excellence (NICE), recommended only 56% of them for reimbursement even though they had received marketing authorizations from the European Medicines Agency (EMA).¹³

HTA agencies and payers are the gatekeepers to the resource-constrained health care marketplace. They're demanding value for money, and many have negative perceptions of pharma's approach to innovation.¹ Yet there is evidence that drugs developed using innovative trial designs (ie, adaptive designs, patient-centric designs, precision medicine trials, and real-world data trials) make their way onto national

formularies and/or reimbursement lists faster than those developed using traditional trial designs.¹

That's important because the industry currently is struggling to gather the right evidence to quantify a drug's risk-benefit profile both during development and postapproval, and to communicate that transparently and effectively to HTAs. A similar communication rift once existed (and, sometimes, still does) between the industry and its regulatory agencies.

For example, in the 1980s and 1990s, interactions between pharmaceutical companies and the US Food and Drug Administration (FDA) routinely verged on adversarial, with companies bemoaning the agency's glacial, or opaque, approach to reviewing marketing applications, and the FDA suspecting the industry of taking shortcuts and obfuscating submissions. But in a decades-long, halting process that included passage of the Prescription Drug User Fee Act (PDUFA) in 1992 and the establishment of multiple accelerated regulatory pathways (APs), the relationship between industry and regulators in the United States has matured. Today it is more transparent, reliable, and productive. (A similar evolution has occurred in Europe and Asia, thanks in good measure to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use [ICH] and the collaborations it helped to create and foster.) FDA review times are now among the shortest in the world: Of the 174 new drugs the FDA approved between January 2012 and December 2016, 105 (60%) used 1 or more of 4 expedited mechanisms, or APs: breakthrough therapy designation, fast track, priority review, and accelerated approval.¹⁴ The figure was 61% for 2017.¹⁵ Drugs that used at least 1 of these mechanisms shaved almost a year (0.9 years) off overall time to market (ie, from IND application to FDA approval).¹⁴

The next frontier for industry is to achieve a similarly transparent and productive relationship in its communications and collaborations with HTA agencies, payers, and other bodies that evaluate the value and cost-effectiveness of new drugs and decide on pricing and reimbursement.

The EMA is currently at the forefront of HTA-industry process innovation with its initiatives to formalize consultation and collaboration among industry, HTA agencies, patients, and payers to improve access to affordable, reimbursable medicines; indeed, the European Union may emerge as the key locality that inspires productive negotiations around the globe among these critical stakeholders. For example, the EMA now offers a formal process that allows sponsors with eligible products to consult with the EMA on their initial evidence generation plan and reimbursement, as well as their postlicensing evidence generation plan.¹⁶ And the European Network for Health Technology Assessment (EUnetHTA), funded by the EU Health Program, seeks to facilitate HTA collaboration across Europe to conserve resources and reduce overlap.¹⁷

FDA officially no longer objects to industry sponsors communicating with payers about unapproved new drugs as long as the information is objective, data-driven, and truthful.¹⁸ Industry should take advantage of this new openness to initiate a dialogue with payers about the potential benefits and value of

new therapies while they are still in development and while the development plan can be adjusted to meet the payers' needs.

Standardized, high-quality new product assessments that reflect the priorities of multiple health care stakeholders could increase R&D efficiency because they can facilitate disinvestment from low-value services and reinvestment in high-value ones.¹⁹ However, industry-HTA agency communications will not improve overnight, and solutions will be local for the foreseeable future as the HTA-payer frameworks remain highly fragmented by nation and even locality, and cross-border standards, requirements, and interests currently are not converging. Yet, as we have seen with industry-regulator relations, successful innovation in one key locality can lead to a more globalized solution.

Diversity and Inclusion: Designing a Learning Culture

In drug development, only about 1 in 10 compounds makes it from Phase I testing to market.²⁰ That metric should make it obvious that pharmaceutical companies need to learn from those failures, and quickly. That requires a culture that can absorb failures and leverage them rapidly.

Unfortunately, too many drug developers are eager to put their failures (90% of their efforts) behind them, cutting their losses to invest in their next treatment or compound. This is a missed opportunity, and a critical one.

In her book, *Teaming: How Organizations Learn, Innovate, and Compete in the Knowledge Economy*, Amy Edmondson characterized 3 types of failures: (1) preventable failures caused by skill deficiencies, or a lack of attention to detail that easily can be fixed through process redesign; (2) complex failures (triggered by process or system breakdowns) that require large-scale remediation efforts; and (3) intelligent failures (caused by thoughtful experiments gone wrong) that are best handled by formal processes that will incentivize companies and individuals to identify, analyze, and learn from them.²¹

In Edmondson's framework, drug development failures are "intelligent failures." That's why successful drug development demands a culture that encourages failure due diligence. That means applying scientific methodologies and specialized technical expertise to examine failures fully, viewing them as pathways to future success. Given the high rate of failure inherent in the drug development process—and the equal volumes of data both successes and failures generate—developers need to leverage those data to master it.²¹

A crucial aspect of a culture that can learn from failure is workplace diversity, which is coming to be understood widely as a source of business advantage. When companies create a diverse and inclusive workplace by securing and leveraging talent with different perspectives, experiences, and expertise, it has been demonstrated that they produce a more innovative culture than from a more homogenous workforce. An inclusive work environment can also help break down organizational silos that can stifle knowledge sharing and creativity. Today's emphasis on diversity comes precisely and fortuitously at a

time when drug development must become more creative, faster, cheaper, and more efficient.

A 2013 *Harvard Business Review* study suggests that diversity unlocks innovation by creating an environment where nontraditional ideas and solutions are more welcome and seriously considered. Data show that firms with a “strong diversity orientation” were 45% more likely to report year-over-year growth in market share and 70% more likely to report expansion into new markets.²² A more recent study argued that diverse companies may be more innovative for 3 reasons: (1) teams with a broader range of people have a wider range of interests, experiences, and backgrounds to draw upon; (2) diverse teams understand the variety of potential users of their products better than less diverse teams; and (3) diverse teams tend to be more effective at problem solving.²³

As clinical development becomes increasingly global, companies that have a strong culture of diversity and inclusion will have the advantage of a more diverse leadership team and workforce that reflects and can align more closely with desired markets.

This is also true at the macro level. For example, the ICH has steadily diversified its membership from its original 3 members (Europe, United States, Japan) to its most recent inclusion of Brazil, Canada, China, Singapore, South Korea, and Switzerland. Diversity within the ICH community has produced tangible gains in efficiency, including harmonized guidelines (which are continually updated) on nonclinical safety studies to inform human trials,²⁴ creation of the electronic Common Technical Document (eCTD),²⁵ standardizing medical terminology with MedDRA,²⁶ and harmonization of product quality risk management and Good Manufacturing Practice (GMP),²⁷ and pharmacovigilance.²⁸

Harmonization has paved the way to regulatory convergence and, more recently, to regulatory reliance, a framework that will allow agencies in lower-income countries to focus on narrower components of regulation and rely on the expertise of other countries to help promote and protect the health of local patients without compromising their statutory accountability.²⁹ Agencies with diverse cultures and capabilities are demonstrating that by working together and combining their areas of expertise, they can advance health care for their constituents in more efficient ways.

A “Virtual Global Organization”

Today’s drug development enterprise has become so global, cross-disciplinary, and interconnected that it behaves like a “virtual global organization” of diverse stakeholders with shared values (eg, ethical clinical trials), standards (eg, ICH Guidelines), and goals (eg, affordable health care for all); one that requires its different people, processes, and cultures to work collaboratively and in synchrony to ensure that health care innovation is both vibrant and economically viable. The opportunities and challenges involved in this multi-institutional endeavor occur at the intersection of science, medicine, regulation, technology, patient needs, health care delivery, and funding. In its present inharmonious state, it is not delivering the efficient, economically viable care the world’s patient population demands and deserves. This is not sustainable, either socially or economically.

It will take a global effort to change the game. Workers must be trained appropriately to leverage new technologies and the data they collect, generate, and use to produce insights. Industry, governments, HTA agencies, and payers must find a way to examine, debate, and resolve their differences on what constitutes value, how treatments and medicines will be priced, and who will have access to them. Institutional cultures must change to embrace diversity and learn to develop new processes and tools to take advantage of scientific advancements.

Addressing these challenges successfully will require a concerted effort by industry, academia, governments, and NGOs to connect silos (administrative, cultural, and technical) and devise innovative solutions. This “virtual global organization” may be approaching a tipping point³⁰ wherein a critical mass of evidence and effort will make efficient drug development and affordable medicines a sustainable reality.

However, much work—the bulk of it of necessity collaborative—lies ahead.

Authors’ Note

Certain elements of this content were presented at the DIA Japan Annual Meeting, November 2017, Tokyo.

Declaration of Conflicting Interests

No potential conflicts were declared.

Funding

Drs. Grignolo and Siu receive financial support as full-time employees of PAREXEL International, a contract research organization and consulting firm.

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