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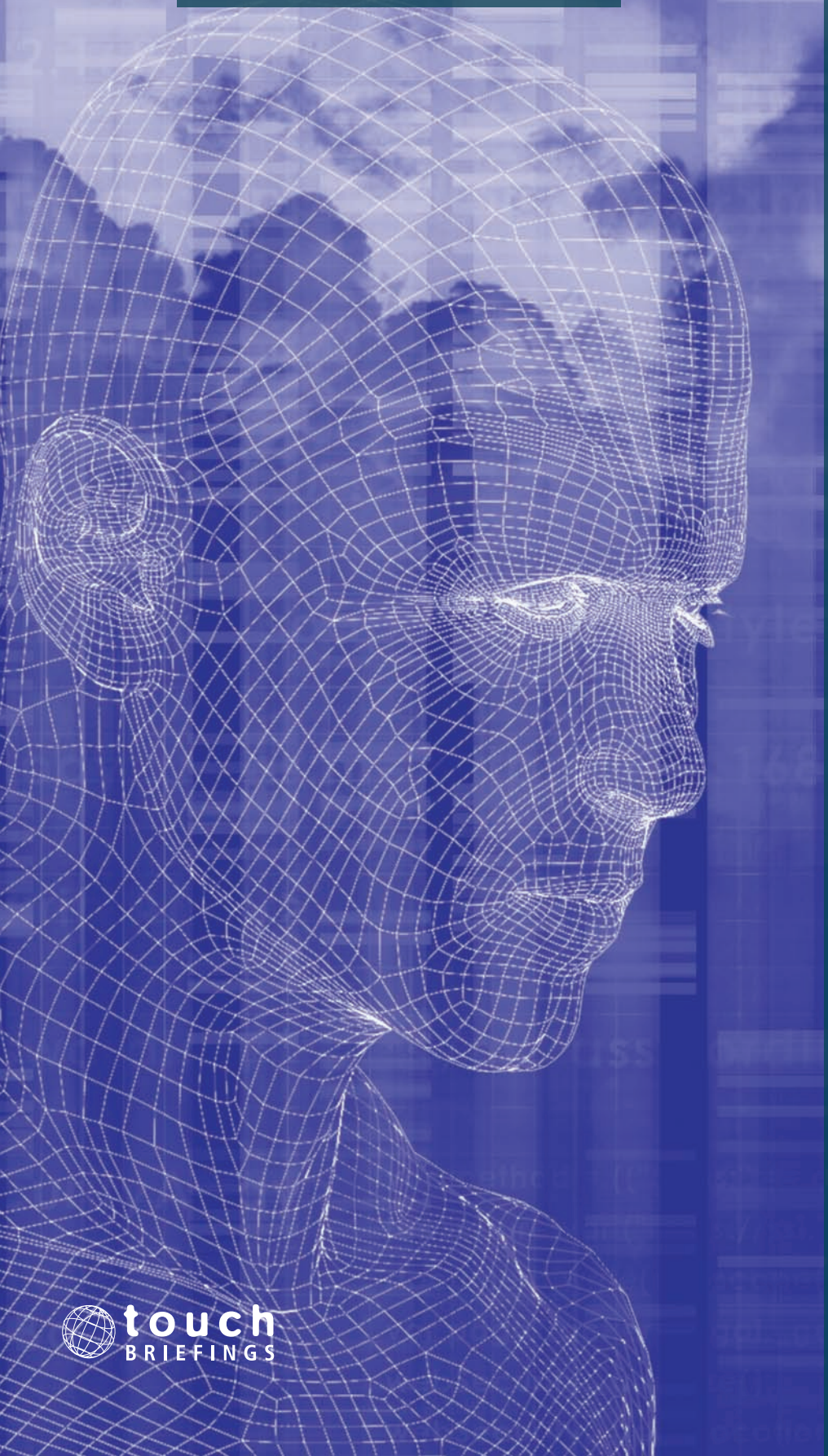
VIRTUALIZATION IN PHARMA R&D



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THE BUSINESS OF VIRTUALIZATION IN RESEARCH AND DEVELOPMENT

Sandy Johnston, Kate Moss, and Andy Brown
PricewaterhouseCoopers

EMPOWERING VIRTUALIZATION, ENABLING NEXT-GENERATION PHARMA

Nick Giannasi
Oracle

RE-THINKING PHARMA R&D—THE MERCK EXPERIENCE

Clark Golestani
Merck & Co

TECHNOLOGY AND PEOPLE—SHIFTING THE R&D PARADIGM AT GLAXOSMITHKLINE

Alex Lancksweert, Peter Milligan, and Robin Dement
GlaxoSmithKline

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Tomorrow's Virtual World—Big Pharma's Big Chance

Sian Bithell

Tough times for Big Pharma indeed, but the pharmaceutical market is out there and there is little doubt that it's growing globally. Unsurprisingly the pharmaceutical industry is facing challenges from the weak global economy, downward pressure on prices, and increased public scrutiny over ethical and business practices—driving development and regulatory costs sky high. Cost control measures can be employed and go some way to counter these problems, although it is by addressing the demand for innovative medicines where real progress can be made.

For too long pharmaceutical companies have relied on modest improvements in existing research and development (R&D) pipelines while their blockbuster drugs 'pay the bills', but this strategy is no longer working. Evidence demonstrates that spending in R&D has been increasing exponentially while the annual number of new drug approvals remains relatively low. Add to this the well-documented fact that patents for many of the industry's blockbuster medicines will expire over the next few years and it is evident that tactical changes must be made.

Reflex action sees like-for-like mergers as a quick fix. Looking to combine existing drugs in novel ways also provides a solution to unblocking the pipeline in the short term. Yet, as governments worldwide attempt to shift the spotlight from disease treatment to prevention, it appears that focusing on disease rather than individual compounds should generate new business opportunities for pharma—but can such shifts be done alone with any great degree of success?

Moving into a new decade, senior management acknowledge that adopting new business models could provide them with long-term solutions to their problems, offering much more than a glimmer of hope for the future. Fundamental to the future success of the industry is the need to improve on the return on R&D investment. This will require a shift from the integrated in-house model of R&D to models that embrace external innovation from creative alliances and outsourcing—the virtualization of R&D.

Here, in our focused report 'Virtualization in Pharma R&D', we have commissioned a collection of articles from expert commentators and practitioners in the new R&D landscape.

From PricewaterhouseCoopers, Sandy Johnston, Kate Moss, and Andy Brown provide a brief state-of-the-nation overview of the biopharmaceutical industry in their article, 'The Business of Virtualization in Research and Development'. They identify and review potential virtualization business models and strategies, presenting an excellent introduction to the subject matter and a comprehensive analysis of the methods used to implement a suitable approach.

Complementing this, our second review, 'Empowering Virtualization, Enabling Next-generation Pharma', written by Nick Giannasi, goes even further. This article underlines the fact that the virtualization of R&D will need to be supported by enabling IT, predicting that IT-empowered data/knowledge management will drive efficiencies and facilitate the much-needed push for continued innovation that remains elusive.

'Rethinking Pharma R&D—The Merck Experience' provides us with an insightful 'view from the ground'. Clark Golestani harnesses Merck's progressive hands-on experience of virtualization and discusses the new strategies that have been employed at the company, the challenges faced, and the resulting benefits to their business.

The final article in this report, 'Technology and People—Shifting the R&D Paradigm at GlaxoSmithKline', written by Alex Lancksweert, Peter Milligan, and Robin Dement, highlights how GSK, among others, are revisiting 'virtual' IT solutions to improve R&D productivity.

We would like to thank all of our authors for their contributions and trust that you, our readers, will find our report informative and engaging. ■

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The Business of Virtualization in Research and Development

Sandy Johnston, Kate Moss, and Andy Brown



Sandy Johnston leads PricewaterhouseCoopers' (PwC's) consulting practice for the Pharmaceuticals & Life Sciences Industry Group in the UK. He has over 20 years of experience in consulting, mostly focused on the pharmaceutical industry. He has considerable experience in business performance improvement and change management enabled by new technology and has led a number of major performance improvement and cost reduction projects for many of the world's largest pharmaceutical companies. He has also led the implementation of new processes and systems across the pharma value chain, including electronic data capture, clinical trial management systems, clinical data management systems, clinical trial supplies, performance management, document management, and data warehouse projects in research and development, as well as enterprise resource planning systems in finance and the supply chain.
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Kate Moss is a director at PricewaterhouseCoopers (PwC), leading the European research and development (R&D) practice. She works solely with pharmaceutical clients, and her client work is focused on managing change and general R&D performance improvement. She has been integral to the recent Pharma 2020 publications from PwC. Ms Moss has extensive pharmaceutical industry experience across multiple therapeutic areas, geographies, companies, and roles. She began her career as a sales rep, but the majority of her industry career was within clinical development and program management within pharma, biotech, contract research organisations, and virtual companies. In 2000 she moved into consulting.
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Andy Brown is an experienced international blue chip project executive and management consultant specializing in pharmaceutical research and development (R&D). With 20 years of successful direction and delivery of major international new product development and performance improvement projects, he has worked with many of the world's leading pharmaceutical companies. He has particular expertise in directing complex global pharmaceutical R&D time compression, cost reduction, and fast-track cross-functional drug development projects. In addition, he has started, developed, and sold his own technology-based business. As VP of Global R&D, Dr Brown has directed new product development strategy and execution at one of the major scientific information and business intelligence providers to the pharmaceutical industry. He currently leads the UK Pharma R&D Practice and Pharma Cost Reduction Service Line at PricewaterhouseCoopers. He has a BSc (Joint Hons) in zoology/microbiology, a PhD in cellular immunology, and an MBA, and will complete a BSc (Hons) in psychology in 2010.
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In this article the authors provide a brief 'state of the nation' overview of the biopharmaceutical industry. While the industry faces a number of influences for change, this article focuses on the critical issues and then identifies potential business models and strategies. The models suggested—the federated and the fully diversified—are representations of the evolution of the biopharmaceutical industry and how new business models will be created, not in terms of structure but in terms of risk sharing and financing.

Balancing on the Precipice of the Patent Cliff

The biopharmaceutical industry is at a significant point in its evolution. Fundamental changes across the industry are gathering pace, creating divergence away from the uniform model currently in use across most of the industry. The principal force driving this need for change is the unprecedented number of market-leading drugs facing patent expirations. Between 2008 and 2012, branded drugs with revenues amounting to $157 billion (measured in 2005 terms) will lose market exclusivity. For the leading pharmaceutical companies, between 14 and 41% of their existing revenues will be lost as a result of patent expiries.[1]

With so many blockbuster drugs going off-patent, the imperative for companies is to replace them with similar high-earning products in order to sustain both rising research and development (R&D) costs and market and shareholder expectations. However, the shortage of suitable replacements in the pipeline together with declining productivity exacerbates the challenges faced by the biopharmaceutical industry.

In 2008, biopharmaceutical R&D spending by the member companies of the Pharmaceutical Research and Manufacturers of America (PhRMA) reached a record $50.3 billion, while the total industry spend was an estimated $65.2 billion[2]—yet the US Food and Drug Administration (FDA) approved only 24 new therapies in the same year. Contrast this with the 53 new molecular entities (NMEs) and biologics approved in 1996 when R&D expenditure was estimated at $15 billion (see *Figure 1*).

Declining productivity has also affected the revenues generated by the industry. In terms of total corporate expenditure, sales and marketing account for the greatest corporate expense and rose from 28.7 to 33.1% of expenditure between 1995 and 2005. The need to spend heavily on promotion not only affects the bottom line but could also be seen as yet another sign of the paucity of innovative medicines reaching the market. Furthermore, aggressive promotion of pharmaceuticals also generates considerable criticism and poor public perception, leading to legislation and stricter industry codes of practice regarding the promotion of medicines.

1. PricewaterhouseCoopers, Pharma 2020: The vision – Which path will you take?, 2007. Available at: www.pwc.com/gx/en/pharma-life-sciences/pharma-2020/pharma-2020-vision-path.jhtml (accessed March 2010).
2. Pharmaceutical Research and Manufacturers of America, Pharmaceutical Industry Profile 2009, Washington, DC: PhRMA, 2009. Available at: www.phrma.org/files/attachments/PhRMA%202009%20Profile%20FINAL.pdf (accessed January 2010).

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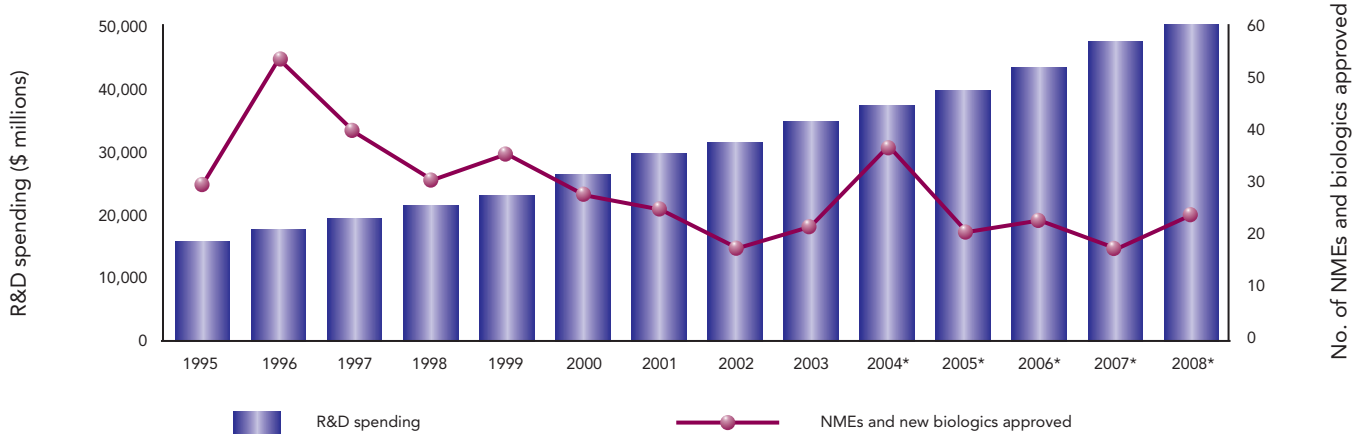
Figure 1: Increased R&D Spending Against Decline in the Number of New Therapeutics Approved by the FDA



**Includes biologics. Data on R&D spending for non-PhRMA companies are not included here, because they are not available for all 11 years.*
Sources: FDA/CDER data; PhRMA data; PricewaterhouseCoopers analysis: PricewaterhouseCoopers, 2007.[5]

Barriers to Innovation

As R&D processes within the biopharmaceutical industry have become increasingly complex, it is hardly surprising that productivity has tumbled. At the beginning of the millennium, the mapping of the human genome was expected to greatly increase the number of therapeutic targets, which would in turn help improve productivity. This has not proved to be the case, with the human genome proving even more complex than originally envisioned. At the beginning of the decade, the estimated cost of bringing a new medicine to market was $802 million. This estimate took into account the cost of financing the R&D and the expense of failed drug candidates.[3] The current estimate is $1.318 billion for an NME and $1.2 billion for a biological drug.[4] PricewaterhouseCoopers estimates that the average cost of drug development is in the region of $454 million.[5] Obviously, there is considerable variation in development costs depending on the therapeutic area,[6] but these numbers still point to a considerable financial risk. Indeed, Pfizer was widely reported to have spent 13 years and $800 million on developing the failed cholesterol-lowering drug torcetrapib.[7,8]

The current structure of the political and legal framework surrounding drug development also means that companies do not know whether their product will be eligible for reimbursement if it does reach the market. In other words, after significant investment and expenditure a newly licensed drug might not even gain market access due to pharmacoeconomic barriers. This is a substantial risk for an organization to take on, which is why the strategic decision for many companies is often to 'play it safe.' Research from the Centre for Medicines Research International found that 10 of the largest pharmaceutical companies invested over 20% of R&D expenditure on line extensions rather than new development projects. In smaller companies, the percentage was over 40%.[9]

The industry will need to adapt and transform to address the changing environment, which will add to the challenges already facing the industry. These changes include:

- chronic diseases placing increasing pressure on healthcare budgets;
- greater influence on prescribing by payers and healthcare policy-makers;
- more pharmacoeconomic barriers and outcomes-based pricing;
- the provision of healthcare moving closer to the patient;
- the growing markets of the emerging economies;
- the shift from treatment to prevention of disease; and
- even tighter regulation.

The current cyclical model of reliance on a few billion-dollar blockbusters and the subsequent race to develop new medicines to replace the income lost from these high-value drugs as they come off patent will not suffice. Nevertheless, the trends affecting the industry will also provide some major opportunities.

The necessity for change will have to be managed without forfeiting the confidence of the capital markets. There are examples of major pharma losing billions in market capitalization after issuing unfavorable news (such as withdrawal of 'potential blockbusters' from phase III trials). The biopharmaceutical industry will therefore have to balance the need to meet short-term earnings targets with long-term aspirations.

The 'one size fits all' approach to R&D will also shift as technological and scientific advances enable the development of more targeted drugs that will more likely have the desired responses in specific populations.

Many Paths to Dynamic Change

The decline in R&D productivity underlies many of the challenges faced by the biopharmaceutical industry. This innovation deficit and

3. DiMasi JA, Hansen RW, Grabowski HG, The price of innovation: new estimates of drug development costs, *J Health Econ*, 2003;22:151–85.
4. DiMasi JA, Grabowski HG, The cost of biopharmaceutical R&D: is biotech different?, *Managerial and Decision Economics*, 2007;28:469–79.
5. PricewaterhouseCoopers, Pharma 2020: Virtual R&D – Which path will you take?, 2008. Available at: www.pwc.com/gx/en/pharma-life-sciences/pharma-2020/pharma2020-virtual-rd-which-path-will-you-take.jhtml (accessed March 2010).
6. Adams CP, Brantner VV, Estimating the cost of new drug development: is it really $802 million?, *Health Affairs*, 2006;25:420–8.
7. Wadman M, When the party's over, *Nature*, 2007;445:13.
8. Cutler DM, The demise of the blockbuster?, *N Engl J Med*, 2007;356:1292–3.
9. Centre for Medicines Research International, 2005/2006 Pharmaceutical R&D Factbook, 2005.
10. PricewaterhouseCoopers, Theme of the Pharma 2020 series. Available at: www.pwc.com/gx/en/pharma-life-sciences/pharma-2020/index.jhtml (accessed March 2010).

the imminent patent cliff have fueled another round of mergers and acquisitions. However, the defensive nature of these traditional mergers and acquisitions raises the question of whether there is value and sustainability in these consolidation strategies.

The PricewaterhouseCoopers Pharma 2020 series presented the argument that despite the many challenges faced, significant improvements in R&D productivity are possible over the next 10 years. These improvements include shortening R&D processes by two-thirds, reducing attrition rates or bringing about earlier attrition, and lowering the costs of clinical trials.[10]

There is no longer a one size fits all business solution for this industry. The changes to the roles and responsibilities of each of the current functional areas and the overall business models adopted by each company will depend on the nature of their strategic priorities. PricewaterhouseCoopers predicts that two principal models—federated and fully diversified—will emerge.[11] The federated model is based on a network of separate organizations linked by a shared purpose and infrastructure. Two variants of the federated model have been identified: in the virtual version, a company outsources most or all of its activities; in the venture version, it manages a portfolio of investments. The fully diversified model comprises a network of entities owned by a single parent company. The company expands from its core business into one that also provides related products and services, such as diagnostics and devices, generics, nutraceuticals, and health management (see *Figure 2*).

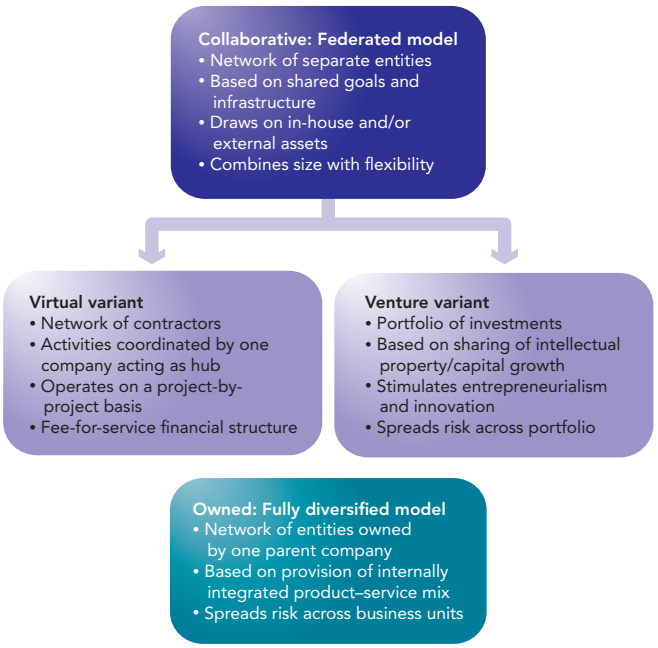
The evolution of the biopharmaceutical industry will create new business models, not in terms of structure but in terms of risk sharing and financing. The transition will be painful. Disrupting the existing order can have a major impact on a company's short-term performance. Furthermore, collaborative business models are far more complex than the existing integrated models. While the models are not mutually exclusive, the federated model has the advantage of being faster and more economical to implement. The federated model relies on the formation of opportunistic alliances; these will create the building blocks for the forging of more strategic, longer-lasting coalitions. The most successful of these coalitions will in turn create a fully federated network of long-term partners.

Whichever path is chosen, in order to increase productivity, the industry will have to use new technologies to improve its understanding of disease, significantly reduce its R&D costs, and reduce risk.

The Virtualization of Research and Development

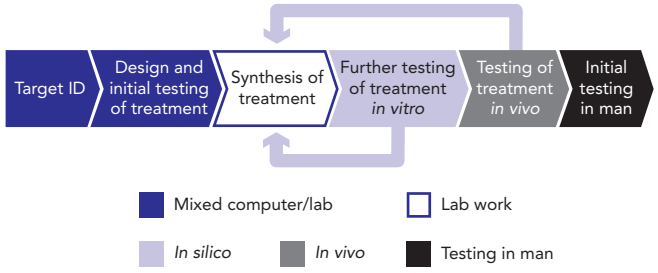
The paramount question the industry is currently trying to answer is 'how do we find new products now?' Many of the lower-hanging fruit have gone. The traditional R&D process has been to define the target by which a molecule, biologic, or diagnostic can be applied. However, in order to fully identify the targets and to dramatically increase the success rate of the molecules that do enter preclinical development, it is essential to have an intrinsic understanding of the pathophysiology of the disease under investigation. A better understanding of systems biology that underpins both the disease and the human body will also be fundamental to helping researchers develop a finer grasp of how to modify or reverse pathophysiologic changes. This is an enormous task, but this knowledge, gained through increased collaboration between the industry, academia, the regulators, governments, and healthcare providers, and facilitated by greater use of new technologies, will enable the virtualization of the research process and accelerate the development life-cycle.

Figure 2: Business Models in the New Paradigm



Source: PricewaterhouseCoopers, 2009.[11]

Figure 3: What the Research Process Might Look Like in 2020



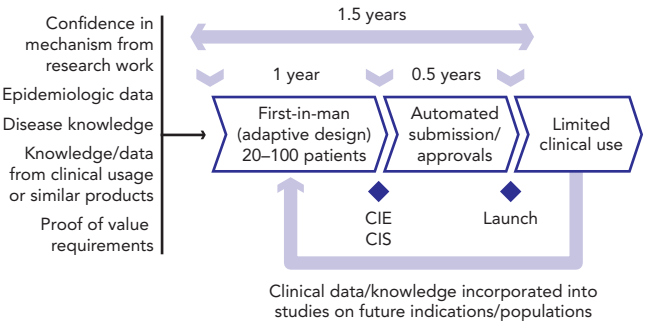
Source: PricewaterhouseCoopers, 2008.[5]

Expediting Research—From the Virtual Human to Networked Pharma

Traditional R&D processes are too complex, too cumbersome, and too prone to expensive late-stage failures. Change has been relatively slow, although continuing scientific and technological advances are providing the momentum to transform the paradigm of drug development. The classic R&D model will transform into new R&D processes that are more connected, iterative, and predictive (see *Figure 3*). In the future, semantic drug-discovery processes, enabled by a comprehensive understanding of how the

11. PricewaterhouseCoopers, Pharma 2020: Challenging business models, 2009. Available at: www.pwc.com/gx/en/pharma-life-sciences/pharma-2020-business-models/index.jhtml (accessed March 2010).

Figure 4: What the Development Process Might Look Like in 2020



Source: PricewaterhouseCoopers, 2008.[5]

human body works at the molecular level, will help make the connections that identify the links between disease and pathophysiologic pathways. This knowledge will then be used to build virtual models. The ultimate goal will be the creation of the virtual human—a single validated mathematical model that is able to predict the effects of modulating a biological target on the whole system and is capable of reflecting common genetic and phenotypic variations. Current research, encumbered by our limited knowledge of physiologic processes, has been aimed at building models of different organs and cells or creating 3D images from the resulting data. Predictive biosimulation is already playing a growing role in the R&D process. The creation of a virtual model will be facilitated by the utilization of computer-aided or *in silico* design. Computational approaches can expedite hit identification and hit-to-lead selection, optimize absorption, distribution, metabolism, excretion, and toxicity profiling, and alleviate safety issues.

It is generally recognized that biotechnology companies, smaller drug companies, and academic research centers are often at the forefront of innovation. Collaborations with these external sources of innovation will be a key component of the new paradigm. The collaborative networked R&D approach provides greater potential for cross-fertilization of technologies and access to key competences. However, promoting effective communication and knowledge transfer will present a significant managerial challenge.

Expediting Development—Biomarkers, Bioinformatics, and Connectivity

The clinical development of new drugs remains the significant bottleneck. Existing processes have been expedited by the move toward the adoption of new technologies, resulting in more trials being conducted in an eClinical environment.

Another development on the horizon that is likely to have a profound impact on clinical development processes is the increasing use of biomarkers that will enable segmentation of patients with different but related conditions and allow for the testing of new medicines only in patients who suffer from a specific disease subtype. Using clinical biomarkers that are reliable surrogates for longer-term end-points, such as survival, will help to reduce end-point observation times.[12] Regulatory authorities in both the US and Europe are supporting various biomarker initiatives, such as the Predictive Safety Testing Consortium—an alliance between the C-Path Institute and 15 pharmaceutical companies[13]—and biomarker qualification programs.[14]

Semantic technologies are also expected to play a major role in improving the development process. Such technologies will enable the industry to link the vast amounts of clinical trial data generated with epidemiologic and early research data, expedite the identification of any significant patterns, and use that information to modify the course of clinical studies—the adaptive clinical trial—without compromising their statistical validity. The use of electronic medical records will also become much more pervasive. Intelligent use of the vast and disparate data sources will be facilitated by common electronic data interchange standards—such as those in development by the Clinical Data Interchange Standards Consortium and the Society for Clinical Data Management—and informatics tools that enable Bayesian analysis of complex data sets. This will enable development processes to become much more iterative.

Ultimately, the current model of development, with its four distinct phases of clinical testing, will gradually evolve into a process that is more flexible, integrates advanced bioinformatics data, and is more receptive to rapid feedback from patients and providers (see *Figure 4*).

The regulatory process will also need to adapt and evolve. A shift in the way new medicines are approved, from the current 'all-or-nothing' approach toward a cumulative process, will need to be supported by a cultural change, with greater collaboration between regulators, industry, patients, and payers. The cumulative process will be based on the gradual accrual of data for a new drug, which will include further in-life testing to substantiate its safety and efficacy in larger and/or different populations, or for the treatment of other conditions.

Balancing the Need for Long-term Fundamental Change with Meeting Current Goals

For many big Ppharma companies the arrival of the patent cliff edge in 2011–2012 may put as much as 41% of their revenue at risk through generic erosion. An unprecedented response to this threat has been cost reductions in R&D. In the past, cost reduction has largely been achieved with relative ease through consolidation/outsourcing of manufacturing and through sales force reduction. R&D has been the sacred cow, but not any longer. The lack of R&D productivity and the associated cost escalation as more complex disease areas are investigated has changed the game. Companies have reviewed the way they manage their R&D and, as a result, reductions in the number of R&D personnel over the last few years have been dramatic. Multiple and duplicated R&D sites across the globe are no longer affordable and site closures are happening more swiftly post-merger.

To balance different business horizons, the more decisive companies realize that whatever is done to address R&D productivity will be

12. Biomarkers Definitions Working Group, Biomarkers and surrogate endpoints: preferred definitions and conceptual framework, *Clin Pharmacol Ther*, 2001;69:89–95.
13. US Food and Drug Administration, FDA and the Critical Path Institute Announce Predictive Safety Testing Consortium, March 16, 2006. Available at: www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2006/ucm108617.htm (accessed January 2010).
14. Woodcock J, The Role of Biotechnology and Bioinformatics in FDA's Critical Path Initiative, September 25, 2007. Available at: ieeeusa.com/volunteers/committees/mtpc/documents/JWCPBioeconomicsNIST092507.ppt (accessed January 2010).

painful. The only difference is that the longer the cost issues are not addressed the more painful it becomes, and R&D leadership will lose control. Thus, it can be argued that it is better to be the architect of change now rather than become the victim of dramatic and sudden arbitrary corporate actions later on.

Hence, the optimal approach for R&D is to achieve transparency of the cost base and then apply surgical precision to identified areas for cost reduction, without affecting ongoing critical R&D projects. Unfortunately, in many R&D organizations transparency of cost has not been a priority over the years. Often, there are inadequate systems in place to capture, analyze, and report costs—a traditional functional-based cost-accounting method that does not capture the true cross-functional costs of drug development—with only rare examples of true activity or process-based costing. To make informed decisions about R&D cost reduction without simply cutting projects through portfolio analysis, there needs to be cost transparency across functions, processes, therapeutic areas, sites, projects, and staff mix. Fortunately, with the increasing adoption of demand and supply management processes across R&D enabled by integrated portfolio management, enterprise-wide project management systems, and finance systems, there is the opportunity to achieve this desired transparency with integrated activity-based costing as an output. Keeping the transparency around costs will always be a challenge; hence, ongoing tracking of savings realization is essential.

Overall, there are opportunities to make significant cost reductions without affecting ongoing R&D projects. This requires change by design through better cost information and hence more targeted cost reductions. Those companies that address this in the short term will transform their R&D organization to fit future requirements rather than having to face disruptive and damaging imposed cuts.

Outsource, Outsource, Outsource

The range of external providers delivering high-quality work to the pharmaceutical industry has expanded outsourcing into most areas of R&D. In the past five years, the growth in externalization of laboratory work in particular has been significant, with new services being provided by vendors and greater uptake by major pharmaceutical players. Gone are the days when all chemistry and biology activities were conducted in-house; instead, the pressure to increase throughput, reduce costs, and reduce internal headcount are helping new companies to flourish in an ever-changing marketplace.

Clinical research and the conduct of clinical trials has always been the most costly and time-consuming element of the drug development process. Outsourcing of clinical trials to full-service contract research organizations (CROs) such as Quintiles, Parexel, PPD, and Covance has been the norm for many years. However, some major pharma companies only outsource some 30% of their phase II–IV studies. The use of functional service providers (FSPs) to undertake specific activities, such as trial monitoring using sponsor standard operating procedures (SOPs) and systems, is another route that has grown. This strategy is aimed at reducing costs, with more control than fully outsourcing studies. Companies such as i3, K-force, and Innovex/Quintiles have been some of the key players in this arena of clinical development outsourcing. The maturation from transactional and often adversarial relationships to strategic relationships with input into product development plans (PDPs) and clinical development plans (CDPs) has the potential to significantly reduce costs. CROs can help pharma companies move from the 'gold-plated' approach to the 'fit for purpose' approach if they are allowed to sit at the strategy table as well as the operational one.

Further cost saving and cost flexibility opportunities come from strategic outsourcing of activities to business process outsourcing (BPO) providers such as Cognizant, Tata, and Accenture. These companies combine process management skills while leveraging their IT application skills to deliver integrated services to the industry. Pharmacovigilance and clinical data management have been fruitful areas for BPO providers, with likely expansion to adjacent areas of the clinical data chain such as statistics programming, analysis, and medical writing. As the pharma industry matures and approaches the next generation of outsourcing deals, it is possible that new models may emerge, and areas other than clinical will utilize the BPO model.

However, in the race to reduce costs there is the potential risk that increased outsourcing may cause a capacity issue in the industry—bigger global players may be needed in order to cope with this scenario, and there may be competitive advantages to early adopters of larger-scale strategic deals.

Access to skilled resources in lower-cost locations such as the BRICS countries (Brazil, Russia, India, and China) is part of the solution. To maximize cost efficiencies it is important to allow the service providers to utilize their own operational infrastructure and processes. The key is to agree the desired outputs and quality along with appropriate service-level agreements (SLAs) and operational-level agreements (OLAs) or reverse key performance indicators (KPIs) for the sponsor. In other words, agree 'what' must be achieved as opposed to telling the partner 'how' and thereby reducing or even losing benefits.

Owing to the cost transparency issues discussed earlier, combined with some issues around corporate and international overhead allocation practices, true internal/external cost comparisons are not always easy. For these reasons it is important to rigorously scrutinize internal options during business case development.

It is reasonable, however, to expect 30% or greater savings over time with year-on-year improvements being incorporated into the contract with strategic outsourcing. Care must be taken when predicting forward volumes so as to maximize contractual value through novel pricing mechanisms. Benefits tracking is also vital here to ensure that unnecessary costs do not creep back into the organization. With constrained budgets, the bundling of additional services can also be an attractive option.

Major changes in strategic direction affect individuals at all levels of organizations. A very robust approach to change management, communication, human resources processes, and business continuity is needed to ensure a smooth transition, with sensitive support for all those affected and for those driving the changes.

Transitioning to new partners requires early and detailed collaboration to ensure scope and interface issues are resolved, thus avoiding the dreaded productivity dip. A robust retained

organization structure and model is also required, along with a joint governance structure for the contract. Business continuity and managing the risk of impact on ongoing vital R&D projects needs to be planned from the outset.

In summary, the biopharmaceutical industry to date has focused on the one size fits all approach, but one size medicines do not fit all patients, and the same is true of the R&D process. The limitations of this approach—on which the industry has relied for many years—have become increasingly clear. The risks associated with major changes in R&D can be, and have been, successfully managed. Success requires the highest caliber cross-functional collaboration as well as high levels of commitment from talented project team members who are fully supported by their leadership. ■

Empowering Virtualization, Enabling Next-generation Pharma

Nick Giannasi

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In response to both internal and external pressures there has been a global paradigm shift in the pharmaceutical industry, resulting in greater outsourcing across the value chain. Within the core functions of pharmaceutical research and development (R&D), the outsourcing of fundamental processes—essentially the virtualization of R&D—will need to be supported by enabling information technologies (IT). IT-empowered data/knowledge management will not only drive efficiencies but also facilitates the much-needed push for innovation in the industry.

The Globalization and Virtualization of R&D

Pharmaceutical research and development (R&D), under the traditional model, was generally performed within the walls of one single company or entity. With the increasing recognition that innovation can come from a wide variety of sources, this centralized hub model is gradually being transformed into a multihub, integrated, networked structure. Innovation is now accessed from within pharma, from scientific or licensed partners, from academic centers, and even from sources traditionally thought of as 'only' service providers, such as contract research organizations (CROs). The definition of the virtualization of R&D is essentially an externalization or virtualization of processes, with a multitiered network of innovation that traverses multiple entities—commercial and academic—with a coordinated research or development goal. Rather than confining creativity to one physical place where all the core activities are conducted, the new model is very much a kinetic network of research centers or skill centers, together with a global network of clinical development sites.

There are two significant drivers for this change: the first is the innovation deficit and the second is cost pressure. The innovation deficit is a direct result of the lack of productivity in terms of new drug approvals. The failure to produce the innovation warranted by the enormous R&D spend has precipitated the search for external, complementary innovation. This is exemplified by the figures showing biopharmaceutical R&D spending in 2008 to be around $65.2 billion, yet the US Food and Drug Administration (FDA) approved only 24 new therapies in the same year.[1] The cost pressure or process efficiency aspect of drug development also needs to be seriously addressed. Clinical drug development as it currently stands is too complex and too costly. Add to this the impact of the impending patent cliff—an ominous phrase that is now firmly established in the industry vernacular—downward price pressures, and earnings pressure—these factors all point to a real need to improve efficiency.

Enhancing Productivity—Reducing Costs

Over the last 15–20 years, R&D spending has continued to increase while the number of new drug approvals has been flat or declining. Enhanced productivity through better innovation is needed to change the trajectory of that curve. With traditional value or cost measures such as site consolidations having run their course, the increasing virtualization of R&D is expected to help achieve much-needed cost savings. The industry is changing—large-scale fully integrated 'within-a-company' business models are being transformed into diverse models encompassing more strategic outsourcing with fluid development–manufacturing partnerships and clinical development partnerships.

It is difficult for any single company to be excellent at research across multiple therapeutic areas. In the biopharmaceutical industry these difficulties are made more complicated by the specific intricacies of this highly regulated business. Companies not only need to have core competencies in R&D across multiple therapeutic sectors, but are also required to have expertise in specialized manufacturing processes and the recruitment and management of global clinical trials. It is difficult for any single company to excel in all of these areas. Consequently, there has been an increasing trend by certain companies of establishing a 'best-in-class' presence in a specific therapeutic sector by partnering with other companies who may have best-in-class capabilities across the R&D pipeline. This scenario includes partnerships with academic medical centers, for example oncology specialists, or collaborating with a manufacturing partner with expertise in complex products, such as biologicals, proteins, or vaccines. Active relationships with CROs with excellent credentials in site management/patient recruitment in specific therapeutic areas are also integral elements of this trend.

In the current biopharmaceutical space, companies such as Shire represent one extreme of the new paradigm—it has embraced the

1. Pharmaceutical Research and Manufacturers of America, Pharmaceutical Industry Profile 2009, PhRMA 2009, Washington, DC. Available at: www.phrma.org/files/attachments/PhRMA%202009%20Profile%20FINAL.pdf (accessed January 2010).

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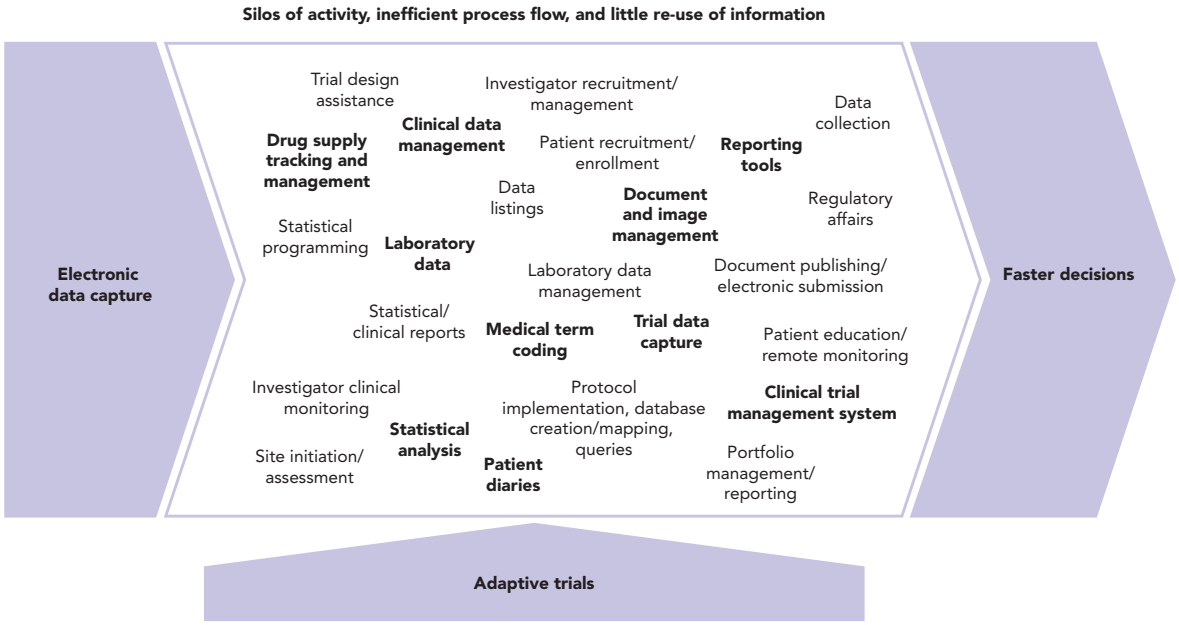
Figure 1: Clinical Development—The Landscape Today



virtualized R&D model since its conception. Companies such as Novartis, GSK, and AstraZeneca represent the middle ground, with R&D starting in the home base and expanding through the development of international integrated R&D networks. Companies such as Pfizer and Merck & Co represent the other end of the spectrum, with R&D structures evolving historically through a consolidation approach. However, notwithstanding Pfizer's recent acquisition of Wyeth and its re-organization of research groups into small, focused scientific teams as a means to innovate internally, the company has not neglected the virtualization strategy, and has pursued active collaborations with academic centers[2] and CROs.[3] Merck has also started to implement its own virtualization strategies, a key example being their External Discovery & Preclinical Sciences (X-DPS) group.

The global trend is one of more research centers outside of western Europe and the US. This aspect of virtualization also capitalizes on the emerging high-quality and highly educated personnel available in lower-cost centers such as India, China, and Singapore.

Data Logistics and Networked R&D

A consequence of the drive to increase productivity that is affecting biopharmaceutical companies, research organizations, and academic centers alike is the tremendous volume of data that is generated and processed (see *Figure 1*). The challenge is how to manage effectively these increasingly large volumes of data. Current bandwidth limitations can affect the ability to move large volumes of data and data types, such as electronic data capture (EDC) and electronic patient-reported outcome (ePRO) data, laboratory data, trial supply information, and medical images, across global networks. However, this situation is generally improving across the world, almost on a weekly basis. Another important challenge relates to data governance, or data providence—ensuring that only the appropriate people can access and share these data across different companies or entities is critical. This is one of the largest challenges for the industry. Providing a good solid audit trail across several networks also presents a significant challenge. Finally, there is the issue of data integration. To be able to share data effectively and leverage vast information sources, semantic tools will be required to make sense of all of the data relationships. The utilization of such tools will certainly need open standards, such as those being developed by Health Level Seven (HL7) and the Clinical Data Interchange Standards Consortium (CDISC) projects.

Meeting the Demands for Virtualization in R&D

Drug development is evolving from a laboratory-based model where chemical entities are discovered that might have an effect to one that makes greater use of data from patients and translational methodologies. There have certainly been signs of an increasing adoption and implementation of electronic medical records (EMRs) across the world, in particular in the US with recent changes in the administration and the announcement of new stimulus packages in the form of the Health Information Technology for Economic and Clinical Health (HITECH) Act. The greater use of patient data will enable more collaboration between healthcare organizations and pharmaceutical companies. Research will have a more patient-centric approach. Data sets from a sub-population or from longitudinal clinical data have the potential to expedite the development of targeted therapies in terms of both patient population and disease. This model of research is in its infancy but has tremendous implications for future drug development and healthcare. At a basic level, the use of EMRs can facilitate targeted recruitment and specific sub-populations for clinical trials. Screening for disease-specific biomarkers not only aids further patient differentiation but also helps from a safety perspective.

2. Hughes B, Pharma pursues novel models for academic collaboration, *Nat Rev Drug Discov*, 2008;7:631–2.
3. Pfizer and Crown Bioscience announce a collaboration to research and develop new treatments for Asian cancers, 2009. Available at: mediaroom.pfizer.com/portal/site/pfizer/index.jsp?ndmViewId=news_view&newsId=20091208006647&newsLang=en (accessed January 2010).

Increasingly, data sets from real-life databases, for instance IMS Disease Analyzer, Ingenix, and CEGEDIM, provide valuable proactive pharmacovigilance information. Importantly, healthcare institutions, especially in the US, are showing a willingness to leverage EMR data. The collaborative use of these data by healthcare institutions and pharmaceutical and life sciences organizations offers potential benefits, such as improved analysis of the efficacy of different therapies across large populations and predictive modeling. The increasing digitization of patient medical records, driven by initiatives such as the HITECH Act, will need the implementation of information technology (IT) tools that will ensure data accuracy and aid data mapping.

A Dynamic IT Infrastructure—Tools for a Leaner, Shorter Development Cycle

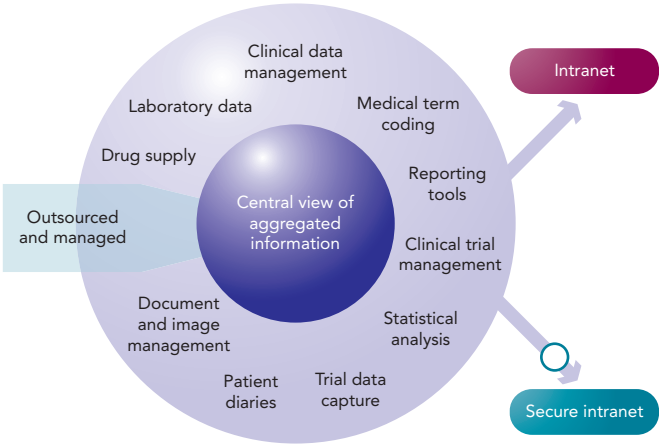
With the increasing globalization and virtualization of R&D through outsourcing and offshoring, effective innovation can be achieved only with effective knowledge and technology transfer. The constraints of geographic distance and dispersed organizational structure can be overcome by the strategic deployment of IT resources. Traditionally, data have been locked in silos and enterprise-wide IT resources underutilized. However, efficient management of disparate data sources, from data integration to the mobilization of information across various projects, will facilitate decision-making. As the data sets grow in size and thus value, semantic data management, reporting, and analysis tools together with advances in processing power could translate to a leaner, more efficient pipeline. Increased speed and the time savings in processes can translate to cost savings—if the go/no-go decisions are made more quickly across the sequential elements of the R&D pipeline, the overall pipeline will benefit from less costly failures in later phase II/III development.

Currently, data aggregation and clinical data warehouse tools such as Oracle's Life Sciences Data Hub (LSH) allow the rapid consolidation of data from multiple sources into a single environment where they can be analyzed, visualized, and reported on (see *Figure 2*). The flexibility offered by clinical data warehouse tools is supported by strong identity management tools that allow for secure sharing of data across networks and between internal and external users and enable collaborative development. These tools will allow data to be integrated, aggregated, and processed more efficiently. Another benefit is the layering of business intelligence and analytic tools that will allow much more efficient, earlier, and stronger testing of hypotheses, which in turn will translate into more informed decisions. Results can be obtained in minutes or hours rather than days or weeks. IT infrastructure is evolving and advancing exponentially, from greater internet access through to superior hardware processing, intelligent software, and the extension of computing capacity by virtualization of computing resources. This will create a flexible, scalable technology platform that can be optimized quickly when business demands change while enabling the leverage of valuable data assets that will improve the quality and speed of processes within the R&D pipeline.

Sharing Data—Improving Knowledge

The traditional approach for many organizations has been to build data silos in separately owned domains. Applications were developed to serve these silo-ed data. The limitations of these legacy systems are a barrier to the virtualization of R&D because the

Figure 2: Integrated Clinical Development



inherent inefficiencies of silo-ed databases are counter to effective knowledge sharing. Moreover, historically, data have been aggregated centrally—the data warehouse approach—or handled by a federated approach, where data come through a set of dynamic links to disparate sources. Both options present data to the user as a single data source and both systems have their advantages and limitations. Data warehouses are built for queries based on static hierarchies; thus, if the nature of the queries changes as the data evolve, the system may not be optimized to meet these changing demands. The implementation of clinical data warehouse tools, such as the LSH, with robust communications layers based on open standards that can communicate with other applications will facilitate communication between formerly silo-ed databases as well as providing another option to the federated or data warehouse approaches to data aggregation.

This third option is a process-based approach and is a hybrid of data warehousing and the federated approach. A process-based approach allows data views into source systems and scheduled copying of data to a central repository, and is designed to support changing environments through workflow to automate business processes. The integration of middleware-based messaging provides dynamic event-driven processes. The use of adapters allows integration with source systems and data structures and enables the intelligent loading of data. Support for interoperable data models enables organizations to adopt emerging standards such as CDISC and HL7. Moreover, these standards can co-exist and interoperate with company-wide standards.

Analytics for Delivering Efficiencies

New processes will generate greater amounts of data. These data, if not effectively shared or used for reporting and performance improvement efforts, are not being leveraged for full competitive advantage. Analytic applications can help to provide deeper insights into captured data, and leveraging these insights can enhance processes.

Analytics is not simply a function of math or statistical analysis, but the use of data to arrive at optimal decision-making based on the results of that data analysis. While the use of data-mining techniques to inform business decisions has become customary in other sectors, the use of historic patterns to predict the future is currently not so

widespread within the pharmaceutical industry. There are valid reasons for this, including regulatory constraints, which need to be overcome if we are to use these data to improve outcomes for both business decisions and patients.

A process-based approach can reduce the overall cost of IT systems ownership by replacing multiple analytic systems with a single integration and reporting system. Applications for data integration, metadata management, blinding and unblinding, report execution, report storage and retrieval, workflows, and data visualization can all be built into the framework. The layering of analytics on top of a global data repository framework will reduce the global programming effort by providing a standard environment for generating the tables, listings, and figures for reports. Pooling of data from multiple sources can be sliced for formal reporting and *ad hoc* visualization. As well as enabling deeper insights by leveraging the available data, immediate real-time access enables a new kind of process improvement to what has previously been a more retrospective environment. This shift from retrospective analytics to prospective analytics will provide data to the right individuals at the right time to enable them to make informed decisions.

To further empower the end user, it is important to design the system from an information-centric rather than a data-centric perspective. Data repositories that can be maintained by clinical programmers and statistical programmers without the need for constant support from IT specialists will enable researchers to focus on extracting scientific knowledge across the entire development portfolio, from microarrays to defining population subsets.

While these systems are within reach in the pharma environment, easily accessible pooled patient data in a useable format is a distant reality outside its confines, such as in hospitals and surgeries. Here there are yet more valuable data that could be brought into play, although the aspects of the arguments for and against accessing this data are for wider discussion.

Delivering Virtualized R&D

The virtualization of R&D has begun. We are beginning to see the implementation of a worldwide network with R&D activities located globally to augment and acquire new assets. This integrated network structure utilizes flexible units that are able to take decisions more rapidly and establish collaborations with external partners. This virtualization is being supported by a global ecosystem of software vendors providing integrated applications based on open standards and using common data elements. These technologies, developed on secure and scalable infrastructure, provide support across different process flows and break down traditional silos. This change is driven by the need to access global innovation, access multiple parallel data sets, and enable more informed decisions more quickly. It is the evolution of biopharmaceutical R&D. The vision is the integration of life sciences and healthcare to provide an economically sustainable model that benefits the biopharmaceutical industry, industry partners, and patients. ■

Re-thinking Pharma R&D—The Merck Experience

Clark Golestani

Clark Golestani is the global head of IT for Merck's Research and Development (R&D) division, with IT responsibility for all areas of R&D including basic research, pre-clinical, clinical, and regulatory areas of the company, spanning target identification through to post-marketing trials/pharmacovigilance. Additionally, he serves on Intel's Enterprise Advisory Board and the PhRMA Foundation Informatics Advisory Committee, and is a co-founder of Cross Road Technologies, Inc., in Cambridge, Massachusetts. His previous responsibilities include leadership of Merck's global IT capability supporting finance, HR, procurement, legal, public affairs, site services, real estate, and related shared business services operations as Vice President of Corporate IT; leadership and development of the company's IT strategy, portfolio, and enterprise architecture as Chief Architect; leadership of the company's global computing services, eBusiness, and information security as Executive Director of IS Global Computing Services; leadership of the company's technology architecture as Senior Director of IS Architecture; and various leadership and management roles within Merck's research laboratories as IT Director. Prior to joining Merck, Mr Golestani was responsible for establishing and managing strategic client relationships from business development through to consulting services engagement delivery as a principal with Oracle Corporation's consulting practice. Mr Golestani has a degree in management science from Massachusetts Institute of Technology's Sloan School of Management.



Reliance on a single source for innovation is an obsolete model. To plug the innovation gap, research and development (R&D) organizations have recognized that creativity and innovation need to come from multiple sources. Industry players are now recognizing the need to re-think and transform the R&D model by building a 'virtual lab' that utilizes internal research, external collaborations, or both. Technologies that are now in their infancy, such as semantic technologies, may yet prove to be the solutions for the challenges created by the need to effectively share and exchange the growing volumes of complex data.

The general consensus is that the pharmaceutical industry is under unprecedented pressures: diminishing returns despite spiraling research and development (R&D) costs; the substantial impact on revenues from major patent expirations; pricing pressure from payers and healthcare systems; and regulatory pressures. When you examine these pressures closely, it is important to reiterate a number of key points. Undoubtedly, external influences such as pricing pressures and generic substitution of major products losing patent protection will have a significant impact on revenues. We need to examine this further, however, especially in the context of R&D. The well-publicized decline in the R&D productivity curve over the last decade running in parallel to an almost constant increase in the cost of R&D paints a most worrying picture. Since the high of 1996, when the US Food and Drug Administration (FDA) approved 53 new medicines, there has been a steady decline in new approvals. In 2008, the number of new approvals was half that of 1996, yet the cost of R&D had increased three-fold for the same period. It could be argued that the peak seen in 1996 was an anomaly due to several factors—not least the introduction of the Prescription Drug User Fee Act (PDUFA)—and that the recent decline is a natural reverse to more historic averages. Nevertheless, the current numbers, in terms of average R&D cost per new approved drug, show that the formula is not sustainable.

Declining productivity despite major increases in investment in R&D is the crux of many of the problems facing the industry today. Compounding this issue is the fact that the industry has not been able to innovate its way out of the problem. The trend since the 1970s has been a fall in the number of products originating from 'internal' R&D efforts (see *Figure 1*); at the same time, the number of external deals has been on the increase. This trend has led to many of the larger R&D organizations asking the following questions: How do we respond to cost pressures? How can we more effectively leverage the innovation that is being generated outside of the fully integrated pharmaceutical company model (FIPCo), where the majority of core functions are fully controlled by a given company?

Creating a Global Network of External Expertise

Engaging and collaborating with external expertise has traditionally been less efficient when performed as an extension of the larger organization. To create a more effective environment for innovation it is necessary to develop a strategic, integrated network of external partners. While partnerships and alliances are not a new concept to Merck—the company has entered into more than 250 significant new alliances in the past five years and about 65% of the company's revenues in 2008 were derived from alliance products and patents (based on 50/50 split of joint ventures)—the wide range of challenges needs to be addressed by re-defining the approach to drug discovery and development.

A recent Merck initiative has been the creation of the External Discovery & Preclinical Sciences (X-DPS) group. The X-DPS aims to build on the recognition that access to external research can greatly extend the company's research capacity. Thus, the ethos is to build a 'virtual lab' by mounting the best scientific program possible in defined areas of medical interest, whether it comes from internal research, external collaborations, or both. It is much more difficult to maintain a strong pipeline when innovation comes from only one source. The X-DPS research team, therefore, is a move away from the old FIPCo model and toward a fully integrated pharmaceutical network (FIPNet) model that relies on a highly networked, partnered infrastructure. The networked model is a reality that can take advantage of the innovation that occurs outside of the larger R&D organizations and encompass the entire R&D value chain from early discovery to late-stage clinical development. Certainly, industries such as defense and aerospace have already undergone similar successful transformations.

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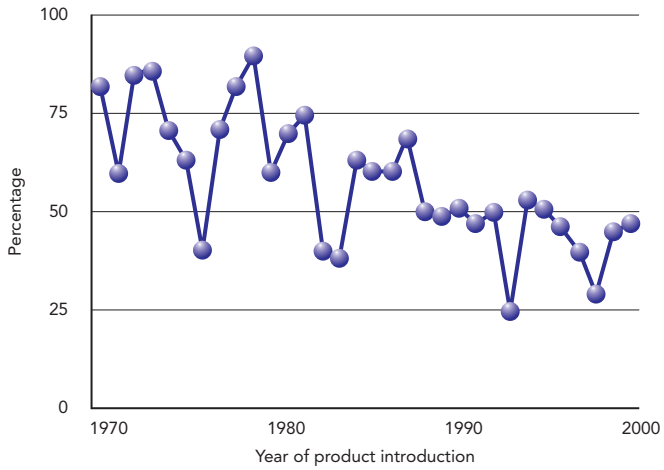
Figure 1: The Percentage of Pharma Products Originated In-house is Declining



Adapted from Growth Strategies for Large Biopharma Companies, Deloitte Research, 2004. Available at: www.deloitte.com/assets/DcomFrance/Local%20Assets/Documents/Growthstrategiesbiopharmacompaniesfeb2004.pdf

The X-DPS group is designed to focus explicitly on external sources of science and innovation as a means to expand the scope and size of Merck's early pipeline. The group's goal is to deliver 25% of Merck's early pipeline from multiple external sources within the next three to five years. The X-DPS group is also aligned with Merck's internal R&D strategies and pipeline priorities. The R&D strategy is intended to support an environment that encourages open collaboration, risk sharing, and increased flexibility not only with academic partners but also with biotech and contract partners.

Sharing Risk

Looking beyond cost savings, many of the global collaborations and partnerships are designed to drive creativity and innovation. Examples of these partnerships include Piramal Life Sciences/Merck (a drug discovery program through proof-of-concept in oncology) and Orchid/Merck (a drug discovery and development collaboration focusing on bacterial and fungal infections). These collaborations are driven primarily from the partner R&D facilities, with Merck providing scientific input and access to Merck resources and expertise. Additionally, the partnerships are designed to share the business risks of the R&D processes, with Merck often retaining late development and commercialization rights and the partner receiving financial incentives.

A Strategic Partnership, Not Just a Service Supplier

Increasingly, there has been a move away from the traditional service provider relationship, focused primarily on cost performance, to one that is more strategic: contract partnerships or strategic sole-source full-time equivalent (FTE)-based relationships. These partnerships are about more than just utilizing the specific capabilities of third-party contract service providers to reduce costs; the partnerships now reflect the drive for innovation by taking advantage of external specialized skills, expertise, and resources. A good example of this type of relationship is Merck's research collaboration with the Chinese company Wuxi PharmaTech Ltd. The research collaboration between the two companies is focused on accelerating drug discovery chemistry, including creation of new drug discovery libraries and constituents to advance lead optimization programs. The original agreement between the two companies was based on the traditional third-party supplier model, with Wuxi developing custom libraries for Merck. This agreement has now evolved into the current contract partnership, with Wuxi providing Merck with dedicated teams of research chemists, biologists, and pre-clinical sciences support, including drug metabolism and pharmacokinetics (DMPK) and scale-up. The objective of the program is to provide an external streamlined, customized early discovery program that is aligned strategically and operationally with Merck's goals. Additional benefits include greater efficiency and productivity through reduced procurement and monitoring of contract research organizations (CROs). The partnership with Merck also helps Wuxi to gain world-class experience.

Breaking Down Silos to Foster Innovation

For the integrated network model to work, a critical issue will be to ensure that, within that network of collaborators, information is shared correctly and efficiently.

Merck was an early adopter of the concept of knowledge sharing as a means to foster innovation, with the implementation of the 'PartnerNet' Network, over a decade ago. The intention behind that initiative was recognizing that there would be many third parties that needed to either share information with the organization or would require access to relevant information from certain areas of the business process. The Internet-based virtual private network (VPN) allowed Merck scientists to collaborate on research projects, enabling anyone with the right credentials to access databases. PartnerNet was created as a model by which this network could be extended to third parties to open up secure lines of communication. This enabled Merck and its partners to share information in several ways. In its simplest form this would be the secure sharing of emails and files; in its most complicated form sharing would enable full access to applications facilitating participation in the part of the business process specific to the partner's requirements and access privileges. More importantly, the network has allowed stakeholders to share information in real time against a core repository. PartnerNet is still very much in existence today, and it has evolved over the years as enabling technologies have matured. Certainly, networking technologies have matured substantially since the inception of PartnerNet, which has allowed for a much richer set of services to be provided to various partner organizations. The advent of the worldwide web and web applications has also facilitated knowledge-sharing processes. Furthermore, PartnerNet has expanded beyond the initial target of the company's research division to a platform that is also utilized by Merck's sales, marketing, and financial departments.

The creation of integrated networks supported by easily accessible data allows transformation of those data into knowledge. The knowledge created cultivates innovation and expedites the development of safe medicines. This is a vision that is already in progress. The lifeblood of the pharmaceutical R&D process is information. Wherever one is able to collaborate on and drive greater access to information, one may then fuel greater advances in R&D. Merck's partnership with the H Lee Moffitt Cancer Center & Research Institute (MCC) is a clear example of PartnerNet's pivotal role in facilitating this type of relationship. The MCC partnership involves transferring substantial volumes of data between the organizations to further drive research in oncology. That, in and of itself, has brought some challenges in sharing those data. PartnerNet has needed to evolve and expand to handle much more complex data types as well

as greater data volumes. The MCC partnership also sets a precedent in that it breaks down silos between pharmaceutical and medical communities. The exchange of clinical and biomarker data between MCC and Merck is an example of the potential future of drug development. Today, clinical research requires the building of substantial infrastructure to capture clinical data for study. In the future, as clinics automate and as electronic health records (EHRs) become much more pervasive, EHRs may become the electronic source of data that drives clinical research.

The Promise of Semantic Technologies

As mentioned previously, the data to support R&D create specific challenges in themselves. The biology of disease is a moving target that changes on a constant basis. Thus, the data are quite often very complicated and, by their very nature, hard to standardize. Each clinical trial may also have unique data capture needs. This complexity is an issue that is very specific to the pharmaceutical industry. The promise of semantic technologies is to leverage information that is not easily, or cannot be fully, standardized in a strategic way, thereby allowing much more flexibility in data modeling and data management. This can help researchers reach novel insights from large volumes of data. However, the technology is still in its infancy. To exploit the capabilities of the technology it will be essential for the industry to think about how to leverage the technologies in a more practical and pragmatic way and create enterprise-level semantic solutions.

The networked business model holds incredible promise for semantic technology. The focus now is to apply the technology to scientific domains to enhance knowledge insights from the vast amounts of data generated. Further ahead, as the technology and standards mature, the application of semantic technology could drive business improvement by capitalizing on the networked business models. The sharing of both transactional/structured and semi-structured data across a network of organizations could be facilitated by semantic technologies that enable better connectivity and integration of the information chain.

In the area of semantic technologies, Merck has collaborated with Cambridge Semantics. The proof-of-concept project has been to examine whether semantic technologies can improve the company's ability to share data with external partners. Using Cambridge Semantics' Anzo semantic engine, the project found that Merck and its research partners could manage the ontology, easily and effectively upload the data effectively, and reduce cycle time. Data sharing and data exchange can often be a hurdle for many pharmaceutical organizations, and semantic technologies may be the potential solution to this costly bottleneck.

The Last Reel—The Future Landscape

The move toward a networked business model that strategically leverages third-party expertise is an important step for the industry. Looking at the future landscape, an analogy can be made to the film industry. The production of a movie is a highly complicated and complex project where the ingredients, such as the actors, the setting, and the script, can be world-class, yet at the end of the day the movie can still be a failure. There are many parallels to movie-making in the pharmaceutical industry. Notably, the film industry is an extreme version of a networked model, with the major studio bringing together various specialty companies to produce that movie. Within this framework is often a financial risk and reward-sharing model. In the future, the pharmaceutical industry may reflect this business model, with large cap companies bringing together independent units to supply the innovation. Currently, the pharmaceutical companies take on the majority of the financial risk in terms of investment in R&D. This needs to be re-addressed so that the risk is not so disproportionate. The shared financial risks and shared rewards with collaborative partners is a business model that may be more sustainable for the pharmaceutical industry. Creative collaborations rather than straightforward transactional relationships are also likely to help to drive innovation. Integration of operating procedures and systems will help to facilitate the creation of the networked model and deliver greater value. ■

Technology and People—Shifting the R&D Paradigm at GlaxoSmithKline

Alex Lancksweert, Peter Milligan, and Robin Dement

Alex Lancksweert leads Simplifying Clinical Development, a critical change program to transform the way GlaxoSmithKline (GSK) collects, reports, archives, and retrieves clinical trials data, involving different types of change (people, process, technology, and standards) over a prolonged period and designed to deliver twice the current output of regulatory submissions per year. He has considerable experience in business performance improvement and change management enabled by new technology and has led a number of major performance improvement and cost reduction projects during his tenure at GSK. Prior to joining GSK in 2003, he was part of Accenture's consulting practice for the Life Sciences & Healthcare Industry Group in the UK where he led the implementation of new processes and systems across many of the world's largest pharmaceutical companies.

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Peter Milligan leads the IT aspects of Simplifying Clinical Development, particularly for all aspects of the design and integration of the many systems in which GSK is investing. He led the diagnosis effort preceding the investment in Simplifying Clinical Development, along with the thought leader for the strategy and design GSK is now executing. Peter began his career at the Wellcome Foundation in 1989 and has led the design, implementation, and support for many of the clinical, medical, and regulatory systems used in Development.

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Journalist and author Sebastian Junger called it a "Perfect Storm" when three major weather-related phenomena converged off the coast of Massachusetts in 1991 to create a cataclysmic tempest. The term has also been used to describe the unprecedented convergence of economic, regulatory, social, and political forces which have converged on the pharmaceutical industry in the 21st century. Ever-spiraling drug prices, product recalls, and recent warnings about popular prescription medications have caused doctors, patients, investors, and government regulators to seriously examine an industry once admired for its contributions to society. Compounding these challenges is the widening gap between R&D expenditure and the number of new drug approvals.

With its image under assault, and its profitability and growth prospects under pressure, the industry is critically re-examining its R&D practices and seeking to transform how it discovers and develops novel and more-effective medicines. A number of leading companies are revisiting how information technology (IT) systems can streamline the processes of collecting, organizing, storing, sharing, and analyzing data to improve R&D productivity and, by doing so with greater transparency and openness about the way they operate, restore the public's faith in the integrity and motivation of this valuable industry.

Data Rich, Information Poor

Information, along with innovation, is the lifeblood of the biopharmaceutical industry. Data are the major asset created in R&D. They are the endpoint of every experiment that is performed. They are the basic ingredient to making informed decisions throughout the drug discovery and development process—data to progress a drug candidate, data to enable regulators to approve new safe and effective medicines, data to demonstrate the innovative value of medicines to payors, and data to assure patients that the approved medicines are safe, effective, and will enhance their quality of life. Ensuring the appropriate governance and integrity of these data is part of the commitment companies like GlaxoSmithKline (GSK) make to investigators and patients when they undertake a clinical study. It can also be the source of new innovation and increased productivity. The ability to harness information has already transformed many other industries, from proactive monitoring of credit card transactions to prevent fraud to the mining of daily transactions to transform supply chains and marketing practices.

Yet finding, accessing, and using this information can be a time-consuming and cumbersome activity. As is the case at many pharma companies, many of the information systems involved in the planning, execution, analysis, and submission of clinical trial data have evolved over time and, while GSK's systems have significantly improved efficiency and data quality, the customization of these systems to functional needs has not encouraged standardization. Common reported difficulties included: entering the same data into multiple systems; manual reconciliation of data; multiple logins and other sources of redundancies and frustration—all of which have a major impact on productivity.

Compounding these challenges for GSK is a healthy development pipeline with some 38 projects in Phase III.[1] The drawback of a healthier pipeline and a larger number of potential submissions is more concurrent trials, higher R&D costs, and added pressure on resources. To meet its stated intent to run twice as many late-stage

1. EvaluatePharma, 30-Apr-2010 (Source: PAREXEL'sBio/Pharmaceutical R&D Statistical Sourcebook 2010/2011)

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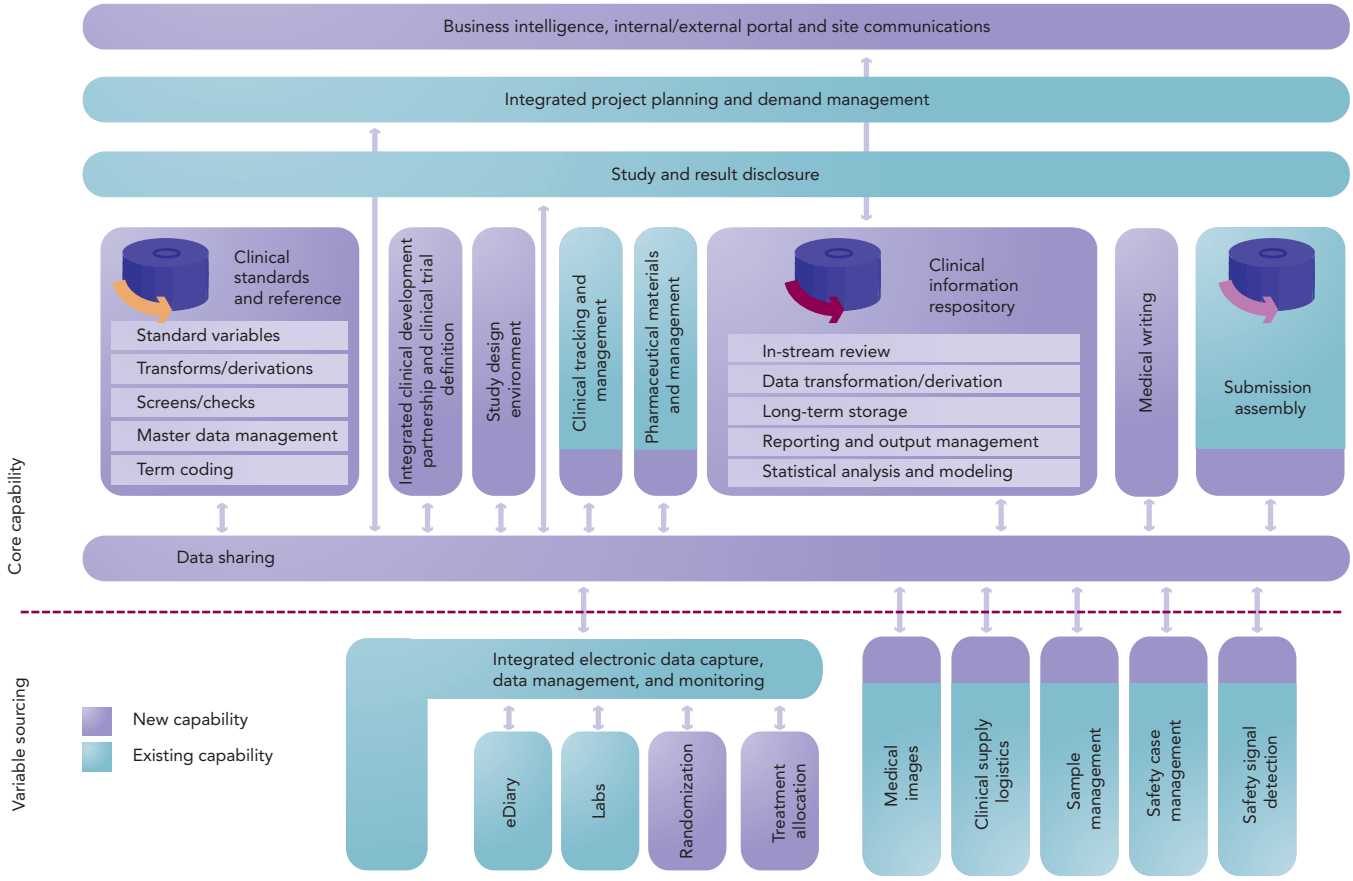
Figure 1: Blueprint for GlaxoSmithKline's Simplification of Clinical Systems



programs with the same amount of resources, and raise the return on investment on R&D from 11 % to 14 %,[2] a significant transformation of clinical development practices is required.

It is against this backdrop that the Simplifying Clinical Development (SCD) program was launched—one of several key change initiatives designed to deliver the three GSK strategic priorities, namely, diversifying its business, delivering more products of value, and simplifying its operations.[3] Anchored around intricately intertwined investments in IT, processes, behaviors, and standards, SCD is a five-year change program designed to transform clinical development by reducing the complexities of clinical development, improving the focus of internal resources on higher value scientific activities, and accelerating the delivery of new, differentiated medicines.

Simplifying the Clinical Information Landscape

GSK's vision for a simpler clinical development landscape is for a more streamlined, simplified environment with fewer, better-integrated "best of breed" systems that create a seamless end-to-end flow of information based on the use of common standards and data formats, such as those developed by the Clinical Data Interchange Standards Consortium (CDISC), and where data are captured once and then used many times. An environment consisting of configured, not customized, off-the-shelf systems that will enable GSK to more easily support the externalization of R&D and collaboration with investigator sites, contract research organizations (CROs), and other joint development partners. An environment that transforms GSK's ability to access, aggregate, analyze, re-use, and share clinical trial data, which enables GSK to unlock the potential of the accumulated research data and enable its scientists to leverage research performed on related compounds to validate findings, perhaps even address queries, without the need to run additional trials. An environment where it will be easier to find and access data, navigate processes, and make more-informed decisions, leading not only to faster and more cost-effective trials but ultimately to more patients having earlier access to new and improved treatment options.

To deliver on this compelling vision, GSK is focusing on three areas: acquiring the right data; making sure they are consistently organized, stored, and accessible; and, finally, using these data to make better decisions.

By taking a clean-sheet approach to its clinical information landscape, GSK is seeking to integrate its clinical development systems to allow information to flow unimpeded from planning through to submission. Enabling the more efficient acquisition and re-use of data is an information blueprint that provides a comprehensive view of the flow of data from system to system. This effort to define the flow of information has been accompanied by a comprehensive and on-going overhaul of several of GSK's key data acquisition systems, such as its Electronic Data Capture (EDC), Clinical Trials Management System

2. "GSK Goes Back to return on investment", Interview with David Redfern, Chief Strategy Officer. www.scrip100.com
3. 2010 GSK annual Report http://www.gsk.com/investors/reps10/GSK-Annual-Report-2010.pdf

(CTMS), and Interactive Voice or Web Recognition system (IV/WRS)—many selected following real-life evaluations of alternative vendors. A process which was designed to ensure the selection of "best of breed" systems, as well as to assess the ability and willingness of the vendors to collaborate with GSK to help it avoid the costly customizations that today constrain its flexibility.

In developing its vision for a more flexible, interoperable IT environment, GSK is also seeking to future-proof its investment to reflect the ways in which it is partnering and collaborating to execute clinical trials. Its goal is to become agnostic to the particular data acquisition vendor or system used by its partners, acquisitions, or CROs, while still being able to efficiently integrate the data with the systems it uses to analyze, review, and interpret this information. This vision is already being put to the test. The decision to establish closer, longer-lasting collaborations with fewer vendors has led to joint investments in common information models and common processes designed to enable the seamless exchange and integration of data and facilitate a more effective collaboration between GSK and its vendors.

The benefits of its investments in streamlining how it acquires and stores data are clear: reduced cost of ownership, increased focus on delivery of higher-value scientific activities, and reduced effort on tedious data manipulation tasks. However, some of the less tangible benefits associated with unlocking the 'nuggets of gold' buried in the data offer the higher-value rewards: validating new toxicology screens to reduce the need for studies involving animals; amplifying hard-to-detect safety signals by pooling data across multiple trials; or applying advanced analytics to detect a problem before it becomes a problem—some of the many ways GSK anticipates being able to mine this treasure trove of information while protecting the health and wellbeing of patients.

Investing in Cultural Change

New technologies imply change—typewriters changed the way we wrote, calculators changed the way we did math, and the internet has changed the way we work; but technology alone cannot deliver the scale of meaningful change required to transform clinical development at GSK. SCD requires a cultural change, a new style of leadership.

Developing this cadre of leadership takes time. While systems and processes can be mandated, behaviors cannot. To deliver on the promise of simplifying clinical development, and for the change to become sustainable, GSK is investing heavily in these leadership skills, and in bringing the organization along throughout the change process. Through broad business engagement, the program is seeking to ensure that those impacted by the change are its architects. After all, as much as IT systems can tweak the environment it is the commitment, not the compliance, of its people to planning, to seeking peer input, and to becoming more rigorous and disciplined that will transform clinical development at GSK.

A Brave New World

Information, along with people, is the most valuable resource a pharmaceutical company has. Imagine a world where this information flows from beginning to end, where access to relevant, accurate information to make informed decisions with clarity and confidence is the norm, where the accumulated results of clinical studies are readily retrieved and mined for insight that will eventually lead to the delivery of new quality medicines. This is the environment GSK's SCD program is seeking to create, halving the effort of current activities to meet its goals of delivering more products of value, simplifying its operations, and delivering GSK's challenging and inspiring mission of improving quality of life by enabling people to do more, feel better, and live longer—a goal we can all get behind. ■

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