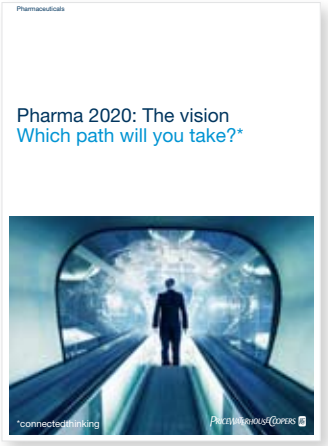
Pharmaceuticals and Life Sciences

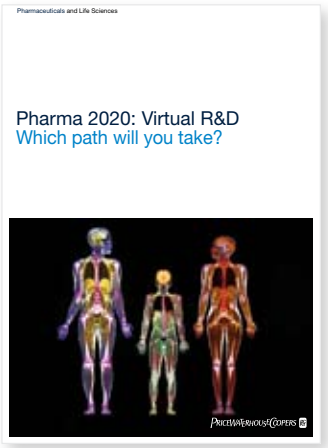
Pharma 2020 Series Executive Summary

PricewaterhouseCoopers

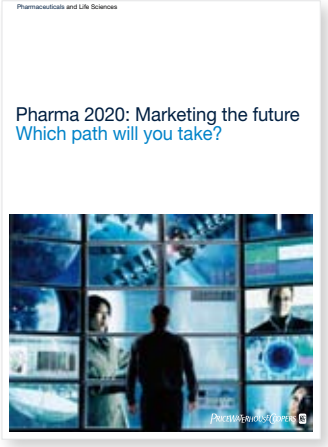
Previous publications in this series include:



Published in June 2007, this paper highlights a number of issues that will have a major bearing on the industry by 2020. The publication outlines the changes we believe will best help pharmaceutical companies realise the potential the future holds to enhance the value they provide to shareholders and society alike.

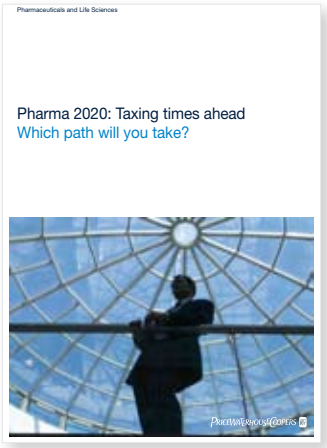


This report, published in June 2008, explores opportunities to improve the R&D process. It proposes that new technologies will enable the adoption of virtual R&D; and by operating in a more connected world the industry, in collaboration with researchers, governments, healthcare payers and providers, can address the changing needs of society more effectively.



Published in February 2009, this paper discusses the key forces reshaping the pharmaceutical marketplace, including the growing power of healthcare payers, providers and patients, and the changes required to create a marketing and sales model that is fit for the 21st century. These changes will enable the industry to market and sell its products more cost-effectively, to create new opportunities and to generate greater customer loyalty across the healthcare spectrum.

Fourth in the Pharma 2020 series and published in April 2009, this report highlights how Pharma's fully integrated business models may not be the best option for the pharma industry in 2020; more creative collaboration models may be more attractive. This paper also evaluates the advantages and disadvantages of the alternative business models and how each stands up against the challenges facing the industry.



The fifth report in our series, published in December 2009, focuses on the opportunities and challenges from a tax perspective. It discusses how the political, economic, scientific and social trends currently shaping the commercial environment, together with the development of new, more collaborative business models, will exert increasing pressure on effective tax rates within the industry. It also shows how companies can adapt their tax strategies to support the provision of outcomes-based healthcare and remain competitive.

All these publications are available to download at: www.pwc.com/pharma2020

Pharma 2020: Executive summary

Pharma's traditional strategy of placing big bets on a few molecules, promoting them heavily and turning them into blockbusters worked well for many years, but its R&D productivity has now plummeted and the environment in which it operates is changing dramatically. We believe that seven major trends are reshaping the marketplace:

- The burden of chronic disease is soaring – placing even greater pressure on already stretched healthcare budgets
- Healthcare policy-makers and payers are increasingly mandating what doctors can prescribe
- A growing number of healthcare payers are measuring the pharmacoeconomic performance of different medicines, and widespread use of electronic medical records will give them the data they need to insist on outcomes-based pricing
- The boundaries between different forms of healthcare are blurring, as clinical advances render previously fatal diseases chronic and the self-medication sector expands
- Demand for medicines is growing more rapidly in the emerging economies than the industrialised economies, a pattern that will continue for the next decade
- Governments everywhere are beginning to focus on prevention rather than treatment, although they have not yet invested very much in pre-emptive measures; and
- The regulators are becoming more cautious about approving truly innovative medicines.

These trends will compound the challenges Pharma already faces, but they will also provide some major opportunities. So what must the industry do to capitalise on them? We think that it will have to improve its understanding of disease, reduce its R&D costs significantly and spread its bets to improve its productivity. It will also have to tap the potential of the emerging economies and switch from selling medicines to managing outcomes. However, few, if any, companies will be able to perform these activities alone.

The global market for medicines is growing but the industry must transform to capitalise opportunities

The virtualisation of R&D

Let's begin with R&D. If Pharma is to develop safe, efficacious new medicines more economically, it will have to learn much more about how the human body functions at the molecular level and the pathophysiological changes disease causes. Only then will it be able to develop a better understanding of how to modify or reverse these changes. This is a huge task – but one that several emerging technologies can help to facilitate.

Semantic technologies will, for example, make it much easier to identify the links between a particular disease and the biological pathways it affects, or the links between a particular molecule and its impact on the human body. Similarly, computer-aided molecule design will give researchers a much better starting point in the search for potent molecules.

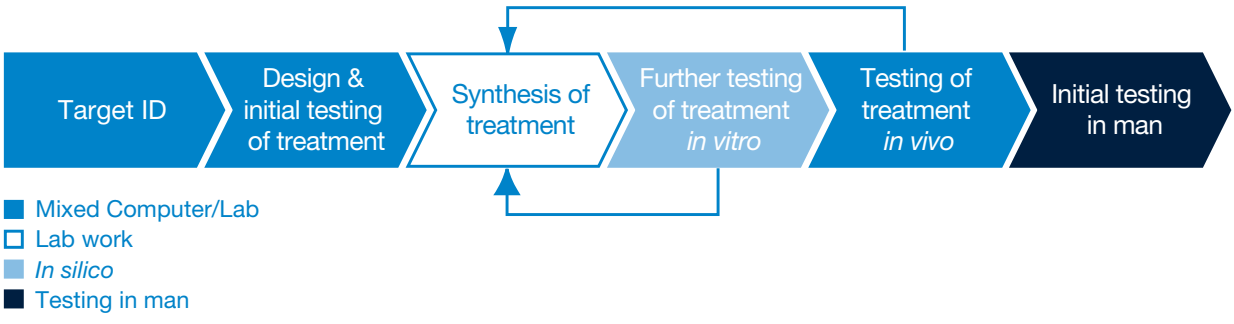
Various academic institutes and bioinformatics firms are also building computer models of different organs and cells, with the ultimate aim of creating a "virtual man". Developing such a model will require a massive collaborative effort far exceeding that needed to complete the Human Genome Project. Nevertheless, predictive biosimulation is already playing a growing role in the R&D process and we anticipate that, by 2020, virtual cells, organs and animals will be widely employed in pharmaceutical research (see **Figure 1**).

Of course, even the most robustly modelled molecules will still have to be tested in real human beings. However, here too, we expect some dramatic changes. When biomarkers for diagnosing and treating patients more accurately are more widely available, for example, the industry will be able to stratify patients with different but related conditions and test new medicines only in patients who suffer from a specific disease subtype. That will enable it to reduce the number and size of the clinical studies required to prove efficacy. Semantic technologies will also play a major role in improving the development process, while pervasive monitoring will enable Pharma to track patients on a real-time basis wherever they are.

We think that these scientific and technological advances will ultimately render the current model

Companies will use virtual R&D to increase innovation and reduce commercial deficit

Figure 1: What the research process might look like in 2020



Source: PricewaterhouseCoopers

of development, with its four distinct phases of clinical testing, defunct. A company will start by administering a treatment to a single patient who has been screened to ensure that he or she has the right medical profile. Once there is evidence that the treatment does not cause any immediate adverse events, it will be sequentially administered to other patients – from as few as 20 to as many as 100. The data they generate will be compared to data from the modelling that preceded the study and subjected to techniques like Bayesian analysis to adapt the course of the study, but the study itself will be conducted in a single, continuous phase (see **Figure 2**).

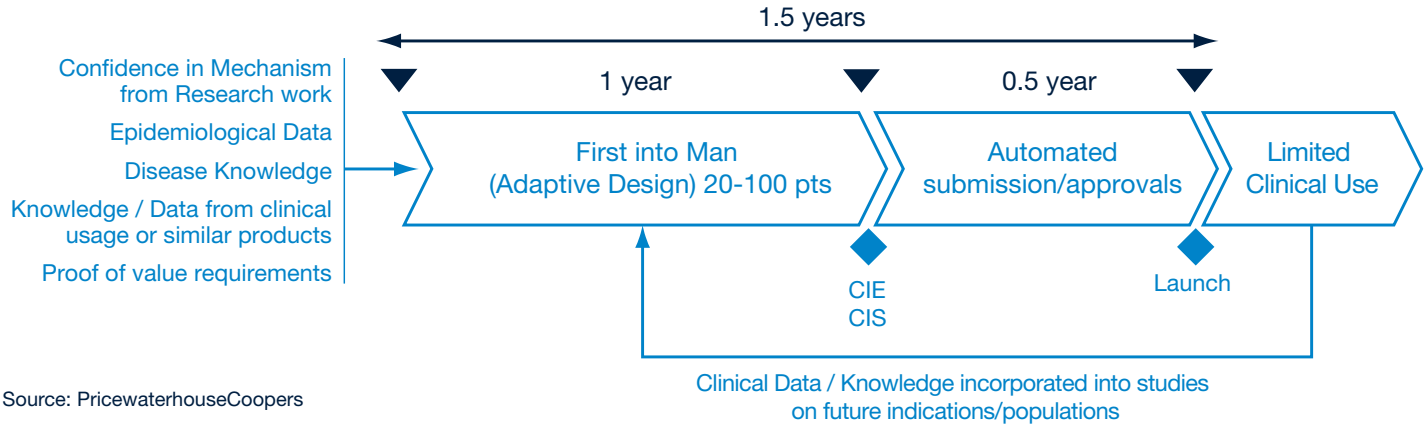
The development process will also become much more iterative, with data on a molecule for one disease subtype getting fed back into the development of new molecules for other disease subtypes in the same cluster of related diseases. And the current system of conducting trials at multiple sites will be replaced with a system based on independently managed clinical supercentres.

The regulatory process will change equally substantially over the next decade. First, there will be a common regulatory regime for all healthcare products and services, rather than separate regimes for pharmaceuticals, medical devices, diagnostics and the like. Indeed, there may even be a single global system, administered by national or federal agencies responsible for ensuring that new treatments meet the needs of patients within their respective domains, although we think the latter is less likely.

Second, the current "all-or-nothing" approach to the approval of new medicines will be replaced by a cumulative process, based on the gradual accretion of data. In other words, all newly approved therapies will receive "live licences" conditional on further in-life testing to substantiate their safety and efficacy in larger populations, different populations or the treatment of other conditions.

However, if they are to capitalise on the new technologies now emerging and the creation of a nimbler, more collaborative regulatory regime, many companies will have to make significant organisational and behavioural changes. They will, for example, have to decide whether they want to focus on mass-market

Figure 2: What the development process might look like in 2020



Source: PricewaterhouseCoopers

medicines or speciality therapies, and whether they want to outsource most of their research or keep it in-house. Those that regard R&D as an integral part of their activities may also need to review the way they manage their R&D and remunerate their scientific staff.

A new approach to marketing and sales

The industry's marketing and sales model will likewise have to undergo major alterations, as pay-for-performance becomes the norm in many countries and the opportunities for generating value from pure product offerings diminish. Many companies will have to analyse their own value chains to identify opportunities for working more closely with healthcare payers and providers. They will, for instance, have to consult payers, providers and patients when deciding which compounds to progress through their pipelines. Some companies now look at whether the products they are developing are more effective than other existing therapies, but very few focus on understanding the payer's perspective.

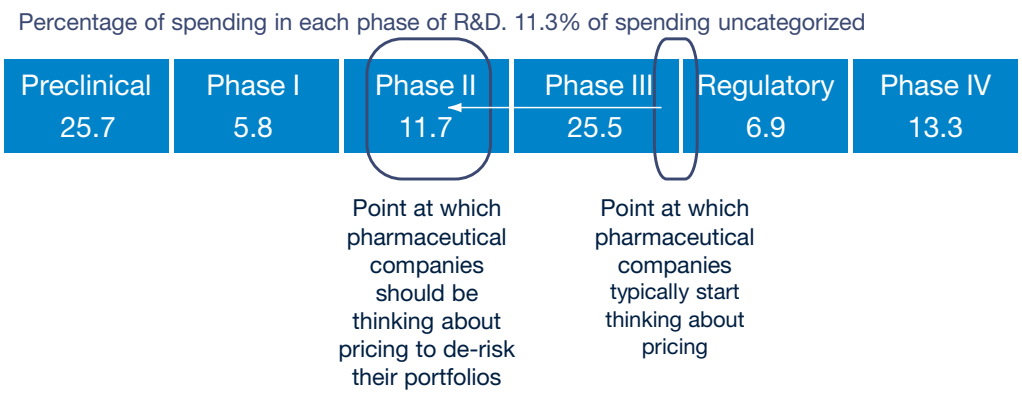
We believe that all companies should extend the concept of "de-risking" from the clinical to the commercial sphere to ensure that they are making medicines the market really wants to buy (see **Figure 3**).

Similarly, many companies will have to supplement the therapies they develop with a wide range of health management services. Most treatments perform much better in clinical trials than they do in everyday life. So, any pharmaceutical company that wants to command premium prices for its therapies will have to provide a range of products and services from which patients can choose all but the core prescription.

This route has several significant advantages. It will enable companies to generate new sources of revenue, differentiate their offerings more effectively and protect the value of the medicines they make. But it will also entail the formation of numerous alliances with local service providers and even rival manufacturers; the development of a secure, interoperable technological infrastructure; the management of new intellectual rights issues; the creation

Smaller, refocused sales force will enable pharma companies to create greater value for patients

Figure 3: Pharma needs to use a price de-risking strategy in early development



Source: PricewaterhouseCoopers

of much stronger brands; and the redefinition of the industry's role. Instead of trying to stimulate prescription sales, its task will be to help patients manage the disease lifecycle.

The shift to performance-based pricing will dictate other changes, too, including the need for a more flexible approach to pricing. The introduction of live licences and increasing importance of the emerging markets will reinforce this trend. Any company that launches a new healthcare package will have to negotiate price rises in line with the extension of the terms on which that package can be marketed. And if it wants to establish a stronger footing in the emerging world, it will have to use differential pricing – both within and between countries.

Increasing payer pressure on pricing and outcomes is forcing companies to increase its efforts to improve patient compliance. Improved patient compliance provides numerous benefits, not least, individual health outcomes, but it also helps to drive healthcare cost and improved revenues for companies. With performance based pricing becoming more common, a focus on patient compliance through education and technology will be a necessity.

Lastly, the industry leaders will have to develop comprehensive strategies for marketing and selling specialist healthcare packages, a process that will require the development of new skills and routes to market; and they will have to revolutionise their marketing and sales functions. By 2020, the role of the traditional sales representative will be largely obsolete. Conversely, the industry will have much greater need of people with the expertise to build brands; manage a network of external alliances; negotiate with governments and health insurers; liaise with secondary-care specialists; and communicate with patients.

The need for new business models

The changes we have outlined above will all necessitate the development of multinational, multi-disciplinary networks drawing on a much wider range of skills than Pharma alone can provide. Most companies will therefore

need to adopt new business models.

We believe that two principal models – federated and fully diversified – will emerge. The federated model comprises a network of separate organisations linked by a shared purpose and infrastructure. The fully diversified model comprises a network of entities owned by a single parent company. We have also identified two variants of the federated model. In the virtual version, a company outsources most or all of its activities; in the venture version, it manages a portfolio of investments (see **Figure 4**).

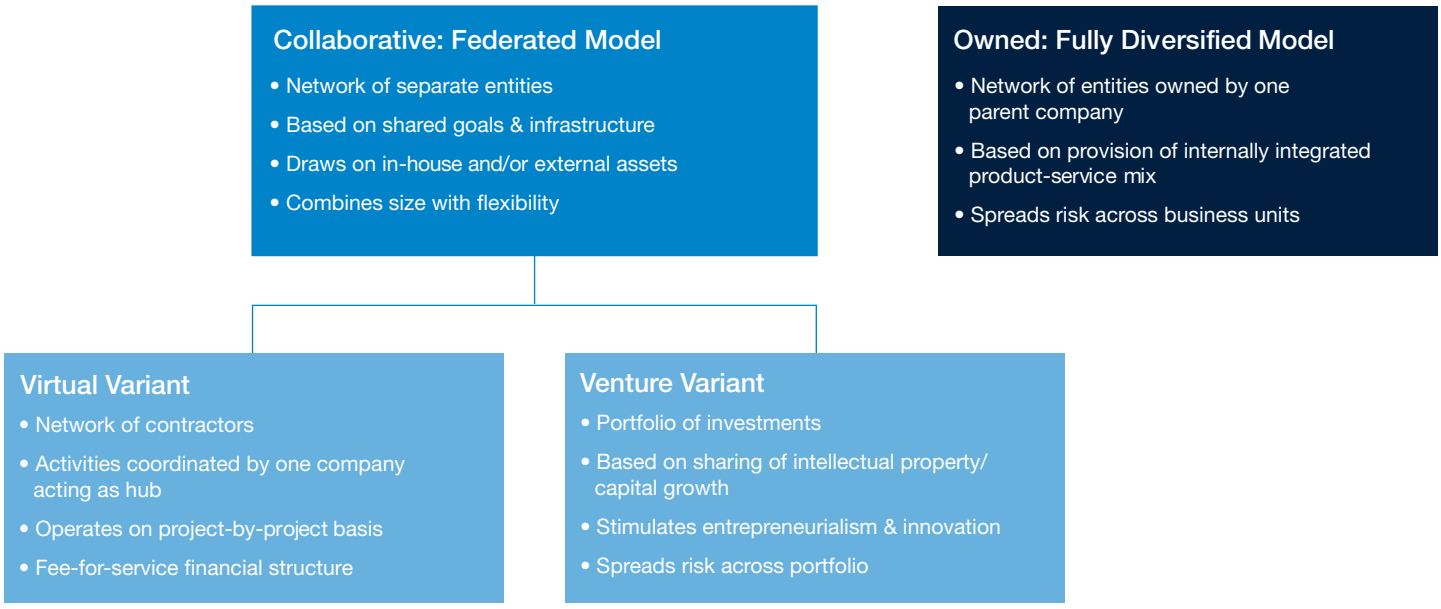
These models are not mutually exclusive. A fully diversified company might choose to use a federated model for certain aspects of its business, and vice versa. But we think that the federated model will ultimately dominate, primarily because it is quicker and more economic to implement.

The transition will not be easy, because collaborative business models are far more complex than the integrated model that has previously prevailed. Disrupting the existing order can also have a major impact on a company's short-term performance. We anticipate that many companies which choose the federated model will therefore adopt a progressive approach. They will start with opportunistic alliances; use the most successful alliances as building blocks to create more strategic, longer-lasting coalitions; and, finally, use the most successful coalitions to create a fully federated network of long-term partners.

However, the prospects for any pharmaceutical company that can make the switch are very promising. To date, Pharma has focused on the profits it can earn from the estimated 10-15% of the health budget that goes on medicines. Yet there are many opportunities to generate revenues by improving the way in which the remaining 85-90% is spent. It is these opportunities the industry will need to address in the brave new world of 2020.

Challenging times require bold moves if pharma companies are to survive immediate storm

Figure 4: The different business models



Source: PricewaterhouseCoopers

A heavier tax burden

The collaborative business models will enable Pharma to deliver healthcare packages that comprise medicines and supporting services supplied locally (such as drug administration training, home delivery, physiotherapy, health screening and exercise facilities). This new way of doing business, combined with the political and economic trends already shaping the general commercial environment, will have major tax repercussions. We anticipate that the industry's corporate tax burden will rise significantly over the next 10 years — unless it undertakes various strategies to mitigate the impact.

Governments of the industrialised world will struggle to repair public finances deeply damaged by debts accrued in managing the global recession. They will clamp down on opportunities that have allowed the industry to reduce corporate taxes by moving profits from higher-tax to lower-tax territories.

Along with imposing more stringent tax regulations, the major powers could place trading restrictions on traditional tax havens that refuse to cooperate. The tax authorities in most countries will work more closely with their counter parties in other territories to curb multinationals' tax-reducing practices.

As Big Pharma moves toward the provision of integrated healthcare packages, the proportion of income generated in the industry's end markets will increase. Demand for such services initially is likely to be greatest in the industrialised world, where corporate income tax rates are often higher. That will make it more difficult for companies to assign profits legitimately from high- to low-tax jurisdictions.

Undertaking or managing more business activities in end markets also will make it harder to prove that a company has not created a permanent business establishment in countries where services are delivered. This may increase the risk of failing to obtain double tax relief, as allowed under international tax treaties, and thus of being taxed on the same earnings in the home country and the country where the services have been delivered.

The provision of direct-to-patient services also will make it even more difficult for the industry to negotiate its way through the maze of withholding tax regulations. Countries have traditionally adopted a more diverse approach to the application of withholding taxes to payments for services than they have for goods. These variations can produce more fodder for tax disputes.

The provision of services also may affect the way the income of controlled foreign corporations (CFCs) is taxed. In many developed countries, tax laws provide that CFC profits may be attributed to the holding company and taxed immediately, rather than being taxed only when (and if) they are repatriated. However, CFC legislation often distinguishes between "passive" income (i.e., interest, dividends, annuities, rents and royalties), which is taxed, and "active" income (i.e., income from commercial activities), which is not taxed. Some of the new healthcare services pharmaceutical multinationals will provide may fall into the taxable category.

Providing integrated packages also could increase compliance costs and risks associated with indirect taxes, such as value-added tax (VAT). Some VAT regimes may apply the appropriate rate of VAT to each component of a

Tax strategy will be the crux, not an afterthought, of long-term business plans

package, while others may treat the package as a composite and apply the rate of the principal element to the entire bundle.

The increasing importance of emerging markets, an evolving supply chain, and a shift to services could also have a major bearing on customs duties and other trade-related tariffs pharmaceutical companies incur. Some countries levy significant import duties on key active pharmaceutical ingredients and finished products, and the valuation of combined product-service offerings for customs purposes could prove complicated.

Finally, because of more complex supply chains, it may become more difficult to use transfer pricing — i.e., the allocation of income among related business entities via the pricing of intellectual property, tangible goods, services, and loans or other financial transactions — to avoid double taxation. Many tax authorities already are clamping down on abusive transfer pricing practices, such as shifting profits artificially from a high- to a low-tax jurisdiction, by maximising expenses in the former and income in the latter.

To deal with these multiple pressures, companies will need to rethink their tax strategies. The choice of legal entity and structure of commercial arrangements, for example, will have a significant impact on taxation. One solution for multinationals might be to locate more business activities, such as R&D, manufacturing, and marketing, in regional hubs in low-tax countries. Some might choose to move their entire operations to a low-tax location.

On the positive side, the competition to attract companies engaging in R&D will intensify. Some countries will offer generous tax incentives and credits — and several will be new competitors keen to build knowledge-based economies. Tax departments will need to keep abreast of these incentives so they can advise leadership on how to take advantage of tax-reduction opportunities.

Tax departments also will have to build much closer relationships with the operational parts of the business and acquire a much more detailed understanding of the complexities of supply chain arrangements. Those tax departments that combine a strong grasp of long-term strategy and effective lobbying with a detailed tactical understanding of the way in which products are distributed and value is created will be best placed to help pilot their companies along the path to future prosperity.

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