



INNOVATIVE FUTURES

A Scenario Analysis of Pharmaceutical Innovation
and Access to Medicines in Europe

This report was commissioned by EFPIA, the trade association of the research-based biopharmaceutical industry in Europe. The views represented here are those of the authors only.

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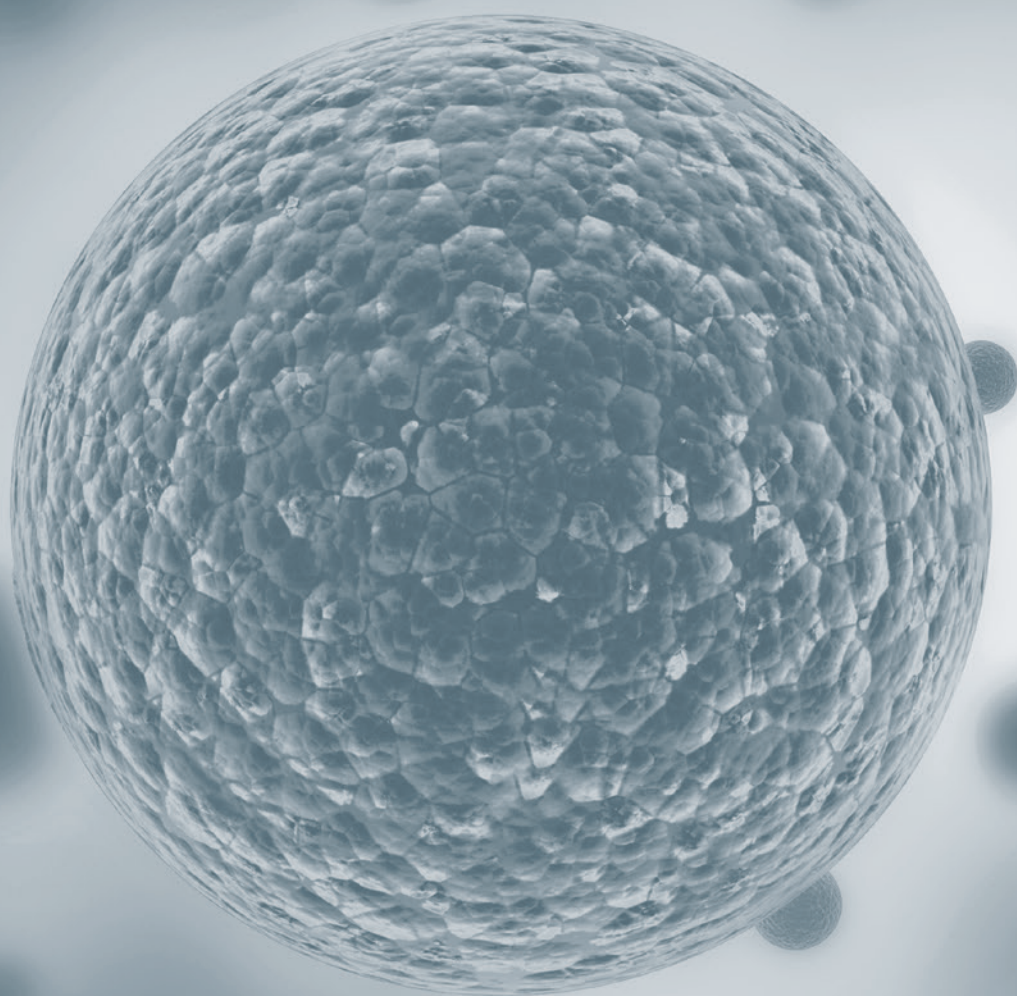
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LIST OF ABBREVIATIONS

EMA	European Medicines Agency
EPO	European Patent Office
EPR	External Price Referencing
GDP	Gross Domestic Product
HSA	Health Savings Account
HTA	Healthcare Technology Assessment
IQWiG	The Institute for Quality and Efficiency in Healthcare (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen)
IPRs	Intellectual Property Rights
NHS	National Health Service (UK)
NICE	National Institute for Health and Care Excellence (UK)
NMEs	New Molecular Entities
OECD	Organisation for Economic Co-operation and Development
OOP	Out of Pocket Expenditure
P&R	Pricing and Reimbursement
PPM	Pharmaceutical Portfolio Management
R&D	Research and Development
ROI	Return on Investment
RP	Reference Pricing
TRP	Therapeutic Reference Pricing
VAT	Value Added Tax



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WHAT ARE INNOVATION SCENARIOS?

Scenarios are stories that describe different future horizons stemming from the same present. In this report we aim to provoke new thinking and to challenge existing preconceptions by imagining two different sets of stories that might take place in the European healthcare sector of the future.

Of course, the only certain thing about the future is that we do not know yet what will happen. So should we even try to predict it? We believe that the answer is 'yes' since scenarios provide a useful as well as a thought-provoking tool for an interdisciplinary conversation about the future. As well as provoking debate, they can be immensely helpful as a means of stimulating new ideas and new thinking.

So who might use these scenarios? Policymakers may turn to this scenario analysis as a means of understanding the challenges faced by the innovative pharmaceutical industry as well as the pressures that they themselves are likely to face in future as decision makers - balancing the need for jobs and a competitive, innovation-led economy with the future costs of the healthcare system including the continued funding of new medicines and treatments.

Industry can use these scenarios as a means of 'gaming through' how the policy landscape may shift in the future and what impact this could have on their business model and strategic planning.

Other healthcare experts, be they in academia or policy research, will find these scenarios interesting in their own right as stories which tell us something about our possible future as citizens of the EU and future users of the healthcare systems of tomorrow.

“Innovation distinguishes between a leader and a follower.”

Steve Jobs

WHY DOES EUROPE NEED INNOVATION SCENARIOS?

Innovation is the buzzword of the moment in Europe. It is perhaps too often seen as the potential saviour of all our ills. Innovation, it is said, will cure the diseases of the future, help us all to live longer and healthier lives, provide new jobs, stimulate the ailing economy, help us to compete against the burgeoning economies of the BRIC nations, and so on and so forth. The word innovation is certainly loaded with a heavy weight of expectations.

Indeed, Europe's new growth strategy, known as Europe 2020, which replaces the old and heavily criticised Lisbon Strategy, aims to put innovation at its heart. According to its own rhetoric "We are facing a situation of 'innovation emergency'. Europe is spending 0.8% of GDP less than the US and 1.5% less than Japan every year on Research & Development (R&D). Thousands of our best researchers and innovators have moved to countries where conditions are more favourable. Although the EU market is the largest in the world, it remains fragmented and not innovation-friendly enough. And other countries like China and South Korea are catching up fast. The Innovation Union is a crucial investment for our future. For example, achieving our target of investing 3% of EU GDP in R&D by 2020 could create 3.7 million jobs and increase annual GDP by €795 billion by 2025".¹

Containing over thirty action points, the Innovation Union project aims to improve overall conditions and access to finance for research and innovation in Europe, to ensure that innovative ideas can be turned into products and services that create growth and jobs. This very pressure to innovate, however, means that the use of the term *innovation* comes loaded with a heavy weight of expectations, whether for policymakers under pressure to help create jobs or for the biopharmaceutical industry trying to convince a new generation of investors and shareholders to place their faith in a research pipeline.

It is clearly essential for Europe's economy that we create the right climate for the research-based industries and for a competitive market to flourish but it is also important that we make sure we can afford to pay for the innovations we want.

Why does pharmaceutical innovation in particular matter so much to Europe? It is fundamental not just to the economy and to our need to create new jobs but also to quality of life for future users of Europe's healthcare systems; particularly in light of most EU countries' rapidly ageing populations. Patients naturally want access to the latest medicines and treatments, which makes innovation a political (some might even say ethical) priority.

But innovation is also a double-edged sword. Some innovations will save money by reducing illness, cutting down the length of time patients spend in hospital or making healthcare systems more efficient but in other cases, we may need to pay more for the most innovative treatments. In a period when so-called 'austerity measures' are severely affecting the level of budgets available to Europe's largely tax-financed healthcare systems, this is becoming a major problem. As a recent OECD report has shown, health spending per capita fell in 11 of 33 OECD countries between 2009 and 2011, notably by 11.1% in Greece and 6.6% in Ireland, two countries most severely affected by the financial crisis.² The report, *Health at a Glance 2013*, says that this makes it all the more important that European countries make their

healthcare systems more productive, efficient and affordable both now and into the future.

Likewise, in a recent issue of the UK's *Health Service Journal* (July 2013) Stephen Dorrell, Britain's health secretary under John Major and now chairman of the respected Health Select Committee in the British Parliament, said the disciplines of the "Nicholson challenge" (a set of policies that seek to find £20bn of savings in the NHS by 2015) will have to stay in place *under any political scenario*. He said the conclusion had been reached on a cross-party basis by his Committee and reflected the political and economic realities facing Britain's NHS.³

Much public policy discussion and also business strategy is based on the assumption that things will continue evolving in the same way or at least in a similar way. But what if they don't? What if external shocks or seismic changes radically alter the economic and political landscape?

Scenarios can help us to negotiate our way through the imagined future in both the best and worst case settings and in a form which is politically neutral. Scenarios do not aim to judge whether an outcome is good or bad but merely to predict what might happen in this imagined reality.

Indeed, many well-respected organisations in both the public and private sectors have commissioned and then used scenarios to useful effect to help inform their thinking and future strategy. The European Patent Office⁴, the energy company Shell (who have been conducting energy scenarios for over 40 years⁵) as well as public policy think tanks such as the Stockholm Network⁶ are just a few examples of organisations who have used scenarios effectively to inspire their own thinking as well as to help shape and inform public policy debates.

Looking at the example of Shell, we can see how companies have effectively employed scenarios for a variety of purposes. To quote from their own material:

*"Shell has been using scenarios since the early 1970s to allow generations of leaders to make better business decisions. Over time, the Shell Scenarios have gained a global following among governments, academia and other businesses. They have helped deepen understanding of how the world might appear decades ahead. Scenarios help decision makers reconcile apparent contradictions or uncertainties, such as how political change in one region impacts global society. They also have the potential to improve awareness around issues that could become increasingly important to society, such as increased urbanisation, greater connectivity or loss of trust in institutions. By exploring plausible, as well as predictable, outcomes scenarios challenge conventional wisdom. Organisations using scenarios find it easier to recognise impending disruptions in their own operating environment, such as political changes, demographic shifts or recessions. They also increase their resilience to sudden changes caused by unexpected crises."*⁷

Shell, of course, focuses its forward-thinking efforts on issues affecting the future of energy supply – or the state of the environment more broadly – but scenario thinking can also be applied to many different contexts. When it comes to the future of the patent system in Europe, which is recognised as one of the preconditions for driving innovation, the EPO has done some important work in trying to identify the forthcoming hurdles as well as the future opportunities to spur on innovation.

In March 2004, incoming President Professor Alain Pompidou decided to prepare for his forthcoming role by sponsoring the EPO *Scenarios for the Future* project. The project considered what the patent system might look like 20 years ahead.

The EPO website describes the rationale for the project as follows:

*"The purpose of scenarios is to examine possible uncertainties that might arise in a complex and turbulent environment. By deploying this methodology, a wider view can be taken and more relevant questions can be asked. This approach encourages a holistic examination of the system and exposes the complex interactions that might impact it. By thinking the unthinkable, and questioning structures that are ordinarily taken as a given, it is possible to better anticipate and adapt to future changes."*⁸

The OECD's Knowledge Bank also provides a useful description of the academic rationale for the use of scenarios:

- *"Scenarios provide a picture of the future from which we may 'back-cast' to discover what decisions may be required at each stage to get there.*
- *Scenarios can be used to encourage discussion and aid strategic planning among policy makers; to stimulate public discourse; to support decisions on complex issues with long-term implications.*
- *Scenarios are participatory tools that can be adapted to different tasks. They should always be used within a 'culture of curiosity' and with good working practices."*⁹

In order to stretch our ability to think beyond the here and now, this report takes on board this approach to blue sky thinking and, for the first time, applies it to the case of the innovative pharmaceutical sector in Europe.

As will be discussed at length in the next section, healthcare systems in general and the pharmaceutical sector in particular are currently subject to a great deal of discussion about the future when it comes to quantifying the value of healthcare expenditure, working out the long-term sustainability of financing European healthcare systems in a period of upcoming demographic change, or indeed how we define what constitutes 'real' healthcare innovation more broadly.

This investment is needed not only because innovation is broadly a priority for Europe's economy but also because research shows that the pharmaceutical sector is the most R&D intensive of all of the high-tech industries. To illustrate, Table 1 shows how the pharmaceutical industry in Europe invests just over 91 billion euros in R&D and the highest percentage of total R&D spending exceeding the amount spent by other successful high-tech sectors such as technology companies, automobiles and software/computer services.

TABLE 1:R&D Investment, EU Industrial Scorecard, R&D ranking of the top 1500 World companies, 2011, Pugatch Consilium analysis¹⁰

INDUSTRIAL SECTOR	R&D INVESTMENT IN €BILLION	R&D BY SECTOR AS A % OF TOTAL R&D
Pharmaceuticals & biotechnology	91,06	17,90
Technology hardware & equipment	83,98	16,50
Automobiles & Parts	80,53	15,83
Software & computer services	39,86	7,83
Electronic & electrical equipment	37,90	7,45
Chemicals	21,67	4,26
Industrial engineering	19,32	3,80
Aerospace & Defense	17,95	3,53
Leisure goods	16,19	3,18
General industrials	14,35	2,82
Health care equipment & services	10,17	2,00
Fixed line telecommunications	9,50	1,87
Banks	7,65	1,50
Oil & gas producers	7,25	1,43
Food producers	7,04	1,38

Source: European Commission (2012)

As we discuss in the forthcoming chapter, such intensive investment in R&D makes the pharmaceutical industry even more sensitive to changes in public policy which affect the 'innovation landscape' making a good understanding of the likely future opportunities, threats and challenges ahead all the more important.

Innovative Futures therefore takes a probing look at the future from two quite radically different perspectives and tries to use these scenarios to see what might happen next when it comes to creating the innovative medicines and healthcare systems of the years ahead. The results may surprise, entertain or even shock but whatever reaction they provoke, their intention is to stimulate a new way of looking at the future. We hope they succeed in doing just that.

METHODOLOGY

This report provides an outline of the possible evolution of two different innovation scenarios:

- Scenario 1: Suspicious Minds; and
- Scenario 2: Convergence.

Each scenario is built around a matrix including a clear set of assumptions which evolve around three dimensions:

Time: The scenarios unfold over a 12 year period, broken into three chunks of four years each (roughly equivalent to a parliamentary term of office)

Players: The Players are divided into three groups – The EU region (i.e. the Member States), the pharmaceutical industry, and the general public

Dimensions: Key dimensions are identified which affect each player over time (all dimensions are defined below):

- For the EU region – Expenditure
- For Industry – Products and Income
- For the Public – Products and Out of Pocket Expenditure (OOP)



SYSTEMIC ASSUMPTIONS

In order to simplify and define the basis from which each scenario proceeds, we have made the following broad systemic assumptions about the state of Europe's economy and the political context within which its healthcare systems operate.

1. Within the scenarios, we have treated the EU as one homogenous region. It should be stressed that this approach has been taken purely for illustrative and analytical reasons. In reality, of course, in terms of innovation, there are major differences in the EU between countries with high rates of innovation and R&D activity (as measured by R&D spending and international rankings such as the Global Innovation Index) and countries with less

innovation output and lower rates of R&D spending and activity. Whilst acknowledging these differences, for the sake of these scenarios, we nevertheless treat the EU region as a single entity.

2. Likewise, although, in reality, there is enormous variety within European healthcare systems, for the purpose of creating scenarios, it would be too complex a process to incorporate all of the economic, social and political nuances of the various Member States as well as explaining the differences in how their financing and delivery models operate. Overall, therefore, a set of simplified assumptions has been made about healthcare innovation and system dynamics, which can then be broadly applied to the European healthcare environment as a whole.

Socially, for example, it can be argued that in virtually all EU Member States the notion of social solidarity is still fundamental to the public and to governments however their healthcare systems are financed. For example, while the UK operates on Beveridgean 'single payer' lines the principle of a social safety net nevertheless remains central to the political consensus behind the system and to its ongoing popularity with the British public.

Economically, Europe's healthcare systems focus primarily on efficiency, whether in the form of implementing direct cuts and cost savings or attempting to implement more efficient management of existing resources. Quality measurements, organisational re-structuring, and transparency take precedence. Innovation is now linked to these concepts of process innovation just as much as it is related to technological innovation.

Politically, governments tend to react or to generate reform largely in the event of an imminent visible crisis or due to a political crisis (or both) rather than responding to arguments about long-term considerations, which do not always generate action.

3. Medicines and treatments form an important part of the funding discussions and healthcare activities of EU Member States. Even so, wage bills for medical staff, hospital maintenance and new buildings as well as the cost of new medical equipment are now fighting for priority against funding of medicines at a time when public budgets are severely squeezed. At the EU level too there is an increasing focus on the pharmaceutical industry's role in contributing to economic growth at a time of constraints on the public purse. On the one hand, public healthcare budgets are being squeezed – which ultimately affects the price paid for pharmaceuticals by governments. Yet at the same time, and perhaps paradoxically, Europe is looking optimistically at the pharmaceutical sector as one of the key players in the innovative knowledge economy hoping it will help to provide new jobs and fuel Europe's economic recovery.

TERMINOLOGY

In this report, the following terms are used in the manner defined below:

Expenditure – relates to public healthcare expenditure only. In other words, government healthcare budgets in general and pharmaceutical budgets in particular.

Products – relates to new medicines or treatments developed by Industry.

Income – industry income from the public purse and private sources (including external investors who may ultimately be influenced by the policy environment).

Access – patients' ability to access medicines and treatments either via the public healthcare system or by private means.

Out of pocket – private spending by patients above and beyond their mandatory tax funding or compulsory insurance.

Government – references to government in these scenarios refer collectively to the governments of EU Member States. In other words, we assume for the purpose of simplification, that all of the EU Member States will react in the same or similar ways to the changing dynamics we artificially introduce into the scenario process. In reality, of course, there would be a good deal of variation, although long-term trends in pricing and reimbursement policies, for example, do suggest that EU Member States are increasingly copying and being influenced by one another into pursuing similar sets of policies.

Indeed, these long-term trends and similarities in pharmaceutical policies is ultimately what forms the basis for Scenario 1: Suspicious Minds. The next section examines this policy trajectory and details how EU Member States have been steadily moving in a direction of 'innovation freeze'.

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THE PHARMACEUTICAL SECTOR AND INNOVATION

Over the last few years the EU, and particularly the Eurozone, has experienced a prolonged economic recession. Even though the full impact of this recession is still unknown, some of the negative consequences are already clearly noticeable, especially amongst the Southern countries most affected by the crisis such as Greece, Spain, Italy and Portugal.

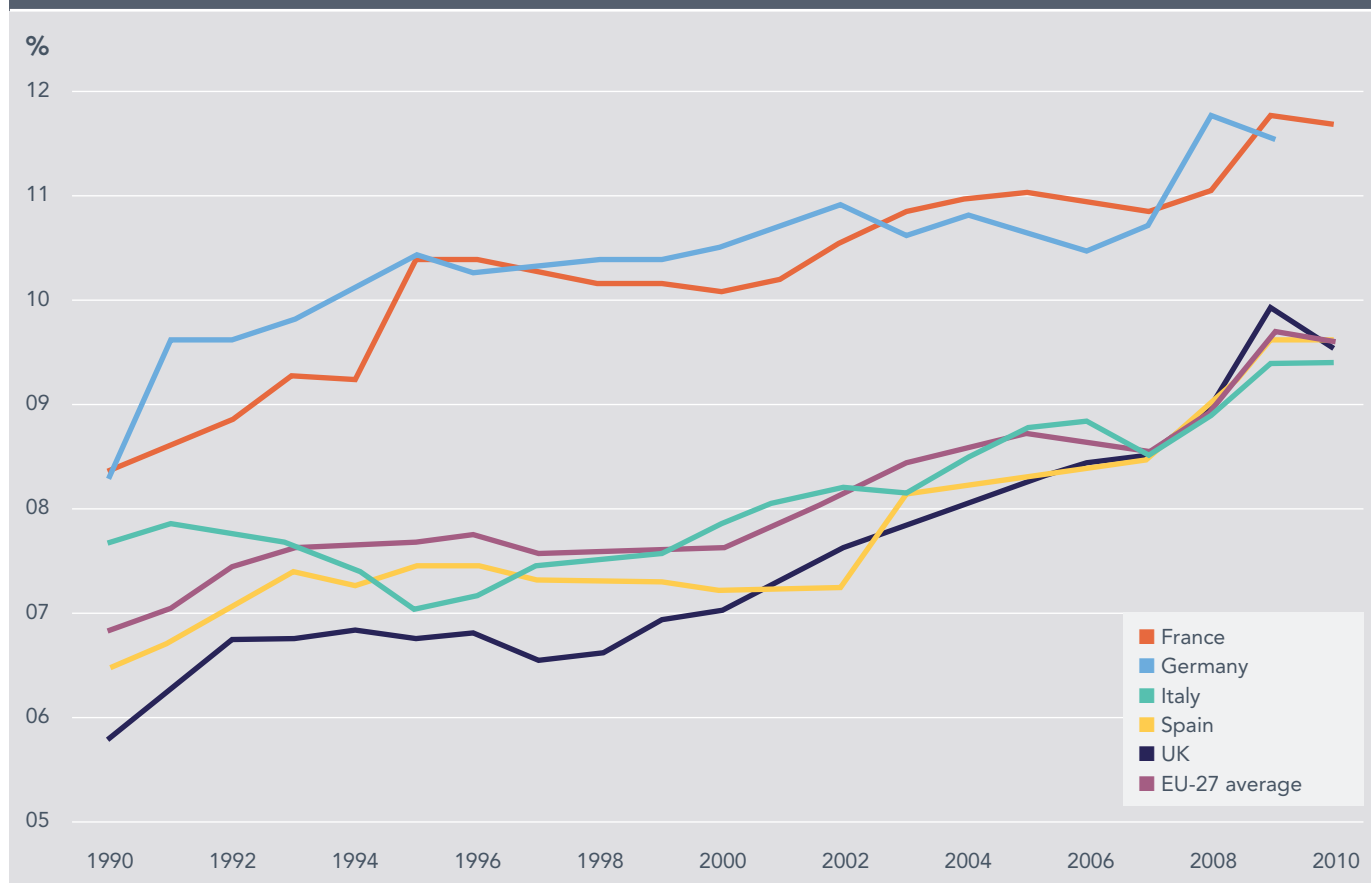
It comes as no surprise that several sectors of the European economy are suffering from a lack of investment. The biopharmaceutical sector has been one of the most severely affected, as it is one of the industries that is most dependent on the one hand on public expenditure on healthcare (as most EU states are primarily financed through the public purse) and on the other the need for long-term, sustainable investment to support its research and development operations. As this section will detail, the cost of drug development has steadily increased and the challenges of developing new medicines and medical technologies have also steadily escalated. In 2012, the estimated cost of researching and developing a new chemical or biological entity was approximately USD1.56 billion.¹¹

The current model of R&D financing allows pharmaceutical innovators to recoup their investments through a system of market exclusivity primarily provided through IPRs such as patent protection. The protection of these IPRs puts the inventor in a monopolist position and allows innovators to charge a premium price for their products in order to pay for the high costs of developing them. But recent economic developments have started a fundamental debate in the public arena centred on the desirability of this R&D model. To begin

with, innovating is becoming more and more challenging, leading the biopharmaceutical industry to increase spending on the development of more sophisticated drugs and technologies. Empirical estimates based on annual rates of R&D spending and the records of NMEs brought onto the market suggest a downward trend in direct R&D productivity, that is, the cost of developing each new product and technology continues to increase.

In essence there are two forces moving in opposite directions: companies have fewer resources to spend on R&D and yet, at the same time, R&D outputs are becoming more expensive. This trajectory could ultimately lead Europe into what may be labelled an 'innovation freeze' which is the story outlined in Scenario 1: Suspicious Minds, subsequent to this section. And even though the international biopharmaceutical industry's historical ability to adapt makes this an unlikely scenario in the short-term, a longer term perspective points to an undesirable trend that should raise our immediate concern.

The primary purpose of this section is to show that while the reality described in Scenario 1: Suspicious Minds may seem far-fetched there is, in fact, a good deal of evidence pointing to just such a future. This section explores this negative

FIGURE 1:Healthcare expenditure in % of GDP, 1990-2010¹²

Source: OECD

trajectory over the last few decades. It starts with a description of the current macroeconomic landscape with regards to healthcare and pharmaceutical expenditures in the EU. This is followed by an explanation of the pricing and reimbursement measures often used to contain costs in Member States. The nature of the pharmaceutical R&D process is explained, which sets the stage for an explanation of the current state of pharmaceutical innovation in Europe; highlighting the difficult environment pharmaceutical companies face nowadays.

The macroeconomic picture: healthcare and pharmaceutical expenditures

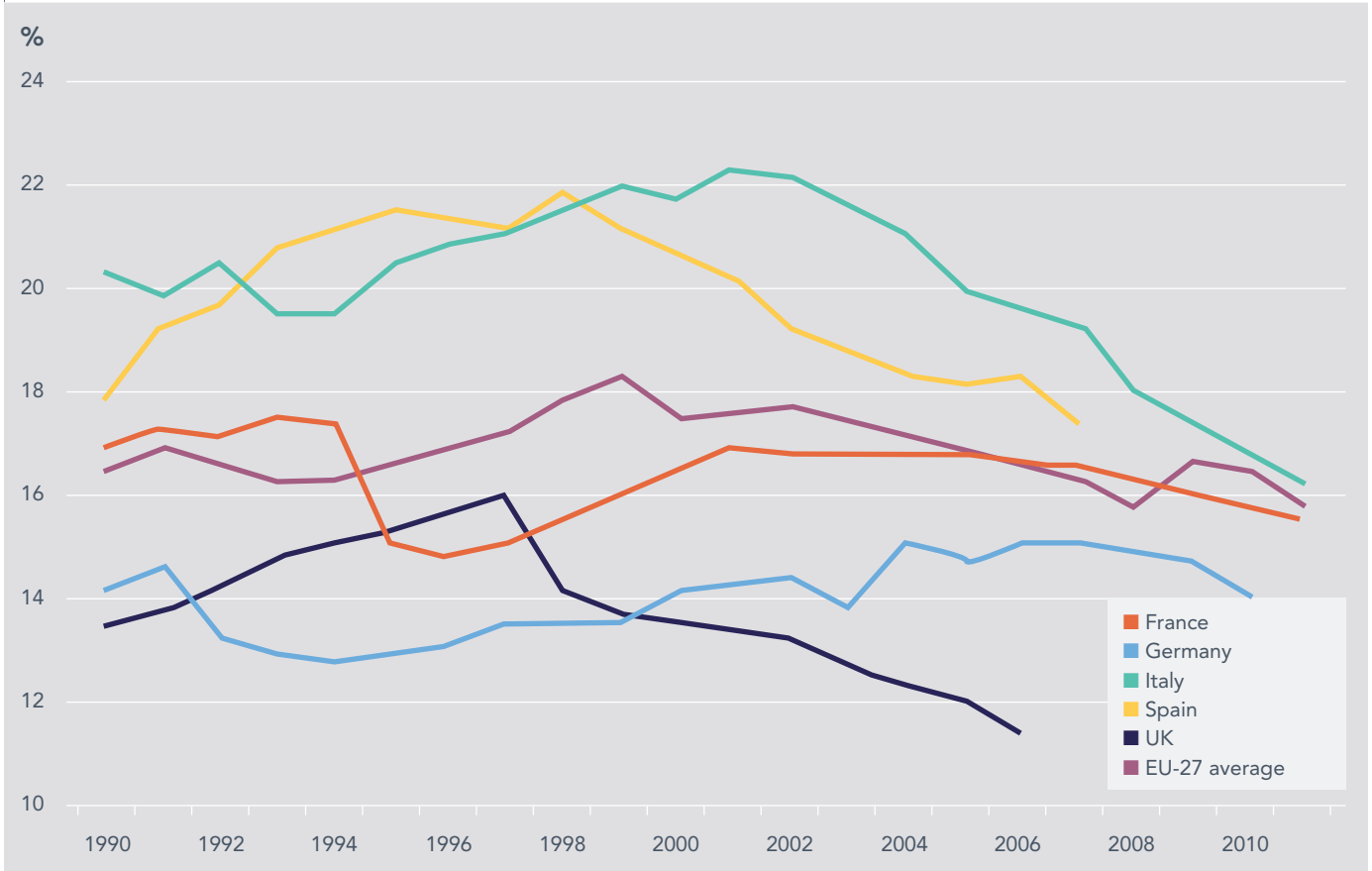
Healthcare expenditure across the European Union has steadily increased over the last two decades. In particular large Member States like Germany and France have experienced record healthcare expenditures as a percentage of GDP, higher than both any other country in the EU-5 as well as the EU-27 average (see

Figure 1). An ageing population, more costly health technology on account of higher R&D costs, and the shift towards chronic diseases are some of the reasons for the rising costs in healthcare, which are stretching public healthcare budgets to their limits.

Healthcare now assumes a larger proportion of public and private spending as a share of GDP. But not all of this expenditure is due to the cost of pharmaceuticals. In fact, pharmaceutical expenditure represents a rather low proportion when compared to other components of healthcare expenditure such as hospitals and out-patient care, even revealing a downward tendency in the EU-5 in recent years (see Figure 2). Still, there are large differences between European countries and the percentage of health care expenditure on pharmaceuticals. National differences in the type and quantity of pharmaceuticals consumed, as well as other factors like the

FIGURE 2:

EU-5 countries' average of total expenditure on pharmaceuticals and other medical non-durables as % total expenditure on health¹³



Source: OECD

labour costs of medical professionals, lifestyles of patients, prescribing behaviour of physicians, level of generic entry, level of parallel trade, and government regulation, all have an impact.¹⁴

Pricing and reimbursement and cost-containment policies in Europe

While being home to some of the most advanced and comprehensive health systems, EU Member States also have in place the most extensive and widely used cost-containment and Pricing and Reimbursement (P&R) policies in the world.

Although cost containment and P&R policies have been in place for decades, the financial crisis that hit the EU and particularly the Eurozone in 2007-8 onwards has prompted public payers to act to redefine healthcare budgets and to strongly intensify their use.

Some frequently adopted measures include:

- Administrative price reductions
- Discounts, rebates, 'clawbacks'/payback and other agreements
- External price referencing
- Therapeutic reference pricing
- Margin control in the supply chain
- Tariffs/sales tax on medicines
- Positive and negative reimbursement lists
- Co-payments
- Health technology assessment
- Promotion of the use of generics

There are numerous examples of countries hard hit by the economic downturn imposing harsher P&R policies. For instance, in 2010 and 2011 the Greek government introduced several P&R policies including price cuts, the re-introduction of a positive list, changes in the profit margins of pharmacies and wholesalers, and tenders for hospital drugs. The result was a decrease in public drug expenditure from €5.09 billion in 2009, to €4.25 billion in 2010, to €4.10 billion in 2011.¹⁵ Similarly, Portugal also implemented extreme measures for controlling pharmaceutical expenditure: price cuts for original medicines and generics (following annual price reviews), an increase in the VAT rate, reference pricing of countries with the cheapest price, and strong incentives for the use of generics. The overall results of these measures are mixed. Empirical studies have found that the introduced measures in Portugal did not change the trend of increasing expenditures. Barros et al (2010) show that the implemented policies merely resulted in a shift of pharmaceutical expenditure from the public healthcare system to patients through an increase in out-of-pocket payments, leaving total health expenditure unchanged.¹⁶

In neighbouring Spain, price cuts of 30% were introduced in the first months of 2010 together with 7.5% discounts on original medicines and 4% on orphan drugs. These policies built on existing cost containment measures started even before the single currency came into place. Puig-Junoy (2004) describes the reforms of the Spanish healthcare system introduced between 1996 and 2002, which included negative listings, a Reference Pricing (RP) system, settlement of pharmacies' margins in accordance with consumer prices, and general agreements between the government and the industry.¹⁷ In fact, looking again at Figure 2, we can observe that the introduction of these policies coincides with the decrease of the average percentage of pharmaceutical expenditure as a percentage of total health expenditure. However, as observed in Figure 1, total health expenditure in Spain continued to increase growing from just over 7% of GDP in 2002 to close to 10% of GDP in 2010. From this example it would appear that pharmaceuticals *per se* are not the main reason for soaring health expenditures.

The widespread use and recent intensification of these P&R and cost-containment policies has been especially hard on the pharmaceutical industry. Cost-containment measures often lead to reduced revenues and profits. This downward pressure on income from the demand side has been accompanied by the increase cost and difficulty in developing new medicines and technology from the supply side.

The process of pharmaceutical research & development

In order to comprehend the full complexity of the pharmaceutical market, one has to be familiar with the R&D process and all the crucial steps needed to bring a new molecular entity into the market. The process starts with basic research into pharmacological active ingredients. From thousands of screened compounds, only a few selected molecules make it through to safety and toxicology tests on animals. The following steps – known as clinical trials – concern human testing. Clinical trials are organized in phases: safety testing on healthy volunteers for dose-ranging (phase I); testing the drug on a small group of patients to assess efficacy and safety (phase II); and finally, up-scaling to a larger group of patients (phase III). After all of these stages, the drug candidate should have built a strong core of information regarding the three main pillars of pharmaceuticals regulation: Quality, Safety, and Efficacy. Only then can a medicine file for a marketing authorization application (registration). After registration, all products need to obtain a price and reimbursement status through negotiations (often lengthy) with each jurisdiction's responsible body. And when a drug finally reaches the market, post-marketing surveillance or pharmacovigilance studies – frequently referred to as phase IV clinical trials – must be carried on as long as the product is maintained in the market.

The R&D process is a rocky road for the majority of new drug candidates. On average, only one to two of every 10,000 synthesized, examined and screened compounds in basic research will successfully pass through all stages of R&D and go on to become a marketable drug. Furthermore, this is a time-consuming process: it takes between 10 and 15 years from the filing of a new patent to the day when a new medicine finally becomes available for patients to use.¹⁸

The state of innovation

In the past 60 years, over 1,220 new medicines have gained access to the pharmaceutical market, accounting for significant improvements in public health and life expectancy.¹⁹ But if we take a look at the number of new chemical or biological entities approved in Europe since the early 1990s, it may seem that output has been decreasing in recent years (see Table 2), which has been raising concerns about a possible lag in innovation.

Examining new drug entries for 5-year periods from 1990 to 2009 it would seem that innovative output has fallen quite significantly from an average of 43 new chemical or biological entities in 1990-1994 to 29 in 2005-2009. This is a drop of a third. However, if we examine the figures from a longer historical perspective it is not at all clear that pharmaceutical innovation has actually decreased. Indeed, looking at the US market (for which data is available and which,

by and large, shows the same trends as the European pharmaceutical market) from 1950 to the early 1990s, NMEs approved ranged around 20 per year hardly ever exceeding 30 NMEs. The source of confusion may be the abnormal peak of 53 NMEs approved in 1996, which extends for the next few years and then returns to historical values between 20 and 30 NMEs (see Figure 3).

Indeed looking at the figures for Europe in Table 1, they correspond with this observed trend in the US, with the number of new drugs introduced on the market during the early to mid-1990s significantly higher than later periods.

TABLE 2:

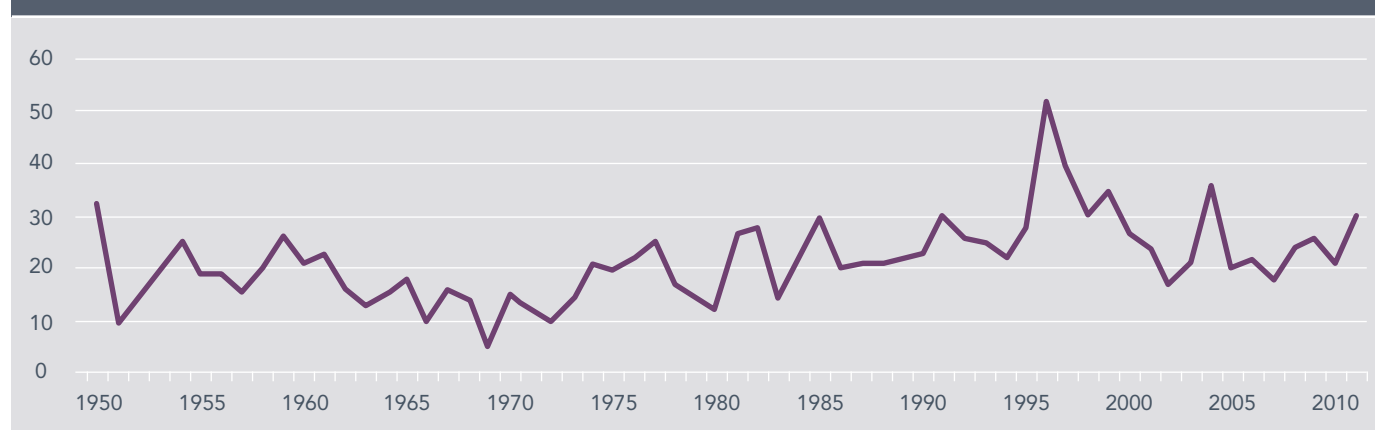
Number of new chemical or biological entities (1990-2009)²⁰

NUMBER	1990-1994	1995-1999	2000-2004	2005-2009
Total	215	207	162	146
Average per year	43	41	32	29

Source: EFPIA

FIGURE 3:

New molecular entities approved by the FDA between 1950 and 2011²¹



Source: FDA

Furthermore, the *a priori* assumption that pharmaceutical innovation is best measured by the number of NMEs introduced is in itself questionable. Cockburn (2006) has convincingly argued that focusing solely on NMEs as the primary measure of pharmaceutical innovativeness is fundamentally incorrect:

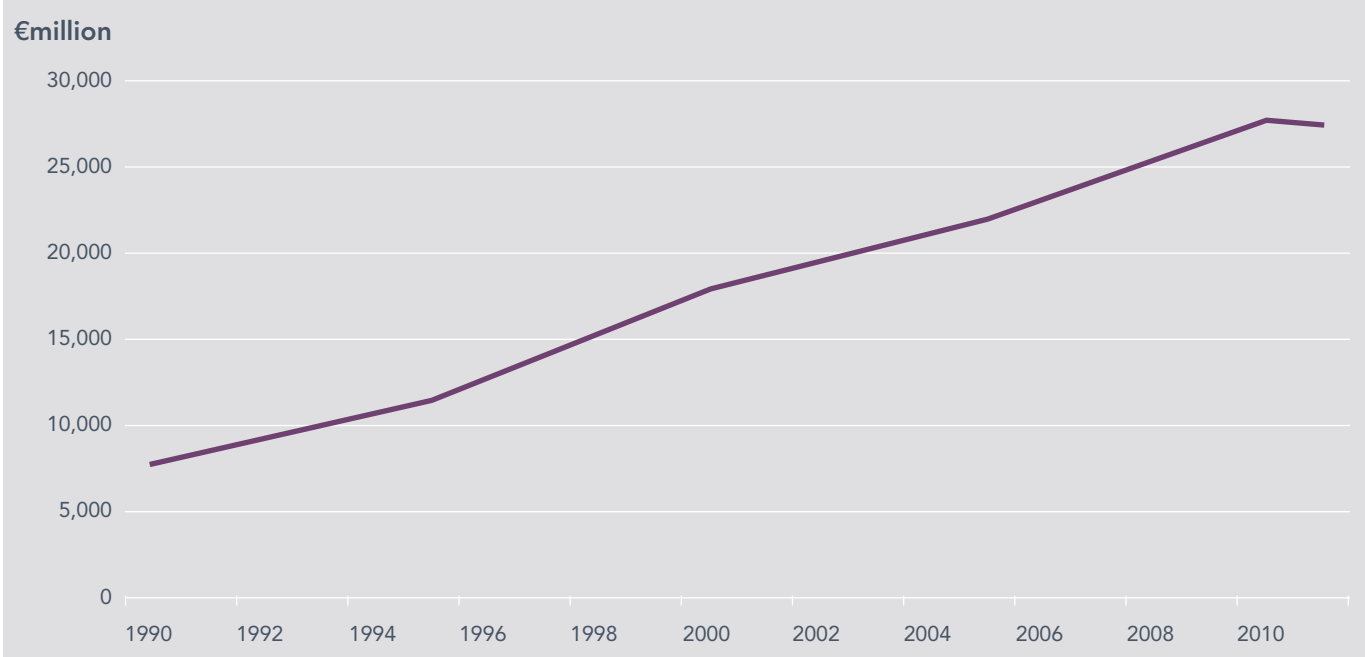
*"Drugs vary significantly in their scientific significance, health impact and economic value. This heterogeneity in "quality" of drugs means that simple counts of NMEs may seriously mismeasure R&D performance. Blockbusters with more than \$1billion in annual U.S. sales, for example, are given equal weight to newly approved drugs that achieve only \$50million in annual U.S. sales, and drugs which represent a major advance in the treatment of disease are given the same weight as the "me-too" products that appear in their wake."*²²

It is also worth asking whether this recently observed decrease in the output of new medicines is a synonym for pharmaceutical industry's low investment in R&D. In fact, the answer is a resounding "no". The total amount of R&D expenditure in Europe in the period 1990-2010 more than tripled (see Figure 4).

But how is it possible that increased R&D expenditure does not translate to a higher number of approved NMEs? The answer is, in fact, simple: a steady increase in the capitalised cost of developing a new drug over the past 30 years. In 1979, the total cost of developing and approving a new drug stood at \$138m. Almost 25 years later, in 2003, this figure was estimated by DiMasi et al (2003) to have sky-rocketed to a stunning \$802m.²⁴ And a more recent estimate by Mestre-Ferrandiz et al (2012) points to approximately \$1,506m (€1.2 billion).²⁵

FIGURE 4:

European R&D spending (€million) in Europe between 1990 and 2011²³



Source: EFPIA

TABLE 3:Capitalized cost per successful medicine (2011 US\$m), Cited verbatim from Mestre-Ferrandiz et al (2012)²⁶

INTERVAL	HYPOTHETICAL SPENDING (US\$m)	TIME FROM INTERVAL MIDPOINT TO 1ST CORE LAUNCH (YEARS)	BASELINE COST OF CAPITAL	CAPITALISED SPENDING PER SUCCESSFUL MED (US\$m)
1: Pre-1 toxicity dose	76.5	9.6	11%	207.4
2: 1st toxicity dose to 1st human dose	86.8	7.2	11%	184.1
3: 1st human dose to 1st patient dose	149.5	6.2	11%	284.0
4: 1st patient dose to 1st pivotal dose	316.9	4.4	11%	501.6
5: 1st pivotal dose to 1st core submission	235.9	2.1	11%	293.8
Launch	33.3	0.5	11%	34.9
Total	899.0			1,506

The different estimates reflect variations in the four main cost-factors of R&D: out-of-pocket costs, success rates, development times and the cost of capital. To give a concrete example, the most recent estimate of the cost of bringing a drug onto the market by Mestre-Ferrandiz et al (2012) assumes a lower overall probability of success for clinical trials than that reported by DiMasi et al (2003), which in part explains the higher estimate for the overall cost of R&D. And this analysis was conducted before the current discussions on transparency of clinical trials in Europe which is likely to increase the costs and reduce the attractiveness of conducting European trials even further.²⁷

Table 3 contains the breakdown of the components of capitalized cost per successful medicine as presented by Mestre-Ferrandiz et al (2012). It is interesting to highlight the observation that the different stages of R&D do not contribute equally to the composition of total cost. For example, clinical trials from Phase I to III (intervals 2 to 4 in Table 3) account for approximately two thirds of the total cost of bringing a medicine to the market, even though they do not represent the longest period of drug development.

Given the high share of total costs attributable to clinical trials, it is worth exploring them further. It is a fact that the probability of success has decreased, but this is not the only reason for the increased cost. Regulations governing clinical trials in terms of generated data requirements have become more detailed and demanding in recent years.²⁸ The complexity of conducting new clinical trials and collecting important data for regulatory bodies now therefore demands a higher level of investment by biopharmaceutical companies.²⁹ This may be dangerous for the viability of some R&D projects, given that these are highly risky, lengthy and costly processes. In this sense, Pharmaceutical Portfolio Management (PPM) has become critical for biopharmaceutical companies. PPM originated from the necessity to identify the optimal portfolio in terms of value creation for a given set of constraints. For this to happen, companies are bound to make trade-offs among: (1) maximizing expected economic returns, (2) minimizing risk, and (3) maintaining product-mix diversity. And while the rationale for PPM makes complete sense, the pressure put on the biopharmaceutical industry through lower revenues may result in such extreme trade-offs that the withdrawal of projects with potential to generate added value may become inevitable.

Negative effects of cost-containment and decreased biopharmaceutical industry revenue

Even though the overall effect of many of the P&R measures used in EU Member States is still unknown, the use and intensity of these policies demonstrates that both the present and future developments of the biopharmaceutical industry are tightly linked with the overall P&R environment in Europe and globally. P&R policies have a direct and significant impact on all stakeholders in any health system – patients, providers, payers and the biopharmaceutical industry. After income and healthcare needs, the regulatory framework of pharmaceutical markets largely determines the level and quality of pharmaceutical spending.

Many academic and international studies have discussed the “double-edged sword” of P&R cost-containment policies by emphasising the negative impact these measures can have on incentives for innovation and access to medicines. A paper by Atella (2000) evaluated the long-run effects of the minimum reference price as a cost containment policy, concluding that this policy does not tackle the fundamental drivers for high expenditures, being unable to change the overall upward trend in public and private expenditure over the long run.³⁰ In another study by Vernon (2005), the author explored the relationship between price regulation of medicines and investment in pharmaceutical research and development, finding that regulating prices results in reduced cash flow and reduced expected profitability for companies, leading to a decline in R&D investment of between 23.4% and 32.7%.³¹ Healy (2011) uses comparative case studies of the US and Europe, drawing on a meta-analysis of existing empirical data to estimate that EU countries have lost \$4.96 billion in R&D spending, failed to discover 46 new medicines and sacrificed 31,925 R&D jobs between 1986 and 2004 as a result of price regulations. Moreover, his paper also calculates that if price regulations were to be introduced in the US, by 2060 European (and American) life expectancy would be reduced by 0.7 years (2.8%).³² In another pertinent and more recent example, Karanikolos (2013) examines the extent to which P&R austerity measures and cuts to public healthcare budgets in Greece, Spain

and Portugal have affected the health system, public health and patients in those countries. Establishing a comparison with Iceland – a country which suffered a similar financial shock but did not impose similar austerity style cuts – the study concludes that austerity-based P&R policies have been responsible for deteriorating health outcomes.

This body of evidence and literature on P&R measures can be further divided into core themes and areas of policy. For instance focusing on reference pricing systems, Kaló (2007) showed that TRP policy introduced in Hungary in 1 September 2003 accounted for 55.9% of statin market growth between September 2003 and March 2004.³³ In a different study, Kaló (2012), also found that TRP may not only influence clinical decisions of the prescribers, but, if based only on the daily therapeutic costs, may also entail additional expenditure for the payer if costs of changing medication are taken into account.³⁴ Brekke (2007) used economic modelling to show that if market entry costs are high, therapeutic reference pricing may have a worse outcome than both generic reference pricing and no reference pricing – once TRP provides the lowest profits to the patent-holding firm, innovation and entry of the new drug treatment are least likely under this scenario.³⁵

Ekelund (2003) used economic modelling to conclude that regulating prices in the pharmaceutical market results in higher relative launch prices and falling real prices over time, also finding evidence to support the view that price regulation discourages price competition between brand-name drugs.³⁶

One more matter that potentially disrupts the balance of pharmaceutical prices is parallel trade. Kanavos (2005) estimated that introduction of parallel trade brings the most benefits to distributors, whereas the branded pharmaceutical industry bears most of the losses. As such, in an R&D context which is primarily dependent on private investment, decreased revenue due to parallel trade does not contribute to a healthy panorama for pharmaceutical innovation.³⁷ Finally, Danzon (2003) used economic modelling which indicated that in the EU the risk of parallel

trade and price spill-overs has an impact on manufacturers' decisions to launch a drug in a given country. The model used suggests that countries with relatively higher rates of parallel exports (Italy, Portugal, France, Belgium, Spain and Greece) and strict pricing regulations tend to see fewer product launches.³⁸

To conclude, although this is a small sample, the cited evidence and studies show how European P&R policies have had – and continue to have – negative effects on innovation and access to new medicines. The following sub-section will turn to the question of what effect this has had on the research-based pharmaceutical industry.

Is the research-based pharmaceutical industry moving away from Europe?

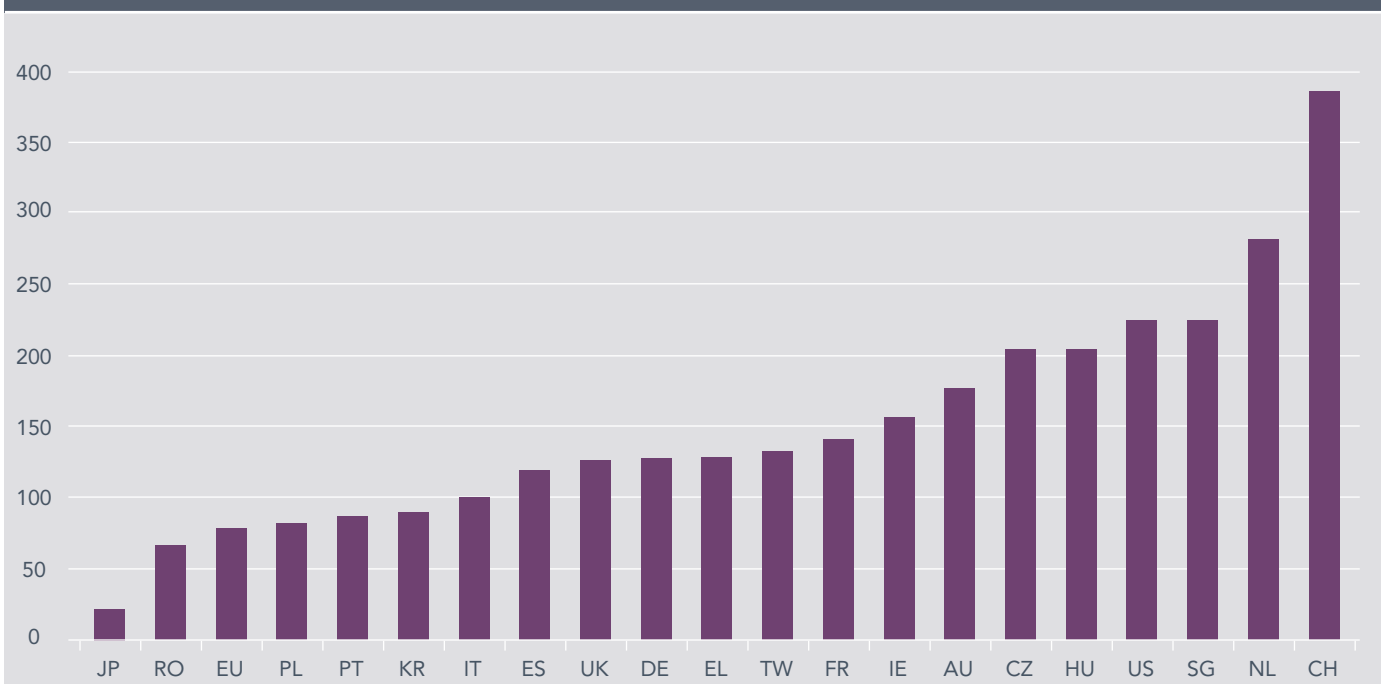
Looking at clinical research the answer seems quite clear: the number of applications for clinical trials fell by 25% from 2007 to 2011, with the majority of this decrease being observed between 2010 and 2011.³⁹

It also seems that Europe is falling behind as a competitive biopharmaceutical environment for the realization of clinical trials. The EU-27 average (together with Switzerland and Norway) is well behind other high-intensity innovation hubs such as the US and Singapore. Furthermore, if we take a closer look at Figure 5 below, it is discernible that, even higher intensive R&D countries within the EU such as the UK, Germany, or France are lagging behind.⁴⁰ In Europe only Switzerland and the Netherlands are true world-beaters.

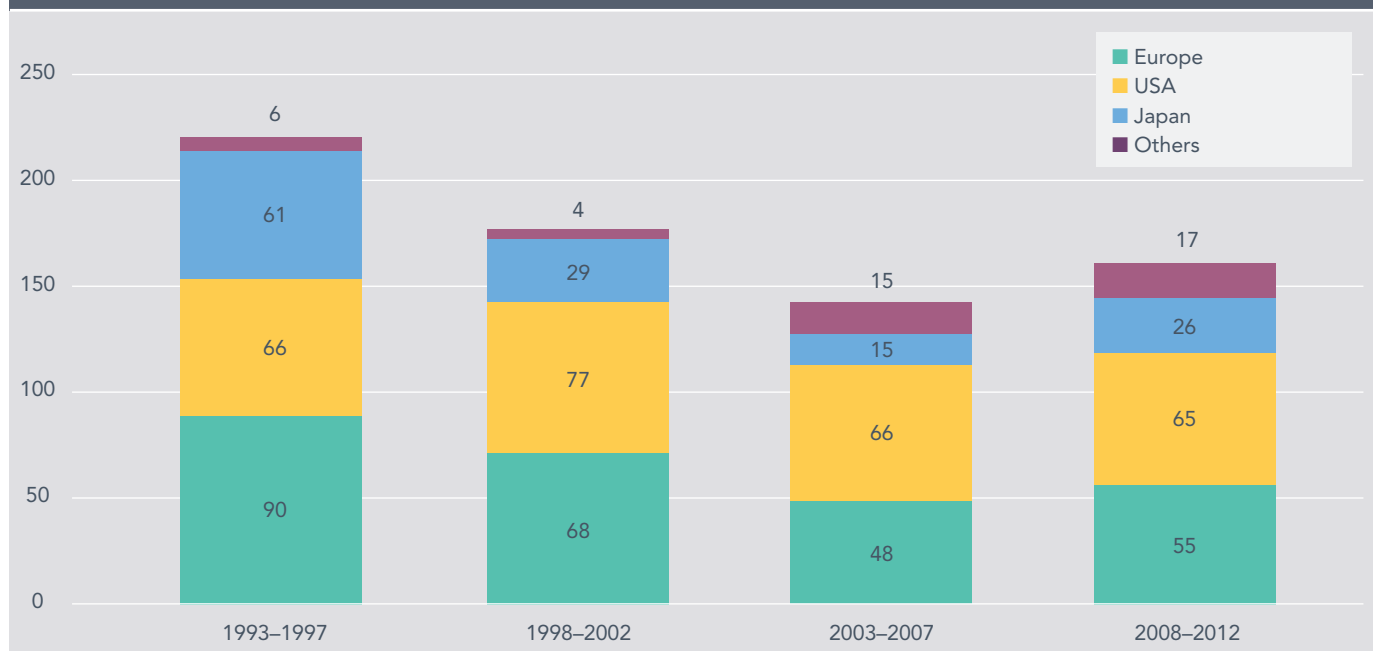
Conscious of this situation, the European Commission is now putting its efforts into issuing a new Clinical Trials Directive. This initiative aims to decrease the costs and increase the efficiency of clinical trials through centralized procedures. These measures are strongly supported by industry, researchers, and patients, who see the Directive as an opportunity for accomplishing the re-launch of EU as an important hub for the conduct of clinical trials.

FIGURE 5:

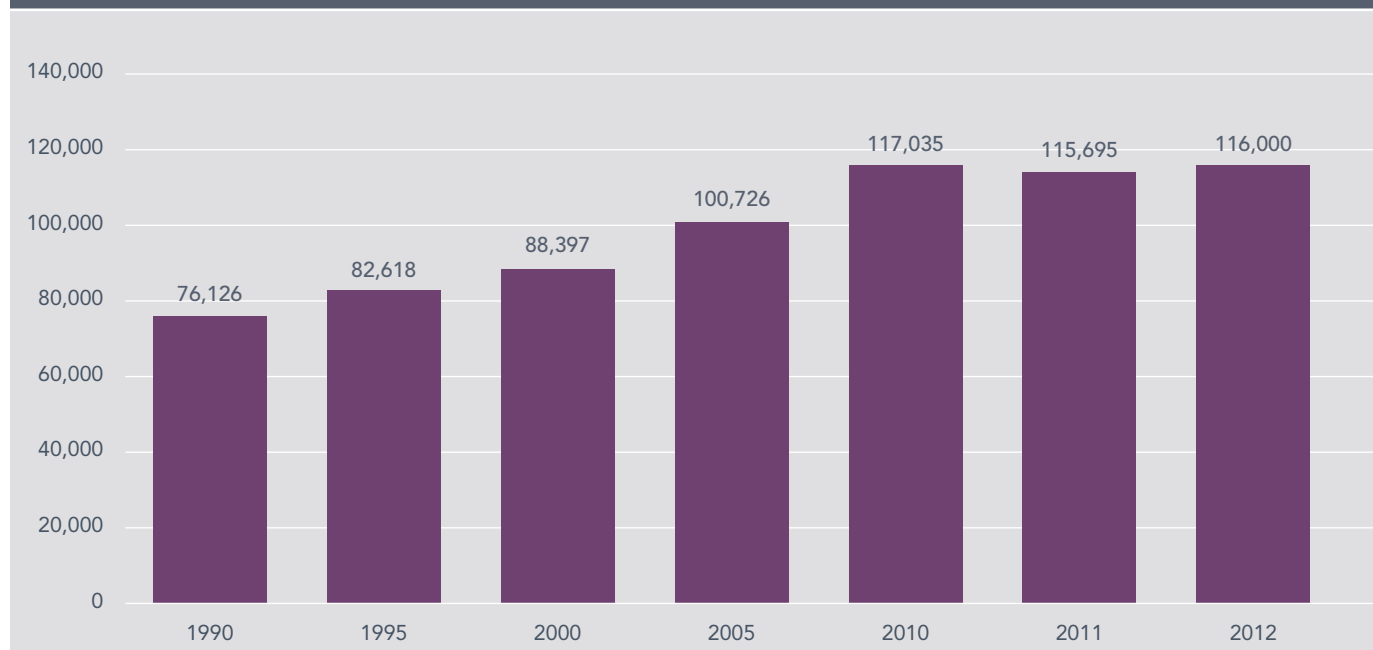
Number of CTs per million inhabitants⁴¹



Source: clinicaltrials.gov

FIGURE 6:Absolute number of new chemical or biological entities approved (1993-2012)⁴²

Source: EFPIA

FIGURE 7:Number of employees in pharmaceutical R&D in Europe (1990-2012)⁴³

Source: EFPIA

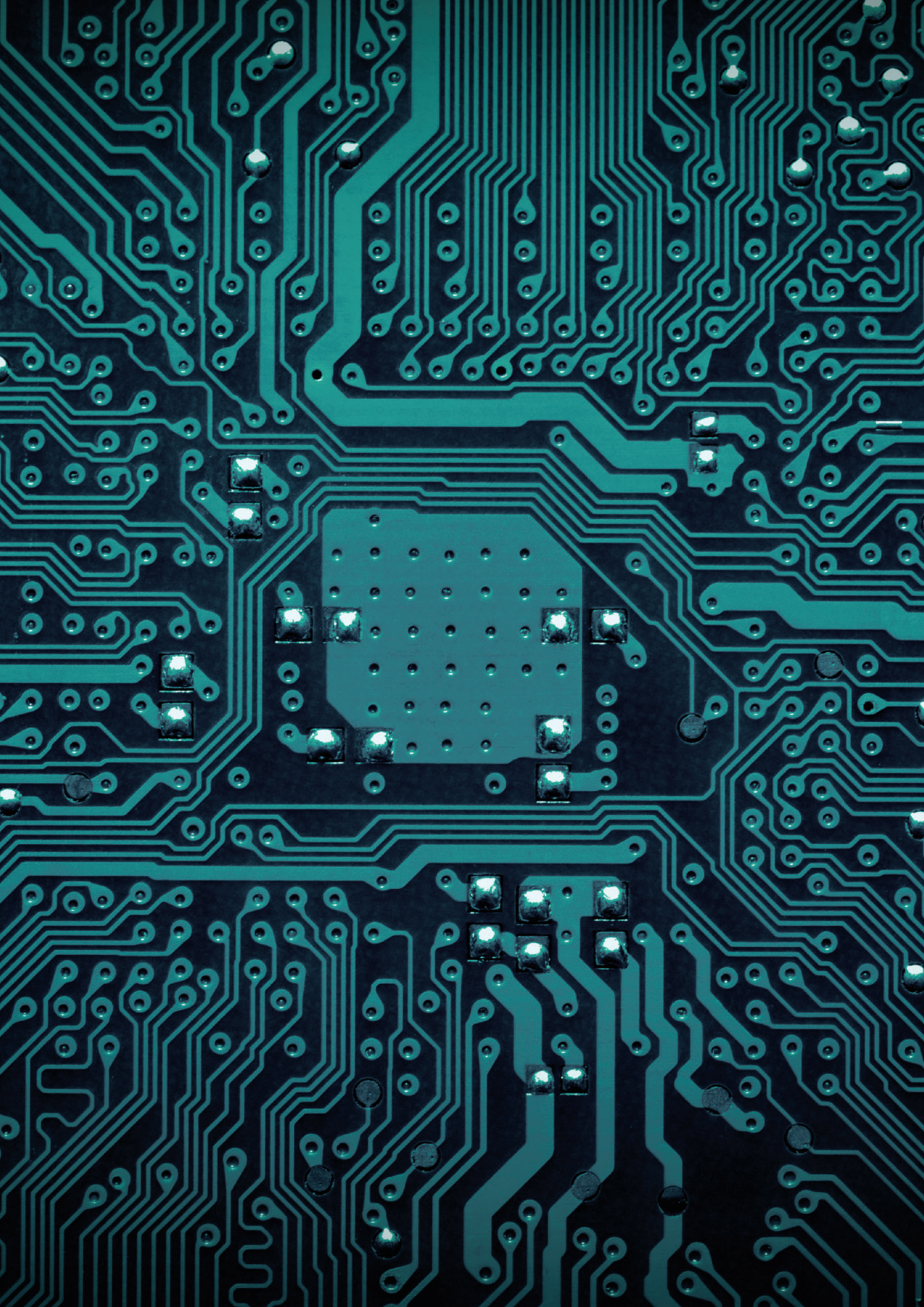
In addition to a weak level of clinical trial activity the EU and Europe more broadly has also seen an absolute and relative drop in the number of new chemical and biological entities approved. Figure 6 shows the number of approvals between 1993 and 2012.

Not only on an absolute basis but also percentagewise Europe has seen its preponderance as a main centre for the introduction of new chemical or biological entities decrease. Europe saw its share of new chemical or biological entities approved globally decrease from slightly over 40% in the period 1993-1997 to below 35% in the recent period 2008-2012. As opposed to the downward trend in Europe, the category 'Others' almost quadrupled its share of new chemical or biological entities approved, surpassing the 10% barrier in the period 2008-2012.

Looking at employment in the pharmaceutical industry in Europe there has also been a noticeable slowdown. Figure 7 shows a decrease in the number of R&D employees between 2010 to 2011, for the first time since

1990. And despite a slight recovery from 2011 to 2012, caution must be taken when assuming that Europe is already on the right track.

This section has provided an overview of what the biopharmaceutical environment in the EU and Europe looks like today and what the historical trajectory has been both for European health systems as well as the research based pharmaceutical innovators operating in them. From the evidence examined – whether it be the twin pressures of decreased income for industry through the increased use of P&R cost-containment policies and higher R&D costs; lower clinical trials activity; falling number of medicines introduced onto the EU market; or the drop in the number of employees in pharmaceutical R&D in Europe – it is clear that the fundamental drivers of biopharmaceutical innovation and dissemination of those innovations is under serious strain. Can this negative trajectory be arrested or reversed? In the next section, we have devised and outlined two potential scenarios which look at how this innovative future may unfold.



3



TWO SCENARIOS – ‘SUSPICIOUS MINDS’ AND ‘CONVERGENCE’

This report defines two distinct scenarios for the future of biopharmaceutical innovation in Europe. We have called them ‘Suspicious Minds’ and ‘Convergence’.

The intention is to create a thought-provoking exercise about the possible evolution of healthcare innovation, access to new medicines and treatments, and the future financing of healthcare systems in the light of different possible external dynamics in the EU. In other words, how can both policymakers and the research-based pharmaceutical industry prepare for a series of ‘what ifs’ by re-thinking, and even challenging, common assumptions and perceptions?

The first scenario, which we have called ‘Suspicious Minds’, is based on an evolution of some of the existing dynamics and trends in European healthcare policy described in the preceding section, even if they are eventually pushed to the extremes in the final four-year period. Using specific data and examples from section 2 to illustrate what the trends are now it is possible to then look at and imagine how these may be pushed to their limits over time.

In the second scenario, called ‘Convergence’, we imagine a much rosier picture in which there is much greater co-operation and collaboration between the public and private sectors. This scenario is, however, much more ‘futuristic’ in attempting to imagine a healthcare paradigm shift which has mostly not yet occurred in Europe (and, indeed, may not ever occur in reality). Empirical data and case studies which might support this type of scenario are necessarily scarcer with the result that the ‘Convergence’ scenario is much more illustrative and less concrete than the ‘Suspicious Minds’ scenario. Despite this, an attempt has been made to find examples of healthcare innovation – be it in delivery, financing or other forms of partnership (including in other areas of public service delivery such as education) – which support the notion that the ‘Convergence’ scenario forms one picture of a credible and possible future for healthcare.

As explained above in section 1, in order to consider the concepts of innovation, access to healthcare technologies and financing in a fresh light some of these different possible assumptions and scenarios are pushed to the extreme ends of the spectrum for the purposes of discussion and for the sake of provoking new thinking.

THE TWO SCENARIOS ARE DEFINED AS FOLLOWS:

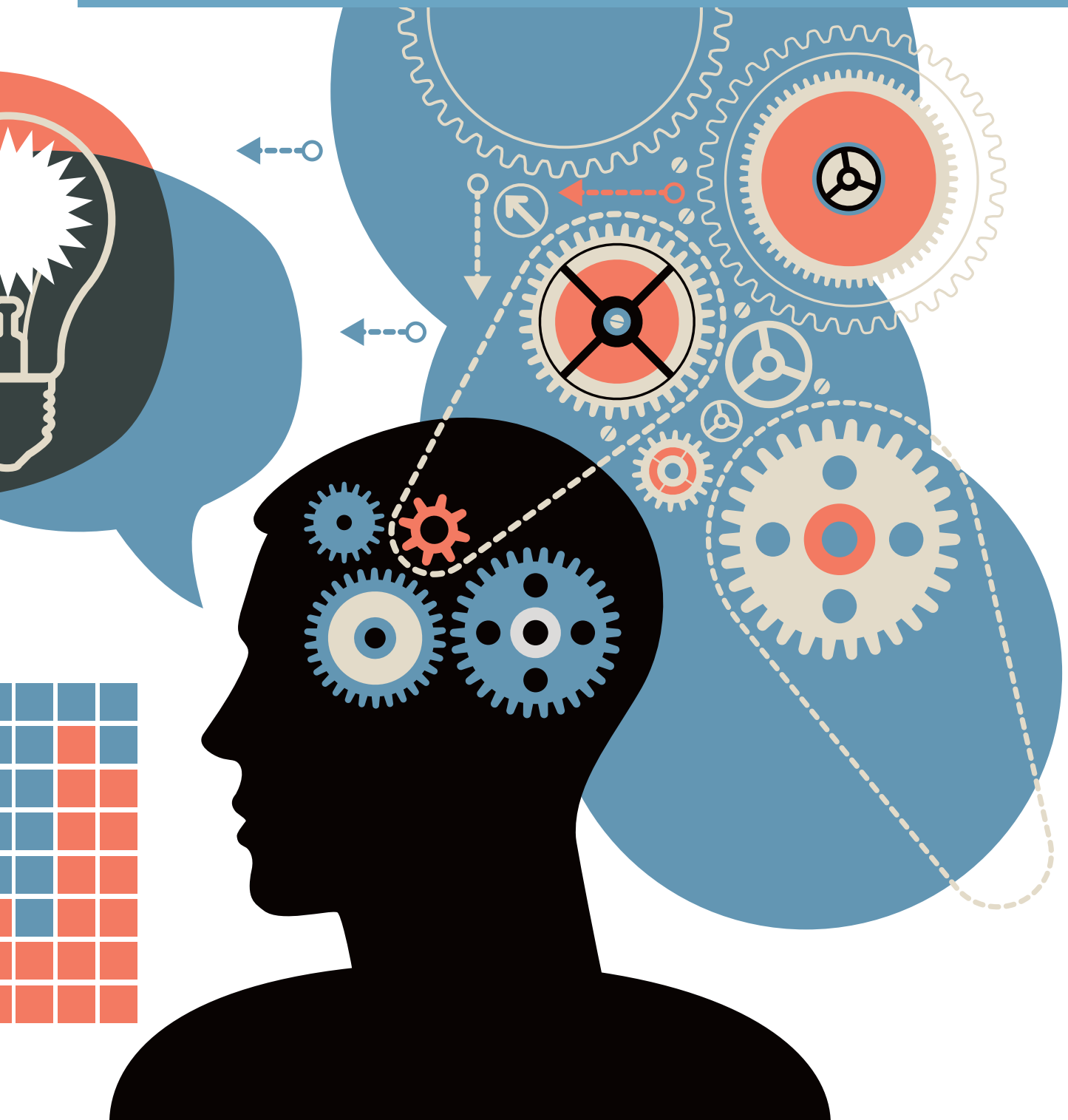
1. SUSPICIOUS MINDS

In this scenario, the EU inherently believes that the pharmaceutical industry is part of the problem when it comes to innovation. In other words, policymakers' view is that medicines are now too expensive and not innovative enough. We begin with a bureaucratic scenario and then move into an 'innovation freeze' before ending up after 12 years with a process of so-called 'closed circuit innovation', a more extreme extension of the scenario in which the EU decides to try to take future biopharmaceutical research into a publicly-funded, publicly-conducted domain.



2. CONVERGENCE

In this more collaborative and optimistic scenario, we describe how the pharmaceutical industry and the EU are working together to enhance areas of strength and deal with areas of weakness. In some areas and countries patients are now using their own out of pocket finances to top-up their funds or governments are beginning to introduce systems of complementary or supplementary insurance. A greater degree of innovation is taking place in healthcare system processes as well as via the introduction of a more holistic delivery of healthcare services. In this scenario, where the public and private sectors tend to co-operate and partner in a variety of ways, the overall healthcare system is strengthened with a greater supply of funding and a more efficient and innovative use of treatments to the ultimate benefit of patients and the public.



SCENARIO 1 – SUSPICIOUS MINDS

PERIOD 1 (1-4 years)

The Suspicious Minds scenario makes the following assumptions in its first four years:

1. The EU region is not happy with the current level of biopharmaceutical innovation and believes it has to “guide” companies to the correct priorities
2. The EU region issues a wish-list of “worthy” innovations
3. The EU region is not willing to pay for failures, only for what it deems to be successful innovation
4. The EU region prioritises disease areas based on its own assumption of what is important to society
5. Follow-on innovations are considered incremental and in most cases redundant



WHAT HAPPENS IN THE EU REGION (Years 1-4)?

Based on the ongoing trend towards harsher rationing and P&R policies as outlined in section 2, EU governments decide to allocate more resources to process innovation i.e. investing public money in new management models, better compliance, and systemic efficiency measures. Overall the EU still believes in converging into fewer areas of priority research, for example, focusing on research into the most important disease areas such as oncology and diabetes.

As time goes on, the EU region no longer sees real value in the new treatments being developed by industry and becomes even more selective about the medicines and treatments it chooses to reimburse. Disparities increase between certain disease areas, which are fully reimbursed, and others which are not.

By the end of the period the EU region reaches an ‘innovation freeze’. New gaps arise in access to medicines between the private market and the public healthcare system.

However, while public expenditure on new medicines is declining fast, patients are forced to buy most new technologies from their own purse leading to a growth in out-of-pocket spending. Health systems also face increasing pressure in non-pharmaceutical areas when older and less sophisticated medicines and treatments potentially lead to more frequent hospitalisation and need for medical care through, for example, the administration of the medicine. There is also a rise in the costs of other public services and facilities such as social welfare services which take on the extra responsibility of dealing with the consequences of the rising (and sometimes unmet) healthcare needs and demands of the public. Patients who are unable to finance medicines which they need and which are no longer reimbursed through the public system need to find money or care elsewhere. As a knock-on effect they are forced to turn to charities, local government services and other forms of support to help meet their ongoing day-to-day needs.



WHAT HAPPENS TO INDUSTRY (Years 1-4)?

Industry continues to pursue its own areas of R&D initially as well as tackling the government-chosen priorities. However, income levels start to decline as profits have to be re-invested in the business to support the shift in emphasis on selected disease areas. A steady trickle of new pharmaceutical innovations is produced but companies now specialise very heavily in government-directed or so-called ‘bureaucratic innovation’ with priorities decided by an arms-length Health Technology Assessment (HTA) body. Only a selected few therapeutic fields are considered to be commercially viable and dominate the stream of research and development. Yet as a whole, income from

the EU markets is dropping, which forces the industry to restructure itself towards only its core EU business priorities. After four years, interest in the launch of new innovations in the EU is declining while priority areas are saturated. Generic entry is also picking up as many of the primary products are losing their exclusivity.

Income rises slightly from the growth in the private market, which still demands new treatments. Yet overall income is down against previous periods due to the decline in public reimbursement.



WHAT HAPPENS TO THE PUBLIC (Years 1-4)?

The public do not notice much of a change in access to medicines over the first four years and remain supportive of government policy, although there is a slight growth in OOP payments for new medicines and treatments, which begin not to be available within the public system. Eventually, however, the public and, in particular, a vocal set of patient groups start to become aware of shortages, rationing and inequalities between disease areas. Access via the public system decreases as only the priority areas secure new funding so the private market develops more rapidly for those who can afford it. Disparities widen between different groups not just based upon income but also upon the type of condition they suffer from. Access declines further as only priority areas are now covered. Follow-on innovations are not reimbursed either. The private market increases and an 'access freeze' occurs for everything except the government-chosen list. There is significant dissatisfaction from the public in the face of systemic and bureaucratic failures as the system appears to 'feed itself' as opposed to serving the patient.

PERIOD 2 (5-8 years)



WHAT HAPPENS IN THE EU REGION (Years 5-8)?

In the middle period of the 'Suspicious Minds' scenario in the EU region, we reach an 'innovation freeze' where the level of technological innovation is static. Public expenditure is also static (yet declining in real terms). Meanwhile, greater resources are allocated towards efficiency models, such as trying to make hospital management processes more efficient.

The use of new pharmaceutical technologies in the EU also begins to lag behind compared with other areas of technological innovation. Public expenditure rises in the face of new healthcare needs and challenges that are unmet by new products and treatments, and which are currently not reimbursed in the EU area. More resources are allocated to hospital care, support programmes, complementary medicine, health promotion programmes, etc. all of which aim to deal with new healthcare challenges in the absence of new pharmaceutical treatments.



WHAT HAPPENS TO INDUSTRY (Years 5-8)?

In the face of a freeze on public reimbursement for a growing number of its products, equating to a drastic fall in its income, industry is less interested in launching new products for the EU market. Instead it invests in support platforms to maximise the commercial potential of existing products in the EU market. Efforts to develop and launch new products now take place outside the EU, including the re-location of research facilities. Industry's income in the EU is declining rapidly, also due to generic competition. As patients begin to spend significantly more money out-of-pocket to gain access to treatment, income begins to rise steadily from private sources (e.g. via the growth of the private insurance market and self-payers) and industry cautiously begins to launch a limited range of new products on the understanding that they have a clear commercial horizon in the EU. At the same time, industry focuses on terminating its large-scale

R&D operations in the EU, both in the basic and in the clinical phases. As the growth of the private market continues, industry begins to invest more significantly in niche markets and populations in the EU. However, the EU becomes a 2nd line market, i.e. products are being introduced in the EU only after they are launched in other countries. Industry has a more predictable, though limited, income stream from the EU market, yet not enough to justify re-investment in R&D in the EU.



WHAT HAPPENS TO THE PUBLIC (Years 5-8)?

Access to new medicines and treatments levels off in the face of public expenditure cuts but patients make the most of what they can get from the public system while standards are still reasonable. Over time, OOP expenditure starts rising as patients realise access is severely limited in the public system and start to contribute their own funds to get the treatments and medicines they want. Access increases for those who are able to pay for it privately. Public opinion starts to focus on gaps in treatment and on the failure of the welfare state to treat patients on an equal and reasonable basis. By the end of the 4-year period, OOP expenditure goes up more rapidly as a new private market grows. Access to the public system becomes poor with only out-dated treatments now available. The universal system breaks down. Public opinion leads to a political crisis and the government is under severe pressure to re-think its strategy.

PERIOD 3 (9-12 years)



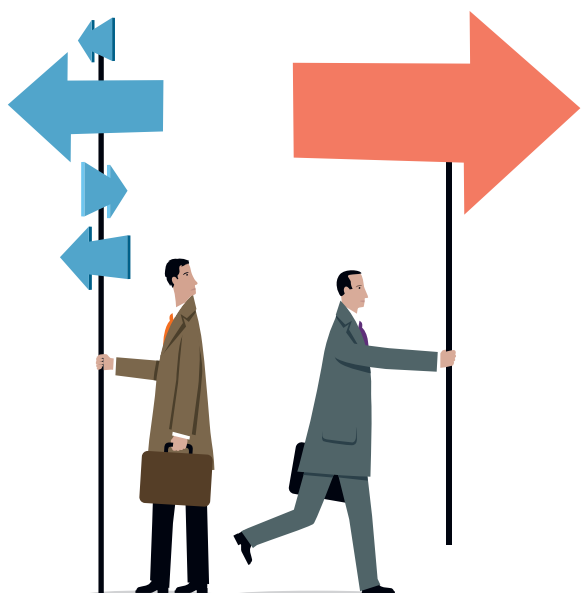
WHAT HAPPENS IN THE EU REGION (Years 9-12)?

Private sector innovation flattens out as industry is unsure of its future role and level of income. Public expenditure rises significantly since governments need to invest in their own R&D facilities to develop the new technologies of the future. The political consensus is that the increased investment from the public purse will produce more innovation at a lower cost. The public also appear convinced that this course of action is the right thing to do and largely support the Government's approach. After a while, innovation picks up slightly but mainly from publically funded contracts and only on a limited set of products and treatments, as prioritised by Government. Both taxes and public expenditure rise sharply as the cost to Government of conducting its own R&D becomes bureaucratic and time-consuming. Government redoubles its effort to produce more cost-efficient committees and innovative processes. By the end of the period, innovation starts to decline sharply as Government runs out of money and industry's income from private sources is now no longer sufficient to bridge the gap.



WHAT HAPPENS TO INDUSTRY (Years 9-12)?

Uncertain about the future climate for investment, industry only works on existing product lines in the EU and ceases new investment in blue sky R&D as well as on product launches in the EU, which it can no longer afford. A significant downsizing of industry occurs in the face of the huge drop in income. The climate steadily declines for technological innovation and income drops too as public funds are squeezed. Industry gradually leaves the EU region except for selected distribution of individual products, mostly generics. At the same time, industry is being approached by the Government to develop clinical activities, in which policymakers want industry to act as a service provider. Industry's income now comes only from selling existing



products or from specific commissions from Government. By the end of the period, the Government tries to court the private sector back via various heavily subsidised activities but industry is now very cautious about any further activities in the EU region.

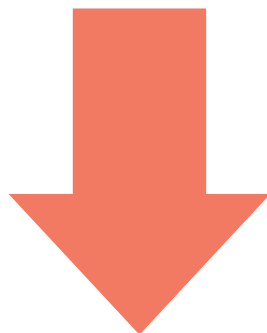


WHAT HAPPENS TO THE PUBLIC (Years 9-12)?

Access to new medicines and treatments via the public system levels off and OOP expenditure remains steady while patients adjust to the new system and wait to see what will happen. Access remains at a similar level for most patients but taxes rise significantly. Dissatisfaction gradually starts to rise in the face of the decline in service accompanied by higher tax bills. Those patients who want more expensive or

new treatments begin to pay more for them out of pocket but many cannot afford to do so given their increased tax costs. By the end of the period, the financial burden of the system on the public increases. Taxpayers balk at what they view as yet another industry being propped up by the public's efforts as banks were during the financial crisis. Public sentiment grows for Government to offload its high level of risk, bringing the private sector back into the business of innovation. The private insurance market for biopharmaceuticals grows rapidly but not enough to keep most companies from deciding to leave the EU region.⁴⁴ The period ends with the biopharmaceutical industry mostly moving its activities outside of Europe and into other priority markets and with a public deeply dissatisfied with the state of the healthcare system and politician's ability to reform it.

Problems Rationing
Freeze Bureaucratic
Closed Circuit Dissatisfaction
Decline Inequalities
Disparities Shortages



SCENARIO 2 – CONVERGENCE

EXPLANATORY NOTE

First it may help to clarify some of the assumptions that inform the upcoming scenario, especially since such a scenario is more futuristic and may be harder to envisage than that outlined in ‘Suspicious Minds’. So, for example, what does ‘partnership’ under the Convergence scenario really mean? Sometimes there is suspicion of the word partnership – especially in healthcare – since partnership has a number of different interpretations. When we talk about partnerships below we may be talking about any type of collaborative approach between the public and private sectors (NB – the private sector can also be taken to include not-for-profit organisations, patient groups and other third parties not simply private companies).

On the research side, such partnerships may include public funding being directed towards stimulation of a better environment for innovation to flourish (a modern form of industrial policy), or indeed the private sector building stronger research partnerships with public bodies like universities or government-funded research councils. On the supply side, different forms of partnership might arise which support better funding for the provision of healthcare itself (such partnerships in and of themselves represent an innovative approach as well as increasing the pot of funding which might pay for new healthcare technologies – a so-called ‘win win’ situation).

The ‘Convergence’ scenario works from the following assumptions throughout the whole 12-year period.

Each of these factors develops gradually over the period, accelerating in the latter stages as partnerships become better established and more successful:

1. The EU region works in full partnership with the private sector
2. There is an understanding that the innovative process entails failures as well as success
3. Flexible financing models exist for healthcare based on both public and private sources
4. Competition between products allows for greater patient choice as well as price considerations by individuals
5. The EU region prioritises the allocation of a ‘safety net’ of healthcare resources to its less privileged population who can’t pay out-of-pocket

PERIOD 1 (1-4 years)



WHAT HAPPENS IN THE EU REGION UNDER CONVERGENCE (Years 1-4)?

In the initial stages of the scenario, a new mindset is emerging which realises that the old way of thinking about healthcare innovation is not working and that new forms of investment and financing are needed if European healthcare systems are to continue accessing the latest medicines and treatments. As a first step, policymakers begin to increase government investment and support for basic and clinical R&D (such schemes exist today, for example, under the Horizon 2020 framework).⁴⁵ Under such partnerships, the EU provides public money not only to support the overall science base but also to help commercialise new innovations, support the use of key technologies and provide greater access to capital and support for SMEs, generally aiming to create a supportive and ‘nurturing’ environment where private sector innovation can flourish more easily.

As the scenario develops momentum towards the end of the first 4-year period, policymakers begin to think more radically about how to shift the healthcare system into a new dynamic. Industry also becomes more confident about the likely success of such partnerships. As trust between all the parties increases, other types of partnership come into effect not just in terms of partnerships between Industry and Government to help create new medicines but also between Government and patients to pay for the costs of treatment. This is seen by the public as much more radical – especially in EU countries which have been used to a single payer or publicly-financed model. New pricing and reimbursement policies come into effect which give patients greater flexibility and choice in terms of how they pay for healthcare. The patients of the future are permitted to top-up government funds using a personal healthcare budget or health savings account. Such HSAs represent an innovative means of supplementing essentially government-funded systems and already exist in Singapore and the US.

Other countries pursue a more fundamental set of reforms, looking at examples of international best practice in healthcare financing and outcomes. They start to look to countries such as Switzerland, which already operates a sophisticated form of social insurance in healthcare, mixing elements of both public and private financing and provision but with a much higher degree of patient choice and competition between providers and insurers.⁴⁶

Policymakers similarly look to other areas of policy to inform their arguments and help to convince the public that healthcare is no more of a special case than, say, education where there has already been more opportunity to experiment with consumer choice and hybrid public-private financing models.^{47, 48}

With the help of such initiatives, innovation increases steadily as governments become more supportive towards the notions of choice and competition in public services and start to support private sector R&D efforts with new funding opportunities and partnership arrangements as well. Over the period, the EU both considers and then develops a more

hybrid model of financing of healthcare technologies based on combining public expenditure with private investment via a mix of top-up models, innovative insurance schemes and more sophisticated outcomes research as well as long-term epidemiological analysis.



WHAT HAPPENS TO INDUSTRY (Years 1-4)?

Industry continues to invest in new research and development efforts and looks to encourage and persuade policymakers to work to create more sustainable, long-term partnerships to finance alternative models and to provide supplementary levels of finance as well as on the supply of service innovation in addition to existing products. Medical device companies, for example, begin to also advise hospitals not just on the use of their products but on how the whole operation of the hospital can be modernised and made more efficient to maximise the value for money of the product for a particular condition or disease area, using a pathway of care.



WHAT HAPPENS TO THE PUBLIC UNDER CONVERGENCE (Years 1-4)?

The public does not initially see a dramatic change in the supply of new technologies or in healthcare budgets. However, patients are starting to be offered a greater choice of products and flexibility in the way they are treated and being offered ideas of new way to pay for healthcare. Initially sceptical, some patients nevertheless begin to experiment with new approaches or are asked to take part in pilot schemes with varying degrees of success.

PERIOD 2 (5-8 years)



WHAT HAPPENS IN THE EU REGION (Years 5-8)?

The EU region is able to deal more effectively with shifting paradigms and healthcare needs by being able to access new breakthrough technologies including in new diseases areas or conditions that were not previously identified as priorities. Health care and pharmaceutical expenditure increases but in a more predictable

manner which also allows for consistent allocation of resources towards systemic and service innovation.

Innovation in the EU area surges as both public and private sector maximise all new opportunities for successful R&D efforts. Governments now start to prioritise the health sector not only as a public good but also as a means of generating new sources of economic growth. Under the scenario, industry and policymakers also begin to develop a range of more collaborative models of working aimed at boosting innovation. For example, both policymakers and industry take much greater interest in developing the type of pilot projects, which already exist today, such as the Innovative Medicines Initiative (IMI). The IMI is self-described as “Europe’s largest public-private initiative aiming to speed up the development of better and safer medicines for patients. IMI supports collaborative research projects and builds networks of industrial and academic experts in order to boost pharmaceutical innovation in Europe.”⁴⁹ The effort is a joint collaboration between the EU and EFPIA. A likely development under the Convergence scenario would be greater allocation of EU monies to expand such schemes or the development of additional and complementary projects which apply a similar approach.⁵⁰



WHAT HAPPENS TO INDUSTRY (Years 5-8)?

As innovation models gradually change, the pharmaceutical industry shifts into new disease areas and technologies, which are not necessarily based on the current model of delivering products but also on so-called service and platform innovations that seek to provide more holistic and comprehensive solutions to patients, based on more innovative services and use of existing IT solutions. Growth continues in the second period as new markets are developed further. This adaptation is supported by a more flexible financing model, which expands the overall pot of funding from both public and private sources. Industry becomes gradually less reliant on the public purse but still considers the EU market to be of significant value and worthy of investment in new R&D efforts.



WHAT HAPPENS TO THE PUBLIC (Years 5-8)?

As new innovative products and treatments reach the market, the public starts to shift its attitude towards the manner in which healthcare should be financed, realising there is a need for the creation of supplementary finance systems be it top-ups, HSAs or supplementary insurance products in order to make sure that Government can continue to provide a social safety net to support the poorest members of society. Public discussion focuses on the modernisation of this ‘social contract’ between government and taxpayers and on the concept of creating a risk pool. Access to healthcare technologies improves both under the public system, which supports innovation, and also under a steadily growing private market for value-added products as well.

PERIOD 3 (9-12 years)



WHAT HAPPENS IN THE EU REGION (Years 5-8)?

The EU is gradually shifting to a fully hybrid health care model in which innovation comes sometimes from the public purse, sometimes from the private market and also sometimes from a combination of both public and private instruments. In addition to more sophisticated means of funding R&D, there is a step change in attitudes to funding the healthcare system itself. Eventually there is a transformation in Europe from the old welfare model into a more dynamic and flexible model of financial management where consumers are in the driving seat. There is a growing recognition that strengthening competition and the role of the private sector in the provision of health services can lead to greater innovation in patient care as well as offering better value for money in the delivery of services.



WHAT HAPPENS TO INDUSTRY (Years 9-12)?

As the pharmaceutical industry sees the transformation of its innovative pipeline and research model so does it see a shift in the way in which it approaches reimbursement in the EU. Industry no longer sees the EU region as

a single payer system but rather as a market with multiple sources of income, which requires industry to change its business and marketing models and the manner in which it tries to launch new treatments. Income gradually decreases from the public purse but overall income from the EU market nevertheless increases as the result of the more mixed financing models of healthcare. After 8 years of successful collaboration there is both a growth in new products and income also shoots up as new avenues of research bear fruit and successful new markets open up.



WHAT HAPPENS TO THE PUBLIC (Years 9-12)?

The public have access to a much greater selection of technologies and healthcare financing models but are also willing to allocate their own money into more holistic schemes. The new focus is on 'bundles' or longer-term

healthcare and wellness 'packages' that reflect a more flexible and sophisticated view of the treatment process. The public see vastly improved access to new treatments in the public system and, convinced of the benefits, also continue to spend more out of pocket. Consumers become more empowered with new sources of information, new sources of healthcare savings or finance and with the ability to use new technologies such as health apps to stay on top of their own care and treatment.⁵¹ Care is more often provided in the home, with the support of medical professionals, or in an integrated care setting such as a polyclinic or other public facility, which provides a set of wrap-around social support services.⁵² By this stage the public's entire understanding of what is meant by 'healthcare' has undergone a fundamental paradigm shift and innovation of all kinds now takes centre-stage in a modern and dynamic healthcare ecology of the future.

Optimistic Collaborative
Holistic Paradigm shift
Working together Future
Radical Co-operation
Momentum Modern Dynamic
Partnership Efficiency





4



CONCLUSIONS AND FURTHER THOUGHTS

What does the process of creating these scenarios tell us about the approach that the pharmaceutical industry might choose to take to its interactions with policymakers both now and into the future?

The first conclusion that must be drawn from the process is just how difficult it really is to predict the future, especially when it comes to innovation. This lesson applies not just to the writers of scenarios or to policymaking but even to innovators and businesses themselves. We only have to remember the now infamous pronouncement of Ken Olson, president, chairman and founder of Digital Equipment Corp. in 1977 that “There is no reason anyone would want a computer in their home” or Thomas Watson, Chairman of IBM who apparently said in 1943: “I think there is a world market for maybe five computers.” Similarly, if we are looking for hubris, we might quote from a Western Union internal memo written in 1876 which said: “This ‘telephone’ has too many shortcomings to be seriously considered as a means of communication. The device is inherently of no value to us.”

Yet, foolhardy as it may seem to even attempt to gaze into the crystal ball of future innovation or indeed of future policymaking, without such efforts we may end up being even worse off. We may fail faster by not managing even to anticipate the future trajectory of the ongoing trends of today and how they may impact our innovative industries, let alone failing to predict the paradigm shifts of tomorrow.

Based on the stories we tell in these scenarios, there would seem to be two options for industry when it comes to its strategic planning for the future of healthcare policy in the EU. Without passing any judgement on its merits

or demerits, the ‘Suspicious Minds’ scenario is inevitably the more realistic of the two scenarios in the sense that it takes a set of existing trends and essentially extrapolates what might happen to these trends under an artificial set of external circumstances.

Were such a scenario to take place, it would suggest that industry is best placed to undertake a cautious approach to its future in Europe. The likely trend under this scenario is that pressures of all kinds intensify with the European healthcare environment eventually becoming really quite hostile to the innovative industry and to its ability to do business in the EU. Under these circumstances, the industry’s approach to dealing with policymakers is more likely to be one of damage limitation and an approach of maintaining whatever share of the market is viable to continue doing business in Europe, yet without making enormous losses.

Were the ‘Convergence’ scenario to develop, or even some elements of the scenario in some selected Member States (which may be a more realistic prospect) the approach by industry would need to be far more nuanced and sophisticated. Under such a scenario, relationships between industry representatives and policymakers would need to be built in a sustained and multi-faceted way over many years, gradually developing into a true partnership. Such relationships will rely on building trust, investing in research, creating new partnerships on a practical level including financing such partnerships and entering into a

degree of both financial and political risk. These are uncharted waters and the evidence from other sectors such as education which has tried this approach to some extent already, suggests that those who enter them will have to be both brave and bold, as well as extremely focused, to ensure they are successful.

The same rationale also applies to policymakers. Under the 'Suspicious Minds' scenario, policymakers are to some extent making up their own minds which societal objectives they want to achieve and assuming the industry will bend to their will, although they nevertheless cannot risk making policy in a vacuum without considering the impact it will have on the European economy and levels of innovation.

Under 'Convergence', however, there would need to be a cadre of policymakers willing to be much more entrepreneurial and dynamic in shaping and building the innovative healthcare systems and markets of the future through a conversation with the industry. Thought leaders in the policy space may need to be persuaded of the moral impetus for pursuing such an agenda, which may at times be politically unpopular and risky to their own reputations. Given the mounting challenges that Europe faces both in a broad economic sense and more specifically in the modernisation of its social welfare systems to meet current and projected demographic changes, it is clear that neither of these scenarios will be easy. And, of course, there are a myriad of other scenarios that may play out instead.

Is there one over-riding message that we should remember from these stories? The ultimate goal is to make sure that not only does Europe become a global hub for innovation in the life sciences and an economically successful trading bloc but also that the European healthcare systems of the future include us all.

Putting the patient at the heart of what every type of future healthcare innovation means will be key to successfully building that vision.

FURTHER THOUGHTS FOR INDUSTRY

- How can the industry redefine its value in a period of austerity measures so that it works in partnership with healthcare policymakers and builds long-term trust?
- Does industry need to work to change perceptions of what it can be expected to do from the perspective of social responsibility at a time of crisis?
- Are there better ways to establish collaborative partnerships between the public and private sectors, which would improve access to medicines but also allow industry to develop new sources of revenue to support innovation and longer-term growth?
- Can other sectors such as education provide examples for the healthcare industry to show that public-private partnerships can be effective and fair?

FURTHER THOUGHTS FOR POLICYMAKERS

- Do current healthcare policy decisions effectively take into account not only the short-term costs of medicine but also the longer-term value to society (quality of life, economic contribution etc.)?
- Is there enough 'joined up' thinking between healthcare and economic ministries when it comes to pharmaceutical policymaking?
- Are governments doing enough to support the science base and provide an environment where all forms of innovation can flourish?
- Are we good enough at defining what we mean by innovation and in what context?

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