

LIFE SCIENCE INDUSTRIES

EUROPE BETWEEN AMBITION AND WAIT-AND-SEE

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September 2013

The Institut Choiseul's
Strategic Papers

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Executive Summary

The financial and economic crisis, whose unremitting turmoil has disturbed and hindered global growth since 2007, has highlighted the solidity of the life sciences market. This apparent good health, however, masks divergent currents and a far-reaching shift in the balance of the market. Much more than the ageing of the population, the reservoir of growth lies in the emergence of new technologies, likely to increase the effectiveness of care and the performance of the health systems. Their spread leads to the creation of new markets or accelerates the growth of the existing markets.

Although for the moment, Europe remains competitive in this sector, it owes this more to its industrial and scientific heritage than to a new dynamism injected into it by Brussels or the Member States. The competitiveness of its industry, which has managed to adapt as well as it can to a changing market whose prospects remain promising, and the excellence of its academic research which goes back a long way, are by no means guaranteed. These advantages are fragile in an increasingly competitive environment. There is a high risk, as in other technology sectors, of being outdistanced by the United States or caught up by the emerging Asian nations.

In a globalised economic world, maintaining a competitive European life sciences industry is in fact a necessity and a factor for survival. This must involve as a priority maintaining, or rather consolidating, an environment which is conducive to innovation. The efforts and spending devoted today to R&D are in fact the guarantors of the future creation of wealth and jobs. The European Union and the Member States play a crucial role in this innovation cycle. Like the space industry, the life sciences industry, which can also be regarded as an issue of sovereignty, cannot develop without solid and pro-active support from the public authorities.

The model on which Europe has been built since the Second World War is currently under threat from the economic crisis which is obliterating growth and the sovereign debt crisis which is leading most countries into a race to make savings. Much criticised, the policies of budgetary rigour have also weakened, in their sometimes blind and obsessive search for savings, the European social model. This is the case in the area of healthcare where the reduction in reimbursements for treatment in some countries and the pressure exerted on the prices of drugs

are emblematic of these excesses. Since the benefit of the savings seems meagre in terms of the collateral damage that is immediate (reduced access to treatment, impossibility for the pharmaceutical industry to amortise R&D costs) and future (increase in the financial burden linked to the deterioration in the health of the population, risk of offshoring of research centres, etc).

Given these dangers, the challenge is to rebuild a European ambition in the life sciences sector. The right time is not to wait until the crisis is over to face up to the future but to lay the foundations now for a proactive and courageous strategy which is able to bear fruit tomorrow.

Satisfying this renewed ambition for Europe first involves a strengthening of cooperation between the Member States. This must lead to greater cohesion. It must also enhance the efficiency of public management by reducing costs, improve competitiveness by avoiding time being wasted, give some member States scientific expertise which they do not yet have and which is able to take into account in a balanced way the range of benefits, both health and economic, brought about by medical and pharmaceutical progress. This enhanced cooperation may, finally, constitute an important step towards improved coherency of Europe's health systems.

This ambition then involves the strengthening of research projects thanks to the launch of major joint projects. These must be organised, in the interests of performance, with the aim of pooling financial and human resources, creating a strong dynamic that compensates for the fragmentation of the European R&D effort and the weakness of coordination between countries, academic institutions and private companies. The launch of major research programmes continent-wide would allow Europe to compete more effectively with the American model, built around the National Institutes of Health (NIH), a single organisation for financing public medical research in the U.S.

Finally, it involves ending the fragmentation of measures at the community level and the establishment of a coherent policy refocused on the public health mission of the European Union. This requirement means simplifying the management of health issues currently divided up between several directorates of the European Commission. This fragmentation is a source of contradiction in deploying a coherent public health policy, able to take into account all the health, industrial, economic and scientific issues.

AN INDUSTRY OF THE FUTURE

A DYNAMIC, FAST MOVING, MARKET

The financial and economic crisis, whose unremitting turmoil has disturbed and hindered global growth since 2007, has highlighted the apparent solidity of the life sciences market. It is first necessary to define its scope, in so far as this varies according to the definitions adopted in the articles, studies and reports that are devoted to it. In this document, 'life sciences' means all ways biology and industrial technologies are applied to human and animal health. Besides the production of so-called traditional medicines produced by the pharmaceutical industry which represents almost two-thirds of the market, the sector comprises the biotechnology and medical technologies (or medical devices) fields. Taken as a whole, this market experienced an average annual growth rate of 6.7% between 2007 and 2011, higher than global growth, with turnover reaching \$1,100 billion ¹. This surprising performance contrasts with the misfortunes of some industrial sectors at the height of the crisis. But this apparent good health, which, it should be stressed from the outset, is not led by Europe, masks divergent currents and a far-reaching shift in the balance of the market.

The priority given to health care expenditure both on an individual and collective basis, cannot in itself explain the resilience of the sector. Several favourable structural trends contribute more widely to feeding growth. They are not a sum of bullish movements which have come together but rather comprise a complex set of forces that collide and clash with each other.

Whether demographic, scientific, economic or social, their currents resemble the movements of tectonic plates, shifting the market's centre of gravity, both geographical and technological. Its horizon, until now limited to the sole treatment of mass illnesses by the famous blockbuster drugs (more than a billion dollars

1. *2013 Global life sciences outlook*, Deloitte, 2012.

in turnover annually) in the richest countries (North America, Western Europe and Japan), are becoming multi-centred and dispersed between multiple niche markets, created by the increase in the standard of living in certain regions of the world and the emergence of new medical and industrial technologies.

In the next few years, these factors of change will sustain activity, even if a slight slowdown in overall growth is forecast, as well as precipitating the decline of the dominant business model, based on the blockbuster drug culture in the so-called mature markets. If one event should be remembered which alone shows the magnitude of these transformations, the expiration of the Lipitor® patent in the United States in late 2011 is particularly representative of the new environment. This anti-cholesterol drug was, again that year, the most sold therapeutic treatment worldwide. But in just one year, following the opening up of the American market to generic competition, its global sales fell by 59%, from \$9.5 billion in 2011 to \$3.9 billion in 2012, and those in the United States by 81 % ².

This spectacular collapse does not only highlight the now fast diffusion of generics. In its wake, it highlights other market trends such as the increasing strength of biotechnologies and emerging countries. Thus, Lipitor® has relinquished its number one spot as the most sold drug worldwide to Humira®, used to treat, in particular, rheumatoid arthritis in adult patients and produced by the American drugs company Abbott. With two-digit growth, its sales reached \$9.3 billion in 2012 and are expected to exceed the \$10 billion mark in 2013. Especially, it is the first time that a biological drug and not a "traditional" chemically synthesised drug has occupied the top place in the rankings. In total, seven drugs of the biotechnology sector, such as Enbrel®, Remicade® or Rituxan®, in 2012 were among the top 10 sales by value. Another shift has emerged that highlights this event: driven by the decline in sales of Lipitor®, the Pfizer group's pharmaceutical activity fell by 11 % in 2012 but grew by 7 % in the emerging countries (+12 % discounting exchange rate effects).

This episode is indicative of the new currents and tensions which are transforming and will, in the future, continue to play out in the market, increasing competition between the countries and the industrial players, weakening some or strengthening others in response to patents expiring, authorisations for marketing new therapies being issued, regulatory changes, reforms to public health policies, the health of public finances and geographical disparities in growth. Certainly, life sciences are, there is little doubt, a sector of the future but, in a world in constant and accelerating change, the competitiveness of the industrial players is put under pressure because never have market share and profitability seemed so fragile.

2. « Pfizer reports fourth quarter and full year 2012 results », *Performance report*, Pfizer, January 2013.

GLOBAL TRENDS THAT SUSTAIN DEMAND

Among the structural developments which in the medium and long terms will sustain demand, demographic factors are the most obvious - which explains why they are sometimes overstated. Despite the observed decline in fertility, the world's population is expected to grow from approximately 7 billion people at the end of 2011 to 8 billion by 2025 and to more than 9 billion by 2050³. This increase, however, needs to be put into perspective, in terms of market creation because the bulk of population growth is expected to be in the poorest nations. However, the life sciences market remains concentrated in the rich countries - the developed and developing countries account for nearly 90% of sales. The population of the most developed countries should, for its part, remain broadly stable. But this part of the world has faced, since the end of the Second World War, another demographic phenomenon: growing life expectancy. Under the effect of this unprecedented development in the history of mankind, the number of people over 65, as those over 85, is strongly increasing in Europe, the United States and Japan.

All forecasts confirm the continuation, acceleration and spread of this phenomenon. In 2030, the number of people over 65 is expected to rise to 72.1 million in the United States, i.e. more than twice the number as compared to 2000. With regard to people over 80, their population is predicted to rise from 5.7 million in 2010, to 6.6 million in 2020 and to 14.2 million in 2040⁴. In Europe, the trend is similar. Between 2010 and 2060, a near doubling of the population of people over 65, living in the European Union, and a tripling of those over 80 are forecast. Their number will increase respectively from 87.5 million to 152.6 million, and from 23.7 million to 62.4 million⁵. Asia and Africa will be also concerned, leading overall to a tripling by 2050 of the world's population aged over 65. If the direct influence of growing life expectancy on the demand for care and drugs is difficult to measure and subject to variable and sometimes contradictory assessments, it remains true, however, that health expenditure increases with age, particularly after 55 years for men and 60 years for women and that some diseases, such as Alzheimer's disease or cancer of the prostate, are closely linked to age.

However, more than age, it is the health, or rather the morbidity i.e. the occurrence of a disease or disability, which truly influences an individual's health care expenditure. Many indicators reveal a worsening of the prevalence of chronic diseases (cardiovascular diseases, diabetes, cancer, chronic neuro-degenerative and respiratory diseases, etc.) in older people especially, but not

3. *World population prospect : the 2010 revision*, United Nations, New-York, 2011.

4. U.S. Administration on Aging et U.S Census Bureau, 2008.

5. *The 2012 Ageing Report*, European Commission, 2012.

only, of a kind which leads to higher demand. To use the phrase of a physician : "the increase in the number of people with a chronic illness is in some way the flip-side of the coin of increased life expectancy" ⁶. According to an American study conducted on a sample of around 30,000 individuals, 45% of people over 65 living in the United States suffered from at least two chronic conditions in 2010, compared with 37% ten years earlier ⁷. Although the frequency of most chronic diseases rises with age as in the case of diabetes or high blood pressure, it is also significantly increasing in the younger age groups.

The reasons for the epidemic of chronic diseases, the leading cause of mortality and morbidity in the world and described by the World Health Organization (WHO) as "a major health challenge for the 21st century", are therefore not so much to be sought in the ageing of the population but in changes in lifestyle and eating behaviours, related in a large part to urbanisation and a sedentary lifestyle. It is a worldwide social phenomenon. The diabetes epidemic, which affects 366 million people around the world ⁸, is characteristic of the consequences of these transformations. By 2030, under the effect of demographic and social changes, the number of ill people is set to increase by 51%. Growing life expectancy only amplifies the prevalence of this "disease of civilization", due to the changes in carbohydrate metabolism which accompany ageing. In France, for example, the prevalence of diagnosed diabetes increased continuously between 2000 and 2011, at an annual average rate of 5.4%. In 2011, prevalence amounted to 4.6% of the population, i.e. more than 3 million people with diabetes. The peak is reached between 75 and 79 years of age when diabetes affects 20% of men and 14% of women ⁹.

This expansion of chronic disease affects all regions of the world. Taking four Asian countries as a whole (China, India, Thailand and Indonesia), the prevalence of diabetes quadrupled between 1970 and 2005, whereas it increased only by 50% in the United States during the same period ¹⁰. In the developed countries and the countries of so-called "intermediate income", this increase in cases of chronic diseases is contributing more markedly to the increase in demand for drugs and medical technologies. Thus whereas in France for the first time in 2011, expenditure on drugs stabilised, anti-diabetic agents recorded their strongest

6 J. Bloch, "Chronic Diseases - Importance of the problem: frequency, contribution of the various pathologies", *Actualité et dossier en santé publique* (adsp), September 2010.

7. V. M. Freid, A. B. Bernstein, et M. A. Bush, « Multiple Chronic Conditions Among Adults Aged 45 and Over : Trends Over the Past 10 years », *NCHS Data Brief N° 100*, National Centers for Disease Control and Prevention, July 2012.

8. International Diabetes Federation, *IDF Diabetes Atlas*, 5 Edition, 2012.

9. "Diabetes in a few facts and figures", www.invs.sante.fr (consultation February 2013).

10. A. Dans, N. Ng, C. Varghese, S. Tai, R. Firestone, R. Bonita, « The rise of chronic non-communicable diseases in southeast Asia : time for action », *The Lancet*, February 2011.

growth, with an increase of 6.8% by value ¹¹. The same observation can be made in the United States: the sale of anti-diabetic agents grew by value by 10.7% in 2011, compared to an overall increase in drug expenditure of 3.7% ¹². Although the growth of generics may curb market growth, it still remains true that increased life expectancy will sustain demand in the medium-term because most of these so-called long-term disorders currently require life-long treatment.

INNOVATION, THE TRUE GROWTH DRIVER

But much more than the ageing of the population, the reservoir of growth lies in the emergence of new technologies, likely to increase the effectiveness of treatment and the performance of the health systems. Their spread leads to the creation of new markets or accelerates the growth of the existing markets. It is reasonable to estimate that between a quarter and half of the increase in health expenditure, in the past few decades, is linked to changes in medical practice, made possible by technological advances ¹³. The development of the life sciences is, in fact, closely linked to the notion of scientific and medical progress, materialised in the form of radical (or breakthrough) innovations which accompany the creation of new therapies for diseases for which there was previously no treatment or, more frequently, by gradual (or incremental) innovations which lead, for example, to the placing on the market of drugs with enhanced performance (improvement of tolerance, reduction of side-effects etc).

There is an endless number of illustrations of these leap forwards or technological advances, whose proven health benefits sustain the demand for treatment. "The example of cataracts is eloquent. The replacement of the old technologies by the new has led to significant gains in productivity: stability in the cost of cataract surgery is observed between the end of 1960s and the end of 1990s, while it has gained in efficiency and safety, leading to better results in terms of visual acuity and a reduction in complication rates. Expenditure associated with the treatment of cataracts has only increased because the operation has been extended to a larger proportion of patients. Less risky and more efficient, it can be performed on older patients or those who experience less severe discomfort" ¹⁴. Led by the advances in the materials used during the operation and the development of intra-ocular implants, cataract surgery is also "now the most common surgical

11. "Primary Care Drug Expenditure in 2011", Assurance Maladie, December 2012

12. *The use of Medicines in the United States : Review of 2011*, IMS Institute for Healthcare Informatics, April 2012.

13. Congressional Budget Office, *Technological Change and the Growth of Health Spending*, January 2008. S. Smith, J.P. Newhouse et M.S. Freeland, « Income, Insurance, And Technology : Why Does Health Spending Outpace Economic Growth ? », *Health Affairs*, September-October 2009.

14. B. Dormont, "Ageing and Health Expenditure", *Globalisation of Research*, Conférences du Collège de France, Paris, 2011

operation performed in a large number of OECD countries". And if "the ageing of the population is one of the factors which explain this growth", "its proven success and safety and the cost/effectiveness of operations performed in day surgery have probably been the most important factors" of the boom in this market ¹⁵.

Over the past thirty years, technological and medical progress has thus very widely sustained the growth of the health care market. Think of replacement surgery operations, whose number for hips increased by more than 25% between 2000 and 2009 in the countries of the OECD, and almost doubled for the knee, thanks to the progress made in the manufacture of prostheses ¹⁶. Think also of kidney transplants, whose number increased in the OECD countries from 15 to 36 people for every 100,000 inhabitants between 1990 and 2009, thanks in particular to the "development of new anti-rejection drugs which have enabled more transplants to be performed and their rate of success to be improved" ¹⁷.

Think also of the therapeutic treatment of rheumatoid arthritis, whose market is experiencing very strong growth since new biological drugs were placed on the market in 2000, four of which are among the top ten best-selling drugs in the world. In 2011, sales in this market in the United States, Japan and the five main countries of Western Europe reached \$11.5 billion and are expected to rise to \$15.7 billion in 2018 ¹⁸. Finally think of the vaccination against cervical cancer caused by the human papillomavirus (HPV), recommended in many countries and developed thanks to the contributions of new technologies stemming from genetic engineering: cumulative sales of vaccines totalled \$1.8 billion in 2012, whereas this market was non-existent in 2005. Because it increases health performance, reduces disability and mortality and improves patients' quality of life, therapeutic innovation is the impetus behind the future growth of the life sciences' market. The new therapeutic approaches (gene and cell therapy, tissue engineering, nano-drugs, biological drugs such as targeted cancer therapy, robotic surgery), developed in the past ten years appear to have a promising future. As also have, in the areas of prevention, diagnosis and medical monitoring, the potential for digital health (or e-health).

Still virtually non-existent at the end of the previous decade, applications of the new information technologies (remote medicine, remote monitoring, remote consultation and remote diagnosis) could exceed \$160 billion in turnover in 2015 ¹⁹, backed both by the desire by States to control costs and the strong expectation of patients.

15. «Panorama de la santé 2011», in *Les indicateurs de l'OCDE*, OCDE, November 2011.

16. *Ibid.*

17. *Ibid.*

18. GBI Research, *Monoclonal Antibodies Market in Rheumatoid Arthritis to 2018*, January 2013.

19. *GSMA Research Reveals Growing Opportunity for Mobile Operators in Healthcare*, GSMA Press Release, April 2012.

THE EMERGING ECONOMIES, A SOURCE OF GROWTH

Although innovation remains the growth engine, globalisation has opened up new perspectives by broadening the market's geographical horizons. Growth potential has switched from the developed countries, which are struggling to find a way out of the economic and public deficit crisis to emerging countries, where a higher standard of living and health system reforms are sustaining demand. In fact, the trend seen in recent years of a slow-down in pharmaceutical demand in the mature countries compared to that of the emerging areas should continue and become greater in the short term. This movement will reshape the balance of the market. By 2016, the share of developed countries (North America, Japan, Great Britain, Germany, France, Italy, Spain and South Korea) in the purchase of drugs should total 57 %, compared with 73 % in 2006. During the same period, that of the 18 "pharmerging" countries, already higher since 2010 than Western Europe, will increase from 14 % to 30 %²⁰.

Several factors explain this growth differential. Firstly, the so-called "mature" markets of western nations are faced with the growth of generics and the measures taken by countries to limit health care expenditure. Secondly, emerging countries' markets are enjoying more sustained growth of their economies, the emergence of a middle class concerned about its quality of life, longer life expectancy and the spread of health insurance cover. Among this group of countries, the BRICS (Brazil, Russia, India, China, South Africa) stand out clearly with overall growth of their health expenditure of 22.6 % in 2011²¹. The vitality of their economies is the surest promise of the growth of their domestic market. "GDP growth is an important driver of health expenditure despite the low impact of household income, if they are insured, in deciding to favour health in their spending"²².

The growth and, to a lesser extent, the expansion of health insurance systems therefore stimulate scientific research, the rapid spread of new medical technologies and improvement in the quality of care. In fact, if the health expenditure growth model in the developed countries over the past few decades is examined, it reveals not only a close link between economic growth and health spending, but also a faster increase in health expenditure than in GDP. Between 1970 and 2002, the growth differential between health care spending and GDP per capita was

20. IMS Institute for Healthcare Informatics, *The Global Use of Medicines : Outlook Through 2016*, July 2012.

21. PriceWaterHouse Coopers, *Pharma 2020 : From vision to decision*, 2012.

22. S. Smith, J.P. Newhouse et M.S. Freeland, « Income, Insurance, And Technology : Why Does Health Spending Outpace Economic Growth ? », *Health Affairs*, September-October 2009.

as high as 1.1 % per year in the OECD countries (excluding the U.S.) and 2 % in the United States²³.

Although the share of spending devoted to health increases in proportion to a nation's wealth, the growth potential of the market of emerging countries remains high in the light of their economic growth. In 2009, China and India spent respectively 4.6 % and 4.2 % of their GDP on health expenditure compared with an average of 9.6 % in the OECD countries (and up to 17.4 % in the United States)²⁴.

Health indicators are another means of revealing the significant needs of emerging countries and the effort that remains to be made to bring the performance of their health systems into line with the developed countries. Thus, although infant mortality (under five years old) has declined significantly in the-called BRICS, it remains significantly higher than in the developed countries. It totals 61 deaths per thousand births in India, 16 % in Brazil and 15 % in China compared with a rate of 7 % in the most developed countries²⁵. Indicators which reinforce the conviction that the emerging countries, led by the BRICS, will play a leading role in the life sciences market and serve as sources of growth at a time when the most developed countries are struggling to retrieve growth and a balance in their public finances.

23. C. White, « Health Care Spending Growth : How Different Is The United States From The Rest Of The OECD ? », *Health Affairs*, January 2007.

24. OECD, « Panorama de la santé 2011 », *Les indicateurs de l'OCDE*, November 2011.

25. *Levels & Trends in child mortality – Report 2012*, Estimates developed by the UN interagency group for child mortality estimation, United Nations Children's Fund, 2012.

A STRATEGIC INDUSTRY FOR EUROPE

A SECTOR WHICH IS BETTER AT WITHSTANDING INDUSTRIAL DECLINE

The industrial decline of Europe has been headline news for several months. The use of this expression is neither a fad used by a few editors short of ideas nor a fantasy of people with alarmist temperaments.

According to the European Commission, "the persistence of the economic crisis has put European industry under pressure: production has fallen decreased by 10% compared to its level before the crisis and industry has lost more than three million jobs" ¹.

In this bleak picture for Europe's industrial fabric, life sciences, like aeronautics, can be held up as a technological showcase. The European companies compete for the leadership of this sector with their American counterparts. Five European groups, namely the Swiss, Roche and Novartis, the British, GSK and AstraZeneca, and the French, Sanofi, are in the top ten largest pharmacy and biotechnology groups worldwide. Many others, such as Boehringer Ingelheim, Bayer, Novo Nordisk, Merck KGaA, Shire, Menarini or Servier, are also ranked among the 50 world leaders. In the medical technologies market, largely dominated by American companies, European industry has a few icons such as Siemens, Phillips, Fresenius or Essilor. The presence of European groups among the world leaders is all the more remarkable in that, whatever sector of activity, the weight of the North American market is much higher than that of the European internal market.

Taken as a whole, and in spite of overall profitability in decline, the European life sciences industry has stood up quite well to the crisis (at least up to now) and to the market turmoil while at the same time having been forced to adapt to it,

1. "A Stronger European Industry for Growth and Economic Recovery ", Communication from the European Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions, October 2012.

sometimes at the cost of implementing strategic restructuring plans, geographical redeployment of some of their activities and massive investment, in particular in North America, in future technologies. Therefore, the margins of the major European drugs companies are approximately 5 points higher than their American counterparts. A telling sign: of the 105,000 job losses in the pharmacy sector over the 2009-2011 period, three out of four were lost in the United States ². With strong proven competitiveness, indispensable for its long-term survival and maintained thanks to correct forecasting of ongoing developments, but which remain fragile in a gloomy European environment and an increasingly competitive global context, the life sciences industry is part of the lifeblood of the continent's economic fabric. It directly employs more than 1.3 million people, of whom over 50% in the pharmaceutical industry and almost 40% in medical technologies ³. This employment rate is however threatened in the long-term by the decline in European research and innovation.

In some regions, the life sciences industry is one of the key drivers of the local economy. Thus, 45% of jobs in the life sciences industry are concentrated in 25 European regions ⁴. By way of an illustration: with 7,000 employees, Sanofi is the leading private sector employer of the Greater Lyon area ⁵. And the investments made on many sites contribute locally to economic dynamism and to the creation of jobs as evidenced by the role played by Roche in Upper Bavaria. Since 1998, the company has invested over €1.8 billion on its Penzberg site, dedicated to biotechnology, resulting in the creation of 2,500 new jobs ⁶. Alongside the pharmaceutical industry, whose industrial presence is concentrated in the area, medical technology firms form a diversified fabric of small and mid-caps, with no fewer than 22,500 firms of which 80% have fewer than 250 employees ⁷.

It should be noted that despite the strong internationalisation of the market, Europe, thanks to the presence of a high-performing industrial tool, acknowledged human and technological skills and a substantial domestic market, remains a solid industrial base. Thus, 40% of GSK employees are based in Europe, whereas the geographical area does not account for more than 30% of the group's sales ⁸. This is also the case for Sanofi, which in Europe employs over 56,000 people (including 7,000 researchers) or more than half of its global workforce, whereas Western Europe accounts for less than 25% of its sales ⁹. In the same way as

2. "The pharmacy world in better shape than its actors", Press Release, Euler Hermes, 2012.

3. E. Giovacchini, « Priority sector report : life sciences », *Insphere*, Europe Innova, March 2011.

4. *Ibid.*

5. "Hearing of Christian Lajoux, President of Sanofi-Avantis France", Employment Affairs Commission of the National Assembly, December 2012.

6. *Annual report 2012*, Roche.

7. *Medical Technology in Europe : Key facts and figures*, Eucomed, 2012.

8. *Annual Report 2011*, GSK.

9. *2012 Reference Document*, Sanofi.

GSK and Sanofi, a number of European firms have a similar ratio, enabling the sector to contribute positively to the European Union's balance of trade: €80 billion for the pharmaceutical industry alone ¹⁰. Despite R&D investment which is increasing outside its borders, particularly in the United States and in the emerging countries, Europe remains one of the main innovation centres, with around €35 billion invested in research and development on its territory by the life science industries ¹¹.

The strong European siting of industrial activities, both production and research & development, guarantees job and wealth creation. The social and financial impact that the pharmaceutical industry makes is even stronger in so far as it is the technology sector which records the highest value-added per employee, far ahead of the other industrial sectors ¹². R&D expenditure by the pharmaceutical and biotechnology sector ranks just behind the automotive industry in Europe but its intensity in comparison to sales is higher (14.7% for pharmacy and biotechnologies, compared with 4.9% for the automotive industry and 6% for aerospace and defence ¹³). A number of firms stand out by the emphasis they put on innovation: Novartis, Roche, GSK and Sanofi which are among the twenty industrial companies worldwide which dedicate the highest amounts to R&D or the world leader in ophthalmic lenses, Essilor, which in 2011 was in 25th place ¹⁴ in the ranking of the most innovative companies published by Forbes magazine and which records 45% of its sales for products under three years old ¹⁵.

In this context, the European life sciences industry has many strengths for playing a key role on the international scene and, accordingly, contributing substantially to the continent's economic recovery provided an environment favourable to support the essential research effort is created. The European Commission was not wrong by placing the life science industries at the heart of its new, "Europe 2020 - A strategy for smart, sustainable and inclusive growth". The implementation of this action plan, which is organised into seven flagship initiatives, in particular provides for the launch of a "policy strategy agenda to strengthen the competitiveness of the pharmaceuticals industry" ¹⁶.

10. *The Pharmaceutical Industry in Figures*, European Federation of Pharmaceutical Industries and Associations, 2012.

11. *The Pharmaceutical Industry in Figures*, European Federation of Pharmaceutical Industries and Associations, 2012 ; *Medical Technology in Europe : Key facts and figures*, Eucomed, 2012.

12. *Ibid.*

13. *The 2012 EU Industrial R&D Investment Scoreboard*, European Commission, Joint Research Centre (JRC), Directorate General for Research and Innovation, 2013.

14. *Ibid.*

15. *2011 Activity Report*, Essilor.

16. "A Stronger European Industry for Growth and Economic Recovery ", Communication from the European Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions, October 2012.

BENEFITS FOR THE ENTIRE ECONOMY

Because of the public deficit crisis, the debate on the control of health expenditure has made a powerful comeback, centre stage. But an approach to the issue which highlights its cost only, including that of its higher rate of increase than GDP growth thereby putting the public finances under strain and increasing the cost of labour, is, to say the least, reductionist. It too easily obscures the many socio-economic benefits generated by the improvement of the health of the population. Because although health has been long regarded as a luxury by economists, it is now widely acknowledged as supporting economic activity. In 1993, in a report, regarded as the document which establishes the foundations of its health policy, the World Bank recognised that "improved health contributes to economic growth"¹⁷. This principle was confirmed in the work carried out by the WHO Commission on Macroeconomics and Health.

In its report, published in 2001, it shows the close links that exist between health and economic development. And asserts that "the economic costs of avoidable disease, when taken together, are staggeringly high. Disease reduces annual incomes of society, the lifetime incomes of individuals, and prospects for economic growth. The losses are dozens of percent of GNP of the poorest countries each year, which translates into hundreds of billions of US dollars"¹⁸. Although today there is virtually no challenge to the paramount role of health in the development policies of poor countries, its influence in the economies of the developed countries remains largely unrecognised and as such under-estimated and rarely taken into account in policy thinking.

Yet, as early as the 1960s, the winners of the Nobel Prize for economics Theodore Schultz and Gary Becker had defined education and health as the main pillars of what they called "human capital" and asserted that expenditure which was devoted to it should be regarded as investment that was as profitable as any other, or even more so. If their theory of "human capital" long provoked controversy because as Theodore Schultz forewarned "our values and beliefs inhibit us from looking upon human beings as capital goods"¹⁹, the many scientific studies carried out in the 1990s and 2000s have underpinned their approach; they have corroborated the importance of health in the industrialised countries both in terms of economic productivity and social cohesion. "Although the economic justification of health in high-income countries may differ from that of the poor countries, there is today sufficient evidence that the health improvement leads to significant economic benefits (...). From this point of view, health must be

17. "World Development Report 1993: Investing in health", World Bank, 1993.

18. *Macroeconomics and Health: Investing in Health for Economic Development*, Commission on Macroeconomics and Health, WHO, 2002.

19. T. Schultz, *Investment in Human Capital*, AER, 1961.

considered as an investment that provides an economic return, and not only as a cost", it is possible to assert ²⁰.

Even if the assessment of the socio-economic benefits of health remains, it must be acknowledged, complex due to the abundance and diversity of the factors that need to be taken into account, increasing the difficulty of building relevant study models, certain recent episodes give us a sharp reminder of how much, conversely, any health crisis, even a minor one, has large financial and social impacts. There is no better example than the epidemic of measles which affected Europe from January to October 2011. In total, more than 26,000 cases were recorded in 36 European countries. Some 83% of the reported cases were in the countries of Western Europe. According to the WHO, this outbreak caused nine deaths, including six in France, and 7,288 hospitalisations ²¹. Despite the absence of an assessment, elements of comparison can be used to appraise the cost, judged to be "extremely costly" by the WHO. "A well-documented 2008 outbreak in Arizona of seven measles cases, traced to a traveler from Switzerland, affected two hospitals, caused significant disruption, and cost \$800,000 to respond to and contain", the WHO notes.

The financial burden of an epidemic, such as that of measles, whose resurgence is mainly attributable to a fall in vaccination even though cheap and advocated by the public health authorities, reveals in its wake the economic efficiency of vaccination campaigns. What is true cyclically for a measles outbreak, is all the more so, acutely and on a completely different scale each year for the epidemics of seasonal influenza, whose vaccination cost must be weighed against the savings generated. These are twofold: the direct costs incurred by the increase in medical consultations and hospitalisations, borne by the health system, to which are added those indirectly caused by time off work (social security payments, loss of productivity etc). Each year, the lack of vaccination coverage against influenza in Europe is a heavy socio-economic burden for the community. It is estimated that among the persons at risk, who amount to almost 50% of the European population, some 145 million of them do not get vaccinated. This failing in the vaccination policy has serious consequences. By ensuring the total vaccination coverage of all the risk groups, the number of cases of influenza would be reduced by 7.2 million, medical consultations by nearly two million and hospital admissions by approximately 800,000 and deaths by 70,000 ²².

Mainly due to this weakness in the vaccination coverage, influenza is not just a health scourge, it is also an avoidable financial burden, even out of place at a

20. M. Suhrcke, M. McKee, R. Sauto Arce, S. Tsoлова, J. Mortensen, *The contribution of health to the economy in the European Union*, European Commission, 2005.

21. *European countries must take action now to prevent continued measles outbreaks in 2012*, Press Release, WHO, December 2011.

22. J. Ryan, Y. Zoellner, B. Gradl, B. Palache, J. Medema, « Establishing the health and economic impact of influenza vaccination within the European Union 25 countries », *Vaccine*, 2006.

time when all European governments are engaged in an active drive to cut public spending and make it more efficient. In Great Britain, for example, among the elderly population, it is responsible for 11,000 hospital admissions for respiratory complications, representing a financial burden for the health services estimated at £22 million each winter²³. For the whole of the European Union, the cost of medical consultations due to influenza is estimated at €267 million and hospital admissions totalling €11.5 billion. These sums are only the most visible part of the consequences of seasonal influenza²⁴.

Although more diffuse, its impact on economic activity is equally, or even more, important. In Europe, influenza is the reason behind around 10% of sick leave. The loss of productivity in France and Germany has been estimated at between \$9.3 billion and \$14.1 billion per year, i.e. 5 to 10 times greater than the direct costs²⁵. According to the Bureau of Labor Statistics of the U.S. Department of Labor, absenteeism is 32% higher during the seasonal influenza epidemic than during the rest of the year. Although some consultants in the American press at the approach of the epidemic recommend reducing the number of meetings and promoting teleworking in order to limit the impact of influenza on firms' activity, some companies encourage their employees to get vaccinated. This is particularly the case of the British company BP which, with a concern "to provide a healthy working environment that enables its employees to achieve their best level of productivity"²⁶, funds vaccination against influenza in its entirety. An approach that far from being a mere anecdote demonstrates that a vaccine is undoubtedly a competitive tool.

Like infectious diseases, chronic diseases are also a significant cost for the economy. Their impact on the career of people affected has been shown in many empirical studies. In this respect they are edifying: a higher risk of unemployment, increased absenteeism, early retirement, low income, a fewer number of worked hours, lower productivity. On reading about their impacts, it is not an exaggeration to conclude that there "is reasonable evidence of the negative impact that chronic diseases have on the labour market, showing that they affect the supply of labour, in terms of employability, attendance at work, job rotation and early retirement, as well as the level of wages and income as well as career

23. European Scientific Working group on Influenza (ESWI), www.flucentre.org (consultation mars 2013).

24. J. Ryan, Y. Zoellner, B. Gradl, B. Palache, J. Medema, « Establishing the health and economic impact of influenza vaccination within the European Union 25 countries », *Vaccine*, 2006.

25. T. Szucs, « Medical Economics in the field of influenza : past, present and future », *Virus Research*, 2004.

26. [http://hr.bpglobal.com/LifeBenefits/Sites/core/BP-Life-benefits/Policies-and-programs/Influenza-\(flu\)-vaccinations.aspx](http://hr.bpglobal.com/LifeBenefits/Sites/core/BP-Life-benefits/Policies-and-programs/Influenza-(flu)-vaccinations.aspx).

development" ²⁷. The significant losses in productivity that they cause affect businesses' competitiveness. In the United States, those caused by cardiovascular diseases alone, the first cause of mortality, have been estimated at \$172 billion ²⁸; those related to visual impairment are reported to be \$8 billion ²⁹.

From a macroeconomic perspective which tends to calculate the impact health has on economic growth, the link of cause and effect is not so easy to demonstrate. However, life expectancy is regarded as a reliable indicator of growth. "Even if only part of the increase in life expectancy is the result of health measures, the benefits are enormous. Health expenditure, whether through health systems or other sectors which have an influence on health, may be considered to generate "social productivity" several times greater than that created by other forms of investment" ³⁰. Other indicators give support to this observation: in high-income countries, an increase of 1% in mortality due to cardiovascular diseases would lead to a drop of 0.1% in the rate of growth of income per head in the following five years ³¹. Thus, even if the studies on this subject are partial, they prove that "health is a significant determinant of growth in high-income countries" ³². And that if the life sciences industry is a strategic sector, it owes it as much to its importance in the European economy and its development prospects as to the social-economic benefits it generates through the improvement in the health of the population.

27. R. Busse, M. Blümel, D. Scheller-Kreinsen, A. Zentner, *Tackling chronic disease in Europe*, European Observatory on Health Systems and Policies, WHO, 2010.

28. *Cost to treat heart disease in United States will triple by 2030*, American Heart Association Policy Statement, January 2011.

29. *The economic impact of vision problems*, Prevent Blindness America, 2007.

30. J. Figueras, M. McKee, S. Lesof, A. Duran, M. Menabde, *Health systems, health and wealth : Assessing the case for investing in health systems*, WHO, 2008.

31. M. Suhrcke, R. Nugent, D. Stuckler, L. Rocco, *Chronic disease : An economic perspective*, Oxford Health Alliance, 2006.

32. R. Busse, M. Blümel, D. Scheller-Kreinsen, A. Zentner, *Tackling chronic disease in Europe*, European Observatory on Health Systems and Policies, WHO, 2010.

AN INDUSTRY THAT MUST ADDRESS NEW CHALLENGES

INCREASED PRESSURE ON PRICES

On the one hand, generic drugs which are eroding market share year after year and on the other, governments that subjected to the crisis in public deficits are increasing the number of initiatives to restrict health care costs: the economic model of the life sciences industry is undergoing increasing pressure, exacerbated by the economic crisis which is forcing many Europeans to abandon certain treatment. A consequence of the weakness of the economic growth and austerity policies put in place, per capita health expenditure declined in 2010 by 0.6 % in the European Union ¹. The first time since 1975.

Between 2000 and 2009, it had grown by 4.6% per year on average. Faced with increased control of expenditure in most European countries (downward pressure on prices, reductions in reimbursements, deferral of investments), the industry is directly affected by this reversal of the historical trend. Drug sales, which represent 16.7% to 19% of health ² spending, thus remained stable in 2010 in the European Union.

Besides the weakness of the European market, one of the greatest pressures which is being exercised on the pharmaceutical industry, wherever the location of the market, is the advent of generics, or rather its cause i.e. the expiration of patents for blockbuster drugs. During the 2012-2016 period, drugs affected by patents expiring will represent a volume of sales estimated at \$127 billion worldwide ³.

1. *Health at a glance : Europe 2012*, OECD, 2012.

2. *The Pharmaceutical Industry in Figures*, European Federation of Pharmaceutical Industries and Associations, 2012 ; *Health at a glance : Europe 2012*, OECD, 2012.

3. *The Global Use of Medicines : Outlook Through 2016*, IMS Institute for Healthcare Informatics, July 2012.

2013 is particularly lively with the opening up to competition of propriety drugs of a market worth \$29 billion ⁴. This movement, which is continuing at a strong pace, has already affected many blockbusters, the traditional driver of the activity of the major European and American drug companies. In 2011 and 2012, five of these flagship products (Zyprexa®, Lipitor®, Seroquel®, Plavix®, Singulair®), representing cumulative sales of over \$22 billion in the United States market alone, have been opened up to generic competition. Their sales are predicted to plummet in 2013 to under \$5 billion: this is what is widely known as the "patent cliff" ⁵. In total, the global market for drugs open to generic competition should thus rise from 242 billion in 2011 to more than 400 billion in 2016, representing approximately 35 % of the market ⁶.

The very strong expected growth of generic sales, mainly in the "pharmerging" countries, will feed almost exclusively the growth of the pharmaceutical market in the next few years, hiding the relative sluggishness of the rest of the activity. The "Big Pharma" companies, whether they are European or American, are bearing the brunt of this divergent movement which is directing the market even though they anticipated it. In 2012, global sales of the pharmaceutical activity alone of the ten largest global groups thus fell "by 5 to 20% depending on the case" ⁷. The desire shown by governments to control their health expenditure, in a climate of strong budgetary restraint, is emphasising this squeeze. Most countries, and not only in Europe, have strengthened their regulatory measures to curb the demand for treatment.

Even if the new measures adopted differ from one country to the other, due to drug pricing and reimbursement procedures based on a different perception of social well-being and economic and health approaches, all substantively have the same goal: to strengthen the control of expenditure by toughening the assessment procedures for new formulations, increasing the requirements for establishing reimbursement rates, making targeted price reductions and encouraging the use of generics. But this quest has its flipside which cannot be ignored. The continual changes to market access conditions is holding back the pharmaceutical companies in developing strategic choices to guide their R&D policies. The absence of transparent and clear ground rules is neither an incentive to investment nor to risk taking.

This is certainly not the most alarming aspect for the European economies. Because although the search for increased efficiency of public expenditure must be continued and encouraged, the risks that short-term savings will be made at the expense, in the medium term, of the public health interest, and accordingly

4. *2013 Global life sciences outlook*, Deloitte, 2012.

5. "A new roadmap for pharmacy?", Press Conference, Euler Hermes, March 2012.

6. *The Global Use of Medicines : Outlook Through 2016*, IMS Institute for Healthcare Informatics, July 2012.

7. "Big pharma in quest of another economic model", Pharm@nalyse, March 2013.

that of public finances, are real. Although we do not yet observe "a deterioration in health linked to the crisis, there is no cause for celebration – it takes time before the effects of bad social conditions or poor quality of care show up in the health results. Policy makers have often done what they can to ensure that access to quality treatment remains the norm in Europe; As to whether these efforts are enough to guarantee the population's health will only become clear in the years to come," the deputy secretary general of the OECD, Yves Leterme, and the director general of the Directorate General for Health and Consumers (DG SANCO) of the European Commission Paola Testori Coggi⁸ have warned. The warning should be taken all the more seriously since some decisions, encouraged by budgetary restraint, are feeding concerns.

This is the case, for example, of France's decision to withdraw severe high blood pressure from the list of long-term disorders, leading to a reduction in the cost of treatment borne by public bodies. "We will actually make €20 million in savings, but in the long term, if people do not get adequate treatment because they do not have the means or do not wish to invest financially in paying for treatment, we will end up paying a lot more for the consequences of this over the next ten years. In my opinion, it is a time-bomb", Claire Mounier Vehier, Vice-President of the French Federation of Cardiology stated⁹. The situation is exacerbated in those countries most seriously affected by the public deficit crisis, widening a little more the health inequality gap that exists between the different European countries. In Greece, many hospitals are unable to obtain basic medical equipment: "there is a shortage of everything: latex gloves, compresses, reagent for blood tests, catheters"¹⁰. The budget for reimbursing drugs fell from €5.6 billion in 2010 to €2.8 billion in 2012 and at the same time stock-outs are also multiplying. "According to the Panhellenic pharmaceutical association, it is now virtually impossible to find 300 drugs and the situation is particularly serious for cardiac and cancer treatments"¹¹.

Although patients are the first to be affected by austerity policies, the shortfall for the life sciences industry is also high because, according to the formula which strikes so true of the Canadian economist Robert Evans, "in the health sector, the expenditure of some are the incomes of others"¹².

In 2011, the pharmaceutical companies thus granted discounts and price reductions on drugs in Greece, Italy, Ireland, Spain and Portugal, for a total

8. *Health at a glance : Europe 2012*, OECD, 2012.

9. "High blood pressure will no longer be fully reimbursed", rmc.fr, November 2012.

10. B. Vitkine, "The inexorable descent into the abyss of the Greek health system", *Le Monde*, November 2012.

11. *Ibid.*

12. A. Gurría, "Impact of the economic crisis on health systems", *Rencontres de la Boétie*, March 2013.

amount of more than €7 billion¹³. Despite this, they had to deal with overall debt assessed at €12.5 billion as of the end 2011 in four countries (Greece, Portugal, Spain and Italy)¹⁴. Faced with the increasing number of unpaid invoices, several firms have in fact threatened to suspend their supplies to Greek public hospitals. At the beginning of November 2012, Merck thus announced that it would cease its deliveries of the anti-cancer drug Erbitux®¹⁵. Other groups such as Roche and Novo Nordisk have also warned that they may take similar measures pending the payment of the unpaid invoices¹⁶.

Just by themselves, these reductions in the price of drugs in Greece (-30% on average in 2010 and -27% in 2011) have resulted in a fall in income for the pharmaceutical industry of €2.67 billion¹⁷. The impact of these financial cuts is not limited to the most seriously indebted countries; it is spreading. "While the industry has agreed temporarily to cut its prices to fill the financing gap as in Greece and Portugal, the other countries which are not subject to the same financial pressure are automatically lowering the prices. Some 26 European and non-European countries are referring in one way or another to the prices charged in Greece"¹⁸. Germany and Austria are included in the countries which take into account the Greek prices in fixing their own rates even though they are not faced with a crisis in their public finances. For a group like Sanofi, the multiplication of drugs which are no longer being reimbursed by the health systems and the freezing of prices of a number of drugs have had a "very significant negative financial impact (...), because this is estimated at €470 million in Europe, and \$300 million (€232 million) for the United States"¹⁹.

This policy of the accountant, based on the search for savings at any price without considering the consequences it has on the industrial tool and the supply of treatment, is all the more illogical since the main purpose of placing generics on the market en masse was to reduce the cost of certain drugs and could have offered a little financial flexibility to support innovation and consolidate the competitiveness of the European research tool. In wanting to insist too much on prices, there is a great risk of becoming trapped in a spiral in which the immediate benefits for the public finances will be quickly swept away. Because if this trend continues in the medium term, the whole balance of the European life sciences

13. *Annual Review*, EFPIA, 2012.

14. « Break Point », *Pharmatimes*, July-August 2012.

15. « Germany's Merck halts supply of cancer drug to Greek hospitals », *Reuters*, November 2012.

16. E. Labropoulou, « Sick man of Europe : Life-support drugs run short in Greece », CNN, March 2013 ; J. Whalen, *Roche Keeps Drugs From Strapped Greek Hospitals*, WSJ Europe, September 2011.

17. « Break Point », *Pharmatimes*, July-August 2012.

18. *EFPIA welcomes Commission decision for a policy strategy agenda to strengthen the competitiveness of the pharmaceutical industry*, Press Release, EFPIA, October 2012.

19. C. Pietralunga, "Sanofi accuses its R&D of not releasing enough new formulations", *Le Monde*, October 2012.

industry and more widely of the health system itself which will be undermined, indirectly inviting companies to concentrate their efforts on other safer and more profitable markets. The recent restructuring plans announced by several giants of the European industry must be heard as an alarm signal.

THE NEW COMPETITION FROM THE EMERGING COUNTRIES

The emerging countries, especially China, appear to be an El Dorado for the life sciences industry. Although these markets with spectacular growth rates no doubt constitute a timely source of growth for the European companies at a time when those of the western countries, hampered by the coercive measures taken to control expenditure are suffering from sluggishness, their increasing strength must be regarded as a chance as much as a threat. All the European industrial players have had for the past few years, their eyes fixed on these "pharmemergent" markets, whose attractiveness is growing at the same pace as their economies develop and the standard of living of their middle classes increases. Many industrial players have taken a foothold in these new markets to increase their outlets and to take advantage of the expected growth.

Because of the size of its domestic market and the rapid ageing of its population, China is focusing attention and investment most strongly. Its pharmaceutical market should exceed in value in 2016 that of the five major European countries (Germany, France, Great Britain, Italy, Spain)²⁰. And the prospects for growth are bright in the light of its health data: China has the highest prevalence of diabetes in the world, with 92 million patients (compared with 26 million in the United States) and 150 million people with symptoms of pre-diabetes; it accounts for a quarter of people with haemophilia in the world, i.e. between 70,000 and 100,000 people; it records 300,000 deaths per year from liver cancer, i.e. 24 times more than in the United States²¹. The extension of medical insurance, which has helped to reduce in four years the fraction of the funding of treatment borne by the patients from 40 to 35% and aims to reduce it to 25% by 2015, as well as the launch in 2009 of a \$125 billion plan for modernising health infrastructure are also sustaining demand²².

The European industry is benefiting fully from the Chinese health policy and economic development. Despite barriers to accessing the market which are still significant, a preponderance in volume share of Chinese medicine (70% compared with 30% for western medicine) and the rapid development of the local industrial

20. *The Global Use of Medicines : Outlook Through 2016*, IMS Institute for Healthcare Informatics, July 2012.

21. « Bayer strategically positions portfolio to meet China's critical demands in achieving sustainable growth », *Bayer Corporate News*, April 2012.

22. *OECD Economic Surveys : China 2013*, OECD, March 2013

tool in part through foreign investment, Chinese imports of medical products are rising substantially. They grew by 40% in 2011 to more than \$ 17 billion, of which \$ 4 billion for the European pharmaceutical industry²³. For some companies, such as Bayer HealthCare and Novo Nordisk, China is now part of their three largest markets. In the field of medical devices, Phillips sales in China already exceed one billion dollars and are continuing to grow at a sustained pace²⁴.

Despite its growth, the Chinese industry, highly fragmented and concentrated on the manufacturing of equipment of low technological value and generic drugs which represent the bulk of the local market, is not in a position for the time-being to compete with its western competitors, whose competitiveness is still based on their technological advance and their R&D capabilities. Few local players are able to invest several hundreds of millions of dollars in developing new drugs or equipment. But although imports of medical products are increasing at a rate higher than their exports, Chinese ambitions are real and strong.

The most significant fact which illustrates the increasing strength of the Asian industrial players is observable in the active ingredients market, essential for manufacturing drugs: they already occupy centre stage. In the European market, China and India's market share has increased from 10% in the 1980s to 80% today²⁵. China has taken the lion's share. Its annual exports are estimated at more than \$ 22 billion²⁶. Formerly produced in Europe, most antibiotics such as penicillin, terramycin or gentamicin, the painkiller paracetamol which is the most often prescribed drug in volume and the anticoagulant heparin are now almost exclusively imported. This domination by Asia is accompanied by an increase in fears about health safety, arising from the heparin scandal of Chinese origin which led to the deaths of at least 80 Americans in 2008.

Although the major western drugs companies have invested in means of control for securing their supply chains and monitoring the quality of imported products, the trafficking of counterfeit Asian drugs is exploding, in particular on the Internet. In 2011, European customs seized more than 27 million fake medical products, compared to only 3 million in 2010, representing the largest volume of seized goods²⁷. Of course the European Union has strengthened its controls on the drug chain by adopting in July 2011 a new directive in order to compensate for the weakness of controls in China and India which are a favourable ground for

23. « Analysis of Imports and Exports of China's Western Medicine Products », *China import magazine ;China – UE bilateral trade and trade with the world*, DG Trade, European Union, November 2012.

24. F. Le Deu, R. Parekh, F. Zhang, G. Zhou, *Healthcare in China : "Entering uncharted waters"*, McKinsey&Company, July 2012.

25. T. Scott, C. Oldenhof, *A 25-year landslide in the manufacture and business of active pharmaceutical ingredients in Europe 1993-2008*, European Fine Chemicals Group/CEFIC.

26. M. Lee, B. Hirschler, « China's "wild east" drug store », *Reuters*, August 2012.

27. *Report on EU Customs Enforcement of Intellectual Property Rights : Results at the EU Border 2011*, European Union, 2012.

the trafficking of ineffective or even poisonous counterfeit products. But besides the problems of health safety and the shortfall for the industry that placing counterfeit drugs on the market represents, sometimes protected by patents, this dependency of the European pharmaceutical production in relation to remote industrial players is analogous to a loss of sovereignty. A stoppage, for one reason or another, of Chinese exports would be tantamount to a disaster scenario: in just a few weeks, the shelves of the European pharmacies would be empty.

At discussions organised to resolve the stock-out problems frequently observed in Europe in the supply of certain drugs, the risks created by a dependency on a single source of external production in the European Union were underlined. "A public health issue, the control of the manufacture of raw materials for pharmaceutical use has therefore, in this context, become a strategic issue for Europe", David Simonnet, chairman of Axyntis fine chemistry group, stressed during a day of debates organised by the French National Academy of Pharmacy²⁸. Some political leaders, such as the French minister Arnaud Montebourg, expressed concern about this dependency, advocating the repatriation of the production of "strategic" drugs to defend European health sovereignty²⁹. This legitimate political concern should not, however obscure the reasons which have led the European industry to relocate the production of active ingredients to countries with low labour costs. Let us remember that this strategic movement by the European industrial players was motivated by the desire to satisfy the governmental policies of reducing the cost of drugs without calling into question their competitiveness. This situation reflects the dilemma of European policy, and its inconsistencies, between the desire to maintain a powerful industrial tool and the desire to put downward pressure on the costs of drugs. It also shows the hold of the emerging countries over a whole raft of pharmaceutical production: it is a reflection of their appetite. China makes no secret of its ambitions in this respect. The life sciences industry is one of the strategic sectors identified in the twelfth five-year plan, adopted in 2011. Among the objectives set by Beijing is an increase in industrial production of 20% per year by value and the acceleration of the consolidation of the sector fragmented among hundreds of players (by 2015 the hundred most important local businesses should control 50% of the Chinese pharmaceutical market). This plan should no doubt come to fruition. Because "historically, government backing has considerably accelerated the growth of industries identified as strategic: the automotive sector is an example. With the active support of the central administration and that of the local authorities who will follow quickly, the biomedical industry should experience rapid growth in the coming decades"³⁰.

28. "Drugs: Stock-outs, supply disruptions", thematic meeting of the National Academy of Pharmacy, March 2013.

29. "Health chain: the 'give and take' strategy", *pharmaceutiques.com*, March 2013.

30. "A new roadmap for pharmacy?", Press Conference, Euler Hermes, March 2012.

Two recent events have attracted more attention because they reflect a new phase in China's strategy. The Chinese group BGIShenzhen has acquired for \$117.6 million the American company Complete Genomics, specialised in the sequencing of the human genome. Another Chinese group Joynn Laboratories, specialised in preclinical studies of pharmaceutical formulations, has purchased the Bayer group's former Californian R&D site. These two transactions, carried out in late 2012-early 2013, are the first major investments in the "mature" markets. They are a sign that Chinese industry, relying on its internal market in the course of becoming the second player globally behind the United States, intends to play a leading role in the globalisation process. They testify to the dual nature of the development of the "pharmerging" nations, which in the short-term are new outlets for western industry and in the medium-term, new competitors.

R&D UNDER PRESSURE

Because of the close link between growth and medical progress, the life sciences industry naturally turns towards innovation: this is the true barometer of its competitiveness. Changes to the market have strengthened this requirement for the European firms. Placing new therapeutic products on the market is, in the medium-term, the sole strategy for compensating the fall in sales and their profitability, caused by the loss of patents, the growth of generics and the emergence of competition in the emerging countries which benefit from cheaper labour costs. In 2012, the pharmaceutical industry invested €30 billion in R&D in Europe³¹. But maintaining this financial effort, a guarantee of future innovation, is itself being squeezed, exposed to the current developments in the market and the pressure exerted on prices.

The increase in R&D costs is the main challenge facing the industry. The cost of developing a new therapeutic formulation, from its discovery to its launch on the market, reached \$1.13 billion in 2012³². It has increased four-fold in 15 years³³. Several reasons explain this dramatic inflation. Among these is the growth in the failure and dropout rates before they are placed on the market. Only 10% of new formulations successfully complete all the stages through to marketing, compared with 20% in 1980. The longer time scales, due to the increasing complexity of both of the administrative procedures which surround the tests and the authorisations for placing products on the market in addition

31. *The Pharmaceutical Industry in Figures*, European Federation of Pharmaceutical Industries and Associations, 2013.

32. *Measuring the return from pharmaceutical innovation 2012 : Is R&D earning its investment*, Deloitte, 2012.

33. "A new roadmap for pharmacy?", Press Conference, Euler Hermes, March 2012.

to the scientific research, also increases the R&D cost³⁴. In fact, companies' R&D budget has grown without the launch of the new drugs that it generates keeping pace with it.

This trend, combined with the need for pharmaceutical companies to have increasingly diversified portfolios of products and services to compensate for their dependency on the blockbuster drugs which are declining, marks the end of the traditional fully integrated R&D model. The increase in the costs and risks connected with R&D and its decline in productivity for many reasons, is not sustainable in the medium-term for the companies. To preserve their profitability and their long-term survival in a more competitive and more unstable environment, they are now focusing on their core business, namely placing products on the market and are exploring new avenues to reinvigorate their R&D. Outsourcing and offshoring but also the establishment of platforms or collaborative networks with public and private partners, and even competitors, are models enjoying growing success. Even if it is still too early to really measure the effectiveness of these types of approach, so-called open innovation, European companies have launched themselves, with no holds barred, down this avenue to speed up the development of new therapeutic formulations by pooling skills and resources.

Without going into an off-putting catalogue of these, a look at a few initiatives is needed to assess their extent, diversity and inventiveness. Most of the major groups have created networks of partners or multiple alliances with academic research centres, clusters, innovative SMEs etc. Agreements run into the hundreds. This concept of open innovation is not the preserve of Big Pharma. It may also be advocated by the European biotech companies such as the French Innate Pharma which has signed a licence agreement with the American Bristol-Myers Squibb to finance the development of a new antibody for the treatment of cancer. Other, more original, initiatives also deserve to be mentioned. Thus, GSK has created in Spain the Tres Cantos Open Lab Foundation, a laboratory open to scientists and academics around the world who thus have access to the company's infrastructure and knowledge in order to stimulate collaborative research on tropical diseases. Sanofi has launched the Data Design Diabetes competition in the United States which financially rewards innovative projects each year in the field of the use of data to improve the care of patients suffering from diabetes.

In relation to this movement towards a diversification and redeployment of their R&D effort to which all the major industrial groups are gradually converting, China once again figures as a preferred destination. Since 2006, 13 of the 20 largest western pharmaceutical groups have opened R&D centres in China³⁵. On the part

34. J. Mestre-Ferrandiz, J. Sussex, A. Towse, *The R&D Cost of a New Medicine*, Office of Health Economics, December 2012.

35. F. Le Deu, R. Parekh, F. Zhang, G. Zhou, *Healthcare in China : "Entering uncharted waters"*, McKinsey&Company, July 2012.

of the Europeans, Novo Nordisk, which was the first multinational company to open a research centre in China in 1997, announced in 2012 that it was investing \$100 million to double its capacity; Bayer opened an R&D centre in Beijing in 2009 for a cost of \$ 100 million; Sanofi has transformed its Shanghai R&D centre, inaugurated in 2005, into its main research platform for the Asia-Pacific region. The list is long, and announcements for investment in R&D in China are being made at the same pace as those of closures of sites or of staffing reductions in R&D in Europe and the United States. A necessary rebalancing to take advantage of the expected growth of the Asian markets, this movement, which could however be slowed down by the relative weakness of local scientific resources, is no less a worrying sign for the fabric of European scientific research.

With a permanent concern to reduce the burden of their R&D, the pharmaceutical companies have also strengthened outsourcing downstream of the various development phases of new formulations. Contract research organisations (CRO) are the main beneficiaries of this sub-contracting growth. Mainly specialised in conducting clinical trials, they recorded turnover of \$21.4 billion in 2010, more than a quarter of R&D expenditure by the pharmaceutical industry worldwide. The growth of their income should continue at a fast pace reaching \$56 billion in 2018 ³⁶. This movement is also accompanied by a non-negligible risk of geographical transfer of clinical trials to more attractive countries both in financial and regulatory terms.

Besides the tax incentives put in place to support innovation, the response, today seen as the most appropriate, for maintaining an efficient and competitive research infrastructure in Europe, in a globalised world where transcontinental partnerships are proliferating, resides simultaneously in establishing a drugs cost policy that encourages therapeutic innovation and in the development of so-called "translational" research.

This concept, which emerged during the 1990s, is based on the creation of collaborative research structures between private industrial players, sometimes from different business sectors and academic and university research institutes, with the aim of stimulating and speeding-up the transition from basic research to innovative therapeutic applications. In a budgetary context under pressure both from the States and the firms, this avenue which requires above all the involvement of all the players around shared goals must be promoted. But to be truly effective and to improve the functioning of the medical innovation chain, this development implies creating an environment which is conducive to innovation and a necessary redefinition of the relations between the academic world and commercial enterprises. Despite the proliferation of initiatives, too many cultural and structural constraints still adversely affect, in many European countries, the exchange of information, the sharing of knowledge and the establishment of relationships devoid of mutual distrust between researchers and industry.

36. *Contract Research Organizations (CROs) Market to 2018 - Public-Private Partnerships to Strengthen Research Capacities and Advance Clinical Development Programs*, GBI Research, 2012.

EUROPE BETWEEN AMBITION AND WAIT-AND-SEE

AN INNOVATION IMPERATIVE TO SUPPORT GROWTH

For more than ten years, knowledge and innovation have been the main horizon of Europe's economic policies. This course was set at the European Council of 2000 in Portugal, which adopted the first global and pluriannual economic and social programme in Europe's history. The so-called Lisbon strategy aimed, in particular, to make the European Union in 2010 "the most competitive and dynamic knowledge-based economy in the world" ¹. Suffice to say that its objective was ambitious. Over-ambitious perhaps. Despite results judged to be limited and contrasting by the most generous analysts, or even illusory by the most critical – full employment clearly remaining a distant vision, the promotion of a knowledge-based economy based on education, training, R&D and innovation is still topical.

Certainly, the bursting of the Internet bubble in 2001, the structural constraints which are particular to the European Union and "the glut of objectives" ² have led to a revision of the implementation of the Lisbon strategy of 2005 by redirecting it towards growth and employment at the expense of the initial focus on the knowledge economy. Certainly, the economic crisis, which began in 2007 by the collapse of the U.S. subprime mortgage market and prolonged by the misfortunes of the Euro zone, has wiped out the prospects for growth which supported the European objectives. However, if "for a number of Europeans, the Lisbon

1. W. Kok, *Facing the challenge - The Lisbon strategy for growth and employment. Kok Report*, Brussels, November 2004,.

2. "Information report filed by the Committee for the evaluation and control of public policies on the evaluation of the impact of the Lisbon Strategy on the French economy", P. Cochet and Mr Dolez, National Assembly, February 2012.

strategy continues to be identified with this original, unrealistic, even immodest formula whose rapid transformation into a pious hope has permanently damaged the ambition that it was supposed to serve" ³, it however remains true that everyone now acknowledges the increasingly important role played by knowledge in economic growth and in businesses' competitiveness.

To say that innovation is the lifeblood of the economic struggle is now no longer challenged and was stressed even before the implementation of the Lisbon strategy. Already in 1996, the OECD had, at the G7's request, highlighted the close links between new technologies and economic growth. "In the long run, knowledge, and particularly technological knowledge, constitutes the main driver of economic growth and improvement of the quality of life. Those nations which exploit and effectively manage their knowledge assets are those which show the best performance. Companies which have more knowledge systematically get better results", the experts of the organisation highlighted ⁴.

This awareness has accelerated with the advent, in the years that have followed, of the new information technologies, the extraordinary rapidity of their dissemination and the emergence of a "new economy". The advent in recent years of new information technologies, the extraordinary speed of their dissemination and the emergence of a "new economy", which has swept away entire sections of the "old economy" – we only need to think of the rapid decline of Kodak, have convinced us of the need for innovation. Moreover, since the beginning of the 2000s, all the reports written by economists on the productivity, growth and competitiveness of the European economy are in agreement and insist on the primordial place of knowledge. To be convinced of this it is enough to recall simply that "among the ideas put forward by the 77 economists who met on Rexecode's initiative, to propose ideas to allow France to experience sustainable growth of 3%, the increase in expenditure in research and innovation is that which is the most often mentioned" ⁵.

This consensus explains the durability of principles established in Lisbon, despite the observed weakness of the results. The preliminary discussions in preparation for the new European economic strategy for the 2010-2020 period have been guided by the same goals. They have reaffirmed the leading role of innovation for growth. "The exit from the crisis should be the point of entry into a new sustainable social market economy, a smarter, greener economy, where our prosperity will come from innovation and from using resources better, and where the key input will be knowledge", the European Commission presented

3. L. Cohen-Tanugi, "A European Strategy for Globalisation", *Report in view of the French Presidency of the Council of Europe*, April 2008.

4. "Technology, Productivity and Job Creation: the OECD Jobs Strategy", OECD, 1996.

5. J. Bourdin, «The economic implications of an increase in research spending in Europe», *Information report prepared on behalf of the delegation of the Senate for planning*, June 2004.

in introduction to this work ⁶. In fact, the Europe 2020 strategy, adopted in June 2010 by the European Council, reforms and extends the Lisbon strategy. Subtitled "a strategy for smart, sustainable and inclusive growth", it fixes among its three objectives the implementation of policies encouraging innovation and joint research projects.

This choice of a European economy directed mainly at knowledge and innovation to stimulate growth and employment is not a simple bet. It is directed by both cyclical and structural factors. Firstly, the advent of the globalised economy has resulted in the transfer of a part of manufacturing production at low cost to emerging countries and has highlighted the importance for the developed countries of strengthening their capacity for innovation to maintain their competitiveness. That perhaps appears obvious, but it is good to remember: "In an economy with high production and productivity costs, the requirement to invest in R&D applies to all sectors: in the pharmaceutical sector for example, where the intensity of R&D is "naturally" high but also in the textile sector where the survival of businesses depends on their ability to innovate" ⁷.

Secondly, the new theories about growth, which emerged at the end of the 1980s, forced the process of improving productivity to be rethought significantly. In the wake of the American economist Joseph Schumpeter who at the beginning of the 20th century considered innovation and technical progress as the engines of growth, these, so-called endogenous growth models, bind the competitiveness of the economic fabric to factors such as expenditure on research and development, human capital (i.e. education, training and apprenticeships) and public investment in infrastructure. All elements which carry with them the promise of innovation and productivity gains. The great merit of this work, besides demonstrating a strong interaction between technological progress and economic growth, has been to rehabilitate the relevance of certain investments by highlighting their essential contribution to long-term growth. They thus demonstrated that an increase in R&D expenditure generates an economically virtuous process, which is shown by sustainable growth of GDP and an increase in the employment rate.

According to a simulation, carried out using the macro-economic Nemesis tool, the €8 billion spent in 2013 on R&D as part of the seventh framework programme of the European Union (€13.9 billion in total thanks to the leverage effect) should lead directly to the creation of 210,000 jobs in the short term. Over a period of 15 years – a period long enough to ensure that the financing of R&D is reflected in innovation, the creation of new markets and new industrial sectors, this investment would increase GDP by €75 billion and lead to the creation of

6. «Consultation on the future EU 2020 Strategy», Working Document of the Commission, Brussels, November 2009.

7. J. Bourdin, «Productivity and Standard of Living: Is Europe falling behind?», *Information report prepared on behalf of the delegation of the Senate for planning*, January 2007.

569,000 equivalent jobs per year⁸. This established link of cause and effect between R&D expenditure and growth, de facto legitimises political action and public support in favour of innovation. Which is what a report by the French Senate thus summarised: "the ability of intervening and influencing the long-term growth rate gives at the same time considerable scope to structural growth policies (taxation, aid and subsidies, infrastructure spending) and of course to the policies related to the R&D effort"⁹. This return of the public authorities to the economic field not only legitimises its intervention but also increases its responsibility in establishing an educational, scientific, legal and tax framework favourable to the growth of the knowledge economy.

THE FALLING BEHIND OF EUROPE COMPARED TO THE UNITED STATES

If everyone agrees on the priority given to innovation and knowledge, it is also because the technological gap between Europe and the United States has widened in recent decades. Many reports have highlighted that Europe is falling behind. Most economists consider that the process of catching up with the United States was interrupted during the 1990s. The gap in terms of GDP per head then increased in favour of the United States. The reasons for this divergence are many. If the reforms on time worked in part explain the lower productivity gains in Europe, other studies have stressed the contribution that the "new economy" is making to the dynamism of the American economy, marked by a faster spread and more profitable use of information technology by businesses¹⁰. Which confirms "the idea of the difficulty that Europe has in moving from a model of imitation, characteristic of an economy in a catching-up phase, to a model of continuous innovation, which would allow it to remain in the vicinity of the technological frontier"¹¹.

As part of the Lisbon Strategy, the European Union however had set as an objective an increase to 3% of GDP expenditure on R&D in 2010 to support growth. Although this ambition was widely shared by all the member countries, the objective was not met. Then, despite a few reforms carried out successfully here and there, the move towards the knowledge society has not been made. The observation speaks volumes: "The Member States have experienced near-stagnation in research and development expenditure over the period, whether

8. P. Zagamé, A. Fougereyrollas, P. le Mouél, « Consequences of the FP7 call for proposals for the economy and employment in the European Union », *Erasmus*, May 2012

9. J. Bourdin, «The economic implications of an increase in research spending in Europe», *Information report prepared on behalf of the delegation of the Senate for planning*, June 2004.

10. D. W. Jorgenson, M. S. Ho, K. J. Stiroh, « A retrospective look at the U.S productivity growth resurgence », *Journal of Economic Perspectives*, winter 2008.

11. J. Bourdin, "Productivity and Standard of Living: Is Europe falling behind? ", *Information report prepared on behalf of the delegation of the Senate for planning*, January 2007.

public or private" ¹². The persistence of Europe's weaknesses reveals an inability to change the economic paradigm that the proliferation of declarations of intent and initiatives are unable to conceal. The observation in 2010 is the same as that made ten years earlier: "we are under-investing in our knowledge base, spending every year 0.8% of GDP less than the US and 1.5% less than Japan in R&D" ¹³.

According to the European innovation scoreboard, based on a dozen criteria, US performance exceeded by 50% that of the European Union and that of Japan by 40% ¹⁴. Europe is largely outclassed by its two rivals on a number of criteria such as R&D spending in the private sector, public-private publications, the filing of patents in relation to GDP, the income generated by the exploitation of patents abroad, etc. Not only has Europe not managed to reduce the gap with its two main rivals but it has seen, in the last decade, its technological advance over other countries, such as South Korea and China melt away.

By relying on proactive public policies, the first has raised its R&D to GDP spending ratio to the highest level in the world and the second has become the leading employer of researchers in the world. Other facts, at the very least significant, reveal the falling behind of the European Union or its corollary, namely American domination. According to the Academic rankings of world Universities annual ranking, 17 American universities in the first 20 places compared with just two European establishments. A 2008 study by the Rand Institute ¹⁵, on behalf of the U.S. Department of Defense, established that American R&D spending accounted for 40% of the total of the OECD countries, that 37% of researchers of the OECD were employed in the U.S., that 63% of the most cited academic articles in science and technology had been published by researchers working in the United States and that 70% of winners of the Nobel Prize lived in that country.

Finally, the United States is, very largely, the preferred destination for students who continue their university studies outside their country. The number of foreign students in the science and engineering sectors thus increased from 91,150 in 1990 to 148,900 in 2009 ¹⁶. This aspect deserves to be stressed. In most countries of the world, scientific and technical careers attract young graduates less and less, who

12. P. Cochet and Mr. Dolez, *Report of information filed by the Committee for the evaluation and control of public policies on the evaluation of the impact of the Lisbon Strategy on the French economy*, National Assembly, February 2012.

13. *Europe 2020 Flagship Initiative - Innovation Union*, Communication from the European Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions, Brussels, October 2010.

14. *Background on innovation in Europe*, European Commission, 2011.

15. T. Galama, J. Hosek, *U.S competitiveness in science and technology*, RAND Corporation, 2008.

16. R. E. Wasem, *Immigration of foreign nationals with science, technology, engineering and mathematics degrees*, Congressional Research Service, November 2012.

instead of industry prefer finance, consulting, the luxury sector or communication, considered financially and socially more rewarding. This disaffection for industrial careers is "a global phenomenon, which affects equally France, Germany, North America and China", acknowledges, for example, Jacques Aschenbroich, CEO of Valeo, one of the most important recruitment firms of researchers for European industry ¹⁷.

If the United States has been able to retain and even strengthen, its technological leadership, it is not absurd to think that it owes it in large part to the attractiveness of its universities which has made up for the lack of interest in scientific and technical careers. A large number of foreign students trained in the United States indeed continue their career on American soil once they have obtained their diploma. Thus, 66% of foreign citizens who received a doctorate from an American university in 1999 were working in the United States ten years later ¹⁸. The idea according to which the too large opening up of American universities helps strengthen the competitiveness of the emerging countries, primarily China, seems to be based more on fantasy than reality. Five years after their doctoral degrees, 89% of ex-Chinese students are still in America.

The performance of the United States and its predominance on the scientific and technological stage reveals the strong interaction between education and technical progress and, in its wake, how much Europe is behind in this field. Aware that the creation of an environment conducive to innovation starts with investment in human capital, the United States has increased its effort to train and attract talent. Despite the freezing in public spending, the overall budget of grants awarded to students from low-income backgrounds almost doubled between 2008 and 2010 reaching \$ 34.9 billion in 2011 ¹⁹. At the end of 2012 and the beginning of 2013, the Republican and Democrat representatives multiplied parliamentary initiatives in favour of a relaxation of the rules governing the granting of work visas for science, technology, engineering and mathematics graduates.

This attention given to human capital reflects a genuine culture of innovation which is disseminated at all levels of American society, in public administration as in private entrepreneurship, and largely contributes to the strength of the American economy. It is not a coincidence if startups are the driving force of the American jobs market. Between 1977 and 2005, American firms less than one year old by themselves created 3 million jobs on average per year when all the others

17. V. Aubert and E. Botta, «Motivating involves giving love and money», *Management*, December 2012.

18. M. G. Finn, *Stay rates of foreign doctorates recipients from U.S universities, 2009*, Oak Ridge Institute for Science and Education, January 2012.

19. P. Delisle and I. Schöninger, «The 2011 Budget proposal by President Obama for higher education: new federal investment promoting reforms», *BE United-States* No. 197, Embassy of France to the United States /ADIT, March 2010.

combined destroyed a million per year²⁰. Innovation is the key to the success and dynamism of young American companies, some of which such as Google and Facebook, to mention only the most well-known, have become, in the space of a few years, heavyweights of the world economy. They are not the only ones. Thus, firms less than fifteen years old in the United States account for nearly 40% of R&D spending of the most innovative companies compared with just 5% in Europe²¹. In 2009, Google's R&D budget amounted to approximately €2 billion, more than the annual amount spent by the European Union on information technology under its FP7 research programme (€1.3 billion).

LIFE SCIENCES: EUROPE DISPERSES ITS EFFORTS

Although life sciences are one of the most dynamic elements of the knowledge-based economy, a pillar of the economic policy of the European Union, European strategy in this field suffers from an obvious lack of clarity, a lack of coordination between the various national initiatives, and contradictory economic, health and budgetary goals pulling in different directions. Although for the moment, Europe remains competitive in this sector, it owes this more to its industrial and scientific heritage than to a new dynamism injected into it by Brussels or the Member States. But the competitiveness of its industry, which has managed to adapt as well as it can to a changing market whose prospects remain promising, and the excellence of its academic research which goes back a long way, are by no means guaranteed. These advantages are fragile in an increasingly competitive environment. There is a high risk, as in other technology sectors, of being outdistanced by the United States or caught up by the emerging Asian nations.

The difficulties experienced by Europe in moving down the biotechnology path are in fact a serious warning. Despite an equivalent number of biotechnology companies on both sides of the Atlantic, the performance of the European sector remains way below that of its American competitors. The success stories alone attest to this gap in competitiveness. In less than thirty years of existence, many American biotechnology companies have risen to become among the leaders of the pharmaceutical industry. Created in 1980, AmGen is the iconic flag-bearer of this success. The largest biotechnology company, which recorded sales of over \$17 billion in 2012 and employs 18,000 people around the world, is part of the top fifteen global pharmaceutical groups.

Other young companies, biotechnology pioneers at the start of the 1980s, illustrate American dynamism: Genentech, founded in 1976 and acquired by Roche in 2009 for \$46.8 billion, which employs more than 12,000 people; Genzyme,

20. T. Kane, *The importance of startups in job creation and job creation*, Ewing Marion Kauffman Foundation, July 2010.

21. *Background on innovation in Europe*, Commission européenne, 2011.

founded in 1981 and acquired in 2011 by Sanofi for more than \$20 billion, which employs more than 10,000 people; Gilead Sciences, founded in 1987, which had sales of \$9.7 billion sales in 2012 and employs more than 5,000 people. In total, in 2011, the United States had 16 independent biotechnology companies whose sales were greater than \$500 million. Three exceeded this threshold for the first time (Salix Pharmaceuticals and Vertex Pharmaceuticals, created in 1989, and ViroPharma, founded in 1994) and three others for the second year only (Alexion Pharmaceuticals founded in 1992, Gen-Probe founded in 1983 and United Therapeutics founded in 1996) ²². In comparison, the circle of European biotechnology companies whose sales come to more than \$500 million has remain unchanged since 2007, demonstrating the difficulty of the continent's innovative companies to reach a critical size. This observation is confirmed by a few figures: the American biotechnology sector records three times higher sales, has four times greater capitalisation and employs three times more people.

This obvious disparity between American and European biotechnology demonstrates less a lack of creative initiatives than a European environment that is not conducive for transforming research and innovation into the creation of value and jobs. There is no single cause. If most European companies suffer from a growth deficit when compared to their American competitors, there are many reasons: a less attractive tax regime, difficulties in raising capital, a more complex relationship between public and private research, the fragmentation of support policies between multiple national programmes that are often overlapping and the weakness of trans-European collaboration. To measure the extent of the competitiveness gap between Europe and the United States, a comparison of their public policies is useful. In contrast to the complexity of support for public biomedical research in Europe dispersed among multiple national organisations (85% of the funding) and the European Union (15%), the United States relies on a single organisation which is dependent on the Department of Health, the National Institutes of Health (NIH), whose budget amounted to \$30.9 billion in 2012.

An essential link in the innovation chain, basic research, due to its costs and the uncertainties and time scales that characterise it, cannot be conducted by private companies, subject to capitalistic rules of return on investment. Public funding is necessary and indispensable to support and thus create the foundations of an environment which is conducive to private innovation. It is certain that the effectiveness of American fundamental research, its single window and its ability to harness large budgets, is a major competitive advantage for stimulating innovation. In 2007, investments by the NIH accounted for 27% of the total

22. *Beyond borders : Global biotechnology report 2012*, Ernst&Young, 2012.

amount spent on biomedical research in the United States²³. The European countries cannot compete with the power of the NIH. Even nationally, funding of research in the life sciences and health is often complex and fragmented. The example of France in this respect is enlightening. A profusion of agencies with differing statuses but sometimes similar objectives are involved managing and financing public research in the life sciences and health: Inserm, placed under the dual authority of the Ministries of Research and Health, the National Research Agency (ANR), the main source of financing for biomedical research projects as well as the CNRS, the National Cancer Institute (INCa), the National Agency for Research on AIDS (ANRS) and the Aviesan, which does not have a budget but whose role is to coordinate the activities of all these players.

This complexity in the way public research is organised in Europe, exacerbated by a culture of entrepreneurship which is less mainstream than in the United States, is a major obstacle to infusing innovation in the industry. "A study by the American National Bureau of Economic Research concluded that, contrary to the received wisdom that public investment prevented or drove out private initiative, every dollar invested in research by the NIH led to an increase of approximately 32 cents in private sector R&D spending"²⁴. This complementarity between public fundamental research and private clinical research is an essential element in the competitiveness of American industry. Many promising young American companies, such as Syntouch founded in 2008 by researchers from the University of Southern California or Protea Biosciences created in 2001 thanks to technology developed at the University of West Virginia, have benefited from research conducted in public institutions thanks to NIH funding.

The example of research on the human genome is indicative of the impact public funding has on the economy. Managed by the NIH, research has resulted in reducing the cost of sequencing a genome from more than \$100 million at the beginning of the 2000s to around \$20,000 just ten years later. According to the NIH, U.S. public investment of 4 billion dollars in the Human Genome Project generated GDP growth of \$796 billion between 2000 and 2010, i.e. a return on investment equivalent to 141 times the funds invested²⁵. And some experts believe that the sequencing activity should grow by more than 20% per year to reach sales of \$1.7 billion in 2015, demonstrating how efficient public research stimulates business and economic growth²⁶.

23. A. Gerbin, M. Drnovsek, *Innovation in the biotechnology industry : The role of university-generated intellectual property rights, knowledge base investments and funding mechanisms*, Druid Society, 2012.

24. *An Economic Engine : NIH Research, Employment, and the Future of the Medical Innovation Sector*, United for Medical Research, 2011.

25. www.nih.gov (consultation March 2013).

26. *An Economic Engine : NIH Research, Employment, and the Future of the Medical Innovation Sector*, United for Medical Research, 2011.

The dispersion of European efforts is not seen just in the way public research is organised but also in the multiplication of clusters in the countries of the European Union. The American clusters directed at biotechnology such as the San Francisco Bay area, New England or Orange County, each generate sales equivalent to that of the whole of Europe's biotechnology industry. Most importantly, the very high concentration of research organisations and businesses provide an environment in these places which is conducive and ideal for finding complementary partners and exchanging information. Europe has more than twenty clusters spread over all the countries few of which however reach a truly critical size. The search for a greater pooling of financial and scientific resources dedicated to health research and life sciences in Europe is more than ever needed to compete with the United States and as protection against the growing threat of the emerging nations.

REDEFINING A EUROPEAN PROJECT IN SUPPORT OF A POSITIVE ECONOMIC VISION

In a globalised economic world, maintaining a competitive European life sciences industry involves maintaining, or rather consolidating, an environment which is conducive to innovation. The efforts and spending devoted today to R&D are the guarantors of the future creation of wealth and jobs. States play a crucial role in this innovation cycle. Like the space industry, the life sciences industry, which can also be regarded as an issue of sovereignty, cannot develop without solid and proactive support from the public authorities. R&D is directly and indirectly funded by the States through subsidises given to academic institutions capable of carrying out basic research projects, essential for paving the way for the development and placing on the market of new therapies, and the implementation of policies for the pricing and reimbursement of treatment which offer both fair access to healthcare and an amortisation of private R&D spending. Disengagement, whether through the pursuit of a policy of pressure on prices or weakening of support for fundamental research, would only make limited savings but would precipitate however the decline of one of the showcases of European science and technology, and even more serious, would certainly slow the pace of medical progress. Through the questions that are currently expressed about the future of the life sciences sector, it is not only the question of the long-term survival of a scientific heritage and industrial capacity that Europe has built up over the decades in this sector which is at stake. It is the very essence of the European social model combining economic growth with improved quality of life which is at issue.

This model, on which Europe has been built since the Second World War is currently under threat from the economic crisis which is obliterating growth and the sovereign debt crisis which is leading most countries into a race to make savings. Both have created a social crisis, marked by a worsening in unemployment, a reduction in social protection, an increase in poverty, greater inequality and deterioration in the health of the most fragile population groups. Much criticised, the policies of budgetary rigour have also weakened, in their sometimes blind and obsessive search for savings, the European social model. This is the case in the area of healthcare where the reduction in reimbursements for treatment in some countries and the pressure exerted on the prices of drugs are emblematic of these excesses. Since the benefit of the savings seems meagre in terms of the collateral damage that is immediate (reduced access to treatment, impossibility for the pharmaceutical industry to amortise R&D costs) and future (increase in the financial burden linked to the deterioration in the health of the population, risk of offshoring of research centres). The finance director of the Boehringer group thus explained recently that the pressures exerted by the regulatory authorities which are reducing access to the market access for new drugs made it "extremely difficult to maintain investment in the research and development of new drugs". "A health policy that targets only cost reductions will lead, sooner or later to an increase in costs for society", he added ¹. An alarm signal currently echoed across the industry.

Given these dangers, the challenge is to rebuild a European ambition in the life sciences sector. The right time is not to wait until the crisis is over to face up to the future but to lay the foundations now for a proactive and courageous strategy which is able to bear fruit tomorrow.

STRENGTHENING COOPERATION BETWEEN THE STATES

The European life sciences industry is suffering from a lack of competitiveness in particular held back by a complex environment, exacerbated by the absence of standardisation between the different national regulations within the European Union. This situation more specifically affects R&D policies (complexity of administrative procedures, time scales and costs) and strengthens the temptation of relocating to countries with less restrictive rules. Since 2001, the administrative complexity of the authorisation process for clinical testing in Europe has thus resulted in the need for the industry to double its human resources to be able to follow the procedure ². Given the importance of clinical trials in the R&D budget, the consequence in a globalised environment is immediate: the number

1. « Boehringer : Tough HTA threatens future of German research », *PMLive*, April 2013.

2. European Commission, *Proposal for a regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive*, July 2012.

of applications for the authorisation of clinical trials in the European Union fell by 25% between 2007 and 2011, with a marked acceleration between 2010 and 2011.

At the same time, the market share of the emerging countries in conducting clinical trials is increasing sharply. For those drugs for which an application has been made for authorisation for placing them on the market from the European Medicines Agency, the proportion of patients originating in the Asia/Pacific/Middle East region, having participated in clinical trials, increased from 2% in 2005 to 12.8% in 2011. Over the same period, the proportion of the countries of the Community of Independent States (CIS) also underwent sustained growth, from 0.8% in 2005 to 7.5% in 2011³. Europe's decline in conducting clinical trials is not anecdotal. It has both economic and health consequences. Firstly, European decline is weakening continental scientific expertise, leading, according to the OECD, "to a decrease in the number of international trials conducted by academic organisations for non-commercial purposes"⁴. Secondly, it delays new therapies from being placed on the market and access to them, both for medical professionals and patients.

In an effort to improve the competitiveness of both private and public research, the European Commission has planned to review the current directive. It has proposed a new regulation to simplify the procedure. Similarly, the issue of a single European patent, an old well-worn issue of European policy, has recently experienced significant progress. The establishment of the single patent is expected for 2014. For years, this standardisation has been called for by the industrial players and European leaders because of the complexity and additional cost of the current procedure. In all, including the costs of the procedure and especially of translation, the cost of patent protection in the 27 member States of the European Union can reach €36,000, whereas the average cost of a patent in the United States is €1,850⁵. Despite the unanimously recognised need for a single patent, it has not been introduced without difficulty, first coming up against linguistic quarrels, then struggles between Member States about where to host the headquarters of the new authority. This bickering demonstrates the weight of the difficulties which are an integral part of the European Union in harmonising community regulations.

And yet, this streamlining effort, which may be carried out at no extra cost for the public finances, or even may, we hope, generate economies of scale, must not only must be checked regularly to ensure that it generates the expected benefits,

3. European Medicines Agency, *Clinical trials submitted in marketing-authorisation applications to the European Medicines Agency*, April 2013.

4. "OECD urges countries to harmonise clinical trial regulations to boost medical research and save lives", Press Release, OECD, February 2013.

5. "Commission proposes unitary patent protection to boost research and innovation", Press Release, European Commission, April 2011.

but also continued and broadened. Collaboration between national bodies, when it does not affect the prerogatives of the States, must be one of its priority goals. Maintaining a European research capacity in the current competitive environment comes at this price. Although authorisation for placing new formulations on the market are already taken at the European level by the European Medicines Agency, the Health Technology Assessment (HTA), whose goal is to inform the public authorities by examining the consequences (health, economic, social etc.), in the short and long term, of the use of a medical technology on individuals and society, remains the responsibility of the Member States, creating a complex and inefficient environment. "The industry players are then faced with the problem of trying to understand what is expected by each of the 30 HTA European agencies, all independent, with varying levels of expertise and which may make contradictory decisions" ⁶.

If the creation of a European health technology assessment agency is not desirable because of the differences in approach and attitude at the European level with respect to the assessment criteria are too diverse and considered by the States as the domain of their sovereignty, it is necessary in the interests of efficiency to encourage better coordination and sharing of scientific expertise. This collaboration would not call into question the sovereignty of the Member States in respect of the policy of reimbursement of drugs and setting prices but it would lead to greater cohesion. It would enhance the efficiency of public management by reducing costs, would improve competitiveness by avoiding time being wasted, would give some member States scientific expertise which they do not yet have and which is able to take into account in a balanced way the range of benefits, both health and economic, brought about by medical and pharmaceutical progress. Finally, it would be an important step towards improved coherency of Europe's health systems.

STIMULATING RESEARCH THROUGH JOINT PROJECTS

Whereas the cost of developing new drugs or medical technologies is rising continuously and the pressure exerted by the new players is increasing, European research is fragmented among multiple initiatives, national and transnational, sometimes redundant and often competing with each other. This fragmentation is obviously counter-productive for the European economy. It does not allow the best use to be made of its scientific resources nor to bring the many cutting-edge public and private research teams together to work on joint projects. In the current environment marked by renewed and strengthened competition and by increased pressure on the public finances, this situation is a burden on the competitiveness of European R&D. Certainly, some initiatives aim to infuse

6. "Proceedings of the ISPOR Congress 2010", College of health economists and Novartis France, March 2011.

a new dynamic such as the Innovative Medicines Initiative programme (IMI), launched jointly by the European Commission and the pharmaceutical industry, represented by the EFPIA (European Federation of Pharmaceutical Industries and Associations). With a budget of two billion euros funded equally by each partner, this programme aims to promote collaborative transnational research between industrial players and academic centres in Europe.

But this response, laudable as it is, only partially meets the challenges facing the European life sciences industry and the political desire expressed to make Europe the most attractive region for pharmaceutical R&D. Ultimately it just adds one extra layer to the already existing tiers of the many research partnerships. The establishment of a new European dynamic needs a will to bring together some of today's research efforts dispersed among the various R&D programmes of the Member States to tackle major health problems, able to harness the energies of all the countries and all the citizens. The success of industrial programmes such as Airbus or Ariane which have demonstrated their effectiveness in enabling Europe, despite public financial support which is just a fraction of that deployed in the United States, to become a major world power in aviation and space and in developing a competitive industry must show the way forward. The flexibility and pragmatism of these models based on open membership and their industrial logic have enabled them to overcome national differences (not without difficulty sometimes, it is true) and to play a catalytic effect in Europe, able to stimulate the streamlining of activities and provide a coherency for European ambitions.

There is no shortage of subjects for research that could drive these major programmes in the health field. Accompanying ageing through the development of e-health, prevention against chronic diseases such as diabetes and obesity, the promotion of vaccinations or research on Alzheimer's disease and cancer are subjects of transnational engagement, already identified, in which Europe could assert its legitimacy. The launch of major joint programmes such as the IMI (Innovative Medicines Initiative) are organised, with a concern for performance, with the aim of pooling financial and human resources, of creating a strong dynamic that compensates for the fragmentation of the European R&D effort and the weakness of coordination between countries, academic institutions and private companies. The launch of major research programmes continent-wide would allow Europe to compete more effectively with the American model, built around the National Institutes of Health (NIH), a single organisation for financing public medical research in the U.S.

Such a policy must create a new impetus capable of reconciling Europe with its citizens, the pharmaceutical and medical industry with the patient and public research with private industry, while at the same time creating economic growth and well-being. Through its discoveries, it would strengthen Europe's image, currently very downgraded, in the eyes of its citizens, who in contrast profess very strong faith in the abilities of medical research – thus 75% rate medical progress among the three factors that have contributed most to the improvement

of well-being in the past few decades, way ahead of the Internet (37%), the development of transport (21 %) and widespread access to leisure (20%)⁷.

REVIVING GROWTH THROUGH A TRUE PUBLIC HEALTH POLICY

The debate on the recovery of the European economy changed track in the spring of 2013. Noting that "the reduction of social expenditure has been much stronger than in past recessions" and has "neutralised the economic stabilisation function of social protection systems in many Member States", the European Commission recognised in a roundabout way that this policy had "may have contributed to aggravating the recession, at least in the short term"⁸. The observation also applies to the health systems, subjected, in order to limit spending, to growing pressure and whose counterproductive effects have been under-estimated. "Although recessions pose risks to health, the interaction of fiscal austerity with economic shocks and weak social protection is what ultimately seems to escalate health and social crises in Europe", note, as if to echo the words of the Commission, the authors of a study published at the same time by *The Lancet*⁹.

In wanting to regard health spending as a financial cost that can be squeezed, there is a risk that the cure indeed turns out to be worse than the disease. Greece, Spain and Portugal are already experiencing this. They "have adopted strict fiscal austerity; their economies continue to recede and strain on their health-care systems is growing. Suicides and outbreaks of infectious diseases are becoming more common in these countries, and budget cuts have restricted access to health care", continue the authors of the study of the Lancet study. And this is without taking into account the economic and social impact caused by the consequences of these drastic cutbacks on the life sciences industry. Between the pressures on certain Member States to drastically reduce their healthcare spending, the statement in the Investing in Health plan, presented in February 2013, that "health is a precondition for economic prosperity and that spending devoted to it is 'growth friendly' expenditure" and the desire to revive growth by consolidating the pharmaceutical industry, the European Commission has made its strategy in the health field unreadable.

The confusion is even greater in that by requiring Greece to limit public health spending to 6% of GDP, the European Commission and the Troika, of which it is a member, "have created a precedent in the European Union by taking over

7. "Health care in Europe and the United States", *Baromètre cercle santé Europe assistance – CSA*, May-June 2012.

8. *EU Employment and Social Situation – Quarterly Review*, European Commission, March 2013.

9. M. Karanikolos, P. Mladovsky, J. Cylus, S. Thomson, S. Basu, D. Stuckler, J. Mackenbach, M. McKee, « Financial crisis, austerity, and health in Europe », *The Lancet*, March 2013.

the control of a national health system" ¹⁰ even though the organisation of the health system and the planning of medical care on their territory are part of the internal prerogatives of the Member States. This episode has contributed to damaging the image of the Commission among European citizens even though Europe has made ageing in good health one of its priority objectives. It is therefore very important politically for the European Commission to reappropriate a topic which is held dear by Europeans through a proactive policy directed at medical progress and its dissemination. This direction involves the establishment of a coherent policy refocused on the public health mission of the European Union as defined in Article 152 of the Treaty of Lisbon, in particular through the fight against major health scourges, by promoting research into their causes, their transmission and their prevention.

This requirement means simplifying the management of health issues currently divided up between several directorates of the European Commission. This fragmentation is a source of contradiction in deploying a coherent public health policy, able to take into account all the health, industrial, economic and scientific issues. Today, several directorates-general of the European Commission may address health issues (Directorate General for Health and Consumers, Directorate General Internal Market and Services Directorate, General Competition, Directorate General Enterprise and Industry, Directorate General Research and Innovation) based on different or even divergent approaches and sensibilities. Thus, the Commission has launched concomitantly different initiatives related to policies for health, which are currently the subject of negotiations, without any coordination or overall vision. Among them are the Research Framework Programme 2014-2020 led by the DG Research and Innovation, the European Health Programme for the 2014-2020 period under the auspices of DG Health and Consumers, the revision of the regulation on the protection of personal data, which has important implications for research in the medical field conducted by the Directorate General Justice and the proposal for revising the "Transparency" directive related to the pricing and reimbursement procedures for medical products desired by the DG Enterprise and Industry. Since this profusion of initiatives is not at all coordinated, they are counterproductive.

In a globalised and uncertain world where responsiveness and cohesion are more than ever needed, defining and conducting an effective health policy requires thinking in terms of sector, starting from the academic research institutes right through to the consumers and taking in the industry on the way. It is high time Europe set up a single, coherent strategy in terms of health. The competitiveness of its industry and the effectiveness of the health care systems depend on it.

10. *Ibid.*

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16, rue du Pont Neuf
75001 Paris
www.choiseul.info
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ISBN : 979-10-91525-09-1

Print in France

Printing Office DUPLI-PRINT, 2 rue Descartes, ZI Sezac, 95330 Domont

Registration of copyright : September 2013

The Institut Choiseul think tank considers the major issues affecting international economics, politics and strategies.

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