

**FRENCH ATTRACTIVENESS AND COMPETITIVENESS:**

**LEEM SURVEY OF THE HEALTH INDUSTRY**

*Final report*

*September 2010*



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## I. KEY MESSAGES AND CONCLUSION

### A. Objectives and outline of the survey approach

In the beginning of 2009, the President of the LEEM, Mr. Christian Lajoux, wanted to conduct a wide-reaching survey **of the way France is seen by decision centres of large industrial pharmaceutical companies** as an investment destination. This initiative was aimed at preparing for the CSIS coming up in October 2009, and today it is intended to provide **further proposals** for the directions that have been taken since then.

The **methodology** retained was based on qualitative interviews meant to record the perception of France's attractiveness from a panel of **important pharmaceutical players, world leaders** from countries with a strong track record in the pharmaceutical industry (France, United Kingdom, Germany, Switzerland, the United States, and Japan) and some **key national players in France**.

The 20 world leaders in the pharmaceutical industry were asked to participate in the survey, as well as the 5 biggest actors in France. As sanofi-aventis was part of both groups, 24 pharmaceutical companies were asked to participate in the survey and 19 accepted. Among the **73 people**<sup>1</sup> who were questioned in these groups, **55%** had a **worldwide perimeter of responsibility** and **18%** had a **European perimeter of responsibility**.

As public research was quickly pointed out as one of France's potential advantages, it seemed important to complete the survey afterwards with interviews with managers of **public research organizations** that are active in the field of health and life sciences and a selection of **key actors in the environment** (public financing organizations, other health industries, etc.)<sup>2</sup>

### B. Prominent points of the survey

1. A market that remains relatively attractive
2. A high-quality industrial tradition, burdened with a perception of the social environment that does not reflect reality
3. A high-performing research and development environment, with under-exploited potential
4. The positive perception of a political environment that is changing

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<sup>1</sup> See list in annex 1

<sup>2</sup> See list in annex 2



## 1. A market that remains relatively attractive

- France, in terms of size, is one of the two biggest European markets and the third world market after the United States and Japan (2008).
- On the other hand, like the other Western European countries, it is currently caught between the two great geo-economic forces with strong attractiveness:
  - The **United States of America**, largest market in the world, almost four times larger than the second, where the predictable drop in prices will be compensated by the inflow of more than 30 million additional patients;
  - The **emerging countries**, with expected growth that is much higher than the developed countries, whose mature markets are greatly constrained by the necessary limitations of healthcare costs;  
The attractive force these emerging countries exert on investment flows is even stronger when:
    - The expected growth is associated with large market size (China, India, Russia, Brazil, etc.);
    - These countries require local investments to access their markets.

## 2. A high-quality industrial tradition, burdened by a perception of the social environment that does not reflect reality

The perception of the French industrial environment is very positive in many ways, which explains its position as the **number one producer and exporter of medicinal products in Europe**, and the third exporter in the world:

- The quality of the engineers and technicians;
- The existence of transportation and telecommunication infrastructure;
- A strong industrial tradition in the field of medicinal products, due to investment policies implemented at the end of the 20<sup>th</sup> century;
- The quality of the system for distributing medicinal products.

On the other hand, **the perception of the social environment is not good**. This is mainly due to three factors widely relayed in the media outside of France:

- The legislation concerning the 35-hour working week;
- The social climate, particularly strikes in public transportation and civil service;
- Occurrences of confinement of company directors as part of labour disputes.



This **perception** is **nuanced** by industrial actors who have more insider knowledge of France, and in their opinion **does not actually reflect the reality** of the situation:

- The good productivity of the work force makes it possible, according to some responders, to be more competitive than countries that have implemented extremely favourable fiscal policies (Ireland, for example, where high salaries absorb fiscal savings);
- The country is reforming in a social climate that remains, to date, rather peaceful: relaxing of the 35 hours and legislation on overtime, reform of special retirement regimes and health insurance plans, introduction of minimum service for civil service strikes, etc.;
- Other countries also have a complex and restrictive work environment and social relations that can sometimes be tense (Italy, Germany, and Holland).

The “equipment rate” in factories producing medicinal products is already high in France, while the traditional medicines industry is facing a global over-capacity situation due to the growth of generics. Considering the rarity of large industrial investment projects (capillarity of existing sites, ongoing rationalization of manufacturing base, related investment figures) and the attractiveness of emerging countries, large investments in this field are not to be expected in Western Europe.

However, efforts to accompany and improve productivity are necessary to limit the risk of disinvestment and to defend the existing industrial base. According to the industrial actors, there is a certain French resistance to transformation which, though it can limit job losses in the short term, condemns attractiveness of industrial facilities in the medium term due to a lack of adaptation and competitiveness.

Finally, capturing investments in new production facilities for biomedicines (which will not be of the same extent as those provided for “traditional” drug factories, either in value or in terms of jobs) will depend more on the competitiveness and attractiveness of the upstream part of the chain, during the research phase. That is where important efforts must be made.

### **3. A high-performing research and development environment with under-exploited potential**

**France has important advantages** for being a high-performing actor in the global setting of research and development in the life sciences, particularly:

- The strength of Public Research in the biomedical field, with large internationally reputable organizations (INSERM, CNRS, Institut Pasteur, Institut Curie, CEA, etc.), which are highly-ranked in the citation indexes;
- French excellence in fields like engineering, math, physics, etc. as multi-disciplinarity is emerging as an important lever in the performance of research;
- The quality of the health system and the level of expertise of physicians in “field” medicine as well as clinical research;
- The reputation of being international opinion leaders in several therapeutic fields (cancer, AIDS, infectious diseases, CNS, etc.).



France, unlike other countries, **is unable to transform these advantages into true competitive advantages**. There are many and different kinds of reasons for this:

- In the past, there was no strong, focused and coordinated investment policy for research in life sciences:
  - In a similar vein to what France has been able to accomplish in fundamental and applied research in recognized fields of excellence today (atomic energy, aeronautics, etc.);
  - As the investment policy of the 80's and 90's in the drugs sector successfully promoted the industrial side.
- The dispersal of Public Research, which results in the existence of numerous actors (national research organizations, evaluation agencies, financing agencies, universities and university hospital centres, centres for excellence, etc.), and which led to the implementation in 2009 of the National Alliance for Life Sciences and Health.

Industrial actors appreciate this initiative, as they understand it and consider it to be a step in the right direction, which should quickly result in visible measures, particularly the implementation of a “one-stop shop” entry point.

- The relative dispersion of public investment does not promote ease the emergence of large bioclusters with the critical mass necessary to demonstrate visible ambition internationally.

Even if the independence of universities and the emergence of competitiveness centres are appreciated in principle, their number and the way in which they are spread out does not promote an effective interface with industrial partners, particularly when R&D decision centres are located outside of France. In the same way, the number of cancer and genetics centres (“cancéropôles, genopôles”) is the reflection of a complex and fragmented structure.

On the other hand, the planned selection of five University Hospital Institutes should certainly make it possible to create a structural network that will be internationally visible and better adapted to the needs of industrial actors.

- The insufficient number of Public-Private partnerships shows greater difficulties in collaborating than in other countries, for many reasons:
  - Processes of project evaluation and valorisation need to be optimised:
    - . The need for selectivity, market expectations and the regulatory context are not sufficiently taken into account to ensure projects' competitiveness on an international level;
    - . **Complexity** and **slowness** of processes due to the number of people involved and a lack of convergence;
  - A French cultural environment that is changing, but that **still pits the public and private sectors against one another too much**: training and education, ways in which researchers are evaluated, strong risk aversion of not only researchers, but also industrial and financial actors.

There are many symptoms of this: insufficient **mobility** between the public and private sectors, insufficient **industrial orientation of projects**, lack of recognition of the **usefulness of applied and translational research**, low attractiveness of France for **international researchers** (except for the large centres of excellence), etc.



- **An image problem of French research** that should better reflect its value to industrials and internationally, but also nationwide: to the general public, social partners, the media and political decision-makers.

#### 4. **The positive perception of a political environment that is changing**

In sum, France is perceived to be one of the major industrial countries that offer a stable political environment, quality transportation and telecommunications infrastructure, recognized skills in technical, medical and scientific fields, and an attractive market in terms of size and market access.

It is located in the middle of the natural competitive environment that is Western Europe, caught between the substantial growth gap with emerging countries and the resistance potential of the United States of America (market size and linguistic, regulatory and health-system integration compared to the European mosaic; competitiveness of research, etc.)

However, **France distinguishes itself** from the rest of Europe by the **political willpower** it has demonstrated to consider **health industries** as a **strategic sector**, which is accompanied by numerous **real measures and initiatives** welcomed by industry, particularly:

- Re-launching of the CSIS (Strategic Council of Health Industries) with the involvement of the highest level of the State and of 3 ministries (Economy, Industry and Employment; Higher Education and Research; Health and Sport);
- “R&D Dating” meetings initiated in 2009 under the aegis of the President of the Republic of France;
- Organisation of the General State of Industry meetings, where health industries were one of five industrial branches to have a specific working group;
- Launching of the “Great Loan”, with a special consideration for Higher Education and Research;
- The implementation in 2009 of the “National Alliance for Life Sciences and Health” to coordinate Public Research activities in these fields;
- “Health, well-being, nutrition and biotechnologies”, number one priority axis of the National Strategy for Research and Innovation;
- The reform of the Research Tax Credit in 2008, widely appreciated by industrial actors, but not always understood, particularly in international decision-making centres.





This **political willpower needs to be leveraged**, particularly by capitalizing on and expressing the France's important advantages, especially in the field of Public Research.

The efficacy of French Research in the health field can only be improved on three conditions:

1. Reduce the gap between reality and perception, particularly from the point of view of large international groups;
2. Initiate a communication strategy towards the main decision makers in the French environment in order to develop a convergence of interest, coherent policies and supportive approaches;
3. Pursue reforms of the Research organization and implement a pro-active and ambitious policy of promoting French excellence and developing public-private partnerships.

**C. A set of actual recommendations proposed by the LEEM based on the findings of the survey**

**1. To develop convergence of interests between the actors thanks to targeted communication initiatives**

- Towards large industrial groups, particularly the heads of French subsidiaries, who must be considered as veritable ambassadors of French competitiveness within their group;
- Towards actors in public and private research, to increase reciprocal knowledge of the environments and constraints, and eventually to develop and reinforce partnerships;
- Towards social partners, to help them understand the challenges related to the perception of the social environment in France and to contribute to reducing the gap between perception and reality;
- Towards political decision-makers and authorities at all levels, to remind them of the economic value created by the health industry and of the leverage that health represents for improving the well-being of the population and the competitiveness of French companies ("health, a factor for productivity").



## 2. To realize the potential of French Research

- To support and prolong the action of the “National Alliance for Life Science and Health”, particularly by leveraging on communication about successful partnerships and success stories;
- To activate the “Alliance for Research and Innovation of Health Industries” (ARIIS), created as a reflection of the “National Alliance for Life Science and Health” with the purpose of:
  - a. **Bringing together** the important private research actors in life sciences – drugs, vaccines, medical devices (particularly diagnostics), imaging, animal health, etc. – and constituting a platform for exchanges, discussions and joint recommendations;
  - b. To stand up as a natural, legitimate, and direct **contact** (representative of private industry) of the National Alliance for Life Science and Health and to jointly propose **recommendations** to improve the overall efficacy of the Research organization and to supervise implementation; for example:
    - Identification of **priority Research fields**, in line with **public health priorities**;
    - Platform for actual recommendations to facilitate the **creation and financing of public-private partnerships** intended for **industrializable and economically viable research projects**;
      - Measures meant to clarify the policy of **valorisation** and to adapt the **evaluation** process of projects: evaluation criteria used, level of selectivity, acceleration and non-redundancy of the evaluation by several organizations, etc.;
      - Measures promoting **financing activities and modalities of fundamental and translational research**: evaluation and accompaniment of transfer projects, labels and/or financing decisions related to the valorisation and commitments of the inventors, particularly in terms of control and management of the companies created, etc.;
      - Development of a culture for **creating scientific and medical value**, but also **industrial and economic value**;
      - **International watch on practices** of project transfer and project acceleration;
    - Work on **mapping expertise** and fields of excellence;



- Initiatives to improve **training, education** and **career management** of researchers and to optimize the Research paths and networks in France in the field of life sciences:
    - . Specific training for Research in the field of life sciences;
    - . Career management and mobility;
    - . Evaluation of researchers, which should increasingly take into account the filing of new patents, valorisation and industrial partnerships, and not just publications;
    - . Profit-sharing with researchers for transfers and valorisation;
    - . Establishment of links between disciplines working together for tomorrow's discoveries, etc.
  
  - Proposals to adapt legislation to maintain and improve the **competitiveness of the French regulatory environment** compared to other countries (animal experimentation, stem cells, protection of intellectual property, valorisation of innovation, etc.);
  
  - Measures to facilitate **clinical research** operations (contractualization, weight of clinical research in the physicians' evaluation, etc.);
  
  - Creation of a "**French Award for Research in Life Sciences**";
  
  - Implementation of an **international communication strategy**;
  
  - Federation of the **network of researchers of French origin living abroad** in order to consolidate links between French researchers and international actors.
- ... and thus to reinforce the two public and private pillars of Research and to constitute a strategic lever for French attractiveness in Research and Development in the field of life sciences and health.



## II. INTRODUCTION:

### RATIONALE AND METHODOLOGY OF THE LEEM SURVEY

#### A. Objective: to identify new levers for improving French attractiveness and how it is perceived for the investments of pharmaceutical industrial actors

At the beginning of 2009, the President of the LEEM, Mr. Christian Lajoux, wanted to hold a large survey on the **perception that the decision centres of large industrial pharmaceutical groups have of France** as a destination for their investments.

The objectives of this project, which was carried out by AEC Partners, a specialized consulting firm in the healthcare and life sciences industry, were as follows:

1. To objectivise and document the factors and evaluation criteria that orient the investment decisions of large companies in the pharmaceutical industry:
  - Research and Development investments, particularly in international clinical research;
  - Investments into production capacity and distribution facilities;
  - Operational and commercial investments (for example, choosing France as the location for a European headquarters, decisions concerning the launch of a new product, level of commercial and promotional investment, etc.);
2. To gather their perception of the attractiveness and positioning of France based on these criteria and in comparison with other countries competing for their investments;
3. To list the measures that should be taken to positively change this perception and to increase the planned level of investment in the years to come based on, in particular, an analysis of best practices and examples in France and abroad.

At the time, this initiative was aimed at preparing **the coming CSIS meeting** in October 2009, and today, its purpose is to feed the orientations that were decided on since this meeting with **further proposals**.



## **B. The participation of 73 key actors belonging to 19 major pharmaceutical companies representing more than two thirds of the French market**

### **1. Functions surveyed**

The methodology retained was founded on qualitative interviews intended to gather the perception of French attractiveness of a panel of key actors in the pharmaceutical industry. These are **world leaders** from countries with a strong track record in the pharmaceutical industry (France, United Kingdom, Germany, Switzerland, United States, Japan), and the stars of the French industry.

Different points of view were collected from these companies, in order to provide a complete idea:

- Representatives of important global or regional functions, the best placed to give a view of the comparative position of France, and close to investment decision-making centres on an international level;
- Representatives of commercial subsidiaries located in France, for their intimate knowledge of the environment and the health system as well as market access mechanisms, and for their perception of the vision that their parent company has of France.

The representatives of 3 types of major functions were surveyed:

- Two functions which naturally carry out important investments, i.e. Research and Development on one hand, and Production and Distribution on the other hand (“Supply Chain”);
- Other field functions, mainly Global or European Operational or Commercial entities, General Management of French subsidiaries in certain cases, or heads of important support functions to Commercial Operations: Market Access, Public Affairs, Medical Affairs (particularly for their view of clinical development), etc.;

We will see that these functions, besides their own investment decisions (promotional investments, decision to launch new products and when to launch them, location of certain support functions, or even regional headquarters, etc.) can influence R&D and Production and Distribution investment decisions (particularly in the field of Clinical Research).



## 2. Pharmaceutical companies participating in the survey

The heads of the French subsidiaries of 20 world leaders in the pharmaceutical industry were contacted on behalf of the LEEM.

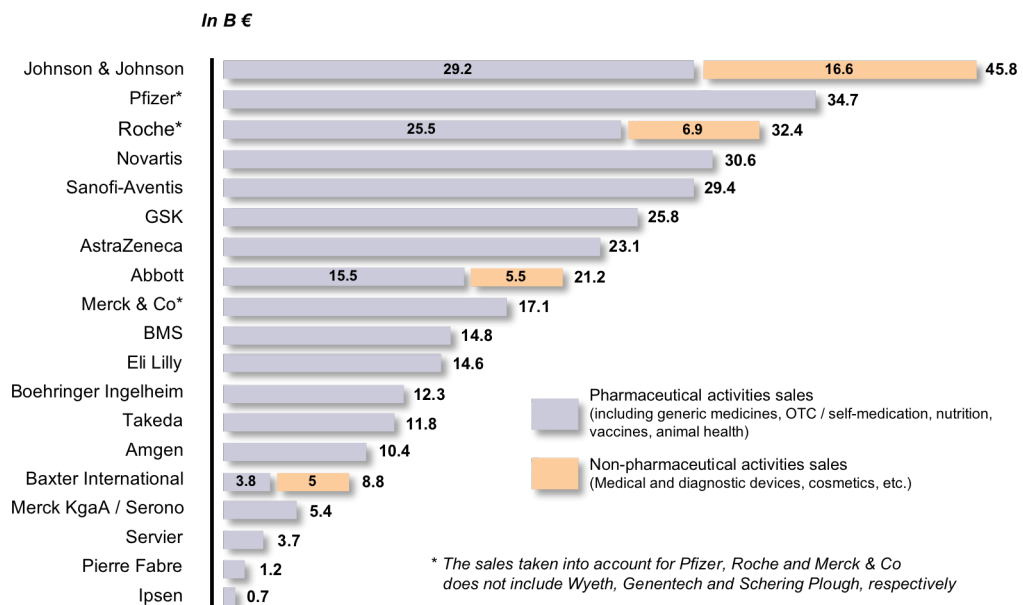
- Selected from a ranking by consolidated 2008 sales (available in 2009), all activities combined (medicines and other divisions for diversified groups);
- Excluding companies whose integration into another group was announced in 2009 (Wyeth, Genentech and Schering-Plough, about to merge with Pfizer, Roche and Merck & Co, respectively).

The top 5 major pharmaceutical companies in France were also contacted.

As sanofi-aventis is a part of both groups, a total of 24 pharmaceutical companies were contacted.

**19 of them agreed to participate in the survey.**

### World Sales in 2008 for 19 industrial pharmaceutical groups participating in the survey

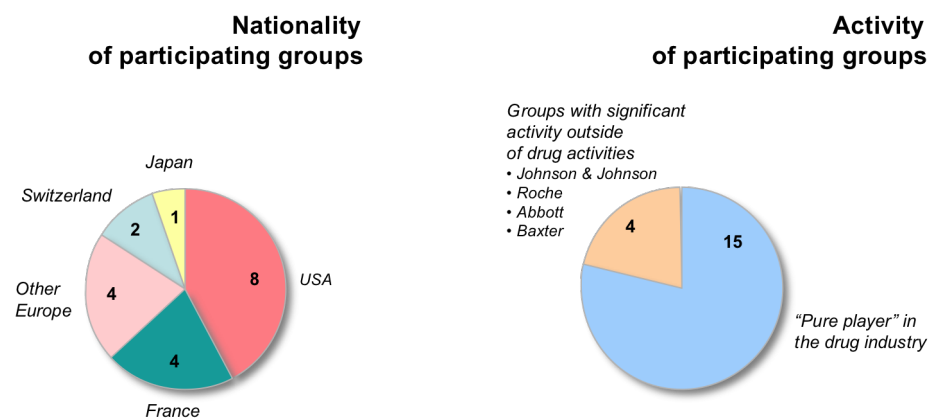


Sources: annual reports, company Internet sites, lefigaro.fr, journaldunet.com



This panel of industrial actors covers all of the nationalities that were originally targeted with a stronger representation from the United States with 8 companies (Johnson & Johnson, Pfizer, Abbott, Merck & Co, Bristol-Myers Squibb, Eli Lilly, Amgen, Baxter International) and France with 4 French companies (Sanofi-aventis, Servier, Pierre Fabre and Ipsen).

It should be noted that the majority of these actors (79%) are pure players in the drug industry, as only 4 of them (21%) are significantly involved in other activities (medical devices and diagnostics, cosmetics, etc.).



The heads and managers of the important target functions were contacted with an introduction from the heads of the French subsidiaries.

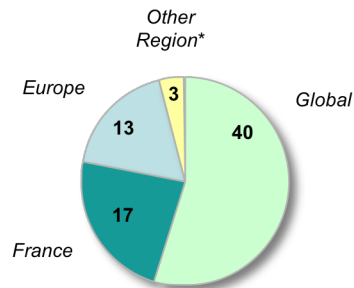
**A total of 73 people were interviewed.**

*See annex 1,  
Pharmaceutical Industry Heads and Managers Interviewed*



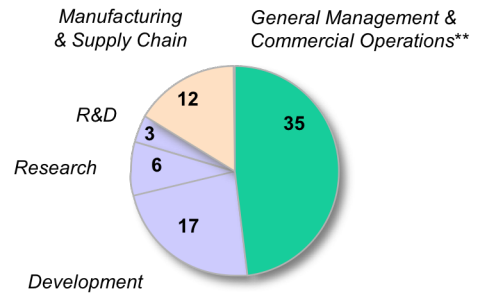
Among the 73 people interviewed in the industrial groups, **55%** had a **worldwide perimeter of responsibility** and **18%** had a **European perimeter of responsibility**.

### Perimeter of responsibility of interviewed managers



\* "Other Region within Europe" (2 people) and "Other Region outside of Europe" (1 person)

### Function typology of interviewed managers



\*\* Including Medical Affairs, Institutional Affairs, Public Affairs and Communication

### 3. Conduct of the interviews

The interviews were conducted in the following manner:

- By telephone or face-to-face;
- Individually (except for a few rare exceptions where 2 managers asked to be interviewed together);
- Generally for 45 to 90 minutes;
- In French or in English;
- After having reminded the interviewees that the report would respect the anonymity of their answers (the companies and individuals participating in the survey are identified, but the confidentiality of their views on each of the points brought up is respected).





Five major themes were brought up during the interviews:

- Decision criteria regarding the location of investments and their relative weight;
- The decision process, their key actors, their possible influences;
- The critical analysis of the environment in France regarding decision criteria; the relative position of France, its strengths, its weaknesses;
- The rationale of recent investment decisions of the group in France and in other competing countries<sup>3</sup>;
- The pre-requisites and key measures to implement that could lead to an increase in planned investment in France.

We defined investment as:

- Investments in the economic and accounting sense of the term, i.e. allocation of resources in tangible assets, including and distinguishing, for example:
  - The creation of production capacities or R&D centres where there were none before (“greenfield”);
  - The extension of existing capacities;
- Investments of resources in assets that are not depreciated from an accounting point of view: internal or external promotional investments, labour or non-labour investments (sales reps, clinical studies and other medico-marketing levers), investments in partnership agreements, as this takes a significant place in research and development activities, external expenses on high-value service providers, etc.;
- Disinvestments, which could possibly be conducted in the least attractive countries in the first place.

We did not include in our definition the acquisitions of a group of companies implanted globally or products commercialized globally, even if these acquisitions represent by far the highest investment amounts, particularly in the context of “big mergers” which are reappearing (Wyeth, Genentech, Scherring Plough, Solvay,...). These investments are generally made for reasons that have nothing to do with the environment where the acquired assets are located.

We tried to include, however, decisions to acquire existing assets related to a local context, for example, the need for a local R&D presence or the need to invest in a production or packaging capacity to access a market, or acquisitions that give access to a technology or competitive advantage due to the location of the acquired assets (factory in a country with low production costs, etc.).

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<sup>3</sup> Finally, in order to feed discussions during the interviews, we sought out the major investment and disinvestment movements in France for the industrial actors participating in the survey. This study was based on public data and was focused on the movements that had an impact in terms of sites (creation, closing, sale, transfer, significant extension or reduction of capacity, etc.) and jobs.



### C. 16 experts on the French health environment provided further insight

As partnerships among key actors and Public Research strengths were quickly brought up as being a major potential lever for improving French attractiveness, it seemed important to complete the study with interviews with:

- Heads of **Public Research organizations** that are active in the field of health or life sciences;
- Members of other components of the health industry;
- A selection of **key actors in the environment** (public financing organizations, etc.).

These experts were interviewed to gather their vision of French attractiveness and to hear their reactions to the major expectations expressed by the industrial actors.

16 people were interviewed, according to the same interview principles as those used for the pharmaceutical industrial actors.

*See annex 2,  
Heads of public research organizations,  
public financing organizations,  
other health industries,  
and key actors in the environment that were interviewed*



### III. INVESTMENT DECISION CRITERIA OF INDUSTRIAL ACTORS AND MAJOR INFLUENCING FACTORS

The first main section discussed during the interviews with the industrial actors was the factors and criteria that influenced investment decisions and the choice of their location.

Several types of factors should be distinguished:

- First of all, the location of investments of industrial actors is closely related to **market size** and **expected growth**; there are two major factors, closely related to the changes that the industry is undergoing, which are impacting them today in an overall manner in industrial groups (i.e. all functions combined):
  - The growing weight of emerging countries in the world market, which is moving the centre of gravity;
  - The development of generic medicinal products in developed countries, which structurally impacts production capacities and forces the rationalization of existing commercial structures;
- Next, the **important criteria for the choice of the location** for investments are not related to the environment itself or the attractiveness of a country on the whole, but rather to **factors within companies**;
- Finally, the criteria related to the environment (besides market size and expected growth) should be approached as per the individual views of major functions: Research, Development, Production and Distribution and Commercial Operations.

#### A. Two main structural trends strongly influence investment decisions and their locations

1. **Growth gaps between the world's major economic areas on one hand and the constraints on health costs in "mature" markets (North America, Western Europe, Japan, etc.) on the other are allowing the "BRIC" countries (Brazil, Russia, India, China) and a few others (Mexico, Turkey, etc.) to emerge as the main source of future growth for health industries.**

The traditional markets of the drug industry are experiencing strong slow-downs due to structural factors, particularly the need to:

- Control the growth of health expenses in a difficult economic context;
- Regulate the growth of demand for healthcare due to the aging of the population, patient expectations and medical progress.

At the same time, some countries are emerging as the new markets of tomorrow, due to their size and dynamics:

- Increase in purchasing power of large population segments;
- New expectations from these populations for their health, in an environment where the social protection system does not allow people to get sick without jeopardizing their job or income;



- Gradual implementation in certain countries of public or private (employer) coverage systems for medical expenses.

The expected growth thus varies between -2 and +2% per year on one hand for mature markets, and between +8 and +15% for emerging countries (according to individuals, types of products and depending on whether we measure in volume or value).

The strategy of industrial actors is naturally to move investments – practically of all types: research, development, production, commercial operations – towards the regions where the **highest growth is expected**, and within these areas, where the **markets will be the largest in volume**.

This underlying trend must be identified as an **essential factor in investment decisions**.

## 2. The development of generic drugs in the large developed markets, due to more pro-active policies and the expiration of patents for many important active substances, deeply affects the level of industrial and promotional investment

- The development of generic drugs, which is more or less rapid depending on the country, but significant everywhere, is one of the essential factors causing the **manufacturing overcapacities** seen in **developed countries**.

A large proportion of generic drugs are produced in delocalized manufacturing sites and/or those that belong to the generic makers. “Innovative” industries are thus forced to rationalize their manufacturing organization in a situation of global overcapacities, caused by the drop in volume of the proprietary medicinal products which have had generics made of them. There are situations where generics are produced in the factories where the proprietary medicinal products were once produced, but this does not balance for the decreases in volume affecting these sites.

The sites are affected (reduction in capacity and employees, sale, closing) because they produce an active substance for which the patent has expired in a number of markets. This can occur **without any relationship to the environment or the attractiveness of the country where the site is located**.

- In the same way, the decreases in commercial volumes of proprietary medicinal products deeply affect the existing **commercial structures**: dimensioned to promote and distribute large “blockbuster” active compounds, they are not always **adapted to the methods of marketing** that are emerging for the **product portfolios of tomorrow**: approaches that are more qualitative than quantitative, more targeted, and focused on products with high added value.

The methods of marketing generics, which are very specific, do not make it possible to compensate for the rationalization effects occurring within groups that commercialize the proprietary medicinal product.



## **B. Three major factors for investment decisions in the choice of the location have nothing to do with the environment of the country**

The decision making processes for investments and the choice of their location are strongly influenced by factors within companies, independent of the attractiveness or the intrinsic quality of the environment of the country.

### **1. Capillarity of investments**

A large portion of investments (and related hirings) are carried out at existing sites or locations, for several reasons:

- Leveraging on existing know-how and infrastructure;
- Better efficacy of teams conducting related activities when they are at the same site, as opposed to a situation where they would be on distinct and distant sites;
- Absorption of fixed costs at the existing site (scale effect);
- Fewer administrative hurdles in extending an existing site than in obtaining authorizations to create a new one.
- General situation of structural overcapacities which encourages the adaptation and reconversion of existing sites, rather than the creation of new sites, whenever technologies make it possible to do so at rational cost levels;
- Valorisation of existing teams and management.

Companies thus often make investments on a site that is already located in a given country. If the decision to establish a new site were to be made, the attractiveness criteria would have their full impact and could orient the choice towards another country.

### **2. Quality of local management and historical performance of subsidiaries or sites**

The quality of the existing management at a site or a subsidiary, regardless of its location or the attractiveness of the country being considered (and levels of training / education in the country) is a key investment criterion. In the same way, sites that have demonstrated superior performance and productivity are preferred in decisions regarding allocation of resources.

These are important factors for managing the risk related to an investment and securing the expected outcome of an investment project.

These factors are often associated with the energy of management to find and gain investments within the group, in a pro-active manner and in an internal environment that is often very competitive. A form of **internal competition** to capture investments of all types often occurs **between subsidiaries**, in a manner which varies depending on the culture and the organization of the groups.



Certain site managers (manufacturing sites but also non-manufacturing entities) develop their own strategy of **performance and efficiency, guaranteeing the future of the site or subsidiary, of jobs and, a key factor, of the quality of labour relationships.**

*In particular, production capacities are sometimes allocated after internal calls for tenders, where several sites within a company compete with each other or even with external service providers.*

*This encourages site directors to “invest in the future” to keep a strong competitive position for their site (instead of strictly optimizing costs in the short term) in order to win internal calls for tenders.*

The heads of subsidiaries are therefore **highly aware** of the way in which the country for which they are responsible is perceived and understood at the group’s headquarters. Some of them consider themselves to be veritable ambassadors of their country within their group.

### 3. Nationality of the investing group

**Certain groups that were surveyed, particularly American or French groups, recognize a strong tendency to invest in their home country,** even if, in certain cases, it is not the most attractive in terms of purely rational criteria. There are many objective advantages to this type of decision.

- Naturally, investing locally appears easier from the point of view of culture, language and proximity;
- The intimate knowledge of the environment makes it possible to get the best out of the benefits associated with investment decisions (for both existing site extensions and creation of new sites):
  - Knowledge of locally offered incentives;
  - Ability to accelerate administrative processes, which can turn out to be very complex for a non-insider or for a subsidiary lacking fully fledged headquarter resources;
- This is reinforced by the capillarity effect mentioned above: as they have a tendency to invest in existing sites (rather than new sites) and as they are mainly located in the home country, some groups go on strengthening their presence at home, sometimes without actually wanting to do so.

*One of the industrial actors interviewed, who had significant international experience, indicated that if he started from scratch, taking into account his current development strategy, he would ideally locate his world headquarters and the world R&D headquarters in Boston, Cambridge (UK) or San Francisco rather than in his home country.*



*Some groups consider themselves to be too present or overexposed in their home country, both in terms of market share and the concentration of their sites.*

*They are confronted with a dilemma between on one hand, the need to internationalize to develop and reduce their exposure in the home country, and on the other hand, rational factors that encourage them to continue investing locally: weight in the local market which remains substantial, capillarity, ease, proximity, perception or reality of political and social pressure that would disapprove of delocalized investments and particularly disinvestments made in the home country.*

*They must therefore implement a delicate policy of transformation and adaptation of their sites (manufacturing, R&D, headquarters, etc.) to tackle the deep changes affecting the pharmaceutical industry.*

The **nationality of the decision-makers** is a factor that is sometimes mentioned. This remains a marginal factor, but it could have tipped the scales in favour of one location or another, all other things being equal. Is the network of French decision-makers within foreign pharmaceutical groups an asset that should be leveraged?

### **C. The importance of the environment in the countries considered for receiving the investment and corresponding decision criteria**

After the fundamental factors such as market size and growth on one hand and the factors within a company on the other, additional criteria influence the location of investments and are directly related to the attractiveness and the competitiveness of a country.

To understand properly, it is necessary to approach these criteria specifically from the point of view of the major functions that were interviewed, and to call to mind some of the major trends of changes that they experience individually.

#### **1. The Research point of view: quality and accessibility of skills to function as a network**

##### **a. A deeply changing environment**

The organizational model for Research is changing considerably, and investment policies are deeply affected by this.

Two factors should be taken into account, which interact with and directly impact investment strategies:

- (i) The **setting-up of global networks of research competencies** makes the internalized “research centre” model obsolete as the main source of innovation for pharmaceutical companies. *“We invest in brain power, and not in bricks and mortar anymore”.*



Industrial actors need more and more to open up to the outside world in order to:

- Expand their sources of innovation in a context of increasing difficulties in finding new active compounds;
- Create therapeutic solutions that combine a drug with other therapeutic components; a classical illustration is the combination of targeted active substances and diagnostic tests, making it possible to:
  - Validate the efficacy of a medicine with a patient beforehand, based on a genetic profile (personalized medicine);
  - Follow-up the efficacy of the treatment.

Research, in a an overall manner, is conducted increasingly via networks, though **partnerships with research organizations, universities, hospitals, centres of excellence, technological platforms, clusters of start-ups in biotechnologies or translational research, or specialized in technological approaches**. This should make it possible to access and integrate all of the disciplines that are now necessary for important discoveries: medicine, biology, computer science and data bases, genetics, robotics, etc.

(ii) Pharmaceutical companies want to **control their risks** even more.

In a context where innovation is becoming rare and the costs of development are increasing substantially, they would like to step in **as late as possible**, ideally on candidate drugs that have passed the “proof of concept” phase.

This also makes it possible for them during the development phase to **focus on the new challenge of personalized medicine**, a more honed adjustment of therapeutic strategies and products to patient profiles.

This causes three major changes in terms of investment in Research:

- (i) **Obsolescence of the fully integrated R&D model**, which was dominant for a long time in the industry;
- (ii) **Development of partnerships with Public Research organizations then Translational Research** actors;
- (iii) **Stronger and stronger attraction to technological “clusters”**, which are veritable pools of skills where actors and specialized partners can bathe in access to strong locally available skills, and enjoy substantial mobility of human resources between actors in the same pool.





**b. Two essential criteria in the choice of location: access to sources of innovation and a critical mass of skills**

The first two **attractiveness criteria** mentioned by the industrial actors in the field of Research were:

- The availability of strong, diversified, complementary and sharp skills, but also basic skills (technicians, etc.), that **can be mobilized quickly** in an environment that guarantees a certain level of **flexibility**, and in **large quantities** if necessary;
- The quality and the richness of the fundamental research environment that feeds development opportunities into the R&D pipelines.

The two criteria of accessibility of skills and accessibility of knowledge should be distinguished: the possibility of **rapidly hiring men and women** and the **ease** with which it is possible to partner with a **pool of existing, established and financed actors who are open to collaboration**.

Visible and internationally known, very attractive technology pools, have formed, which offer access to innovation and skills.

Some were “**spontaneously**” **born around large university centres**, particularly in the United States (Boston, Bay Area, and San Diego) and in the United Kingdom (Cambridge), which are internationally respected and supported by an undeniable track record of discoveries.

Others are the result of **pro-active policies** implemented by states or regions: Singapore, South Korea, China (particularly Shanghai), India, Israel, Canada, the Munich region, the New York region, Dubai, etc.

These policies are based on three main levers:

- Direct (aids, subventions, etc.) or indirect (favourable tax regime) **economic incentives**;
- Implementation of mechanisms that guarantee the **protection of intellectual property**;
- **Education and training** programs, or encouragement of **immigration** of trained people, like in Canada, for example.

*Therefore, “a research laboratory with 100 to 300 researchers can be created in 6 to 8 months in New England. In Europe, it would take at least 18 months, with no guarantees that it will be possible”.*

*Another example shows that the competition is intense and not only localized in major, internationally known “clusters”: a development centre of one of the industrial actors interviewed is located in the city of Campinas in Brazil: “it is a city with 3 universities, efficient road and telecommunications infrastructures, and that is home to one million inhabitants: that is three times the equivalent of the city of Toulouse!”.*



**c. ... Associated with other important factors that impact the choice**

Other factors were mentioned and are considered to be important by the industrial actors who were interviewed:

- The **costs** of research naturally have an impact: cost of accessing skills, and perception of the net cost, **after any economic and/or tax incentives**;
- The **legislation/regulations** and the **pressures of the social environment** on the **way research is conducted** (animal research, stem cells, principle of precaution, etc.) are also considered to be key elements in the strategy of site selection;
- The environment around the **protection of intellectual property** remains an essential factor that must be carefully watched;
- Factors of how “open” the country is are also taken into account:
  - “Cultural” openness, which is important in this field with its high intellectual added value: linguistic abilities, mobility of employees, ability to work in a team and to communicate, etc.
  - “Physical” openness: geographical accessibility, transport and telecommunications network, etc.;
- The **quality of life** in the country can be a plus, in a field where human resources and talents are key;
- Finally, factors of **safety of goods and persons** and **political stability** are naturally considered to be pre-requisites.

**2. The Development point of view: the triangle law of “quality/speed/cost”**

In the field of development, where the weight of clinical development is preponderant, the challenges mainly concern three parameters, which can be translated into factors of competitiveness of a country:

- **Quality** and associated risk management for the design and execution of clinical development plans are critical.

*Naturally, the objective of the industrial actors is to maximize the chances of producing studies whose quality and methodological pertinence will be accepted by all of the organizations that evaluate it: scientific experts, health authorities, healthcare providers and payers. Due to the associated challenges (filing, labelling, reimbursement by public or private payers, price, etc.), concessions cannot be made regarding the quality of a development plan, or its adherence to international standards.*

Quality relies not only on the internal skills of the industrial actors during the design and pilot phases of the clinical projects, but also very much on factors related to environments of the countries where studies are conducted:

- The training of investigators “on the field” to clinical research standards and practices;
- The availability of clinical research technicians;
- The quality of patient recruitment plans and the respect of commitments;
- The existence of hospital excellence centres that are specialized in the therapeutic domains that interest the industrial actors.



- The **speed** of implementing a clinical plan, which will make it possible to shorten the time to market. The control of deadlines is based on two main factors on the country level:
  - The availability of a **sufficient number of patients** to recruit in the clinical studies, which depends among other factors on:
    - The **size of the population**;
    - The **epidemiology** of the disease in question in the country (prevalence, any resistance to diseases or certain types of treatment, etc.);
    - But also the **existence and accessibility of epidemiological data bases** and **patient data bases** that make it possible to rapidly and more effectively identify patients that could be recruited for a study;
  - The **efficacy of the organization** of the clinical research environment:
    - **Time availability**, interest, and **level of involvement** of doctors for clinical research;
    - **Recognition of research** in physicians' activities (evaluation criteria, incentives to publish, etc.);
    - **Organization of the healthcare system**: concentration or dispersion of hospital centres (which impacts the pace of recruiting), existence of centres of excellence or links between primary care practices and hospitals, etc.
    - **Administrative efficacy**, as much for obtaining **authorizations to conduct clinical trials** from the authorities as the **ease of contracting** with establishments and/or doctors;
- Finally, the **cost** of clinical trials is taken into account:
  - Generally ranked third, all other being things equal (at equivalent quality and efficacy, or at least balanced with these two criteria);
  - With variable approaches depending on the industrial actors, that may or may not make it possible to take into account any tax incentives:
    - Tax mechanisms sometimes complex on the local level and that of international tax agreements;
    - Internal organization of industrial groups that does not always make it possible to pass the tax saving to the P&L of the decision centre.

These three parameters are related, and, like the three sides of a triangle, we cannot modify one without impacting the other two.

All countries, however, are not positioned in an equivalent way on these three criteria, and this can vary depending on therapeutic domains; finally, **all industrial groups do not apprehend the relationship between these three parameters in the same way.**

- For example, some groups describe an approach that first takes into account the **level of excellence of the experts** it plans to have participate in the studies that will make up the submission dossier for the authorities, and proceed in two steps:



- (i) Ensuring, in each key country for development and commercialization of the product, the participation of experts that are references in the country (and particularly experts known internationally) to:
  - Participate in the evaluation of the interest of the product (while respecting principles of ethics and with the transparency necessary to avoid conflicts of interest);
  - Identify its position in the therapeutic strategy;
  - To make it known within the scientific and medical community;
- (ii) Next, to allocate remaining clinical development resources to countries and clinical trial centres based on the criteria of “quality/deadlines/costs”, as described above, and based on the track record of the country in the therapeutic domain.
- Other groups have more systematic approaches, based essentially on key **performance indicators**, defined and measured within each therapeutic area, to set up clinical development strategies that are focused on a limited number of countries that are the most efficient in the therapeutic area. **This can lead to disinvesting or reinforcing clinical development resources in a country for a given therapeutic domain.**

In both cases, the subsidiaries of pharmaceutical groups have to sell internally the qualities of the environment of their country in order to “capture” a greater share of the investments associated with a clinical development project:

- **The quality and the reputation of the clinical experts with whom they establish partnership networks in the country;**
- **The quality of the clinical research platform** in the country.

If the subsidiaries themselves are judged on the ability to respect their commitments to headquarters, it is in a direct line with the **ability of investigators in the country to honour their own commitments in terms of patient recruitment, compliance to the clinical trial protocol and the quality of follow-up.**

Finally, the clinical development phases in question must be distinguished: some industrial actors, for example, consider that emerging countries are not mature enough to conduct the initial development phases (phases I and IIa).

Their strategy is thus to conduct:

- The **early phases** (including with healthy volunteers) **exclusively in developed countries**, with suitable centres;
- The **later phases** (IIb and III), which require a larger number of patients and which are more expensive, in a mix where **emerging countries, which are sometimes better positioned in terms of costs**, are more present.



### 3. The Industrial Affairs point of view: to accompany structural changes and to position themselves on production with high added value

#### a. Manufacturing facilities requiring in-depth changes

As indicated earlier, decisions about where to invest in the industrial field are strongly influenced by 3 factors:

- The global overcapacity, which mainly affects developed countries impacted by the decrease in volumes of proprietary medicinal products;
- The movement of the centre of gravity of expected growth towards emerging countries, and therefore the movement of related investment (accentuated by the demands of certain countries for local investments in return for market access);
- The capillarity effect, which promotes the extension of the capacity of existing sites instead of the construction of new sites (“greenfield”).

*The **delocalization** moves aiming at decreasing production costs of proprietary medicines (synthesis products as opposed to biomedicinal products) **have remained rather limited up to now within the drug industry.***

- *It has occurred over the past 10 to 20 years, when the volumes of some major compounds (“blockbusters”) warranted it;*
- *It has particularly affected “primary” production, i.e. the production of the active substance;*
- *This effect has remained relatively marginal for several reasons:*
  - *Risks related to intellectual property in certain “low-cost” countries;*
  - *Strong demands regarding quality, which explains the importance of maintaining a high level of control and therefore a certain level of proximity with the decision-making centres;*
  - *Desire to maintain control over the production of important strategic products;*
  - *Relatively low proportion of labour costs in the industrial cost price of medicines (even if the flexibility of labour is considered an important factor);*
  - *Local subcontracting solutions (outsourcing to contract manufacturing organizations or between drug manufacturers) that make it possible to secure production and provide a certain level of flexibility;*
  - *Dominant criteria in certain cases of proximity to the source of the active substance (for example, a plant that grows only in certain regions, justifying local extraction and production);*
- *Secondary production (pharmaceutical form) is best carried out near the markets for which it is intended for quality control reasons, as well as packaging, to facilitate the “delayed differentiation” (languages of the packaging and package leaflets and other regulatory adaptations);*
- *The delocalization effect today mainly concerns the manufacture of “commonplace” and mature products, production for local markets (sometimes imposed by local authorities to access the market) and the manufacture of generics).*



In the context of overcapacities, big industrial investment projects for “traditional” manufacturing are rare. The base of traditional manufacturing sites has even been subject to a wave of rationalization and disinvestment: mutualisation of production capacities between manufacturers, sale of sites to contract manufacturing organizations and/or generic makers, site closures in the United States, and more rarely in Europe.

- Though delocalization is in fine rather limited (see boxed text above), the expected growth in emerging countries will not make up the difference in the excess capacities in developed countries;
- Legislation concerning intellectual property in Europe does not make it possible for local actors (contract manufacturing organizations for generic makers or purchase of a local site by generic makers) to anticipate the expiration of patents; this does not apply to manufacturing sites located outside of the EU. These are thus favoured, and once the market positions have been taken, it is difficult for local actors to catch up<sup>4</sup>.

In addition, **innovative active substances from biotechnologies** that constitute growth opportunities for industrial actors require **radically different production tools**, leaving few options for reconverting traditional sites. Only one case of reconversion of a “traditional” industrial pharmaceutical manufacturing site into a biomedicines manufacturing site was identified in France.

Furthermore, the manufacture of biomedicines or biotechnology products:

- Is generally carried out in smaller volumes (more targeted products, “denser” pharmaceutical forms);
- Is comparatively less labour-intensive;
- Generates fewer industrial jobs than “traditional” medicines.

The related investments however are high, due to the complexity of the tools in question and the higher demands of quality and control.

Finally, these industrial processes are **more closely related to the R&D phases** than to the industrialization of chemical active substances. The **proximity of skills** that are used in the R&D phases of these products is important during the design, validation and exploitation of these industrial sites<sup>5</sup>. Therefore, **industrial investments in bioproduction are generally made in the country that is the source of the discovery and the development of the new product and/or that manufactured the batches used during the clinical trials.**

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<sup>4</sup> One of the decisions taken by the CSIS in October 2009 had the objective of allowing agreements between proprietary medicinal product manufacturers and generic makers to authorize manufacturing of generics by anticipating the expiry of the patent, and thus preserve jobs within the country.

<sup>5</sup> These sites, the construction cycles of which are relatively long, are generally built very early in the development process, while the risk that the product being developed will not come to market is still high.



**b. Significant challenges for transformation and productivity improvements in developed countries**

Faced with the predictable rarity of large traditional industrial investment projects, the following challenges should be kept in mind:

- Rationalization decisions could impact existing tools. Industrial sites **must be transformed, adapted** and in certain cases reconverted. Measures that make it possible to either slow down or reverse this effect must be identified, particularly those that aim to **improve the productivity and competitiveness** of the sites. Due to the rationalizations that are being carried out on the regional level, it may be **hoped that capacities can be captured** (and thus jobs and investments) **from sites that are closing elsewhere**.
- Maintaining the existing industrial base will also come from the **local manufacturing of generics** consumed locally and/or those replacing proprietary medicinal products that were manufactured locally.
- Finally, there will still be opportunities in packaging and distribution (creation of continental distribution platforms), as these are activities that will remain close to the markets they serve.

**c. Factors of attractiveness that were clearly identified for the industrial investment choices**

When **making decisions about the location of industrial investments** (or disinvestment decisions), industrial actors indicated that they take the **following attractiveness factors** into account:

- The **stability of the political and social environment**, which is a prerequisite;
- The **central geographic location** and/or the **proximity to the markets to be served** (particularly for forms that are very expensive to transport, i.e. liquid forms and cold chain products, especially when their sale price is low);
- The **tax regime** (corporate tax), the impact of which on profitability is higher than the cost of labour and payroll taxes. We noted in our interviews that North American groups were more attentive to this criterion than other groups;
- The **flexibility** of the social and work environment, social relations and the **social climate**;
- **Industrial skills** and their impact on **quality** of manufacturing and productivity;
- **Infrastructure** for transportation and means of communication;
- Regulations and practices related to respect of **intellectual property**, and practices in terms of **counterfeiting** and **parallel trade**;
- **Political willpower** at the local and state levels and **measures to accompany** either investment or transformation;
- The readability and accessibility of **incentives** (an excessive number of mechanisms with complex access conditions can have a discouraging effect, particularly for foreign actors).



As a reminder, an essential factor in the choice of the location for bioproduction sites can be the proximity to R&D skills that are responsible for the development of these products. Capturing investment in new biomedicines production tools will depend mostly on the **competitiveness** and the **attractivity** of the Research environment, at the early stages of the **product lifecycle**.

#### 4. The point of view of commercial operations: predictability and recognition of innovation

Commercial operations representatives (directors of pharmaceutical operations at a regional or global level, or representatives of key functions related to operations), were interviewed for several reasons:

- They orient **investment** decisions that concern their **own** field;
- They are likely to influence the **investment decisions of other functions** (R&D, production, distribution, etc.);
- They are in close contact with the markets and the environment of countries, and they are highly aware of the perception of a country within their group.

##### a. Commercial operations investment decisions

- **Investment decisions in this field** mainly concern **medico-marketing** investment. The main envelopes are for:
  - **Promotional expenses**, of course, which remain concentrated on doctor visits, even if this activity is also undergoing extensive changes. These changes, which are due to the development of generics and the end of the blockbuster model, concern all developed countries and are being carried out with strong inertia because of their social impact and the delays in bringing forth a new promotional model as a substitute;
  - Expenses on **phase IV clinical trials**, conducted to support the competitive position of the products on the local market.
- Another type of investment for which the influence of commercial operations is strong concerns the location of a regional headquarters or a regional platform for a function or a business unit.

What is directly at stake regarding the location of a European headquarters may vary in terms of size (a few dozen jobs to a few hundred), but it can also lead to the creation of an important zone of influence for other types of investments (distribution platform, functional platform such as a call centre or an accounting centre, or even a clinical development centre).





*The criteria for decisions regarding where a regional headquarters or regional functional platform should be located are as follows:*

- *The central geo-strategic position in the middle of a region and/or its accessibility by means of transportation;*
- *The proximity to regional political decision-making centres or authorities (London, Brussels in Europe);*
- *In certain cases, the local tax regime and international tax agreements can impact the choice of a country as the location for an invoicing or distribution platform, and, more for reasons of coherency than for actual need, the Regional Direction and all the support functions;*
- *Infrastructure regarding equipment, transportation, telecommunications, etc.;*
- *The level of training and education, mobility and linguistic openness;*
- *The pre-requisite of a stable social and political environment.*

*As a reminder, this type of decision is rare and is generally made for long periods of time, and for this kind of decision-making, the weight of history can be dominant (for example, acquisition in a country that gives a subsidiary a decisive position).*

- Finally, the influence exerted by the heads of Commercial Operations on the important investment decisions of other functions (production, R&D) is very variable and depends on:
  - A group's organization;
  - A group's size (the decision making power and the independence of large divisions or functions is greater when groups are larger and more complex);
  - The methods of governance in place.

*The changes observed in several global pharmaceutical groups should be noted here, which are moving in the direction of better coordination of major functions on a regional level, particularly in Europe.*

*This is the result in particular of the observation made by these groups that their weight, influence and the image that they project must be better organized and integrated between major functions in order to take advantage of the critical mass that they represent with respect to the people they interact with (decision-makers, authorities, payers, distributors, media, patient associations, etc.).*

*This change is moving towards increased influence of operational functions (which are in contact with the decision makers and authorities in their country) on investment decisions of all kinds.*



## b. The major factors of market attractiveness

Besides the criteria of **size** and **growth**, which have already been mentioned, the directors of commercial operations listed several factors that contribute to the attractiveness of markets and their influence on investment decisions:

- Firstly, the **price level of medicines** and to what extent **innovation is recognized** were mentioned as essential points.

Perceptions were, however, rather variable between interviewees concerning:

- A “spontaneous” preference for countries where prices are set freely (USA, United Kingdom, Germany);
- A more in-depth and open analysis, which sometimes stresses an apparent freedom to set prices which is actually limited to a few rare innovative products (Germany) or which is hindered by recommendations and guidelines on use that are very restrictive (United Kingdom).

Among the administered price systems, those based on indexing mechanisms are particularly criticized for their waterfall effects that impact several countries (Southern Europe, in particular).

The price level is also influenced by exchange rates, and the United Kingdom was mentioned several times as having greatly suffered in terms of attractiveness due to the devaluation of the pound compared to the euro, dollar or Swiss franc.

Price levels have a direct effect on:

- The sequencing of product launches, i.e. the choice of countries where products are launched earliest and thus become references for price setting in other countries;
- In certain cases, on the very decision as to whether or not to commercialize a product. Too low a set price in one country can force industrial actors not to follow through with the launch for reasons related to:
  - . The economic return requirements of the market in question;
  - . The risk of developing parallel trade from that country.

These two kinds of decisions can thus affect patient access to new therapeutic solutions.

- A second essential criterion is the readability **of the healthcare policy** in general and the way in which it is applied to **medicinal products**. This concerns:

- **Regulation of supply**: modalities for setting prices already mentioned, and more generally, **the path of market access**, steps in the registration process, the medical value assessment and negotiation of prices and reimbursement, and the **time this will take**;
- The openness to discussion, **accessibility**, skills and resources **of the authorities** in charge of these processes: industrial actors appreciate powerful contact people, which is a sign of efficacy, rapidity, pertinence of decisions, or even influence beyond the borders of the country on other neighbouring or regional authorities;



- The **governance of market access**, its **transparency** and the **predictability** of decisions, and the **stability of the regulatory and legislative framework**;
- The **regulation of demand**, via recommendations of good usage and other measures that control the use of products as well as all the regulations that constrains the promotion, communication and training on products;
- **Tax regimes** specific to healthcare products.
- All of the factors that impact the **speed of access** to market **and the degree of market penetration** are strong components of attractiveness:
  - Administrative processing time, as mentioned above;
  - **The ability of the country to adopt innovations and new products**;
  - The health insurance system, which ensures **access to healthcare** for the population
  - The existence of **accelerated or facilitated mechanism of access**: orphan drug or paediatric drug status, ATU (temporary authorization for use) or PTT (temporary treatment protocol) in France for example.

Though the existence of a link between investment decisions and the “intrinsic” attractiveness of a market (size, access to care, prescribing habits, expected growth, etc.) is unanimously recognized, opinions differ concerning the delicate link between investment decisions and the decisions of the authorities in charge of market access; two visions must be distinguished:

- For certain interviewees:
  - The criteria for investment choices must be based on objective facts that are specific for each type of investment: political stability, skills and productivity, tax regime, flexibility, quality of the research and clinical development environment, etc.;
  - This can be accompanied by specific and transparent incentives set up by states or regions;
  - Investment choices must remain **disconnected from any expected, hoped for, or negotiated decision concerning market access** of products: price, reimbursement, rapidity of the evaluation process, etc.
- For others:
  - Investment strategies must take into account expected (or past) decisions in terms of market access and “*they must be recognized in all transparency*”;
  - Developed countries cannot ignore and must **fight** “on equal terms” against the **aggressive policies of other countries** that impose, for example, local manufacturing in order to access their market.



#### IV. THE RELATIVE POSITION OF FRANCE REGARDING THESE CRITERIA

The competitive position of France was judged by the industrial actors that were interviewed, based on the identified decision making criteria. We particularly attempted to:

- Distinguish the reality in France from perceptions of the image of the country;
- Obtain a comparative evaluation of France versus the countries with which it competes globally and within Europe.

##### A. A market that remains attractive in terms of size, market access and regulation

- France is, based on its size, **one of the two major European markets** and the **third global market** after the United States and Japan (2008).
- On the other hand, like other Western European countries, it is now **caught** between the two major geo-economic forces with strong attractiveness:
  - The **United States of America**
    - . Largest market in the world (40% in 2008), almost four times larger than the second (Japan);
    - . Large integrated market (as opposed to the mosaic of regulations, paths to market access and ways in which prices are set and reimbursed that is Europe);
    - . Where the predictable drop in prices will be compensated by the inflow of more than 30 million additional patients;
  - The **emerging countries**, with expected growth that is much higher than the developed countries, whose mature markets are greatly constrained by the necessary limitations of healthcare costs.

The attractive force these emerging countries exert on investment flows is even stronger when:

- . The expected growth is associated with large market size;
- . These countries require local investments to access their markets.

China is the major beneficiary of this movement, but India, Brazil, Russia, Turkey, Mexico and South Korea should also be listed, and all of Asia in generally.

- The movement of investments could therefore take place mainly **at the expense of Europe**, and particularly “old Europe”, where for 3 or 4 decades now, the share of investments that Europe was able to capture has already been decreasing to the benefit of the United States.

**Europe** can therefore be considered as a **secondary pool of competition** within a global pool, and **in which France is in competition to capture or hold on to a declining share of investment.**



- **The attractiveness of France remains strong (“a market that cannot be ignored”)**, particularly in the opinion of **international** operational heads, who have an overall view of markets in Europe and in the world. They highlight:
  - The **size of the market**, supported by the quality of the healthcare system and the fundamental principles that ensure a high level of **reimbursement by the state**;
  - The existence of a **conventional system** that maintains constant dialogue between the authorities and the industry, despite its complexity;
  - The quality and the **skill level of the regulatory authorities**:
    - . **Accessible** and open to discussion;
    - . **Influential** in Europe in certain fields;
    - . Ensuring administrative processing times that are relatively good;
  - **Public health priorities** that mobilize resources and skills in certain therapeutic fields (cancer, Alzheimer’s);
  - The **rapidity of adoption of medical innovations** by doctors, who compensate for market access that is slowed down by the price-setting process;
  - A unique mechanism, to be maintained, that makes it possible in some instance for **patients to rapidly access innovations** before the granting of a Marketing Authorization: the ATU (Temporary Authorization for Use);
  - Price levels that are generally in the median of the price range in Europe:
    - . Administered prices, but **recognized skill and pragmatism of the CEPS (French price-setting committee)**;
    - . The stability of the Euro (with regard to the impact of exchange rates on prices in the United Kingdom);
- **Certain local interviewees**, confronted with this environment on a daily basis, have a **more critical view** on certain points:
  - An evaluation system of the medical value of medicines **that does not sufficiently recognize innovation and incremental progress**, lacking transparency and predictability, and that is too strongly influenced by economic considerations;
  - A **lack of visibility** with regard to drug policy (and healthcare policy in general), with the **PLFSS** (Projet de Loi de Finance de la Sécurité Sociale, or laws on the financing of social security) likely to change the rules of the game every year;
  - A lack of national consensus on healthcare policy between the majority and the opposition;
  - A **tax regime, specific to the drug** industry, which is complex and unique in its own right with 11 specific taxes;
- France, as a location for a European headquarters or a regional functional platform, has several advantages:
  - Central position in Western Europe;
  - Quality of the infrastructure, particularly in the Paris region;
  - Quality of life.

On the other hand, it is perceived as poorly positioned on corporate tax criteria (compared to Switzerland and Holland, in particular), and on the social environment (point covered in greater detail in the industrial section, IV-B).



- The perception of the attractiveness of the markets of the large neighbouring countries is more contrasted.
  - The United Kingdom benefits from a generally positive opinion for its free pricing system, often nuanced by:
    - . The drop in prices following the depreciation of the pound;
    - . The slowness and severity of the NICE recommendations;
    - . The slowness and “cultural” shyness of English prescribers to adopt new products.

The predictability of the healthcare policy environment based on the PPRS was praised.

When a location needs to be chosen for an operational direction or European functional headquarters, several advantages are brought up:

- . The proximity to the EMA (ex-EMEA);
  - . The English language, which is comforting for North American groups;
  - . The flexibility of labour law;
  - . The accessibility, quality of life and professional environment that London offers.
- Germany benefits from its status as the number one European market.
    - . Free price setting is often mentioned as an important advantage, though sometimes nuanced (depending on the interviewees, product portfolios and personal experiences) by an application of this rule that is limited to the few very innovative products getting to the market.
    - . Germany is frequently mentioned as an example of a country where the authorities are not very accessible, not very open to discussion, or even influenced more by a form of ideology than by scientific rationale.
    - . Finally, the absence of an announced policy regarding the healthcare industry is also often criticized, particularly by foreign actors.

When a location needs to be chosen for an operational direction or European functional headquarters, several advantages are brought up:

- . Its central position in Europe;
  - . The weight of the country in the region (size of the market, political influence)
  - . The stability of the social environment.
- The Southern European countries are widely criticised for their very low price levels and resulting parallel trade.



**B. A high quality industrial tradition, burdened by a perception of the social environment that does not correspond to the reality**

- The perception of the industrial environment in France is very positive for numerous aspects, which explains its position as the **number one producer and exporter of medicines in Europe**, and number three exporter in the world:
  - The quality of the engineers and technicians and the skill level in engineering;
  - A strong industrial tradition in the field of medicines, due to the investment policies implemented at the end of the 20<sup>th</sup> century;
  - The existence of very good transportation and telecommunications infrastructure;
  - The quality level of manufactured products (recognized for medicines and medical devices, in particular);
  - The quality of the drugs distribution system.
- On the other hand, the **perception of the social environment is not good, particularly for North American industrial actors and decision makers located in the USA**. This is due to three factors that are widely diffused in the media outside of France:
  - The legislation concerning the 35-hour working week, the duration of paid vacation, and the general lack of flexibility of labour law;
  - The social climate, particularly strikes in public transportation and civil service;
  - Occurrences of confinement of company directors as part of labor disputes.

These factors generate misunderstanding and a **strong mistrust**, particularly from North American decision making centres.

*The head of Supply Chain Strategy of one of the interviewed groups said that France is probably “disqualified as a possible location for a European distribution platform or for manufacture of a strategic product because of the risk of blockages or strikes in the transportation sector”.*

The lack of flexibility was mentioned in particular by actors who have conducted or who are conducting layoffs.

More than the hostility of the social partners and local politicians (often conscious of the necessity of adapting existing structures and satisfied with the conditions that are negotiated), the constraints, administrative delays and associated costs are perceived as the major factors stopping transformation.

The lack of flexibility perceived concerns labour law (encompassing work contracts, but also outsourcing, sometimes exposed to the risk of requalification), but also the habits and demands in terms of maintaining employment.

*An industrial actor with R&D centres in France and in the US wanted to hire as part of a project for which the outcome was uncertain (possibility of having to interrupt or externalize). The hirings had to be done in the US, as there were not enough interested candidates in France.*



Some interviewees had the impression that **“generally, in France, it is not legitimately acceptable for a company that is making money to restructure”**.

The countries that were mentioned the most as offering better flexibility were the United Kingdom, and the Scandinavian countries, where social protection is considered to be good.

- However, this poor **perception** is **nuanced** by the industrial actors who know France better, and in their opinion, this perception does **not actually reflect the reality**:
  - The good productivity of the work force makes it possible, according to some responders, to be more competitive than countries that have implemented extremely favourable fiscal policies (Ireland, for example, where high salaries absorb fiscal savings);
  - The country is reforming in a social climate that remains, to date, rather peaceful:
    - Relaxation of the 35-hour working week regulation, which ultimately has made it possible to develop a **work organization with some flexibility**;
    - New legislation on overtime, reform of special retirement regimes and health insurance plans, introduction of minimum service for public service strikes, etc.;
  - Other countries also have a complex and restrictive work environment and social relations that can sometimes be tense (Italy, Germany, and Holland).

*“If we look beyond perceptions, decision-making centres have observed that things do work in France: our group decided to establish an 800-person site in the South of France, and the results are excellent and perfectly in line with the performance demonstrated in other countries”*.

- It should also be noted that **corporate taxes** in France are **not considered to be very attractive**, particularly for North American groups that are more sensitive to this criteria than others.

Ireland is not the only country to have set up incentives in this area: **Singapore, Porto Rico and China** are mentioned as offering tax regimes or attractive adjustments.

In certain cases, the local tax regimes and the international tax agreements can encourage the location of an **invoicing and/or distribution platform** in a certain country. More for coherency than by real necessity, a whole regional site and all the support functions can then be located in the same place. A country that is particularly attractive for this is **Holland**.

- Due to the rarity of large industrial investment projects (capillarity of existing sites, ongoing rationalization of manufacturing base, investment figures at stake) and the attractiveness of emerging countries, large investments in this field in Western Europe should not be expected. In addition, the “equipment rate” in drug factories is already high in France.





- However, **efforts to support improvements in productivity are necessary** in order to limit the risk of disinvestment and to defend the existing industrial base in view of the challenges mentioned above (III-C-3-b).

**According to the industrial actors, there is a certain French resistance to transformation that, if it seems to limit job loss in the short term, condemns the competitiveness of the industrial tool in the middle term via a lack of adaptation and competitiveness.**

*“The French site of an American industrial actor succeeded in maintaining an excellent level of international competitiveness within the group:*

- *By delocalizing a part of its activities in a country with a productivity gap of 25% in this field;*
- *By keeping high added value activities in France, which require skills that are not available elsewhere.*

*Overall, the performance is excellent and everybody has gained”.*

**Finally, capturing investment in new production tools for biomedicines will depend more on competitiveness and attractiveness at the beginning of the chain, in Research. That is where important efforts must be made.**

### **C. A high-performing Research & Development environment with underexploited potential**

- It must be acknowledged that the weight of France in the R&D spending of several foreign leaders of the pharmaceutical industry is not in line with the weight that the country represents in their sales figures.
- However, **France** benefits from **important advantages** to be a high-performing actor in the global setting of Research and Development in life sciences, particularly:
  - The strike force of Public Research in the biomedical field, with large, internationally recognized organizations (INSERM, CNRS, Institut Pasteur, Institut Curie, CEA, etc.).
    - These organizations are known and respected for their quality and their scientific level by the managers interviewed;
    - This is confirmed by the rankings in the citation indexes;
    - The situation is more nuanced for university centres, which are only well known by R&D heads of industries located in or close to France: **“In the USA, the only known French university is the Sorbonne”**;
  - French excellence in fields like engineering, math, physics, etc. as multi-disciplinarity is emerging as an important lever in the performance of research and these skills can become an advantage for new healthcare technologies (imaging, nanotechnologies, bioinformatics, etc.);
  - The cost of research is perceived to be competitive;



- The Research Tax Credit (CIR – Crédit d’Impot Recherche) is praised as a favourable mechanism, but:
  - . It is poorly understood and complex, sometimes difficult to sell in global headquarters, particularly American ones, and requires regular in-house communication;
  - . Some countries can actually be more competitive despite the RTC for certain R&D activities (Spain given as an example) or when their own incentives are taken into account (United Kingdom);
- The quality of the health system and the level of expertise of physicians in “field” medicine as well as clinical research;
- The reputation of being international opinion leaders in several therapeutic fields (cancer, AIDS, infectious diseases, CNS, etc.);
- The proximity to other very rich resources in Europe that can be leveraged, for example:
  - In **proteomics** (while the US has established its hegemony in genomics): European Molecular Biology Laboratory in Heidelberg, Swiss Institute for Bioinformatics, etc.;
  - In oncology: German Cancer Research Centre in Heidelberg;
- The regulatory environment is favourable in the field of animal experimentation, which is becoming more and more sensitive (compared to situations in the UK, Germany, Switzerland, Sweden, etc.).
- Unlike other countries, France **has been unable to transform these advantages into actual competitive advantages**. There are many different reasons for this:
  - In the past, there was no strong, focused and coordinated investment policy for research in life sciences:
    - . As opposed to what France was able to accomplish in fundamental and applied research in recognized fields of excellence today (atomic energy, aeronautics, etc.);
    - . As the investment policy of the 80’s and 90’s in the drug sector successfully promoted the industrial side.
  - The dispersal of Public Research, which results in numerous actors (national research organizations, evaluation agencies, financing agencies, universities and university hospital centres, centres for excellence, etc.), and which led to the implementation in 2009 of the National Alliance for Life Sciences and Health (AViSan).

Industrial actors appreciate this initiative, as they understand it and consider it to be a step in the right direction, which should quickly result in visible measures, particularly the implementation of a “one stop shop” entry point.

Other recent and ongoing initiatives have been praised (INCa, ANR, independence of universities, reforms of the INSERM and CNRS, French Alzheimer’s Network, etc.) by interviewees who were more familiar with the environment, but its complexity remains the predominant impression.



- The relative dispersion of public investment does not promote the emergence of large bioclusters with the critical mass necessary to demonstrate visible ambition internationally.

The availability “in volume” of skills cannot be compared to the power of large “pools” of skills that have been frequently mentioned: USA (best in class) and China, and a few clusters like Singapore.

Even if the independence of universities and the emergence of competitiveness centres are appreciated in principle, their number and the way in which they are spread out does not promote an effective interface with industrial partners, particularly when R&D decision centres are located outside of France.

In the same way, the number of cancer and genetics centres (“cancéropôles, genopôles”) is the reflection of a complex and fragmented structure, even if some organizations stand out (Medicen, Lyon BioPôle, The Strasbourg Biovalley, etc.) and if some industrial actors were able to find their way.

*“One of the Biocentres in France made it possible for us to bring together development and industrial teams with results comparable to those in New Jersey or Singapore”.*

The planned selection of 5 University Hospital Institutes should certainly make it possible to create a network that will be visible internationally and better adapted to the needs of industrial actors.

- The insufficient number of Public-Private partnerships shows greater difficulties in collaborating than in other countries, for many reasons:

- . Processes of project evaluation and valorisation need to be optimised:

- .. The need for **selectivity**, market expectations and the regulatory context are not sufficiently taken into account to ensure projects’ competitiveness on an international level;

- .. **Complexity** and **slowness** of processes due to the number of people involved and a lack of convergence;

- . A French cultural environment that is changing, but that **still pits the public and private sectors against one another too much**: training and education, ways in which researchers are evaluated, strong risk aversion of not only researchers, but also industrial and financial actors.

There are many symptoms of this: insufficient **mobility** between the public and private sectors, insufficient **industrial orientation of projects**, lack of recognition of the **usefulness of applied and translational research**, low attractiveness of France for **international researchers** (except for the large centres of excellence), etc.

*“There is a deep and cultural misunderstanding that is almost dogmatic between the world of public research and the private sector: public research laboratories, universities are places of knowledge, not business”; this is changing according to some, too slowly according to others...*

*“The discussions break down rather often on questions related to sharing economic benefits (valorisation) and the status of personnel who would be hired during partnerships (joint venture, for example)”.*



- Contracting instruments do exist, but their implementation is long, difficult and slowed down by heavy bureaucracy.

*Numerous examples are given of partnerships that were abandoned due to a lack of reactivity of potential partners, exhaustion (sometimes more than 2 years of negotiations) or dropping the process in favour of other collaborations, with other partners, in other countries, where agreements can be made more quickly and easily.*

- **An image problem of French research** that should better reflect its value via “**success stories**” to industrials internationally, but also nationwide: to the general public, to social partners, media and political decision-makers.
- A vision of a world of research that does not communicate enough between organizations, universities and hospital/university centres (where the US seems to communicate a great deal).
- The United States, thanks in particular to the regions of Boston, San Diego and the San Francisco Bay, and to large national organizations (NIH, NCI, etc.) are still considered to be the most attractive country for R&D:
  - Exceptional quality of the research environment and network in terms of skills, critical mass, organization and ease of access (partnerships), etc.
  - ...exacerbated in the case of North American industrials who confess to strongly favouring local investments and partnerships (some of them with several research centres don't have any outside the USA)
  - ... very widely recognized by industrial groups from other countries
  - ... despite its cost, which is among the highest.
- The R&D environment in **emerging countries** (Asia and Eastern Europe) is characterized by:
  - Very competitive cost, due to the emergence of generations of energetic, motivated, hard-working researchers who are increasingly well trained;
  - The attractiveness and the dynamic role of Singapore;
  - A capacity for investment that is increasingly strong (India, China), capable of realizing strategic technological advances in the fields of health and important related domains: telecommunications, data bases, telemedicine, etc.;
  - An environment around the protection of **intellectual property** that still requires great cautiousness, even if perceptions are variable: things have improved for some, not enough for others.
  - A favourable regulatory environment (animal research, principle of precaution, etc.).

*China, “which finances the training of 10,000 PhDs per year, now offers a high-quality R&D environment, that is competitive in terms of costs and linked to a growth of demand that is among the most important”.*

*China is the destination that is the most often mentioned, ahead of India, as capturing a growing portion of R&D investments.*



- The Western European countries mentioned (United Kingdom, Germany, Nordic countries) are positioned in a way that is very similar to France in terms of attractiveness of the Research environment:
  - Caught between American dominance and the competition of emerging countries;
  - Disposing of great scientific skill identified within a limited number of centres of excellence;
  - Distinguishing themselves by a few specificities that could make a difference, depending on the field:
    - Strong pressure exerted in the United Kingdom and in some Scandinavian countries by activist groups, particularly in the field of animal experimentation;
    - An ability to react and set up translational projects that is very quick in the United Kingdom;
    - The cost of research in Germany is perceived as too high by some interviewees.

#### **D. A clinical research platform up to international standards with perfectible efficacy**

- In the field of clinical development, France is still positioned among the leading countries:
  - Recognized excellence of investigators, particularly in the cardiovascular field (and metabolism, according to some interviewees), oncology / haematology, infectious diseases / HIV, neuroscience;
  - Compliance to international clinical standards;
  - Strong influence of French opinion leaders, locally or internationally (depending on the field);
  - The strength of the hospital infrastructure and the organization of the healthcare system;
  - The weight of the French experts and authorities in the field of Regulatory Affairs in Europe;
  - Long-lived partnerships established between doctors and industrial actors;
  - The relatively high pre-tax cost, but competitive when taking the RTC into account, *“even when compared to certain countries that are considered to be among the least expensive”* (Eastern Europe, Asia, etc.).
- However, as is the case for many countries, opportunities have been identified to increase clinical efficacy in the country (some of which have been known for a long time...);
  - Difficulties in recruiting patients and sometimes meeting recruitment commitments
    - Lack of a sufficient reservoir/flow of patients in certain fields, particularly due to the **dispersion of hospital centers** (particularly compared to countries that are more centralized, like Belgium or Holland);
    - Absence of a national patient database (like the ones that exist in some countries: United Kingdom, USA, Canada, Scandinavia, etc.);
    - Need to set up epidemiological databases that make it possible to optimize recruitment in the context of decentralized hospital centres;
    - Productivity is perceived as very variable depending on the industrial actors interviewed;



- Administrative and contractual aspects really need to be simplified (frequent double contracting with establishments and investigators, for each recruitment centre that is opened);
- Clinical research activities need to gain a higher value in the performance assessment of hospital physicians:
  - The medical population is focused on patient follow-up rather than research;
  - Hurdles related to a cultural perception of clinical studies that is sometimes negative (“human guinea pigs);
- Improvement of the readability and visibility of the RTC, praised as a favourable mechanism, but not very well known and difficult to “sell” within global headquarters, particularly American ones: ***“sometimes just a bonus rather than a true deal maker”!***
- The well-received creation of the CeNGEPS has not yet made it possible to observe actual improvements:
  - According to some interviewees, it might suffer from:
    - . An approach that spread the resources out too much;
    - . The integration of Clinical Research technicians into the teams that house them, with no visibility or control on actual activities.
  - For others, it is an initiative that is still recent, and that needs time to leverage the resources (particularly human resources) that it has been granted and to structure its networks.
- Competition between countries is strong, due to the relative mobility of resources and clinical research investments (not within a study, but quite easily from one study to another, based on the historic track record of the country).

Some countries were mentioned several times:

- The Scandinavian countries and Holland, for their remarkable organization and the quality of their clinical trial platforms (as well as Italy in the cardiovascular field);
- The weight of public health policies in the Scandinavian countries, which provides the industrial actors with good visibility;
- The United States and Germany for their generally high costs;
- China, India, Russia and the rest of Asia for their increasingly important share in investments, due to the movement of the centre of gravity of market base and growth;
- The same countries, along with Brazil, the Eastern European countries, South Africa, for the size of the population, making it possible to ensure efficient patient recruitment;
- Emerging countries that can still pose problems regarding the quality of a study, even if they are progressing rapidly.

However, China is perceived as complicated due to its restrictive administrative environment (few possibilities to conduct phase I studies, constraints regarding the exportation of samples of human tissue) and a form of protectionism: projects are deliberately slowed down in order to have enough time to acquire equivalent or competing technologies and to develop them in the mean time.

India has excellent CRO structures, but lacks a network of suitable hospitals.



**E. A rather divided perception of an economic and cultural environment that does not sufficiently promote private companies and their values**

- By and large, the interviewees indicated that France suffers from an insufficiently developed entrepreneurial culture, somehow “low key” compared to other countries such as the United States and the United Kingdom:
  - The aids for the creation of companies are multiple and complex;
  - General administrative heaviness and slowness;
  - Lack of openness towards the rest of the world:
    - . Higher language barriers;
    - . Less mobility of workers.
- This is both a structural and cultural effect, that is not specific to the healthcare industry, but that can be observed in this field via several symptoms, such as:
  - Slow growth and an insufficient network of companies in the biotechnologies sector;
  - Insufficient public and private financing, due to the perception of risk and complexity in the field of life sciences:
    - . Moderate interest of capital riskers compared to their activity in the US (“*we only invest in what we understand well*”); this could change based on a few recent success stories (Fovea, Corevalve, etc.);
    - . Lack of ambition of the “Biotech Fund”: “*It has 100 M Euros ; investing in a spin-off of a development project costs US\$ 30 M; they should have put 10 times more on the table, like for the IMI (Innovative Medicine Initiative)*”;
    - . Absence of large foundations financing research, as there are in the United States;
  - A certain aversion of the research world to companies and the associated risk taking, which does not or only mildly encourages them to launch private ventures:
    - . This is exacerbated by the status of researchers in France, which is particularly rigid;
    - . The worlds of public research and private companies seem much more permeable in the United Kingdom and in the United States, in particular.
- Biotechnology is a field that has not been prioritized by the State for a long time (as biology was before that, and in comparison with historic priorities such as energy or transportation, for example): “*this is changing*”.
- The example of a large-scale industrial investment made in France during the past years in the biological field should be kept in mind:
  - It is, in part, the result of a strong and converging mobilization of private and political actors at the national and local levels;
  - It is proof that France is capable of attracting this kind of project from companies beyond the national circle.



## F. ... But the positive perception of a political environment that is changing

Today, **France distinguishes itself** from the rest of Europe<sup>6</sup> by its announced **political willpower** to consider the **health industry** as a strategic sector, that comes with an ensemble of **actual measures and initiatives** that were welcomed by the industry, particularly:

- Re-launching of the CSIS (Strategic Council of Health Industries) with the involvement of the highest level of the State and of 3 ministries (Economy, Industry and Employment; Higher Education and Research; Health and Sport);
- “R&D Dating” meetings initiated in 2009 under the aegis of the President of the Republic of France;
- Organisation of the General State of Industry meetings, where health industries were one of five industrial branches to have a specific working group in the event;
- Launching of the “Great Loan”, with a special consideration for Higher Education and Research;
- The implementation in 2009 of the “National Alliance for Life Sciences and Health” to coordinate Public Research activities in these fields;
- “Health, well-being, nutrition and biotechnologies”, number one priority of the National Strategy for Research and Innovation;
- The reform of the Research Tax Credit in 2008, widely appreciated by industrial actors, but not always understood, particularly in international decision-making centres.

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<sup>6</sup> Excluding the case of the United Kingdom, which also has pro-active policies, as shown by the implementation of an “Office for Life Science” and the publication of a specific action plan (the “Life Science Blueprint”).





## V. MAIN LEVERS FOR IMPROVEMENT MENTIONED DURING THE INTERVIEWS

The industrial actors and experts interviewed mentioned many **ideas for improving** the competitive position of the country.

Some of these ideas have been identified for a long time, or have even been used in decisions or ongoing action plans. However, they still correspond to **expectations that have been expressed**.

The major points that the LEEM would like to see acted on are repeated in the key messages and conclusion at the beginning of this document.

### A. General levers for the healthcare industry

- To confirm and stress the strategic character of the healthcare industry for France (so as not to be overtaken by the United Kingdom and to distinguish itself from Germany)
  - To express an industrial policy in the field of health that is both clear and responsible;
  - To objectivise the value created by the healthcare industry for public decision makers and to explain the constraints of the environment (teaching role);
  - To highlight the converging interests of stakeholders: politicians, authorities, industrial actors, social partners, and employees, and to protect healthcare policy;
  - To help change the perception of the image of the healthcare industry, with convincing communication based on real cases and success stories:
    - . Valorisation of French biomedical research;
    - . Value created by the health industries (particularly work on the image of the drug industry, which has been greatly criticized, particularly in France);
    - . Need to have them work together more effectively.
- To pursue reforms that are moving in the right direction (independence of universities, reform of Public Research organizations, RTC, etc.).
- To accentuate investment incentives beyond the main existing levers (RTC, CSIS/CEPS credits):
  - Research tax credit based not only on the amounts invested but also on their growth;
  - Intensify aids and incentives for investment in biotechnologies: “How to bring about 2 “Amgens” in France within the next 10 years”;
  - Rationalize and simplify the existing mechanisms, which are perceived as too numerous and as having dissuasive access conditions ;
  - Create a single window (“one-stop shop”) for aids and administrative processes for investment in the health sector (Ministries, Agencies, regional and departmental organizations, etc.).
- To align national and regional policies and reflections in the investment domain.
- To leverage the skills already recognized in France, in certain disciplines such as engineering, math and physics, in a context where the therapeutic solutions of tomorrow will be based, for development as well as manufacturing, on a range of integrated disciplines, and not just on medicine and biology.



- In the same way, the notion of “disease management” will integrate the products and services associated with treatment, but also follow-up of treatment and, earlier on, prevention, screening and diagnostics (personalized medicine, in particular).

If Research and Industry have to adapt to these new challenges, the authorities, and particularly those in charge of the evaluation of healthcare products, must also prepare themselves.

*History is moving towards the convergence and connection of the healthcare industries: integration in the notion of “disease management” of prevention measures, screening, diagnostics, treatment and follow-up, with a special place for imaging and telemedicine.*

*The joint development of the components of a solution will have to integrate scientific disciplines that do not necessarily work together today, and will most likely require adaptations to training curricula.*

*The industrial actors of the healthcare industry remain attentive to the specificities of these activities, which have different life cycles. In particular, the components of a therapeutic solution will not necessarily change at the same pace, which will result in more complex factors.*

*Finally, during the upstream phases, the different health authorities:*

- *that approve marketing authorizations;*
- *that evaluate the benefit for the patient or the community;*
- *that orient treatment reimbursement and the setting of prices;*
- *that create recommendations regarding proper usage;*

*will have to prepare themselves to manage these technological chimerae.*

- To intensify the promotion and valorisation of the attractiveness of France in the healthcare sector;
  - An active promotional programme of the French environment (R&D, Industry) for decision makers of the major global companies:
    - . Go to meet them in their home country;
    - . Invite them to major events in France.
- To identify and implement all the measures that contribute to simplifying this environment.

## **B. Specific levers for the medicines industry**

### **1. Market attractiveness and market access**

- Preserve the attractiveness of the market in terms of volume and price, and in particular, guarantee the recognition of innovation;
- Identify and propose therapeutic fields /diseases that should be addressed in future plans for public health priorities;
- Defend the Temporary Authorization for Use mechanism, without straying from its spirit and use;



- Strengthen the resources, the skills and the reactivity of bodies in charge of regulation and evaluation of medicines (Afssaps, HAS, etc.):
  - The industry has an interest in dialoguing with competent and reactive decision-makers;
  - Influencing factor for France on the European level;
- Investigate new levers to bring more attractive durations of protection and exploitation of medicinal products.

## 2. Research

- Set up a single window for collaboration with research organizations: one of the missions of the “National Alliance for Life Sciences and Health” which has brought out high expectations;
- Help change the mentalities and culture and bridge the gap between the worlds of public research and private financing:
  - Encourage meetings (LEEM symposiums, etc.) and initiate or promote partnerships;
  - Adapt the training of researchers and physician-researchers, the way in which they are evaluated... and their salary: **“Theses should be written like business cases”**;
  - Encourage international exposure and leverage the international network of French researchers;
- Define a national policy of valorisation and general principles in order to rapidly conclude fair and competitive agreements on an international level;
- Professionalize decentralized IP/valorisation teams on the field (universities, regions), and guide them with a clear national public research IP policy, and train them for the expectations of the market, the health authorities, and for industrial and operational constraints (regulations, etc.);
- Identify and leverage future domains where France or Europe benefit from recognized expertise or a head-start on the global level: stem cells, regenerative medicine, proteomics, nanotechnologies, etc.;
- Leverage or gain inspiration from the IMI (Innovative Medicine Initiative) **“which seems more ambitious than the Biotech Fund”** and meets the needs of accelerating technological transfers more than research on new treatments;
- In the short term, compensate for the absence of a cluster or major biotechnology centre in France with the organization of a major event or global meeting in the field of life sciences;
- Improve the image of the industry in the eyes of the Research world (and the general public), ideally by objectivising the value created for the community, the jobs it represents, and the share of profits that are directly and indirectly reinvested, in research and in other domains.



### **3. Development**

- Set up patient databases that make it possible to evaluate recruitment potential:
  - Access to the data of the French national healthcare system;
  - Fund and launch epidemiology studies at the national level;
- Set up a mechanism for consulting the authorities (in the broad sense of the word: EMA, Afssaps, HAS, etc.) in the early stages of development (end of phase IIa), in order to come to an agreement on the evaluation criteria that will be accepted, like the FDA's approach;
- Simplify the modalities for the authorization of clinical trials (effective implementation of the single authorization on the European level) and contracting with establishments and investigators;
- Valorise the contribution of healthcare professionals (doctors and others) to clinical research, including research that is financed by private funds, and identify levers for improved collaboration with physicians (networking, creation of technical platforms, etc.);
- Identify the levers that make it possible for or that encourage private hospitals to contribute to clinical research;
- Communicate with patients or even the public about clinical research activities in order to improve their image.

### **4. Production and distribution**

- Identify measures for accompanying the transformation of industrial tools, for example:
  - Identify and mobilize to capture investment projects in bioproduction;
  - Consider the possibility of setting up specific incentives and acceleration mechanisms for this kind of project;
  - Create an "Industrial Tax Credit" or "Hiring Tax Credit", equivalent to the RTC for production, in order to further the well-received removal of the professional tax;
  - Promote production intended for export via specific tax reductions.
- Create a mechanism for differentiated prices, like the Dual Pricing system in Spain, in order to limit parallel trade of certain medicines from France (for some interviewees, this would be a potential obstacle to setting up a European distribution platform in France).

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## **VI. ANNEXES**



## Annex 1: Pharmaceutical Industry Heads and Managers Interviewed

Group	First name	Last name	Function
Abbott	Karine	Fanous	Clinical Operations, France
	Frédéric	Fleurette	Market Access Director Western Europe & Canada
	Gérard	Goldfarb	Medical Director, France
	Valérie	Hervé-Bannier	Market Access / Government Affairs France
	Laurent	Kirsch	President of Abbott France
	Louis-Charles	Viossat	Public Affairs, Europe
Amgen	Marc	de Garidel	Vice President, Southern Europe
	Will	Dere	Senior VP, International Chief Medical Officer
AstraZeneca	Bruno	Angelici	Executive Vice President, Europe, Japan, Asia-Pacific, Latin America
	Robert	Dahan	President, France
	Anders	Ekblom	Executive VP, Development
	Anci	Kvarnström	Vice President Global Supply Chain
	Ian	Lundberg	Executive VP, Global Discovery Research
	Ulf	Sather	Regional VP, Europe
	Karin	Wingstrand	Vice President Clinical Development
Baxter International	Bernard	Landes	Finance Director, France
	Peter	Nicklin	CVP, President - Europe
	Norbert	Riedel	Chief Scientific Officer
Boehringer Ingelheim	Pascal	Bilbault	Clinical Research Director, France
	Muriel	Haïm	Director of Communication and Public Affairs, France
	Jean	Schefftsik de Szolnok	President, France
Bristol-Myers Squibb	Michael	Giordano	VP Development Teams- Global Development and Medical Affairs
	Eliott	Levy	VP Global Development Operations
	Marie-Pierre	Sbardella	VP Technical Operations Europe & MEAP
	David	Veitch	Sr. VP Europe Marketing & Brand Commercialization
Eli Lilly	Martin	Bott	CFO, Global Manufacturing & Quality
	Timothy	Garnett	VP, Chief Medical Officer, Global Medical, Regulatory & Safety
	Jacques	Tapiero	President, Intercontinental Operations
GlaxoSmithKline	Jean-Noël	Bail	Director of Economic and Governmental Affairs GSK France
	Soizic	Courcier	Medical Director GSK France
	Hervé	Gisserot	President GSK France
	Jorge	Kirilovsky	Director of the "Les Ulis" GSK Research Centre
	Atul	Pande	Senior Vice President, Neurosciences Medicines Development Centre
	Marc	Santesmases	Director of the "Evreux" GSK Production Site
	Patrick	Vallance	Senior Vice President Drug Discovery
Ipsen	Etienne	de Blois	President, France
	Eric	Drapé	Executive VP, Manufacturing & Supply Operations
	Christophe	Jean	Executive VP, Chief Operating Officer
	Stephane	Thiroloux	Executive VP, Corporate Development
	Didier	Véron	Public Affairs and Corporate Communication
Johnson & Johnson	Jane	Griffiths	International Vice President – Area North, Janssen Cilag EMEA
	Jaak	Peeters	Company Group Chairman, Pharmaceuticals, EMEA
	Robert	Sheroff	President, Global Pharmaceuticals Supply Group, J&J
	Johan	Van Hoof	COO, Global Development Organization, Pharmaceuticals, J&J
Merck & Co	Joe	DeGeorge	VP of Preclinical Development and Toxicology
	Peter	Honig	Senior VP Merck Research Laboratories
	David	O'Connell	Directeur of the "La Vallée" Production Site
	George	Rizk	Commercial Operations, Europe
	Nigel	Thompson	Executive Director, Economic Strategy
Merck KgaA / Serono	Roberto	Gradnik	VP Commercial Operations Europe
	Christopher	Huels	VP Research & Development
Novartis	Eric	Cornut	Director of Commercial Operations, Europe
	Trevor	Mundel	Head of Development
	Rick	Priest	Head of Strategy & Operations
Pfizer	Leigh	Bonney	Head of R&D Strategic Management Group
	Olivier	Brandicourt	President, BU Primary Care
	Anthony J.	Maddaluna	VP Global Manufacturing Strategy and Supply
Pierre Fabre	Eric	Ducourneau	Secretary General
	Jean-Pierre	Garnier	Managing Director
Roche	Jean-Jacques	Garaud	Head of Roche Pharma Research & Early Development
	Hervé	Hénaff	Director of Public Affairs and Development, France
	Mondher	Majoubi	Global Head of Medical Affairs, Oncology
	Jacky	Vonderscher	Global Head of Molecular Medicine Labs
Sanofi aventis	Philippe	Alaterre	Director of Strategic Studies - Industrial Affairs
	Marc	Cluzel	Senior Vice President, Scientific and Medical Operations
	Jean Pierre	Lehner	Senior Vice President, Chief Medical Officer
	Philippe	Luscan	Senior Vice President - Industrial Affairs
	Jean-Philippe	Santoni	Director of Industrial Development and Innovation
	Hanspeter	Spek	President, Global Operations
Servier	Marie-Noëlle	Banzet	Vice President — Director of Public Affairs
	Christian	Bazantay	Secretary General
Takeda	Erich	Brunn	CEO Takeda Pharmaceuticals Europe
	Michael	George	Managing Director TGRD (Takeda Global Research & Development) Europe



**Annex 2:**

**Heads of public research organizations,  
public financing organizations,  
other health industries,  
and key actors in the environment that were interviewed**

<b>Name</b>	<b>Organization / Institution</b>
David Appia	French Agency for International Investment
Gilles Bloch	CEA, Life Sciences Direction
Dominique Costantini	BioAlliance
Alice Dautry	Institut Pasteur
Virginie Fontaine Lenoir Annie Geay	OSEO
Thierry Herbreteau	St Jude Medical
Georges Hibon	bioMérieux
Dominique Maraninchi	INCa
Arnold Munnich	Presidency of the French Republic
Patrick Netter Marc Ledoux	CNRS
Alain Ripart	Groupe Sorin
Christian Seux	Snitem
André Syrota	National Alliance for Life Sciences and Health, INSERM
Elias Zerhouni	Former NIH Director

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