STUDY ON THE NATIONAL INNOVATION SYSTEM IN THE SPANISH BIOPHARMACEUTICAL SECTOR

PROJECT: DSTI/STP/TIP (2002)1 - OECD
AUTHOR: Emma Gutiérrez Mesa - UEM
COORDINATOR: Dr. Emilio Muñoz - CSIC
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I. INTRODUCTION

I.1 BACKGROUND

Industry and innovation are concepts that have coevolved during the process of transformation of modern societies contributing together to their socio-economic wealth.

There is a new and important phenomenon that has developed during the last half of the twentieth century in the relation of competitiveness and industry: the growing use of scientific principles for industrial research and innovation. Pharmaceutical industry appears as paradigmatic to this model.

It is nonetheless true that the relationships between science and innovations are as old as the beginning of capitalism, if not older, as stated by A. Gambardella in his book "Science and Innovation. The US pharmaceutical industry during the 1980s" (1995). But is clear also that the second half of the 20th century has witnessed an augmentation in the use of knowledge produced in two scientific realms: information and computation and life sciences. Both domains and their technological applications do affect the pharmaceutical sector.

Even in the periods of more empirical approach to industrial research processes (based on trial and error of chemically synthesized products) the pharmaceutical industry has characterized itself as being highly innovative as judged from the spend in R&D activities. But it is in the rapid change to the use of more scientific knowledge and computerized technologies where the pharmaceutical industry excels among other "high tech" industries.

The mentioned book by Gambardella provides a good synthesis on the characteristics and evolution of the big (USA based) pharmaceutical industry as well as an ample repertoire of references on the subject until mid 1990s. Gambardella's book explores the transition from the approach of new drugs discovery based on empirical tests of many molecules –the so-called "random screening" or "molecular roulette" approach- to the use of new advances of molecular biology and genetic engineering. Less than ten years later, the pharmaceutical industry is experiencing the potential for discovering drugs offered by new upstream research such as genomics, proteomics and cell and tissue engineering.

Having stated clearly that the upstream research is essential to the development of the pharmaceutical industry, the interest to study the situation of the biopharmaceutical sector in a comparative analysis to understand the strengtheness and weaknesses is self evident.

The application of this study to the case of Spain is both attractive and difficult. Within the frame of a country characterized by a low innovative performance of the

economy (Muñoz *et. al*, 2000 a,b), the pharmaceutical industry classified as one of the more, if not the most, innovative industrial sectors in Spain. However, the dimensions of the Spanish owned innovative pharmaceutical industries do not seem to be sufficient for competing in a globalized world, and the participation of the multinational firms, albeit very significant for the national drug market, has not been influential in the R&D and innovation domain. The transition of this industry to the modern biology – based approach is puzzling. But in any case, the advantages of the present study are three fold. First, it serves to analyze the pharmaceutical sector in Spain from which we are not aware of many studies (except for the reports of the industrial sector itself, consult Farmaindustria reports cited in the bibliography and few other works, e.g. Frias, 2000). Second, it allows to delve into the biotechnological sector in Spain, extending previous work (Asebio, Diaz *et al.* 2001). Finally, it provides an international base to the characterization of the Spanish biopharmaceutical sector.

I.2 KEY QUESTIONS

This work constitutes part of the international project carried on by OECD under the title of "Case Study on Biotech Innovation Systems" (DSTI/STP/TIP (2002)1) lead by Christien Enzing from TNO Strategy, Technology and Policy of Netherlands.

The investigation of the systemic characteristics in the participating countries is one of the main goals of this project. Given the specific characteristics of national innovations systems in the participating countries and the role public policies can play in the management of innovation processes in order to correct systems imperfections, a set of questions specific for biotechnology innovations can be formulated.

The project focuses on specific cross-examination dealing with four main issues to be investigated:

1.- Identification of the systemic failures. We can define systemic failures as mismatches between elements in an innovation system; They hinder the functioning of an innovation system, the flow of knowledge and therefore reduce the system's overall efficiency ;

2.- The national – international dimension of system openness. System openness is understood as to what extent a national system is open to international elements such as the presence of foreign companies in a country or cooperation with research groups and companies from abroad. This tension between "national" and "international" innovation system is relevant to policy makers when developing and implementing national biotechnology policies;

3.- The demand side factors. These factors could play an important role in the speed and direction of many new technological developments, for

example biotechnology. It is especially necessary to identify which specific actors and institutions constitute the demand side of the innovation system (for example consumer and patient organizations, national health care systems, insurance companies, etc.) and analyzes their specific function and role in the innovation process;

4.- Systems policies. One of the main goal of the OECD Project is to make a policy assessment based on the perspective of specific innovation system;

Therefore, it will be main goals of this work to study the Spanish Innovation System in Biopharmaceutical Sector in order to answer the four questions mentioned above.

I.3 THEORETICAL FRAMEWORK

The concept of "innovation systems" was proposed and developed by relevant economists (Freeman, 1987, Lundvall, 1992, Nelson, 1993, Edquist, 1997) to explain the differing degrees of competitiveness of economies, especially of their "technological competitiveness" and their ability to innovate as the basis for the wealth of developed societies.

The innovation system concept comprises all institutions and actors involved in scientific, technological and innovation activities. The components of the system are responsible for the accumulation and diffusion of knowledge, are involved in the education and training of the population, develop technology, produce new products and innovative processes, and distribute them.

As Kuhlmann (1999) stated, an innovation system is a "hybrid system" representing a section of society which carries cover into other societal areas and consequently has a decisive influence on the modernization of a society.

Biotechnology has emerged as new field of application of advanced scientific research to industrial innovation activities going far beyond national institutional frameworks and polices. On the other hand, it has been repeatedly stated that the development of biotechnology in a given space requires a good scientific base, an industrial culture and productive propensity, an active participation of capital and an appropriate social environment. It therefore requires a systemic ground. Against this background, it is interesting to look at to the remaining specifities of national systems of biotechnological innovations and in particular to the biopharmaceutical innovation system as subject of this study. The heuristic value of the concept is so tested.

I.4 METHODOLOGY

This work was carried out by following three different research approaches performed in different phases:

1. The first one concerns the descriptive approach, in order to study and identify the most relevant characteristics of a (potential) national system of innovation of the biopharmaceutical sector in Spain.
2. A second one deals with the empirical approach to go more in depth with the industrial component of the sector (and the system).
3. A third one aims to find the explanatory elements of the functioning of the system; failures, degree of openness, which are the roles played by actors not directly involved in the process of innovation as well as which are the effects of governmental policies.

The empirical research was approached through a survey sent to the whole of firms identified as being part of the sector. The questionnaire containing 35 questions was sent the 15th of March 2003 and the reception of responses was closed the 15th of May of the same year. The sample of biopharmaceutical firms was initially estimated at 109, being composed by 39 biotechnology based firms in the health area and 70 traditional pharmaceutical companies that either produce or process biotechnological products. Among the sample surveyed, 12 responses were received stating that the firms were not involved in the object of research and other 17 questionnaires mailed were returned. From the 89 firms of the final sample, we obtained a 25% rate of response, a result that can be considered satisfactory on the light of the usual lack of transparency of the industry in this sector an on time constraints. The statistical analysis was carried out using an SPSS software program.

Finally, to explore the reasons underlying the unanswered issues about the main objectives of this work, semi-structured interviews were carried out with representatives of the different collectives involved in the dynamics of the sector: officers from the Public Administrations, Industrial Organizations, a set of the small biotechnology-based firms and broad biopharmaceutical companies.

I.5 CONTENT OF THE REPORT

It can be said that the dynamics of technology production and its uses is one of the critical aspects in determining the strategic position of the countries as well as the competitiveness of their businesses. At the core of this problem, it is the capacity to produce technological innovations. At this respect, businesses and governments from industrialized countries recognize as a fundamental element of the policy and the strategy of a country, to be able to develop the conditions strengthening that capacity to innovate. In view of the inability of the public sector to generate from itself working in isolation, enough innovation and even to finance it, the need for the intervention of other actors: agents and institutions from private origin is deemed essential. These private actors may cover the deficit and help to sustain the process.

In this multintervention of actors relies the concept of National System of Innovation (NSI). When we are talking of NSI we are not referring to any specific

institution nor to particular activities but to a way to articulate diverse institutions and activities. We talk of system because there are an ensemble of elements or partners (the different agents and institutions that participate in the same) which are internally differentiated but whose joint intervention in harmonic and integrated way represents the "raison d´être" of a NSI. From this, it follows that the general goal of a NSI will be the establishment of a broad frame which improve the concerted action of all the elements (their connection and fluidity) and help to structure, drive and foster the science, technology and innovation activities with the aim to contribute the increase of the cultural, social and economic patrimony of the country.

NSI is composed by several agents and institutions, each one of them playing and which show differences at various levels: public-private; profit-non profit; political-corporate.

This study analyzes each one of the subsystems (elements) which integrate the National System of Innovation in the Biopharmaceutical Sector, through specific analyses of the governmental and research subsystems (Item II.2 and Item II.3.1), the business part (Item II.3.2) and the finance subsystem (Item II.4).

The report is structured on seven chapters whose contents are as follows:

Chapter I: develops in essence the main question to be answered as well as the methodology used;
Chapter II: analyzes the structure of the Spanish National System of Innovation in the Biopharmaceutical Sector, the most relevant policies and the national programmes aiming to support it. Others factors relevant to the biopharmacetical system, are also dealt in, such as the main actors involved, the essential factors which are driving and hindering the evolution, as well as the significant failures observed and their implications to the function of the system;
Chapter III: in this chapter are presented the performance of the Spanish system at various levels: scientific, commercial and educational;
Chapter IV: this chapter analyzes the degree of openness of the system of innovation in the biopharmaceutical sector;
Chapter V: analyzes the role played by other actors from the demand side;
Chapter VI: discusses the main failures of the system;
Chapter VII: the main conclusions of the study are given in this chapter

II. NATIONAL BIOPHARMACEUTICAL INNOVATION SYSTEM

II.1 INTRODUCTION

The effectiveness of a NSI demands the existence of three key factors in a national context: a culture of coordination, an interactive learning and entrepreneurial culture.

1.- The social and public character of NSI (semi-public in its limits) claims for the existence of a profound "culture of coordination". This is a factor deemed necessary to make possible the collaboration between all agents and institutions. The State in isolation can not cope with such responsibility but, at the same time, it can not leave the process in the private responsibility, because the system should not have enough innovation. Since a NSI must be targeted to the obtention of results, it requires to work and produce as a network, what demands the "culture of coordination" as a basic element for shaping a system.

2.- A NSI must be supported by an interactive learning. A NSI is a lively system which requires learning and by the process of learning it is able to embody information and knowledge through a constant and permanent process.

3.- The third key factor concerns to the entrepreneurial side. An adequate "entrepreneurial culture" appears as indispensable for a society with capacity to generate economic and commercial initiatives for its own sake.

A NSI to be well established asks for a very significant number of informal relationships. This type of relationships is vital for building the real bases of consensus which may lead to a normative and legal frame. The dynamics of this process must be driven by the same outcomes of the innovation and so the normative and legal frame should be in agreement with this dynamics.

Two other factors must play a determinant role with respect to the relevance and impact of a NSI: one linked to the demand side, the other to the supply side. The relevance and impact of a NSI will depend on both, from the characteristics of its economic actors and from the own capacity of the system to generate innovations.

Concerning the innovation potential of the firms, the following rank is established from data of expenses collected by the Spanish National Institute of Statistics (INE) [1]; the automotion sector is the first with spent of 1,000 millions of euro in 2000; the food industry ranks second with 700 millions euro expenditure; the specific sector of research and development with more than 500 millions euro. During the period 1998-2000, the innovations recorded by INE amounted to 29,228, whose 99% has been carried out by companies with less than 250 employees, and showing an even distribution between innovations of products and processes. The regional distribution of the innovation expenditure reveals that its 50% correspond to the sum of Catalonia and Madrid. The R & D expenses as percentage of the Gross Domestic Product according to Eurostat data for 1999 amount to 0.89 for Spain, a value well below the average of the EU which rises until 1.92%. Only Portugal with 0.76% devote a lower percentage(s) to those activities.

[1] Survey on Technological Innovation in the Businesses. INE. 2000

Total figures in the year 2001 for R & D activities in Spain, according to the statistics on Scientific Research and Technological Development, amount to 6.227 millions euro, from which the business sector spent 3,201 millions (52%), the higher education sector spent 1,925 millions (31%), the public research sector 989 millions (16%) and non-profit institutions near 52 millions euro (1%).

The 52% share of the total expenses performed by the business sector was contributed in 83% by the same sector (own funds or funding from other enterprises). This figure includes the credits and loans subjected to reimbursement. The value of this item arising from the public sector gives up 255 millions euro, that is 9.5% of the autofinancing expenses and 7.8% of the total expenditure in research carried out in the firms. The public funding comprising the sum of subventions and contracts which goes to business support of R & D activities amounts to 10% of the sector expenditure.

The intensity of the research effort in the different branches of activity, according to the ratio of R & D expenses with respect to Gross Added Value (GAV), provides the following ranking: the industry of transport material occupies the first position with 5.6% of the GAV, followed by the sector of electronic and electric equipment (5.4%). The regional distribution of the business sector expenses reveals the predominant role played by Madrid (1,974 millions euro) and Cataluña (1,334 millions).

In addition to all the official data, the COTEC Foundation (a foundation dedicated to the promotion of innovation in Spain) elaborates an Annual Report on the Analysis and Perspectives of the situation of technology and innovation in Spain which is presented every year in a public ceremony (June 2003). The COTEC report has shown the continuous growth of the resources devoted in Spain to the technological innovation. Data pointing out in this direction are the figures of the number of researches and the number of innovative companies that have doubled in the last eight years. This data is a strong indication of the improvement of the scientific capability of Spain. But this growth and the level attained are insufficient as the mentioned COTEC report concludes. The business contribution to R & D expenses in Spain amounted 0.40% of GDP in 1997, rising to 0.52% in 2001, a percentage clearly below the objective, as expressed by the European Union[2], of going up to 3% of GAP in 2010. This objective means that the firms should invest and spend the 2.25% of GDP, what would imply that the Spanish business sector has to quadruplicate its R & D investment in eight years.

The most encouraging data from the COTEC report refers to the percentage of small and medium enterprises which collaborate with the research institutions, universities, public research centres, technological centres. The rate of collaboration has increased from 29.6% in year 1999 to 35.4% in 2001.

[2] Decisión of the European Council.

Any system is composed of different subsystems possessing similar characteristics that the whole system. Within an industrial system it is likely to find sectoral subsystems that are organized and functioning with similar characteristics.

The analysis of the Biopharmaceutical (National) System of Innovation can be approached by establishing and defining four subsystems:

1. Business Subsystems

   It is composed by the set of biopharmaceutical companies that are using the biotechnology as a tool for their products or in their processes as well as by the whole of small companies based on biotechnology.

2. Research Subsystem

   It comprises the ensemble of the public and semi-public institutions devoted to the scientific research and the technological development. The excellence is a quality of critical relevance for the intervention of the research centres in the system.

3. Financing Subsystem

   It is composed by the set of actors and institutions which support by financial instruments this type of projects and activities: capital firms, business angels, public institutions which promote financing.

4. Governmental Subsystem

   It is composed by the Government and its agencies, responsible for maintaining the cohesion of the whole system through the normative and legal frame. It also supports basic and essential funding to any of the other three subsystems.

II.1.1 COUNTRY CHARACTERISTICS

II.1.1.1 SIZE

Spain, together with Portugal, are forming the Iberian Peninsula, the most occidental peninsulas of the south of Europe. Spain occupies the 4/5 parts of the 580.825 square kilometres that represent the total surface of the Iberian Peninsula.

Spanish population amounts to 41 million of inhabitants with a very limited demographic growth along the last five years. During the last fifteen years a substantial change has occurred in the demographic behaviour, as it reflects in a marked reduction in the rate of national growth, for the first time in the last decades, it has reached similar, or even lower levels than in the other European countries.

The average population density in Spain is 81 inhabitants per square kilometre, a figure slightly higher than that of Greece, Ireland and Sweden but largely lower than that of the rest of Europe.

With respect to birth and death rates, Spain has been experiencing a process similar to that of other more developed countries: the trend has changed from one of high rates of births and deaths to one of low rates of these parameters. The life expectancy at the end of the 90s was 75.5 years for men and 82.4 years for women, according to Eurostat, figures which over passed the European average. The number of sons per woman averages 1.24, the lowest index in Europe as stated by the Spanish National Statistical Office (INE) in its 2001 report. On the other hand, 30.73 years is the average age for having the first descendant.

It is important to underline the increase of the immigrant population that has taken place in Spain. From INE data the total number of immigrants has increased by 23.8% in the period 2000-2001 reaching a total figure of 1,109,060 foreigners living in Spain. The main country of their origin is Morocco, followed by Ecuador and the United Kingdom. In this last case, we are not dealing with working immigrants but retired people coming to Spain to live in retirement.

Among other relevant, non-demographic, social changes in Spain it is worth to refer to the new role of the women in society. They have increased their educational level as well as their share in the working market, what has driven to an increase in their economic independence. The level of legal and social equality of the Spanish women has been continuously increasing in the last five years.

II.1.1.2 ECONOMIC SITUATION

II.1.1.2.1 National economic context in 2002

Under little favourable international situation, the Spanish economy underwent an increase by 2% in 2002, according to the Quarterly National Accountability (NTR from its name in Spanish, Contabilidad Nacional Trimestral). This rate of growth was 0.7 percent lower than in 2001, but higher by more than 1 percent of the rate estimated by the European Commission for the whole Euro zone.

TABLE 2.1: SPANISH GDP

	2000	2001	2002
GDP pm (PIB in Spanish)	4.2	2.7	2.0

Source: Contabilidad Nacional

II.1.1.2.2 Spanish national economic context in 2003

The internal demand of the Spanish economy has maintened a sustainable trend, while exports and imports experienced a decline in their rhythm from January 2003, in good match with the generalized ticking over of the external international commerce in the industrialized economies.

Regarding the industrial sector, the Index of Industrial Production (IPI from its name in Spanish) underwent in January a slight increase. This was the fifth in a row showing the positive trend[3] as an indication of the gradual recovery of the industrial activity that has been observed since the mid of last year.

Concerning tourism, the number of visitors, according to the statistics FRONTUR of the Institute of Studies of Tourism, has evolved positively reaching an interannual growth rate of 5% in January-February, a figure which contrasts with the number of nights spent at hotels (-0.6% in January-February 2003). The air traffic has shown a high rhythm of growth in the first quarter of year 2003, with a rate of 7.9%.

From the demand side, with respect to the issue of private consumption, it is first important to outline the results of the Continuous Survey on Familial Budgets (ECPF, from its name in Spanish, Encuesta Continua de Presupuestos Familiares) of the last quarter of 2002, the data reflect an interannual drop in the average expense per home of 3.5% and in the total spent of 1.1%[4].

The recent indicators on the labour market[5] show a certain degree of intensification in the rhythm of growth of affiliation to the Social Security and a decline of the unemployment level. The inflation rate (IPC) in February raised two tenths with respect to the previous month, with a rate of interannual variation of 3.8%. This moderate rise of the prices derives from the prices of fuels and tobacco.

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[3]The extent of growth by branches of activity reveals the greater increases in production by January 2003 for the chemical industry, machine and electric equipment, tobacco industry and oil refinement. On the other side, the branches undergoing the greater drops were computer equipment, extraction of energy products, machine and mechanical equipment, electronic equipment, radio and television, and dress-making and furs

[4]The Index of Consumers Trust, as prepared by the European Commission, felt down till –18 in the first quarter of 2003, the minimum value from the last eight years. This is a strong indication of the worsening of the expectations on the economic perspectives both at personal and general levels.

[5]The number of affiliates to the Social Security reached in February 2003 a figure of 16.335.700 (interannual variation rate of 3.2%) while the unemployment registered in the offices of INEM at the end of February 2003 was 1,734,061 individuals (increase in 68,012 individuals for the last twelve months).

The harmonized index (IPCUM) recorded an interannual variation of 2.4%, two-tenths above the figure corresponding to the previous month. The acceleration was due to the effect of the prices of energy products, of food and of non-energy industrial goods. The majority of the economies of the eurozone contributed to the inflation increase with the few exceptions of Italy and Luxembourg which showed a decrease in the inflation rate and Spain where it remained stable.

The data on the foreign sector reveals a commercial deficit increase of 9.2% in January according to Customs information, this occurred in an environment marked by the slowing down of the commercial exchanges. A possible explanation to this situation stems in the increase of imported energy products (conflict of Irak) though the valorisation of the euro face to the dollar has absorbed notably the effects of the rise in the oil prices.

II.1.1.2.3 Present international economic context

The landscape of the international economy seems to be influenced by the uncertainty concerning the future evolution of the main economies of the world. All the relevant international organizations performing in forecasting and assessing have coincided in making a prediction to reduce the growth expectations for 2003, most of them are betting for a revitalization of the economy postponed until the second half of the year, though it may be gaining strength along 2004.

II.1.1.3 LABOR MARKET

After the adhesion of Spain to the European Community, the Spanish labour market has been characterized by a high rate of job creation precisely in the period of greater economic expansion (1986-1990). During the second half of the eighties, that rate was extremely high leading to a significant decrease in the level of unemployment, in spite of the significant augmentation in the market of active labour force. In the period lasting from 1986 to 1990 near to two millions of new jobs were created, resulting in 400,000 net new jobs per year as an average estimate.

The survey on active population (EPA) in 2001 reveals a figure of 17.8 millions of active individuals, with 16 millions actually working and 1.8 unemployed. Andalucia is the region with the greatest level of unemployed (almost one third out of the 1.8 million) followed by Cataluña, the Autonomous Region of Valencia and Madrid. Leaving aside the cities of Ceuta and Melilla, La Rioja, Navarra and Cantabria are the Autonomous Regions with the lowest figures for unemployed. On the grounds of the age pyramid, the higher shares for unemployment correspond to the collectives comprised between 25-29 years and 20-24 years. The distribution by home lifes shows that on a total of 13,457 milliards of homes 25% do not have active person whereas the remaining 75% hold at least one active person.

Concerning the distribution of the wages, 74% of the gross total salary corresponds to pay, about 21.5% are the obligatory payments to the Social Security, about 1.3% correspond to direct social loanings and 1.2% for layoff indemnities. The remaining expenses are voluntary contributions.

II.1.1.4 BUSINESS SECTOR

According to the Institute of National Statistics (INE) [6] there were 2,710,400 active businesses in Spain by the 1st of January 2002, from them 49.1% of the firms belong to the Services Sector, including firms whose fields of activity are: hotel business, communications, real state and rental activities, services to businesses, educational, sanitary and social care as well as other types of social activities, including the personal services. Followers are the Commerce sector (29.4% of total), Building (12.4%) and Industry (9.1%).

The Services Sector provide jobs to more than six and half millions of persons and involves a turnover of 760,000 millions of euro. From this sector, the higher share of activity corresponds to commerce, services to businesses and tourism, the highest proportion of small firms corresponds to Services and Commerce Sectors, while de biggest ones belong to the Industry Sector.

From the territorial distribution point of view, there is a strong concentration in four Autonomous Regions: Cataluña (19% of total), Andalucia (14.7%), Madrid and Region of Valencia (10.6%).

II.2 POLICIES FOR R+D+I+T

Science and technology policies are becoming critical elements for the development in modern societies, as it has now been clearly stated that there is a direct relationship between the innovation capacity of a country and its competitivity. Those policies are also horizontal policies that may influence many sectoral policies (education, health, environment), this contributing to the improvement of the wealth and the quality of life of the citizen, the essential goal of all public policies.

Along these policies, the General Administration from the State must assume, on one side, the mission to strengthen the basic research. The production of knowledge should be supported with solidarity as the base for any development. On the other hand, the Administration should favor the existence of a positive climate for the firms adopting the culture of innovation in order to foster their ability to compete. The relevance of the R & D policy has been evidenced in the last years as both an instrument and a goal to attain reasonable levels of sustainable growth for the economic development. The public effort by increasing the budget allocated to this heading must help to stimulate the involvement of the private sector in the R & D activities. There is a historical gap in this effort of the private sector in Spain, as it has been quite impossible to surpass the threshold of the 50% contribution of the sector to the total expenses. In 1997, this level was not attained. With the aim to reverse the situation, it is deemed necessary to design and put into force policies that while keeping the general support to research, development and technological

[6] Estructura y Demografía Empresarial. Directorio Central de Empresas (DIRCE) a 1 de Enero de 2002. Nota de prensa de 8 de Agosto de 2002

innovation, should be able to better coordinate the activities of the two sides of the process: public and private in order to attain the reinforcement of the research quality but also the value of its applications. This last objective must receive special attention since it is obvious by the previous arguing that a major problem of the Spanish System of Science – Technology – Business stems in the poor levels of practical applications of the research results.

The Law 13/1986, (Ley de Fomento y Coordinación General de la Investigación Científica y Técnica) established the Natural Plan for Scientific Research and Technological Development as the instrument to accomplish the task, corresponding to the State, of the promotion and general coordination of the scientific and technical research and created the Interministerial Commission for Science and Technology (CICYT, from its name in Spanish, Comisión Interministerial de Ciencia y Tecnología) as the organ for the planning, coordination and monitoring of the National Plan.

The efforts made from the approval of the First National Plan in 1988 to the present time has led to strengthen the Spanish System of Science-Technology-Business by increasing the capacity of the public component of the system and its opening to the productive sectors.

Under the context of European integration represented by the Economic and Monetary Union and the current setting of sustainable growth of the Spanish economy, Spain should keep the strategy of increasing the investment in R+D+I activities. Moreover, Spain must spare no effort in attempts to converge to improve its position in the European landscape of science and technology. For attaining this aim it is necessary to look for sinergy with the activities of the European Framework Programme and the initiatives associated to the Structural Funds of the European Union.

The main areas of interest in the National Plan for R+D+I for the present report are:

1.- Area of Biomedicine

This area comprises all the research fields based on biology, biochemistry and other related disciplines which are addressed to solve the health problems. The extension of life expectancy and the appearance of chronic pathologies related to aging of population are some reasons contributing to the recognition of the critical role of biomedicine at the onset of the XXI century. The continuous and spectacular advances in molecular genetics and in the sequence of ADN and diverse genomes gave support to the contention that biomedicine emerges as a strategic arm for social wealth in the near future.

Among the specific objectives of the National Plan in this area of biomedicine, it should be mentioned the following:

a. The research, development and applications of new technologies.

A.1. Genomic research and its consequences.
A.2. Development of animal and cellular models for the study of human diseases.
A.3. Gene therapy ant the tissue and cellular engineering.
A.4. Pharmaceutical research.

b. Clinical, physiopathological and therapeutic research.
c. Epidemiological research on public health and health services.

2.- Biotechnology Area.

The possibilities of Spain to take benefits from this emerging, horizontal technology go through, at least, two conditions: to continue the promotion of scientific community performing high quality research and to develop a solid entrepreneurial structure able to carry out important efforts in technological innovation.

The gap of Europe with respect USA in the development of biotechnology imposes the European Union and its members to make additional efforts to bridge that gap. It is therefore logical to think in new initiatives from the public and private sectors in Europe that may result in an increase of the qualified labour market and in the promotion of new jobs.

Specific objectives in the National Plan in relation to the biotechnology are:

a. Biotechnology oriented to analysis and diagnosis.
b. Transgenic organisms.
c. Bioengineering (Engineering of biotechnological processes).
d. The relationships between biotechnology and society.

3.- Sociosanitary Area.

A concept of health based in a triple perspective of wealth including physical, mental and social aspects, implies a great variety of initiatives in relation to society. The attainment of these broad objectives can be achieved by applying health policies which affect preventive, curative and rehabilitation-associated issues.

Objectives of the National Plan related to the sociosanitary area are:

a. Aging processes and the treatment of diseases related to those processes.
b. Health technologies.
c. Relationships between nutrition and health.

The instruments to put into force the attainment of objectives are a series of national programmes like the National Programme for Biotechnology and the National Programme on Health.

There are evident difficulties in Spain to distinguish between policies and special plans and strategies to foster the commercialisation of biopharmaceutical products and to promote knowledge. The borders between both types of strategies are diffuse. By this reason, it is possible to find policies and programmes covering both aims.

II.2.1 POLICIES FOR THE PROMOTION OF KNOWLEDGE PRODUCTION

As mentioned before, there are specific National Programmes for Biotechnology and Health. These programmes aim, among other objectives, to promote knowledge.

The National Programme for Biotechnology (N.P.B.) addresses the four following subsectors:

1. Agrofood

   The N.P.B. proposes the use of technologies supported by molecular and cellular biology advances. The targets are the agronomical and forest species with socioeconomic interest for Spain as well as the agrofood projects holding the greater relevance for the firms operating in Spain.

2. Human and Animal Health

   Priority is given to the projects addressed to solve the problems related to pathological problems for human and animals which hold the greater socio economic relevance. The N.P.B. focuses on technologies and instruments like vaccination, diagnostics, design of experimental models as well as the identification and characterization of genes of potential interest for the pharmaceutical industry, paying particular attention to the use of molecular and cellular biology based techniques.

3. Engineering of Biotechnological Processes

   Particular attention will be devoted to the study of the processes on which there are foreseen entrepreneurial possibilities in Spain for any of the sectors: chemical, pharmaceutical, food, etc. The development of new experimental or therapeutic tools emerges as a critical element for the success of this topic as it will be driving , to great extent, the capacity to compete of the different sectors with biotechnological applications.

4. Environment

   The aim is to use biotechnological instruments to solve environmental problems of specific relevance for Spain with particular emphasis in the processes of bioremediation and utilization of wastes of chemical and biological origin.

The National Programme on Health (N.P.H.) addresses the following main objectives:

1.- The development and application of new technologies in biomedicine
2.- Cancer research
3.- Research on infectious diseases
4.- Research on neurosciences
5.- Research on cardiovascular diseases
6.- Research on chronic ailments
7.- Pharmaceutical research

In this sector of activity, the collaboration between the industry and the public has been stepping up. In 2001, the pharmaceutical industry signed with the Ministry of Health an Agreement for the Collaboration for the Promotion and Development of Scientific and Technical Research in the Sanitary Field. The agreement represented the endowment of 33.06 millions of euro to foster and develop plans, programmes and activities of scientific research through the Health Institute Carlos III (ISCIII).

The most significant event of this collaboration between industry (through the Employers Association, Farmaindustria) and the Ministry of Health, was the signature in 2001, the 31st of October, of an Agreement for the Elaboration and Performance of an Integral Plan on Control Measures of Pharmaceutical Spending and Rational Use of Drugs for the period 2002-2004. This Agreement shapes a pact for the stability and the innovation to benefit the citizens. The pact states the compromise of the pharmaceutical industry to increase the investments in R+D+I by a percentage higher than the GDP growth. The endowment agreed for the period reached a value of 1,352 millions of euro; which should be supplemented with 300 millions of euro to fund projects performed by the public institutions on subjects of sanitary research on topics of general interest.

The ISCIII promotes biomedical research through grants in aid. The grants fund two types of projects.

a. Extramural Projects: support projects of biomedical research and health technologies under the frame of the National System of Health (SNS, from its name in Spanish, Sistema Nacional de Salud). The agency in charge of this programme is the “Fondo de Investigaciones Sanitarias”, FIS (Fund for Health Research).

b. Intramural Projects: support research projects carried out by personnel from centres, institutes and units of the ISCIII. The management of this programme is carried out from the General Secretary of ISCIII, by the area responsible for search.

Concerning the regional realm, some Autonomous Regions have launched programmes to promote biotechnology, such as for example, the Basque Country with its programme "Biobask-10", the Region of Valencia with its programme "Biosoluciones" or the Madrid and Cataluña Regions which have declared the biotechnology as a strategic priority for its Research and Innovation Plans.

In spite of these initiatives, it can be said that the regional support to life sciences and technologies remains insufficient and suffers from lack of strategy and coordination. This situation hampers the development of biotechnology, leading to the loss of opportunities for cluster generation, for the development of scientific parks and bioincubators.

II.2.2 POLICIES FOR COMMERCIALIZATION SUPPORT

The General Measures better known programme of public support to the pharmaceutical research is the "Plan Profarma" which is the programme to promote R & D activities in this sector.

Funding of further steps in the innovation pipeline rests on the responsibilities of CDTI (Centro para el Desarrollo Tecnológico Industrial). This line of public funding to the firms consists in the allocation of credits with zero rate of interest and with a large period for pay-off. The credits assume till the 60% of the project costs. CDTI only supports projects assessed as technically and economically viable, but does not demand general guarantees to the firms proposing the project. The funds allowing the funding activity of CDTI proceed from the own resources of the organism and from the European Fund for Regional Development (FEDER).

TABLE 2.2: CDTI Programmes

	Interest Rate	Term	Credit covers % of project budget
Projects for Technological Development	0%	5 years	50%
Projects for Technological Innovation	0%	5 years	25%
Projects associated to international programmes	0%	8 years	35-60%
Projects of Concerted Industrial Research	0%	6-8 years	60%
Line of bank financing CDTI – Institute for Official Credit (ICO)	Euribor – 0.82%	5-7 years	70%

Source: CDTI

These credits include a clause related to technical risk according to which in the case a project does risk the technical objectives, the firms are exempted of redemption of the credit.

- Projects of Technological Development are those of an applied nature which are put into force by companies, either alone or in collaboration with technological centres. They address the creation or improvement of a process, a product or a service.
- Projects of Technological Innovation are those of applied nature which are put into force by companies, either alone or in collaboration with technological centres. They imply the incorporation and active modification of new emerging technologies to the firms.
- CDTI supports and helps the internationalisation of the R+D+I activities of the Spanish companies through a series of instruments.

    1.- Projects of Technological Promotion.
    2.- External Network of CDTI Representatives and Agents.
    3.- Catalogue of Technologies for International Promotion.

CDTI also assumes the Spanish representation in two big European facilities, CERN (European Laboratory for Particle Physics) and ESRF (European Synchrotron Research Facility) with the aim of getting the maximum return as possible.

- The bank financing line on Technological Innovation carried out jointly by CDTI and ICO (Institute for Official Credit). This line allows the firms not only to opt for the types of CDTI support but to take the option of having access to this line of credit. Its permits to get funding for entrepreneurial projects of technological nature at a privileged interest rate and long term. These credits assume till the 70% of the project cost with a maximum limit of 1.5 millions of euro per year. The decision on the allocation of the credits does not rely solely on CDTI but require the intervention of the financing entities which collaborate with ICO in this initiative.

This line of funding is managed through a natural call with the aim of financing the productive instruments carried out by Spanish companies with the privileged conditions indicated above. The total budget rises to 220 millions of euro until December 2003 and results from the collaboration between 33 financing entities, all of them involved in the management of the line of credit providing facilities to receive the documents and information on the guarantees needed to drive to the end of the operation. Every firm established as commercial entity can be solicitor for financing new investments or performing improvements in the technological dimension of the firm. Though the decision is a shared one, the projects require a previous positive evaluation from CDTI and upkeeping to certain conditions and limits:

- The real-estate investment should not exceed 30% of the total.
- The investment in non-material aspects should not go further the 50% of the total.

The firm owner can receive a maximum of 1.5 of euro per year, either through a single operation or several but it is worth to remind that the credit covers, as its maximum, 70% of the budget. He or she can choose to pay-off during five years, without shortage and one year shortage, or to pay-off during seven years, without shortage or with two years shortage. The option is open to a fixed interest rate (ICO reference +1 percentage point) or a variable interest rate (Euribor six months +1 percentage point).

Orphan drugs and their incentives

The production and commercialisation of the so-called "orphan drugs" (drugs without a commercial interest) have the benefit of incentives and subventions at all levels. Europe and Spain have joined the United States in this direction. The Spanish Law (Ley del Medicamento) defines them as "those (drugs) which being necessary for a certain set of treatments related to symptoms or pathologies with low incidence, show absence or deficit in their supply to the national market". On its side, the EU considers "orphan" that drug aimed to prevent, diagnose or treat of rare diseases which should have serious difficulties for its commercialisation by the lack of sales perspective once being present in the market.

Rare diseases are defined, on a quantitative basis, as those which affect to less than 5 persons in 10,000 of the EU. In addition to matching this epidemiological criterion, this type of diseases must represent a disorder able to put into risk the life of the patient or to generate a chronic or severe handicap. The rare diseases are usually associated to a specific genetic defect (according to the WHO, there are 5,000 rare diseases known currently, 80% of which are based on genetic causes). This is the reason why biotechnology applications have become so important to treat them. Most of the drugs are proteins whose best method of production relies on the DNA recombinant techniques. Most of the traditional pharmaceutical laboratories confront difficulties for producing these molecules: they are separated from their pipeline of production, they are specifically failure and this can not serve as blockbuster. This is the reason for the need of businesses oriented in a specific manner to the biotechnological techniques and applications. Biotechnology-based Companies have emerged as the principal actors for the production of this type of drugs, whose development costs amount to one quarter of those of a conventional drug and whose commercialisation costs correspond to one seventh of the traditional ones. But their research and developed have needed a supplement through a series of incentives to attract the interest of the companies. For it, the European Union approved the Regulation (EC) 141/2000 stating that, once the Committee for Orphan Drugs of the EU grants the qualification of orphan to a drug, "the promoter owner of that drug will enjoy incentives and subventions that will be made effective

when the application for its authorization, previous to the commercialisation step "is made".

There exists, as well, a special programme of the Spanish Institute for foreign Commence (ICEX) entitled "Promotion of culture to export"[7] aiming at to bring SMES about the export culture: its understanding, practice and promotion.

II.2.3 POLICIES WITH A SOCIO-ECONOMIC AND ETHICAL DIMENSION

The situation described above concerning an "orphan drug" drives these drugs to be embedded in very important socio-economic and ethical dimensions. They are products of extreme necessity for small collectives of patients which should be left aside in a commercial structure by their low commercial value. The development of a new therapy represents costs around 200 millions of euro, and economic charge that has to be assessed by the laboratory prior to the decision on producing it. This is the reason why the policy makers and the decision makers have taken steps to regulate the situation of this type of drugs and to promote their development and production. These are the goals of the Regulation put into force from the EU in 2000 following the lines of the "Orphan Drug Act" approved in the USA since 1983.

On the other hand, there are important ethical issues related to new research lines in biology and to its eventual applications. This is the case of the research on "stem cells"; a high controversial issue on which Ethical Committees are giving advice to governments decision makers and society at large. In Spain, the Advisory Committee on Ethics in Scientific and Technical Research, associated to the Spanish Foundation for Science and Technology (FECYT), has made a report on the scientific issues from an ethical point of view and the current legislation. In its report, the Committee while recognizing the intrinsic value of scientific progress for society as a genuine human activity, admits an open attitude towards the new avenues. Consequently, the Committee has made the following recommendations to deal with the research on stem cells:

[7]The programme, settled at national level, has resulted from an agreement of ICEX with the Higher Council of Commerce Chambers, the Autonomous Regions and the Commerce Chambers themselves to foster the foreign promotion and commercialisation of SMES. The Plan is a general one, not specifically addressed to biotechnology-based firms or biopharmaceutical companies, but to any business which can be labelled as SME and have its own product service, possessing a strong commitment to internationalise itself and willing to explore its commercial possibilities in foreign markets. The programme named as "Plan de Iniciación a la Promoción Exterior" (PIPE 2000) (Plan to Initiate Foreign Promotion) has as its main goal to get 3,000 new exporting companies for the period 2001-2006. The programme is qualitative in essence and integral providing to the companies individual and specific advice (by means of tutors, promoters and collaborators from PIPE 2000) as well as the economic support (during the two years the programme would benefit the firms, they will be supported by 80% of the expenses carried on by the firms).

1.- Priority should be given to the research on animal stem cells provided their results can be extrapolated to the results than can be obtained with human cells.

2.- The research on human adult stem cells does not pose any specific ethical problematics as they are obtained from adult tissues.

3.- The research on embryonic stem cells poses ethical issues as they are derived from early embryos, who have their identity and value meriting consideration, though this value has to be weighed with respect to other values.

4.- The Committee makes the recommendation to use the embryos in excess resulting from the Assisted Reproduction Techniques as a positive alternative with respect to their destruction. They could be used for obtaining embryonic stem cells to carry out research on them.

5.- In any case, the Committee does not recommend the specific obtention of human embryos with the sole objective to getting stem cells for research.

Mixed programmes

There is an ensemble of programmes making a bridge between policies addressed to produce knowledge and policies to support commercialisation. Among them it should be mentioned the following:

1.The projects called Projects for Concerted Industrial Research developed and funded by CDTI have as main objective the funding of initiatives from precompetitive research (those researches whose results are not directly driven to commercialisation and involve a great technical risk).

2. Initiative: Torres Quevedo Programme

Programme targeted to businesses that are developing or looking to start R+D+I programmes as well as those which are willing to strengthen their innovative capabilities.

3. Petri projects

The main goal is to foster the transfer of technologies from public research organisms (OPIs) and universities to the productive sector.

4. Profit projects programme

This programme constitutes an instrument designed and managed by the Ministry of Service and Technology. By means of public grants, the programme attempts to get

the mobilization of businesses and other organizations for developing research and technological development activities

5. Other actions

Other initiatives worth of noting are the “Proyectos de Colaboración P4” and the initiative “Neotec”, under the frame of the R+D+I Plan. The first one (Collaborative Projects) aims to the precompetitive development with projects led by a public research organism but with the involvement of a company that is willing to develop a product. A single call was the outcome with 221 projects and subventions approved for a total of 40 millions of euro.

The second one, the initiative Neotec, intends as objective to help the creation and consolidation of new technology-based enterprises. The programme lays out several instruments depending on the phase of life cycle of firms (first phase “idea”; second phase “firm creation”; third phase “risk capital”).

II.3 STRUCTURE AND DYNAMIC OF NATIONAL SYSTEM

II.3.1. PUBLIC R&D SYSTEM

The main public (governmental) organism involved in the R+D+I+T policies is the Ministry of Science and Technology (MCYT), though the Ministry of Health and Consumption (MSYC) also plays a relevant role in this area; particularly in the biomedical realm.

Special mention deserve some public institutions deeply involved in the development of the scientific research and technological development of this country. Among these institutions it should be emphasized at first glance the Consejo Superior de Investigaciones Científicas, CSIC, belonging to the Ministry of Science and Technology. It can be considered as the main representative of the public organisms of research in Spain and a basic element of the public research system as CSIC fosters many linkages with Administrations (state, regional and local), with other research institutions from public and private dependencies (universities, research centres, businesses) to collaborate in joint projects. CSIC also collaborates with social an economic actors at national and international levels to build networks for transfer knowledge and its eventual applications. In administrative terms, CSIC is a public organism, autonomous; in functional terms, it is multisectoral and multidisciplinary, possessing juridical entity and its own patrimony and has its resources distributed along the national territory.

CSIC [8]was founded in 1939 and its present objectives and functions are lying in the "Law for Promotion and General Coordination of the Scientific and Technical Research" (Ley 13/1986m enacted on the 14th April) as well as by its Statute or internal regulation (Royal Decree 140/1993, from 29th January) in operation until December 2000. The Royal Decree 1945/2000 from 1st December settles a Statute of the Autonomous Organism, Consejo Superior de Investigaciones Científicas to comply with the Law 6/1997 and the Law 50/1998, both related to the Organization and Functioning of the General Administration of the state.

Several of CSIC institutes and centres, in addition to perform research activities in "strict sense", devote part of the time of the researchers and of their budget to promote the dissemination of science through Conferences, Seminars, Workshops and to communicate basic knowledge to the society.

The scientific activity of CSIC develops within the frame established by the National Plan of R+D+I (plus technology), the distinct R & D Plans of the Autonomous Regions, and the Framework Programme of the EU. That activity is programmed and channelled by the researchers grouped in the following scientific and technical areas:

a. Humanities and Social Sciences.
b. Biology and Biomedicine.
c. Natural Resources.
d. Agronomical Sciences.
e. Physical science and technologies.
f. Materials science and technology.
g. Food science and technology.
h. Chemical science and technologies.

An Office for Technology Transfer (OTT) aims to make the bridge between the knowledge produced in CSIC centres[9] and institutes and the eventual technological assets to all socio-economic sectors both at national and international levels. Its main goal is the transformation of the capacities and skills of CSIC human resources into economic, social and cultural wealth.

[8]Among the functions; the following should be emphasized:

1.- To prepare and perform projects of scientific and technological research.
2.- To promote the advancement of basic research.
3.- To collaborate with the universities in research activities.
4.- To develop training programmes for researches and technicians.
5.- To collaborate with the National Plan of R & D (now National Plan of R+D+I)

[9]. In specific terms, the OTT-CSIC addresses the following objectives:

1. To spread and promote the living image of CSIC as well as its capacities among the socio-economic environments.
2. To easy and promote the relationships between its personnel and the actors from the production "milien".
3. To foster the creation of technology based firms

Another important organism in the public sphere of the science and technology system in Spain is CDTI (from its name in Spanish, Centro para el Desarrollo Tecnológico e Industrial). It is a public organism ascribed to the Ministry of Science and Technology, whose aim is to help the task of the Spanish businesses to carry out R+D+I projects. CDTI assesses and funds projects proposed by firms irrespectively of their sector of activity and dimensions. The amount of funding usually allocated after positive evaluation of a project fluctuates between 240,000-900,000 euro, amount which includes capital assets, personnel involved in the project, materials and other cost of the project[10].

Another important organization is the yet mentioned Institute of Health Carlos III[11] (ISCIII), with the statute of autonomous public organism belonging to the Ministry of Health and Consumption. This organism holds the mission to develop and offer scientific and technical services of the best quality to the National Health System (SNS of its name in Spanish, Sistema Nacional de Salud) and to the society in general. The ISCIII is ruled by the Law 13/1986 (referred popularly as Law for Science), the Law 14/1986 (Ley General de Sanidad) ands its Statute approved by the Royal Decree 375/2001.

Other public organisms of particular interest to this report are :

CIEMAT[12]- Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas –.

IMIM[13] - Instituto Municipal de Investigaciones Médicas –

CNIO[14] - Centro Nacional de Investigaciones Oncológicas –

[10]These technological projects are divided according to CDTI into three categories:

i. Projects of Technological Development.
ii. Projects of Technological Innovation.
iii. Projects on Concerted Industrial Research.

[11]Among its functions it must be emphasized:

- The applied research of the National System of Health.
- The basic research on health problems.
- The advice and collaboration to the organisms acting in the field of innovation and technological development.
- The specialized training for the personnel involved in the health services and management of the health system.
- The promotion and coordination of the biomedical research activities.

[12]CIEMAT is an autonomous public organism ascribed to the Ministry of Science and Technology, whose objectives are the promotion and development of basic and applied research activities as well as actions of technological development with particular emphasis on the areas of energy and environment

[13]IMIM is a public organism, located in Barcelona and associated to the local administration (it is managed through the local institution of health services – IMAS). The mission of this organism is the management, promotion, coordination and putting with force off the scientific research activities in biomedicine and health sciences, complemented with training actions and programmes for the human resources involved in these areas.

[14] CNIO one of the new incorporations to the public health system and the most brilliant piece of the ISCIII. It is a public organism, organized as non-profit institution with the statute of Foundation but strongly linked to

INIA[15] - Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria –

IRTA[16] - Instituto de Investigación y Tecnología Agroalimentaria –

In the Basque Country there are semi-public institutions that are worth taking into consideration. One of them is IKERLAN[17] -Centro de Investigaciones Tecnológicas with specialization on Mecanotronics- .

Some Data of the Research System of Spain

The total expenses for R & D activities in 2001 in Spain amounted to 6.227,1 millions euro, with a gross increase of 8.9% with respect to the preceding year. This figure represents the highest investment in Spain with respect to the wealth of society. The following Table 2.3 shows the evolution of the main indicators regarding economic resources along the period 1990-2001.

TABLE 2.3: ECONOMIC RESOURCES

	1990	**1991**	**1992**	**1993**	**1994**	**1995**
R & D expenses (millions €)	2,559	2,881	3,245	3,350	3,294	3,550
% R & D/ GAP	0.85	0.87	0.91	0.91	0.85	0.81
R & D/ Researcher FTE – thousands a current €	67.93	70.89	77.85	77.25	68.83	74.99
	1996	**1997**	**1998**	**1999**	**2000**	**2001**
R & D expenses (millions €)	3,853	4,039	4,715	4,995	5,719	6,227
% R & D / GAP	0.83	0.82	0.90	0.89	0.94	0.96
R & D /						

the direction of the ISCIII and the Ministry of Health its main sponsors. The funding of the activities takes place through the Agreement of the Industry for Stability and Innovation dealt in depth before. The mission of CNIO is to foster the research on oncology by means of the promotion, support and improvement of the scientific and medical advances in the field of cancer research.

[15]INIA is a public organism ascribed to the Ministry of Science and Technology whose mission is the management and implementation of all governmental competences related to scientific research and technological innovation in the areas of agriculture and food, the fostering of the cooperation both at national and international levels on those areas as well as the elaboration, coordination and management of the strategic actions on the agro food domain included in the National Plan of R+D+I+T.

[16]IRTA is a public organism under the dependence of a regional government, Cataluña in this case. Its mission is to promote research and technological development in the agrofood sector, to assess the scientific progress and facilitate its application, as well as to coordinate the efforts made by public and private sectors in the most efficient way.

[17]IKERLAN which holds the statute of private non-profit Foundation though it is tightly linked to the regional government and to the University of Mondragón. Its mission is oriented to strengthening the innovative capacity of the industrial sector in the Basque Country as well as to improve its capacity to compete in the international world.

Researcher FTE- thousands a current €	74.62	74.96	78.23	81.14	74.59	77.76

FTE: Full time equivalent
Source: INE, OCDE

TABLE 2.4: R & D Activities in the Most Innovative Entrepreneurial Sectors (1999 Data)

Sectors	R & D Personnel	R&D Expenditures			
		Total M €	Increase over 1995 (%)		
			Total	Internal	External
Pharmacy	3,331	369.95	10.9	9.5	15.6
Radio, TV and Communications	2,935	222.13	6.6	7.9	2.2
Automotion	3,354	500.92	14.8	9.4	32.6
Aerospace	2,339	219.66	6.5	7.7	2.6
Total Industrial Sectors	31,093	2,708.08	80.0	79.7	80.8
Total Business Sector	38,323	3,384.94	100.0	100.0	100.0

Source: Farmaindustria, La Industria Farmacéutica en Cifras, Edición 2002, a partir de Encuesta I+D del INE

II.3.2. BUSINESS SYSTEM

II.3.2.1. PREVIOUS STUDIES

One of the first studies on the characterization of the biotechnological business sector was carried but by V. Díaz, E. Muñoz and J. Espinosa de los Monteros in 1999. The study has been the subject of different publications[18].

One of the first finding of that study was that the business subsystem of biotechnology in Spain was not fitting to the model based on spin-off and start-up companies. Three subgroups of companies were identified:

a. Companies clearly dedicated to biotechnology (ECDB from its name in Spanish, Empresas completamente dedicadas a la tecnología), within this category fall all those firms whose 50% or more of their invoicing is related to development

[18] Working Paper 01-01 UPC-CSIC and Diaz *et al.* (2002)

and commercialization of technologies, products and services based on biotechnology.

b. Companies partially dedicated to biotechnology (EPDB): comprises all those firms which having some relation with biotechnology in their value chain, their commercial activity is not essentially supported by the technology.

c. Companies that use biotechnology (EUB): this group refers to those companies which take recourse to some biotechnological applications or products for their products or production processes.

II.3.2.2. EMPIRICAL STUDY

The empirical analysis has been carried out during the first semester of year 2003 on a sample of 20 firms, a 25% of them were micro-firms (with less than 10 workers), another 25% were small companies (with 10-50 workers), a 20% can be ascribed to medium companies (with a number of workers between 50-250), and finally, the last 30% belongs to big companies (with a number of workers beyond 250).

The empirical study we have carried out in the first semester of 2003 on this subsystem allows to draw some previous conclusions:

1. The 40% of the companies respondents to the survey are located in Madrid, 30% in Cataluña and remaining 30% in other Autonomous Regions.

2. The 75% are national capital owned; 15% from the EU and the other 10% from USA.

3. 45% of the firms have a shared property, belong to various partners and do not stand at the Stock Market; 30% of the firms also belong to various partners and stand at the Stock Market, while the remaining 20 are owned in a great majority (95% or more) by a single person.

4. The 50% of respondents are subsidiary companies.

5. The companies use and value as sources of knowledge the following:

- Own or from the head office (83.4%) valued this source as high or very high);
- Scientific sources (78.9% valued them as high or very high)
- Academic institutions (57.9% valued them as high or very high)
- Conferences, seminars, workshops (47.1% valued them as high or very high)

On the other hand, the less appreciated sources of knowledge are:

- Professional associations and firms unions/local authorities (94.1% of the companies considered both as low or very low)
- Knowledge from private sources (particulars) with 82.3% of the companies stating them as low or very low
- Foreign firms (47.1% valued this source as low or very low)
- Data bases (41.2% considered the use as source of knowledge as low or very low)

Finally, there is a some paradoxical situation with the assessment of Public Institutions: 44.5% valued them as low or very low, while 33.4% considered them as high or very high. This may be due to a misinterpretation of the term Public Institutions – to include in it the public scientific institutions or not – or to the distinct significance for the members of the survey of the normative role of these Institutions.

6. With regard to the issue of exporting biotechnological products, 66.7% declared not to have carried out this activity. The most usual formulas are to make recourse to agents and subsidiary companies for the commercialization abroad.

7. The 85.7% of the respondents are manufacturing their products in Spain.

8. The companies rely on the MCYT for the funding of their research expenses (94.1% of respondents declare that part of their R & D expenses are covered by the Ministry of Science and Technology initiatives). However there is a diversification of sources as 70% of respondents use other such a venture capital, credits and loans from banks, etc.

9. With respect to the question asking for the impact that the emergence of the biotechnology has had on the traditional pharmaceutical industry the two issues deserving the highest appreciation in the responses have been: the broad generalization of alliances and the development of small biotechnology-based firms. The first issue has been assessed as representing a high or very high impact by 55.6% of the respondents, where 50% of them have given the same assessment to the second issue. A somewhat controversial result has been obtained with the issue referring to the creation of a new strategic unit as a main factor for the traditional pharmaceutical industry. In this case, 38.9% have considered it as a law or very low impact while other 33.4% have given a rate to it as high or very high.

To undertake the analysis of the quantitative variables, the sample has been divided into four groups according to the size of company.

The first group, with less than 10 employees, the micro-firms, comprises 5 out of the 20 companies responding to the questionnaire. The second group referred as small enterprises (with a number of employees between 10-50) amounts to another

5 of the respondents. The third group (with a number of employees between 50-250) represents 4 out of the 20 enterprises that responded to the survey, whereas the fourth group (number of employees > 250) comprises 6 of the 20 companies. The first two groups, micro and small businesses, hold the profile of newly created biotechnological firms (NBF) that have arisen in the last years as the result of the positive evolution of the biotechnological activity in Spain. The other two groups are examples of the diversification of traditional pharmaceutical companies to the activity in biotechnology.

The analysis of the data reveals that are the NBF those investing higher percentages of their sales in R&D activities as well as those holding a greater number of biotechnological products in the markets. The medium and big companies are beginning to apply biotechnology as a tool for the discovery and development of new drugs. It is worth to emphasize that the big companies allocate a scarce percentage of their sales to perform research activities. The main reason for this lies in the fact that most of them are subsidiaries to big multinational companies whose research activities are carried out either in their country of origin or in some selected place.

With regard to the establishment of cooperative agreements, all of the groups behave similarly in the use of this strategy. However, the big businesses are those having a great number of strategic alliances. The great majority of these alliances is addressed to opportunities of exploration (oriented towards the acquisition or share of technology and innovation) with minor figures in those alliances driven to exploitation (oriented to the market).

In selection to the type and field of products, the two bigger groups are more focused in the human health area and precisely in the pharmaceutical sector. On the other hand, NBF are essentially involved in the precompetitive realm by performing research trying to sell knowledge and to develop products in other fields (though there is not yet available information on these research activities and eventual commercial portfolios).

With respect to the age, the NBF are quite young businesses with less than 10 years old, while the ensemble of the companies derived from the traditional pharmaceutical companies hold antiquities higher than 40 years old for medium companies and higher than 70 years old for the big companies.

The data collected in the following table (Table 2.5) confirm that the NBF are those essentially or totally dedicated to the biotechnological activities, while the traditional pharmaceutical companies apply or use them only partially.

TABLE 2.5: Characteristics of the Spanish Biopharmaceutical Sector

	Microfirms (Nº Employees ≤ 10)	Small (Nº Employees 10 - 50)	Medium (Nº Employees 50 - 250)	Big (Nº Employees > 250)
Patents 1991-2001	1.50	2.25	7.0	33.4
Biotechn. Prod..	1.0	19.5	0.75	2.20
Total Sales 2001	212,620.89 €	6.022,885.3 €	39,026,466€	261,000,000€
Sales in Biotech activities 2001	162,020.89 €	5,020,714.2€	9,600,000 €	8,448,400€
R&D Exp /Sales	58.5%	78.0%	48.0%	7.0%
Total Salary Cost for Comp.	136,270.60 €	653,094.41 €	7,334,078.8 €	42,172,402 €
Human Health Prod. in market	0.50	18	44.5	18.2
H.H Prod. In development	3.50	20.67	24.25	13.6
Animal Health Prod. In market	0	0	0	5
A.H. Prod. In development	0	0	0	4
Total Other Prod	12.0	16.5	0	0
Total Strategic Alliance is in biofarmac sector	4.0	8.0	4.0	30.83
NºExplotation S.A.	1.50	4.0	2.25	14.0
Nº Exploration S.A.	2.50	4.0	1.75	23.0
Age of the firm	4.20	7.8	42.5	70

Source: Own Survey Data

II.3.3 DEMAND SYSTEM

A series of actors can be identified which to a greater or minor extent, are users of the health system and are directly involved in their processes of innovation. Among

them: the patients association, medical or professional societies, foundations/non-profit organizations, etc.

Among the patients associations, the most prominents are those of patients suffering from some diseases, though none of them has been playing a very active role according to the concept of innovation system. Their general mission is to give support to the patients as well as to their families providing advice on the disease, its potential treatments, secondary effects, initiatives to improve the quality of life concerning both the patients and their relatives. The associations with tighter links to the biopharmaceutical products are:

1.- Spanish Association of Multiple Esclerosis (Aedem)
2.- Foundation Alzheimer España-Fae
3- Federación Española de Asociaciones de Enfermedades Raras-Feder
("Spanish Federation of Associations of Rare Diseases")
4.- Fundación para la diabetes
("Diabetes Foundation")
5.- Asociación para los Enfermos de Ataxia
("Ataxia Patients Association")

On the other hand, the scientific and medical societies also play a role, albeit small, in the system by promoting the dissemination of scientific and technical knowledge through the organization of seminars, congresses, scientific meetings, publication of informative bulletins and reports.

Apart from the two biggest societies in the area of biological sciences which are: The Society for Biochemistry and Molecular Biology and the Society for Microbiology, the scientific and medical societies with greater relationship to the biopharmaceutical sector are:

1.- Sociedad española de bioquímica clínica y patología molecular-seqc
("Spanish Society for Clinical Biochemistry and Molecular Pathology")
2.- Sociedad española de cardiología
("Spanish Society for Cardiology")
3.- Sociedad española de genética-seg
("Spanish Society for Genetics")
4.- Sociedad española de informática de la salud-seis
("Spanish Society on Health Informatics")
5.- Sociedad española de ingeniería biomédica –seib
("Spanish Society of Biomedical Engineering")
6.- Asociación española de bioética y ética médica-aebi
("Spanish Association of Bioethics and Medical Ethics")
7.- Organización nacional de transplantes-ont
("National Organization on Transplants")
8.- Private health companies
9.- Associations and Societies Related to Biotechnology

After the analysis of the goals of that organizations (See Item V.) we can remark the following conclusions:

- Scarce role of patients association, which are basically performing activities targeted to promote the knowledge on the diseases, their treatments and effects and to improve the quality of life for patients and their relatives

- Limited role of the scientific and medical associations and societies, which focus their activities in the promotion of the dissemination of the medical and scientific knowledge through the organization of seminars, congresses, courses, workshops, publication

- Scarce role of the private firms involved in medical care. Particular mention to the case of Sanitas, which by means of its Foundation promotes research and medical and sanitary education by means of the calls for fellowships, grants to projects of research, scientific publications, etc.

II.4 KEY DRIVERS AND BARRIERS IN BIOTECH INNOVATIONS

From the qualitative information gathered from a group of experts and some companies as representatives of the sector, the factors that favor the innovation process and the factors that hamper them can be drawn.

A. FACTORS THAT MAKE EASY THE INNOVATION PROCESSES

- The availability of a good scientific community. It is well known that there is in Spain a good scientific base in qualified scientists and support personnel with international recognition.

  An indicator to support this statement stems in the number of publications by Spanish researchers. According to the bibliometric study carried out by the ISI Fraunhofer, the ratio of publications per 1000 Spanish researchers amount to 679, a figure slightly higher than the European average for the period 1999/2000 (619) and a surprisingly 30% higher than the figure for Germany (525). From the countries studied, only the Netherlands (923) and United Kingdom (891) show higher performances.

  Regarding the publications record in the specific field of biopharmaceutical sciences it also shows a marked positive trend for Spain in the period 1994-2001. The Spanish biopharmaceutical

publications have exactly doubled in that period from 438 in 1994 to 936 in 2001. Moreover, the contribution of Spain to the total of the European Union has grown, going ahead from 5.5% of the EU Biopharmaceutical Publications in 1994 to represent a 7.2% of them in year 2001.

- The existence of a series of policies and tools aimed to promote the processes of innovation (National Plan R+D+I, Profit Programme, Torres Quevedo, etc.). For details see item II.2
- The launching and putting into force of a series of tools targeted to improve the relationships between the public and the private sectors. Initiatives to foster the collaboration between public centers of excellence and the business to carry out cooperative projects in their starting phases.
- The adoption and development of the model of bioincubators, such as the "Parque Científico de Barcelona" (Scientific Park from Barcelona).

The establishment of technological parks and bioincubators has helped the process of innovation in Spain. A technological park provides a series of infrastructures which permit the creation of innovative businesses. It also affords an ensemble of services that make easy the technology transfer process between the University, the researcher centers and the firms, all of them installed in a common place, the technological park. The establishment of these local infrastructures allows to foster the creation and positive development of knowledge based businesses. It also may promote synergies between the different companies settled in the park location as well as the access to contract the knowledge capacities and skills of the university and its personnel. The Scientific Park of Barcelona offers a good example for this type of initiative which is now being followed by the Scientific Park of Madrid located in the Autonomous University of Madrid as a joint venture with the Complutense University and CSIC and there also interesting initiatives in the Basque Country.

On the other hand, bioincubators are a means to help the business beginners by providing minimal infrastructures at low cost to those wishing to develop their own company. Bioincubators are environments specifically designed and prepared to support the development of small entrepreneurial units. These units are provided with human resources, equipments and operational installations to foster the emergence of modern and competitive businesses able both technologically and in managerial terms. Bioincubators are spaces shaped to take in and to shelter those firms, essentially micro-firms, holding an emerging and innovative profile and aiming to transform ideas into products and/or services. A bioincubator is a condominium where these emerging companies receive for a period, lasting approximately two years, support to favor their launching. After the take off, the firm leaves the space to continue its process of development. The establishment of bioincubators

makes easy and gives momentum to the innovation strategies since it allows the creation of micro-firms by helping them to use laboratories and offices at low cost and facilitating links with capital entities, venture capitalists and governmental agencies as well as with the public research sector (University and Public Research Laboratories). There is an interesting case of bioincubator in Madrid, an initiative settled in an industrial park near to Madrid (Fuencarral) named Vivozonia which deserves great attention for its future development. Vivozonia has been the venue for an interesting initiative put into force some years ago by the Spanish Society of Biochemistry and Molecular Biology (SEBBM). This iniatitive named in Spanish "La empresa puedes ser tú" ("You may be your own company") was held in its third edition (2003) in Vivozonia with the aim of driving the "creation of biotechnological businesses".

- A more efficient technology transfer by the Offices of Transfer of Technology (OTRIs).
- The emergence and existence of small firms based on research providing added value by means of services to the big companies. These firms are those involved in the clinical trials of the biopharmaceutical products.
- The development of collaborative initiatives between biopharmaceutical companies. Through this culture of collaboration the firms are complementing their assets to share risks and R & D expenses.
- The steps to a greater flexibility of the full-time concept for the researchers of the public system.
- The increasing interest of the researchers of the public system for opening their research to the interaction with other actors in order to make more dynamic their research.
- The existence of fiscal legislation addressed to give incentives to the scientific research.
- The G10 recommendations to foster the R & D in Europe.
- The "Agreement for the Stability and the Innovation" signed by MSYC and Farmaindustria as has been mentioned earlier in this report.

B. FACTORS THAT MAKE DIFFICULT THE INNOVATION PROCESSES

- The uncertainty of the processes
- The traditional lack of research culture among the decision makers in Spain
- The scarcity of public funds to finance these processes
- The administrative inflexibility at several respects: accountability; financial rules underlying the governmental programmes to fund research projects. The inflexibility makes untenable the situation for small firms
- The absence of a "culture for patenting". There is very low propensity to patent in Spain. A reference study carried out by A. Albert and collaborators at the Centre for Scientific Documentation (CINDOC) has shown that about a 15-20% of North American patents related to biotechnology are supported by research carried out in Spain by Spanish

researchers. There is need for a change in the rewarding system of the public researchers. The current system favors the publication and not the patent.

- The cost increase in the research in general, and in the biopharmaceutical sector in particular. Last estimates go up to 900 million euro as the average cost to make a new drug.
- The cost increase of the technology transfer as a consequence of its professionalism.
- The inadequate dimension of the Spanish companies. No Spanish firm can cope the very expensive costs of the innovation processes in isolation
- The absence of "ad hoc" regulations to promote the development of an industrial web
- The lack of specific regulations and norms for the small firms based on biotechnology
- The absence of a determined action from the government to promote the industrial sector what hampers the consolidation of the research processes and initiatives
- The absence of auxiliary industry to accompany and help the development of scientific knowledge
- The same excellence of the Spanish National Health System whose high level of service cover and giving of help makes it extremely costly. This drives to the establishment of a frame of spent contention and restriction. This environment reduces the possibilities to favor R & D initiatives
- The public intervention in the prices of biopharmaceutical products.

C. FACTORS THAT MAY CONTRIBUTE TO A GREATER AND BETTER R & D

We can perceive some factors that could contribute to improve the R&D and the innovation activities in biotechnology:

1. A greater participation of the biopharmaceutical industry in joint projects with the Public Research Organisms;
2. Higher support from the Public Administrations by the increase in the financing resources aimed to fund the processes of innovation;
3. The development of a venture capital market which help the high costs of research;
4. A clear governmental support to the creation of new companies based on biotechnology. Development of an ad-hoc regulation driven to foster and help the development of this industrial network;
5. The creation of appropriate necessary infrastructures for the expansion of this sector;
6. The development of an adequate system for protecting the innovations; As a consequence of the high increase in costs of biopharmaceutical research, in the last years, there is a need for an

enlargement in the period of patent protection in order to help to recover the huge investments.

7. The fostering of a culture of collaboration between traditional pharmaceutical and new biotechnological companies which can achieve good complementary agreements to share risks and costs of the processes of innovation;
8. The generation of an environment able to foster the innovation by means of a stable regulation frame which may allow to plan investments for a long term, what could favor a sustainable growth of the market and give rise to a general climate in supporting these processes.

9. It's necessary a greater flexibility of the full time concept for the researchers of the public system. In spite of some normative efforts made recently, public researchers are experiencing a lot of difficulties to create businesses or to perform research within private firms due to incompatibility regulations. It seems therefore reasonable to make more flexible the concept of full time equivalent or to establish new rules or instruments to favor the compatibility with this type of activities, e.g, by sharing the time allocation and the salaries.
10. A more efficient technology transfer by the Offices of Transfer of Technology (OTRIs). In spite of some improvements in the last years concerning the process of technology transfer, the mechanism and outcomes of these processes seem to be insufficient

As it has been shown previously, Spain disposes of a good scientific offer. The problem rests in the poor links between the scientific realm and the entrepreneurial domain. In the questionnaire, the issue of knowledge and information sources used by the firms was addressed, according to the following classification:

- Own sources from the company itself or from its head office
- Scientific sources
- Academic institutions
- Public research organisms and institutions
- Private research organizations
- Foreign companies
- Local authorities
- Associations
- Data bases
- Conferences, seminars, workshops, etc.

For the results gathered, the following conclusions were reached with respect to the type and intensity of the sources to whom recourse was made:

- Own or from the head office (83.4%) valued this source as high or very high);
- Scientific sources (78.9% valued them as high or very high)
- Academic institutions (57.9% valued them as high or very high)

- Conferences, seminars, workshops (47.1% valued them as high or very high)

On the other hand, the less appreciated sources of knowledge are:

- Professional associations and firms unions/local authorities (94.1% of the companies considered both as low or very low)
- Knowledge from private sources (particulars) with 82.3% of the companies stating them as low or very low
- Foreign firms (47.1% valued this source as low or very low)
- Data bases (41.2% considered their use as source of knowledge as low or very low)

Finally, there is a some paradoxical situation with the assessment of Public Institutions: 44.5% valued them as low or very low, while 33.4% considered them as high or very high. This may be due to a misinterpretation of the term Public Institutions – to include in it the public scientific institutions or not – or to the distinct significance for the members of the survey of the normative role of these institutions.

With respect to human resources allocated to R & D, the year 2001 has witnessed an increase in the personnel as well as in the number of researchers, in particular in the Higher Education. In fact, the universities are the main reservoir of human resources for research, but it is deemed necessary to design and promote measures aiming to strengthen and develop the human potential in the business sector. Along the period 1990-2001, two years, 1999 and 2000, have seen the highest increase in the number of personnel devoted to R & D (18%) as well as in the number of researchers (24.5%).

TABLE 2.6: HUMAN RESOURCES IN R & D

	1990	**1991**	**1992**	**1993**	**1994**	**1995**
R & D Personnel FTE	69,684	72,406	73,320	75,734	80,399	79,987
% over Active Population	4.5	4.6	4.7	4.8	5.0	4.9
Researchers FTE	37,676	40,642	41,681	43,387	47,867	51,633
% over Active Population	2.5	2.7	2.7	2.8	3.1	3.0
AA.PP. (Public Sector)	24.6	24.2	22.7	22.8	21.8	21.4
Higher Education	33.9	35.0	37.6	39.4	43.1	42.9
Business	40.9	40.3	39.0	36.7	34.0	34.5
non-profit institutions	0.5	0.5	0.7	1.1	1.1	33.7
AA.PP. (Public Sector)	20.2	19.9	18.4	17.8	16.3	17.7

Higher Education	50.2	51.1	53.2	55.4	59.7	58.4
Business	29.2	28.6	27.8	26.0	23.1	22.8
non-profit institutions	0.4	0.4	0.6	0.8	0.8	1.1
	1996	**1997**	**1998**	**1999**	**2000**	**2001**
R & D Personnel FTE	87,264	87,150	97,098	102,238	120,618	125,750
% over Active Population	5.3	5.2	5.7	5.9	6.8	6.9
Researchers FTE	51,633	53,833	60,269	61,568	76,670	80,081
% over Active Population	3.2	3.3	3.7	3.8	4.3	4.4
AA.PP. (Public Sector)	20.5	22.0	20.7	21.8	18.6	18.7
Higher Education	44.6	42.3	42.2	39.7	41.0	43.4
Business	33.7	34.4	35.7	37.5	39.0	37.0
non-profit institutions	1.2	1.3	1.2	1.1	1.4	0.9
AA.PP. (Public Sector)	17.7	19.5	18.2	19.4	16.6	16.7
Higher Education	59.8	56.9	57.3	55.0	54.9	58.6
Business	21.5	22.3	23.0	24.6	27.2	23.7
non-profit institutions	1.1	1.4	1.3	1.0	1.3	1.0

Source: INE

With respect to the personnel involved in R & D activities in the pharmaceutical sector, data from 1997[19] indicates a figure of 3,331 individuals (Full Time Equivalent) with a consequent investment of around 370 millions euro.

As the Annual Report from the Spanish Association of Biofirms (ASEBIO) states, the Spanish ECDB firms have a highly qualified staff with 75% of their personnel possessing university degrees, with a great majority of them holding doctorates degree. This personnel is one of the most important immaterial assets (intangibles) of the sector and a strategic tool to compete in the international world.

On the other hand, industrial activity is strongly linked to R & D. But there are particular branches where the link is essential for survival. The pharmaceutical industry is a case for such requirement. The analysis and exploration of new potential drugs as well as the improvement of properties of previously existing products take place at an accelerated pace. The R&D processes in the pharmaceutical sector posses a pluridisciplinar character, are capital intensive and

[19]R & D Survey. INE. Results 1999

long lasting. As previously stated, the pharmaceutical sector is placed in the nine position among the 100 industrial sectors recorded in the Industrial Survey of INE with a 2.2% of the total turnover of the Spanish industry corresponding to year 2000. However, the pharmaceutical sector contributes to business R & D expenditure in Spain with 10.9% of the total expenses from industry (data from INE in 1999).

The flexible system for patenting existing in Spain for a while which was based on the patent of procedure and not on that of the products has made the companies reluctant to carry out important efforts in the R & D realm. However, the modification of the patent rules to adapt Spain to international ruling has led to a very important change. Today, it can be said that the Spanish pharmaceutical sector has understood and assimilated the need to invest in new knowledge and new technologies to be able to survive. Consequently, the research commitment of several firms is becoming quite significant. According to the employer's association, Farmaindustria, the Spanish pharmaceutical industry invested 532 millions euro in R & D in 2002. This figure accounts for about 18% of the total business expenditure, what means that one from each five euro devoted to R & D by industry in Spain belongs to the pharmaceutical sector.

Another critical initiative to this R & D domain worth to be mentioned is The Agreement on Stability and Innovation subscribed by the Pharmaceutical Industry and the Ministry of Health and Consumption (MSYC from its name in Spanish, Ministerio de Sanidad y Consumo) the 31st of October 2001 for a period of three years (2002-2004). By this Agreement, the Industry assumed the compromise to invest in R & D activities both internal and extramural (Table 2.7) while the MSYC agreeded to avoid any new structural measure to control the pharmaceutical expenditure but to explore in depth those already existing such as the prices of reference and the generic drug uses. The relevance of this contribution of the Spanish Pharmaceutical Industry to the R & D+I system reflects in the following data:

1.- The Biomedical Research Programme for the period 2002-2005 is funded by 56% of its total by the industry, a figure higher than that of the Fondo de Investigaciones Sanitarias (FIS), the second source for its funding with 29% of total.

2.- The budget of the Fondo Sanitario para investigación pública channelled by the MSYC Agency for research, the Institute of Health Carlos III (ISCIII), has incorporated 112 millions of euro, an industry endowment in 2002 to which represents 57% of the budget of that organism.

3.- The industry supported activities from ISCIII allow the funding of Networks of Cooperative research in some thematic areas such as: oncology, neurology, cardiovascular, rare diseases, public health, infectious diseases and transplantation.

The industry has bound itself to allocate 1,352 millions euro to R & D in the three years of Pact in force with increases of the annual endowments higher than that of GDP. The third part of that amount should be addressed to extramural collaboration projects. Assuming a 6.5% increase of GDP, the binding funds for R & D in each one of the years 2002, 2003 and 2004 should be:

TABLE 2.7: R & D expenses bound to the stability and innovation agreement (millions €)

YEAR	R & D TOTAL	R & D EXTRAMURAL
2002	422.7	140.9
2003	450.2	150.0
2004	479.4	159.8

Source: Farmaindustria, La Industria farmacéutica en Cifras, Edición 2002

According to the Survey on R & D carried out by Farmaindustria in the year 2002, the sector has devoted to R & D activities an amount of 531.7 millions euro, from them, 201.4 millions were allocated to extramural R & D (38% of the total) through contracts with hospitals, universities and other research countries of public ownership. Other 135.6 millions euro were devoted to human resources, 55.9 millions to capital expenses and 138.8 millions euro to running costs. It is worth noting that the Spanish pharmaceutical industry spent 62% of the total investment in intramural R & D activities a significant data to display the innovative vocation of this industrial sector. With respect to the geographic distribution, there are logical discrepancies in relation to both types of funding. In the case of the extramural activities there is a spreading all along the Spain territory while the 95% of intramural effort is concentrated in Madrid and Cataluña, a logical consequence of the geographic concentration of the Spanish pharmaceutical industry.

Innovation is a key factor to understand and explain the competitive mechanisms of the sector. On the other hand, the institutional and regulatory framework is a crucial component in the definition of the rules for playing the game. Both aspects – high fixed costs of R & D and markets and prices with a high degree of intervention – are approaching the problematic of the pharmaceutical sector to that of the so called "network sectors" like energy and telecommunications. But unlike these sectors, the pharmaceutical industry works with a very strong competitive intensity, sharing this characteristic with other very innovative industries. In addition to this, the R & D costs are increasingly higher what increases the levels of risk. Consequently, the positive evolution of the pharmaceutical industry requires an adequate environment, which should be built around three key elements:

1.- A regulatory frame with due stability to ensure the planning of long term investments;
2.- A market able to keep sustainable growth;
3.- An adequate climate for innovation

In addition to these main institutions and agencies from private origin that provide funds to finance R & D projects we have to mention the venture capital market and the existence of some private foundations to contribute to finance the R&D projets.

The investments of the companies of venture capital raised up to 932 millions euro during 2002, what represents a 22% decrease as compared to the previous year (data from the "Asociación Española de Entidades de Capital Riesgo – Ascri"). The new resources during 2002 amounted to 650 millions euro, what means a drop of 37.83%, while the number of operations was kept stable in 424. The average amount of the investments declined from 3.3 to 2.2 millions euro, though the number of firms in the portfolio grew a 19.89% to reach 1,350.

The investment in venture capital was targeted to the products of consumption with a 21% of the total, followed by that of chemists with 11% and services with 10%, the same percentage devoted to hotel business and leisure.

A major percentage, 62% of the total investments was driven to operations for supporting expansion, while the first steps in the life cycle of the firms received 11% of the investments and the leverage operations were allocated the 24%. The majority of the investments arrived to an end during the second semester of 2002, since the activity during the first sixth month slowed down as a result of the terrorist attacks of the 11th September against USA and the subsequent deceleration in the world economy.

Among the relevant firms of venture capital operating in Spain, are the following:

1. Apax Partner
2. Najeti
3. BCN Empren
4. Marco Polo Investment
5. Capital Riesgo Madrid
6. Gestión Capital Riesgo del País Vasco. SGECR.
7. Elkano XXI FCR
8. Talde
9. Capital Riesgo Internet
10. Innova 31
11. Gilde

The Spanish legislation establishes a series of requirements to the venture capital entities to be considered as entities of this nature in order to benefit from fiscal advantages (these entities are exempted from paying taxes of the dividends got from the shared societies and also benefit from a 99% exemption of the societies taxes resulting from the added value of the sales of enterprises).

The “business angels” are individuals who invest in entrepreneurial projects or in non-quoted at Stock Exchange firms. They can also provided additional services in consulting and business advice. In Spain, there are several clubs of business angels which are devoted to put in contact potential investors with entrepreneurs and companies in search for capital. Investment through this figure can be easier than going through the official instruments but it also confronts some disadvantages, like the loss of control and the absence of a normative as well as the impossibility to apply for the fiscal benefits which may allocated by the official organizations.

There exits some private foundations - Non-profit Institutions, usually associated to companies, either pharmaceutical (Fundación SKB, Fundación Ciencias de la Salud, Fundación SIS, Fundación Lilly) or private health providing services (Fundación Sanitas, Fundación Mapfre, etc.) - that contribute to support the R&D projects but this, nowadays, contributions is quite low.

Although debated since long time, the fiscal policies remain to be considered as essential for the support from governments to the private decision to invest in R & D, promote the innovation and foster the competitiveness and the economic growth.

It is now generally accepted that Spain disposes of one of the most advantageous normatives on taxes among the OECD countries to attain the above outlined objectives: promoting research, innovation and technological development. According to a report from UNICE, the European Owners Organization, the Spanish businesses can get 31 € for each 100 € invested in technological projects by tax benefits.

The Law additional to the Budget Law of year 2000 (Law on “fiscal, administrative and social instruments” 1999), together with the Law 6/2000 of 13th December have made a very significant change to the fiscal treatment of the technological investments, what has driven to a change in the business strategy. Up to that moment, the Government policies to foster R & D have been based on direct subventions and/or subsidized credits, the new regulation makes a bet for tax savings as a tool to empower the entrepreneurial innovation. Among the advantages the enterprises can find, it is worth to mention the following:

a) It keeps confidentiality on the businesses R & D, because it is not necessary to present reports or protocols of the undergoing activities.
b) It has immediate financial effects, as the deduction for taxes is applied to the following fiscal year where the expenses were made.
c) It is proportional to the real effort carried out by the firms. More expenses lead to more taxes benefits; in the case of negative results, the fiscal benefit can be postponed to the back years.

The new normative has introduced a series of substantive changes with the aim to promote the firms to established and strengthen their own R & D departments, or to subcontract third parties to perform the activity. The tax incentives applied for the

first time to the investments on technological innovations rise when these activities and projects are carried out by Universities and Public Research Organisms under contract.

A critical point for an efficient implementation of the Law concerns the catalogue and definitions of the activities than can get the fiscal benefits. They are:

1.- Research[20]
2.- Development[21]
3.- Technological innovation[22]

Deductions (tax benefits):

a. R & D

1.- A deduction of 30% on the expenses done in the concept of R & D will be applied. When the expenses were higher than the average from the two previous years, an additional 50% will be applied with the figure over passing that average.
2.- An additional deduction of 10% will be applied to the amounts corresponding to the following spends:

A. Spend on qualified research personnel devoted exclusively to R & D activities.
B. Spend on R & D projects carried out under contract with Universities, Public Research Organisms or Credited Innovation (or Technological) Centers.

c. Technological Innovation

1.- Deduction of 15% for the following concepts:

[20]"Research is considered as the process of original and well planned inquiry pursuing to develop new knowledge and a higher understanding within the scientific or technological field" (Art. 32 Law 55/1999, on "fiscal, administrative and social instruments").
[21] "Development is considered as the application of the results of the scientific research or of any other type of scientific knowledge to the manufacture of new materials or products or to the design of new processes or systems of production, as well as to the technological improvement in substantive aspects of materials, products, processes or system already existing…" (Art. 33.2 Law on "fiscal, administrative and social instruments", 1999).
[22]"Innovation is considered as the activity whose result is the obtention of new products or production processes or leading to substantial technological improvements which are relevant as compared to those yet existing. It will be considered as new those products or processes whose characteristics or applications differ substantially from those pre-existing" (Art. 33.2 Law on "fiscal, administrative and social instruments", 1999).

⇒ Spend on innovation projects carried out under contracts with Universities, Public Research Centers or Credited Innovation and Technology Centers.

2.- Deduction of 10% for the following concepts:
⇒ Industrial design and process engineering in relation to manufacture;
⇒ Acquisition of technology by means of patents, licenses, know-how and industrial design;
⇒ Obtention of the certificate of compliance with the norms of quality ISO9000 and related ones, not including the expenses of the introduction of the norms.

The new Law also establishes a specific deduction of 5% on the expenses for personnel training in new technologies, link to internet and equipments required for access to it both inside and outside the working place.

At present, the Ministry of Science and Technology is ending with the preparation phase of the R+D+I National Plan for the next four years (2004-2007). The Government has stated its intention to double the R & D spend with an annual growth rate of 10% to reach investments of 12,000 millions euro in 2007. The goal is to approach the Spanish research and innovation realm to the EU average.

There are also initiatives to increase the investments from the business sector as Spain figures are still distant from those of the industrialized countries.

The general idea pursues the establishment of a pro-innovation ambiance which may drive to foster the entrepreneurial competitiveness and its internationalization, the public research of quality and the development as fast as possible of the information society as well as the best articulation of the main elements involved for its building: science, technology, business and society.

II.5 SYSTEMIC FAILURES AND POLICY IMPLICATIONS

A series of interviews were carried out during June and July of year 2003 in order to complete the study. As outcomes of the interviews, the following conclusions could be drawn on the failures of the system.

- The absence of mechanisms of proactive transfer between the public and private sector. The lack of active instruments for achieving effective transfer of knowledge between public and private sectors induces a failure in their links. If these links were more robust and effective, the innovation activities in Spain would increase.

- The lack of a clear, focused and determined bet by the Government to foster the innovation. There is need for a real prioritization of the R+D+I activities for the Government. The governments must act as promoters of the system.
  It is true that Spain has witnessed the putting into force along the last two decades of several measures and instruments addressed to promote innovation and to create culture on innovative practices but the outcomes are still poor. All of these policies and programmes appear to be still insufficient and inefficient, so it is necessary to continue to make a strong bet for this type of activities. Otherwise Spain would continue to be a laggard in the innovation rush. Europe would also experience difficulties to attain the goal of the European Council of Ministers (March, 2000) and Barcelona Council (March, 2001) to transform Europe into the most competitive economy of the world based on knowledge and by investing 3% of GDP in R&D activities.
- The small public investment in research.
  There is an evident need to increase the investment in the public system of research. The public organisms are playing a great role for the positive evolution of the system, though these centers are totally dependent on the governmental policies and the State General Budget.

- The weak linkage between the university and businesses.
  There is a lack of linkages between academia and industry that hampers the application of many academic innovations to the objectives of the enterprises. The establishment of the Offices for Technology Transfer (OTRIs -Oficinas de Transferencia de los Resultados de Investigación-) has contributed to improve the situation, though the positive results are not yet enough to overcome the Spanish deficit in this type of exchanges.
- The poor level in R & D culture
  It is still a general belief in Spain that the money allocated to R&D activities represents an expenditure rather than an investment. A change in this way of thinking seems as imperative. A change on this direction is slowly taking off but a faster pace seems essential.
- The absence of promotion measures to foster the profile researcher-entrepreneur
  The requirements for the researchers in the public sector pose hurdles to their involvement as entrepreneurs both as for creating their own entreprises or for working in them. New measures to foster flexibility with respect to that situation are required for accelerating the creation of businesses based on biotechnology knowledge.
- The absence of entrepreneurial tradition
  There is a deficit of entrepreneurial culture in Spain. Spaniards are not prone to undertake entrepreneurial intiatives as they prefer to be employees working for a third person or to be civil servants. In addition business failures are considered as irreversible and one single way with no return.
- The absence of seed capital and the absence of a venture capital market with sufficient degree of development.
  The Spanish venture capital market is quite small, thus make difficult to foster innovation initiatives.
- The risk perception associated to those processes

It is evident that R&D activities are risky and this is particularly true for the (bio)pharmaceutical sector. In many cases, and there are examples from abroad and even in Spain, the lack of authorization for a product may lead to the loss of the very important investments made along the R&D&I process.

- The lack of appropriate mechanisms to protect the innovations.
  The modification in the period for patent protection emerges as a claim from the business subsystem The 12 years of rights protection appear insufficient for companies to be able to recover the R&D investments.
- The absence of an industrial web and the lack of R & D promotion from the industrial sector
  The low dimension of the Spanish (bio)pharmaceutical sector impinges on the establishment of synergies between the firms.
- The public opinion
  The Centro de Investigaciones Sociológicas (CIS) in its study "Opiniones y Actitudes de los españoles hacia la biotecnología" (Opinions and attitudes of Spaniards towards biotechnology) from year 2001, states that the Spanish public opinion asks for more and more clear information on biotechnology. It can be said that the positions of the public opinion are different depending on the topic. From the biotechnology applications, the Spanish responding to the survey consider the most acceptable application of genetic engineering that of medical treatments with 8 points on 10, followed by the diagnostic of diseases. The less valued application is that of livestock fattening with 2 points on 10. A possible explanation to this data is that health is a common good highly valued for the public opinion for its direct implication on the wealth of individuals as compared to agriculture which is perceived as more distantly associated to the benefit of the individuals.

Some of the governmental policies have been/are instruments for making easy the innovation processes but other have been hurdles to it. From this way, the fiscal regulation in relation to innovation clearly favors the dynamics of the firms to innovate. Another instrument that helped to promote the scientific research in Spain has been the design and launching of the R & D National Plan in 1986.

However, the very exhaustive and demanding regulation for the authorization of a new biopharmaceutical products, their advertising, the public intervention in the prices (established and regulated by the MSYC), the problems in the legal protection by patents, etc. are poorly supporting this type of innovative processes.

There is a need to launch specific policies targeted to the small biotechnology-based companies in order to foster their development and diminish the hurdles to management and for a need of a greater dynamism and flexibility of the system.

POLICY IMPLICATIONS

We must remark the following factors that could contribute to a greater and better R & D and innovation activities in biotechnology and, as a consequence, to improve the overall efficiency of the Spanish National Innovation System in Biopharmaceuticals:

1. A greater participation of the biopharmaceutical industry in joint projects with the Public Research Organisms;
2. Higher support from the Public Administrations by the increase in the financing resources aimed to fund the processes of innovation;
3. The development of a venture capital market which help the high costs of research;
4. A clear governmental support to the creation of new companies based on biotechnology. Development of an ad-hoc regulation driven to foster and help the development of this industrial web;
5. The creation of appropriate necessary infrastructures for the expansion of this sector;
6. The development of an adequate system for protecting the innovations;
7. The generation of an environment able to foster the innovation by means of a stable regulation frame which may allow to plan investments for a long term, what could favor a sustainable growth of the market and give rise to a general climate in supporting these processes.

III. PERFORMANCE OF THE NATIONAL BIOPHARMACEUTICAL INNOVATION

III.1 SCIENTIFIC PERFORMANCE

Data from the Science Citation Index (SCI) –table 3.1- shows that the Spanish contribution to the scientific production (intervention of at least one scientist with work affiliation in Spain in the scientific publication) in year 2001 represented 2.69% of the world scientific production as recorded in that Index.

On the other hand, the Institute of Health Carlos III (ISCIII) and the Fund for Health Research (Fondo de Investigaciones Sanitarias, FIS) promoted a study entitled “Map of the Spanish Scientific Production in Biomedicine and Health Sciences” (“Primer Mapa de Producción Científica Española en Biomedicina y Ciencias de la salud”) that was presented in July 2002. The study provides relevant information on the evolution path followed in the last decade by a series of scientific areas and disciplines grouped under the name of “Life Sciences”.

TABLE 3.1: SCIENTIFIC PRODUCTION

	1991	1992	1993	1994	1995	
Scientific Production in SCI	11,903	13,824	15,309	16,214	18,283	
Share of Scientific Production with respect to the world total	1.68	1.91	2.01	2.02	2.13	
	1996	1997	1998	1999	2000	2001(1)
Scientific Production in SCI	20,080	22,077	23,783	25,065	24,073	26,349
Share of Scientific Production with respect to the world total	2.23	2.35	2.51	2.57	2.44	2.69

(1) Provisional Data
Source: OEPM

One of the main conclusions of the report underlines the step-up of the Spanish scientific research in the Life Sciences field where it has moved from representing 0.69% of the world production in 1990 to 1.62% in 1999. The total of Spanish scientific publications in 1999 was 2.57% as compared to 1.68% of the world total in 1991.

The study also points out to the concentration of research in two regions as Madrid and Cataluña together do account for more than 50% of the published documents and more than 60% of the citations collected in the Life Sciences field.

The Institute for Scientific Information from Philadelphia[23] (ISI), a reference organism as it makes analytical studies of scientific production from a catalogue of 8,000 journals, has recently given information on the case of Spain relative to the period 1998-2002. The ISI report confirms the step-up of the Spanish production of scientific documents, an indicator to evaluate the performance of one of the subsystems of a NSI, the Research one. Under the period studied, the Spanish universities and public research centers published 106,105 articles, what means 2.95% of the world scientific production. Another point of view to assess the performance of the subsystem is to look at the relevance of the work published as measured by the number of citations which every article does receive and to establish a relative value, the relative impact of those citations figures as compared with the rest of the world.

In the following, Table 3.2, the data of the ISI report are presented. From them, it can be seen that the most relevant disciplines in the scientific production of Spanish centers and their affiliated scientists are physics, chemistry, agronomical sciences and engineering.

TABLE 3.2: RELEVANCE OF THE SCIENTIFIC WORK PUBLISHED

	1998 – 2002	
	% of articles with affiliation in Spain	Relative impact as compared with the rest of the world
Astrophysics	5.67	-6
Agronomical sciences	5.11	+8
Mathematics	4.53	-13
Microbiology	4.40	-22
Chemistry	4.13	+1
Plants and Animal Sci.	3.81	-6
Ecology/Environmental Sci.	3.31	-14
Physics	3.01	+17
Biology and Biochemistry	2.88	-29
Materials Science	2.82	-4
Pharmacology	2.82	-24
Neurosciences	2.69	-20
Immunology	2.61	-28
Molecular Biology	2.60	-25
Clinical Medicine	2.54	-10
Geological Sciences	2.48	-14
Economics and Business	2.29	-37
Engineering	2.11	+2
Computational Sciences	2.05	-31
Psychology/Psychiatry	1.76	-44
Social Sciences	0.75	-18
Global participation of Spain	2.95	

Source: ISI

[23] The ISI data bases are a reference accepted by the actors involved in the science and technology system: though they do reflect all the production of researchers in a given country, they do not count the publications written in languages other than English and do not take into account publications carried out abroad.

From the study carried out by the Fraunhofer Institute of Innovation Systems (Germany) for this project, it has been possible to obtain concrete data on the productivity of the scientific and business subsystem of the biopharmaceutical system. Spain shows quite positive results as it has duplicated during the period 1994-2001 the number of publications from 438 in 1994 to 936 in 2001. This rise is the highest one undergone by any country followed by Germany (increase of 99%) and Belgium (increase 90%). The increase is obviously much higher than the average of the OECD countries (increase 60%) and of European Union as well (increase 63%).

TABLE 3.3: BIOPHARMACEUTICALS PUBLICATIONS

	1994	**1995**	**1996**	**1997**	**1998**	**1999**	**2000**	**2001**
World	20,282	22,072	24,574	26,253	28,145	30,600	32,646	33,273
OECD	19,190	20,883	23,067	24,608	26,368	28,483	30,321	30,733
United States	8,658	9,229	10,217	10,781	11,316	12,298	12,971	13,192
EU	7,986	8,931	9,850	10,420	11,355	12,195	12,896	13,024
Japan	2,143	2,333	2,594	2,899	3,169	3,357	3,780	3,733
Germany	1,588	1,807	2,082	2,250	2,533	2,839	3,022	3,160
U. Kingdom	1,910	2,194	2,277	2,401	2,621	2,734	2,936	2,970
Canada	889	1,027	1,093	1,158	1,210	1,385	1,421	1,453
Netherlands	651	722	745	839	895	952	992	1,001
Spain	438	496	587	642	753	862	938	936
Australia	511	535	596	657	723	709	813	851
Belgium	314	357	369	400	489	516	562	596
Finland	262	274	296	294	377	370	377	392
Norway	114	134	127	169	152	180	181	217
Russia	147	131	152	143	138	119	173	139

Source: OECD – Tip; Bibliometric Data; SCI via STN, searches and calculations by Fraunhofer ISI(2003)

The yearly growth rate of biopharmaceutical publications in Spain attains the 7%, clearly surpassing the EU average (3%), that of OECD countries (2%) and the world average (2%).

According to the representation of biopharmaceutical publications in the total, Spain situation matches with that of the rest of the world. In the period 94/95, 3% of the publications corresponded to the biopharmaceutical sector, proportion that increased to 4% in the period 99/00. The EU average in the 94/9 period reached 4% whereas in 99/00 this figure raised to 5%; in the OECD countries the average value was 3% in the first period (94/95) and 5% in the 99/00 period. Next Table 3.4 illustrates this data.

TABLE 3.4: BIOPHARMACEUTICAL PUBLICATIONS OVER THEIR TOTAL

	1994/1995	**1999/2000**
Belgium	4%	6%
United States	4%	5%
Netherlands	4%	5%
Finland	5%	5%
Japan	4%	5%
OECD	3%	5%
Germany	3%	5%
EU	4%	5%
World	3%	4%
Norway	3%	4%
Spain	3%	4%
Russia	1%	1%

Source: OECD – Tip; Bibliometric Data; SCI via STN, searches and calculations by Fraunhofer ISI (2003)

Bibliometric analysis are consistent by revealing that the position of Spain in relation to scientific knowledge position is quite positive. As judging from the data recorded in Table 3.5, Spain occupies the third rank on the basis of the ratio of publications per researcher (0.68) only overpassed by the Netherlands (0.92) and the United Kingdom (0.89). The figure for Spain overpass the EU average according to this indicator (0.62).

TABLE 3.5: TOTAL PUBLICATIONS PER 1000 RESEARCHERS

	1994/1995	**1999/2000**
Netherlands	967	923
United Kingdom	872	891
Spain	673	679
Belgium	706	673
EU	615	619
Finland	708	578
Norway	505	530

Germany	463	525
United States	482	435
OECD	437	399
Japan	181	228

Source: OECD – Tip; Bibliometric Data; SCI via STN, searches and calculations by Fraunhofer ISI (2003)

However, the situation is not so favourable with regard to the publications in the (bio)pharmaceutical sector (Table 3.6). Though the trend in the number of publications along the period 1994-2000 has been quite positive with a 35% increase, the ratio of publications per researcher (0.027) is slightly lower than the EU average figure (0.028) and ranks below the Netherlands (0.069), Belgium (0.038), United Kingdom (0.037) and Finland (0.030).

TABLE 3.6: BIOPHARMACEUTICAL PUBLICATIONS PER 1000 RESEARCHERS

	1994/1995	**1999/2000**
Netherlands	40	49
Belgium	29	38
United Kingdom	28	37
Finland	33	30
EU	21	28
Spain	20	27
Germany	15	24
United States	18	23
Norway	16	22
OECD	15	19
Japan	7	12

Source: OECD – Tip; Bibliometric Data; SCI via STN, searches and calculations by Fraunhofer ISI. Sources for data on researchers (FTE): main science and technology indicators 2002/2 table 7 and 2002/1 table 7.

By observing the scientific specialization in biopharmaceuticals indicator –RLA- (Table 3.7), calculated as the position of Spain over the rest of the world, Spain had an index –5 in the period 94/95 and –6 in the period 99/00, with averages indexes in the EU of 14 for the first period and 8 for the second, and indexes for OECD countries of 13 for the period 94/95 and 11 for the 99/00 period.

TABLE 3.7: REVEALED LITERATURE ADVANTAGE (RLA)

	1994/1995	**1999/2000**
Russia	-94	-96
Australia	-2	-6
Spain	-5	-6
Norway	1	-3
United Kingdom	6	-1
Canada	-3	6
EU	14	8
Germany	4	8
OECD	13	11
Japan	19	18
Finland	41	20
Netherlands	30	23
United States	21	24
Belgium	29	29

Source: OECD – Tip; Bibliometric Data; SCI via STN, searches and calculations by Fraunhofer ISI

III.2 OUTPUT OF NATIONAL EDUCATION

Spain human resources policies have been characterized by overproduction of doctors, especially during the 1979s and early 1980s. In fact, during the mid –1970s, the average number of students enrolled in the first year undergraduate course was very high, around 20,000. Since then, there have been significant reductions in the number of entrants to medical school following the introduction of restrictions in the number of places in 1978, and especially after the 1987 agreement of the University Council to further limit admission.

In the late 1980s, accordingly, the number of students decreased to less than 10,000. The production of excessive numbers of doctors in the past has left a legacy of difficulties, in particular by medical specialities. The examination entry system for residents could not absorb the high numbers of graduates coming out of the universities and this has caused unemployment among physicians who have been unable to specialize.

As regards the growth of active doctors by subsector and the relative position of Spain internationally, a recent study conducted by González López-Valcárcel and her team points to the trend outlined in the following. As no official data was published on public health care personnel at the time, the study had to rely on figures of health care personnel registered with their respective professional colleges, which do however offer a useful picture of the sector. The most visible figures refer to the low number of primary health care doctor in spite of the explicit priority given to this level of care starting in 1984.

Accordingly to the same study, there is also an over average supply of pharmacists compared with the average European levels during the period 1985-1997. In contrast there is undersupply of nurses, which a ratio of 1.8 nurses per physician in 1997, almost half of EU average (3.4).

According to data collected by the Ministry of Health, the number of active health professionals working in the public sector in 1998 were as follows (Table 3.9). There were a total of 1.6 doctors and 2.4 qualified nurses per 1000 population, as well as 1.4 auxiliary nurses, 0.1 physiotherapist and 0.1 midwives. This gives a ratio of 1.5 per doctor, which rises to 2.4 when auxiliary nurses and midwifes are included in the calculations.

TABLE 3.8: Health Graduates

Health Graduate	1992	1993	1994	1995	1996	1997	1998	1999
ISCED 5B		45	78	882	919	n/a	3,157	3,461
ISCED 5B as % of total Graduates							11.7	9.6
ISCED 5A	6,951	16,676	n/a	19,173	18,988	n/a	23,765	24,472
ISCED 5A as % of total Graduates						11.7	11.1	
ISCED 6	1,449	1,609	n/a	1,465	1,440	n/a	1,316	1,196
ISCED 6 as % of total Graduates						11.7	11.1	

Source: OECD, Health Data, 2002 4th Ed

TABLE 3.9: Health Care Personnel 1970-1997

Per 1000 Population	1970	1975	1980	1985	1990	1995	1997
Active Physicians	1.34	1.56	2.30	3.30	3.82	4.15	4.2
Active Dentist	0.10	0.10	0.11	0.13	0.27	0.36	n/a
Nurses	n/a	0.84	3.16	3.73	4.09	4.40	4.6
Midwifes	n/a	n/a	0.11	0.16	n/a	n/a	n/a
Active Pharmacists	0.47	0.53	0.62	0.80	0.94	1.06	n/a
Physicians Graduating	n/a	n/a	0.21	0.20	0.13	n/a	n/a
Nurses Graduating	n/a	n/a	0.14	0.13	0.14	n/a	n/a

Source: WHO Regional Office for European Health for all database

III.3 INNOVATIVE PERFORMANCE

An important indicator to asses the Business Subsystem and its interactions with the Research Subsystem concerns the number of patents. The following Table 3.10 collects the applications of patents with effect in Spain. The results show a quite stable trend for those presented by the national path (to the Spanish Office for Patents and Marks, OEPM from its name in Spanish) both by residents and non-residents. The patents application by the international path show a step-up trend with a great prevalence of non-residents over residents.

TABLE 3.10: PATENT APPLICATION WITH EFFECTS IN SPAIN

	1991	**1992**	**1993**	**1994**	**1995**	
National Path (OEPM)	2,092	2,637	2,728	2,673	2,554	
Residents	2,156	2,053	2,165	2,136	2,047	
Non- residents	746	584	563	537	507	
European path (EPO)	22,057	22,048	20,108	19,012	18,012	
Residents	63	68	61	80	70	
Non- residents	21,995	21,980	20,047	18,932	17,942	
International Path (PCT)						
Euro-PCT	20,820	24,358	27,317	32,631	37,331	
Residents	81	100	115	135	163	
Non-residents	20,739	24,258	27,202	32,496	37,168	
PCT	34	50	32	32	46	
Residents	0	0	0	0	0	
Non- residents	34	50	32	32	46	
	1996	**1997**	**1998**	**1999**	**2000***	**2001***
National Path (OEPM)	2,760	2,702	2,716	2,859	3,111	2,904
Residents	2,274	2,236	2,270	2,438	2,709	2,523
Non- residents	486	466	446	421	402	381
European path (EPO)	17,506	34,828	47,390	49,166	53,356	61,268
Residents	61	177	324	308	315	361
Non- residents	17,445	34,651	47,066	48,858	53,041	60,907
International Path (PCT)						
Euro-PCT	45,221	52,167	64,470	71,123	87,817	99,789
Residents	261	327	370	440	505	575
Non- residents	44,960	51,840	64,100	70,683	87,312	99,214
PCT	38	31	31	86	83	91
Residents	0	1	1	1	2	5
Non- residents	38	30	30	85	81	86

(*) Provisional data

Source: Oficina Española Patentes y Marcas (OEPM)
National path: applications made directly to the OEPM

European path: applications made directly to the European Patents Office (EPO) and which name Spain as the reference place
Euro-PCT: applications presented directly to the International Office of Patents and Marks (IOPM) and which Spain through a European patent
PCT path: applications which go to the national phase: are the applications PCT which gave the name of Spain directly in the IOPM and have now initiated the procedure in the OEPM.

The patent application of Spain in EPO represented 1.4% of the EU total, whereas Germany represented the 44.1%, France the 15.4% and Italy the 7.5%. Taking into account the applications for patents to EPO per million of active population, the results as shown in the following Table (3.11) confirm the low propensity in Spain to patent (54.6) as in the other southern countries Portugal (10.9) and Greece (18.7).

TABLE 3.11: PATENTS APPLICATION TO EPO (per million of active population)

	1998	**1999**	**2000**	**2001**
Belgium	335.5	339.5	366.1	361.9
Denmark	262.2	313.6	373.6	398.2
Germany	515.8	566.6	635.6	643.6
Greece	16.8	19.1	14.4	18.7
Spain	49.0	53.6	55.7	54.6
France	289.5	299.8	329.4	331.2
Ireland	125.8	154.5	206.3	183.6
Italy	160.0	168.0	188.8	182.6
Luxembourg	346.6	477.1	467.6	494.2
Netherlands	360.4	394.1	449.2	471.0
Austria	299.4	293.9	332.2	367.3
Portugal	4.8	9.3	8.0	10.9
Finland	533.4	574.6	667.1	653.3
Sweden	626.8	622.5	734.1	714.9
United Kingdom	208.2	226.7	260.9	272.0
Iceland	154.8	196.2	199.2	206.1
Norway	224.6	231.9	259.3	550.0
Canada	114.4	124.1	150.5	153.1
USA	206.6	273.8	321.7	327.7
Japan	228.8	245.6	299.3	329.2

Note: The regional distribution of patents is carried out by taking into account the residence place of the inventor. If an application has more than one inventor, the patent application is divided in equal parts between all inventors, avoiding the double count. This criterion is used by the Spanish National Statistical Office (INE) but it may not match with the one used by EPO in its own reports.
Source: INE

With respect to the biopharmaceutical patents Spain shows a positive trend with a very important increase in the number of applications rising from 17 in the period 1994/95 to 43 in the period 1999/00, what means to have more than doubled in a six years period. Other countries which have shown a significant increase have been Belgium, Canada, Germany and Japan. However, the low propensity of Spain to patent emerges when the total figures are made relative to population data (Table 3.12).

TABLE 3.12: BIOPHARMACEUTICAL PATENTS

	Biopharmaceutical patents		Biopharmaceutical patents per million inhabitants	
	1994/1995	1999/2000	1994/1995	1999/2000
Australia	83	116	4.6	6.1
Belgium	49	137	4.8	13.3
Canada	108	220	3.7	7.2
Finland	23	29	4.4	5.6
Germany	274	620	3.4	7.5
Japan	294	608	2.3	4.8
Netherlands	68	152	4.4	9.6
Norway	10	25	2.2	5.5
Spain	17	43	0.4	1.1
United Kingdom	231	456	4.0	7.7
United States	1,899	3,141	7.3	11.5
OECD	3,195	5,779	3.0	5.2

Sources: OECD Quarterly Labour Force statistic 2003.
Federal Statistical Office Germany, Statistical yearbook 1999, 2000, 2001

In spite of the low patenting propensity of Spain, the evolution on this parameter has been quite positive both concerning the number of pharmaceutical and (bio)pharmaceutical patents in the period 1994-2000 (Table 3.13). The former ones have grown by more than 60% while the second ones grew by near 80%. Accordingly, the ratio of (bio)pharmaceutical patents with respect to the pharmaceutical ones shows a positive evolution (in 1994, the percentual ratio amounted to 26%, while in year 2000, this ratio raised to about 30%).

It is worth to mention that the EU members have overpassed the United States in the pharmaceutical and (bio)pharmaceutical fields. Whereas in the case of the United States, the figures for pharma and biopharma patents underwent a positive trend to grow a 75% in the period 1994-2000, the average growth for the pharmaceutical patents in the EU amounted to 88%, and that of (bio)pharmaceutical patents doubled in that period. Belgium and the Netherlands were the most active contributors to that growth.

TABLE 3.13: PHARMACEUTICAL AND BIOPHARMACEUTICAL PATENTS EVOLUTION

	Pharmaceutical patents		Biopharmaceutical patents	
	1994	2000	1994	2000
Australia	116	193	72	102
Belgium	88	201	40	114
Canada	186	368	95	178
Finland	35	63	17	28
Germany	731	1,451	263	650
Japan	816	1,528	283	683
Netherlands	92	254	58	154
Norway	25	40	8	20
Spain	72	116	19	34
United Kingdom	550	1,035	243	411
United States	3,274	5,744	1,736	3,030
EU	2,321	4,360	959	1,920
OECD	6,484	11,769	2,990	5,704
World	6,617	12,926	3,050	6,573

Source: OECD, Patent Database, February 2003

According to the specialization indicator, RPA (Table 3.14), Spain also reveals a positive evolution during the period 1994-2000 as the number of (bio)pharmaceutical patents per million of inhabitants increased by a 60%.

TABLE 3.14: REVEALED PATENT ADVANTAGE -RPA

	Pharmaceutical patents		Biopharmaceutical patents	
	1994/95	1999/2000	1994/95	1999/2000
Australia	1.4	1.2	1.5	1.2
Belgium	1.0	1.4	1.2	1.2
Canada	1.8	1.7	1.1	1.0
Finland	0.5	0.3	1.3	1.0
France	0.8	0.9	0.9	0.8
Germany	0.6	0.6	0.8	0.9
Japan	0.8	0.7	0.7	0.9
Netherlands	0.6	0.7	1.5	1.2
New Zeeland	1.1	1.5	0.9	0.9

Norway	0.8	0.7	0.8	1.1
Spain	1.6	1.1	0.5	0.8
United Kingdom	1.3	1.5	0.9	0.8
United States	1.5	1.4	1.1	1.0

Source: OECD – Tip; Calculations by University of Oslo (CTIC) on the basis of OECD Patent Database

With respect to cooperative behaviour as determined by the number of co-inventions with other countries (Table 3.15), Spain shows also a positive trend in the period 1994-2000 with an increased from 9 co-inventions in year 1994 to 13 in year 2000., what represents an increased of more than 40%. The countries with a more positive trajectory at this respect are Belgium, the Netherlands and Germany, which have doubled their performance on this indicator. On the other hand, Spain has collaborated essentially with United Kingdom, Germany and France, among the European countries, and essentially with United States outside Europe.

TABLE 3.15: CO-INVENTIONS

Co-Inventions	1994	2000
Australia	15	22
Bélgica	17	38
Canada	26	44
Finland	0	11
Germany	74	160
Japan	41	63
Netherlands	23	44
Norway	4	5
Spain	9	13
United Kingdom	75	104
United States	210	355

Source: OECD, Patent Database, February 2003

Concerning the number of products which are being developed by each one of the countries as recorded in Table 3.16, the position of Spain is less favourable when compared to the other European countries, revealing once more that the bottle neck for the biotechnological development stems on the production and industrial side. As a reflection of their potential on this aspect, United Kingdom, France and Germany are the countries with a higher number of products under way.

TABLE 3.16: DRUGS IN PIPELINE

Drugs in Pipeline	Preclinics	Clinics I	Clinics II	Clinics III	Total
United States	2,087	389	471	200	3,147
United Kingdom	521	114	165	43	843
Japan	226	75	150	42	493
France	205	56	78	35	374
Denmark	333	44	81	28	486
Canada	246	34	44	19	343
Spain	31	14	6	7	58
Netherlands	64	7	11	6	88
Belgium	57	9	16	6	88
Australia	88	13	13	2	116
Finland	16	4	5	0	25
Norway	11	5	3	0	19

Source: R&D Focus. IMS Health Incorporated or its affiliates. June 2003

III.4 INDUSTRIAL PERFORMANCE

The year 2002 has witnessed a greater activity of the biotechnological sector in Spain. The following Table 3.17 provides information on the most relevant operations in the biobusiness sector during that period.

The state of ECBD firms belonging to the human and animal health sub sector has shown a positive evolution during the last years (Table 3.18), reinforcing the net profits and solvency and increasing the ratio of sustainable growth. This points out to the increase in the launching of products and services and, to some extent, in the success in their commercialisation.

The increase in the debts rate as well as the delay of the average collection from 121 days to 128 days are indicators of a negative trend. The firms shall be dependent on the achievement of funding from venture capital entities, private investors or the head office company in order to overcome the “hostile” environment, at least for short term.

The consolidation and expansion of newly created companies will depend, to great extent, on the success of launching and commercialisation of their products and services.

TABLE 3.17: RELEVANT OPERATIONS IN THE BIOBUSINESS SECTOR during 2002

COMPANY	OPERATION	ADDITIONAL INFORMATION
Med Plant Genetics / Advancell	Strategic Alliance	Development Toxic genomics platform
Najeti / Agrenvec	Seed Capital	1M € to create firm
Marco Polo Invest / Intersuero	2nd round funding	Acquisition 35% company (2.1M €)
Oryzon Genomics / IRTA	Collaboration Agreement	Development new plant varieties
BCNEmpren / Advancell	1st round funding	Acquisition 12% (0.3M €)
BCNEmpren / Xcellsys	1st round funding	Acquisition 13% (0.17M €)
Seed Capital Bizcaia / Med Plant Genetics	2nd round funding	Acquisition 14.69% (0.08M €)
BTSA / Activos en Renta Fondos	2nd round funding	Acquisition 25%
Najeti / Biotools	2nd round funding	Acquisition 30%
NBT / Proteus	Strategic Alliance	Project on proteomics and genomics
Natra / Natraceutical	Going to public	
EMBL Ventures / FEBIT	3rd round funding	Contribution of 30M € to develop biochips
Zeltia / Pharmamar	Capital extensión	1.34M €
Abengoa / High Plains	Acquisition	Acquisition of 94%
Med Plant Genetics / Agromare	Strategic Alliance	Bioinformatics Platform
Advancell / IPS Cardiotox	Strategic Alliance	
Ebiointel / Oryzon	Strategic Alliance	Bioinformatics Platform

Source: Informe ASEBIO 2002, pp 50

TABLE 3.18: ECONOMICS AND FINANCIAL RATIOS

ECONOMIC/FINANCIAL RATIOS OF THE HUMAN AND ANIMAL HEALTH SUBSECTOR			
	Business year 1999	Business year 2000	Business year 2001
Tied up capital/ Total Assets	56%	58%	62%
Solvency Rate	66%	74%	79%
Net profits Rate	144%	155%	163%
Treasunership Rate	12%	14%	17%
Debts Rate	60%	62%	66%
Tied up cap Cover	90%	95%	92%
Sustainable Growth	1%	1%	3%
Turnover/ Total Assets	110%	122%	129%
Average collection	121	117	128
Stocks turnover (days)	16	10	9
Gross margin over sales	3%	4%	5%
Sales per worker (€)	202.35	214.78	231.01
Benefit per worker (€)	12.55	13.67	15.05

Source: Informe ASEBIO 2002

IV. OPENNESS OF THE NATIONAL INNOVATION SYSTEM

Several indicators may serve to measure the degree of openness of the system of innovation at the (bio)pharmaceutical sector. One of them refers to the presence of foreign companies within that system. Our empirical study allows to draw that owing that 75% of the respondent companies are from Spain, i.e, more than 50% of their capital come from Spanish stockholders, the business subsystem is barely

international. Only a 30% of the companies have subsidiaries and 45% of them export their products to foreign countries. The exports, basically, are directed to European countries. The access chosen to those foreign countries is, fundamentally, by subsidiaries companies and using agents in the export country.

Another indicator to measure the degree of openness concerns the cooperation with foreign partners. As it has been already shown, Spain does not show a high activity in carrying out co-inventions with other countries (Table 3.15). Table 4.1 provides a greater temporal scope on this parameter, a presentation that helps to understand the characteristics of openness of a system. The data recorded in Table 4.1 show a similar behaviour for most of the countries with respect to a given year. Most of them show a positive trend for increasing co-inventions for the period 1996-1998 with a decline starting in 1999 or 2000. Exceptions to this trend are Belgium, Netherlands and Japan. The countries showing the highest number of co-inventions with foreign partners are Germany which doubled this figure in six years, Belgium which doubled the figures in seven years with a stable tendency to grow and the Netherlands which has reached near to a double figure during the seven years elapsed between 1994 and 2000, though with ups and downs during the period.

TABLE 4.1: CO-INVENTIONS

Co-inventions	1994	1995	1996	1997	1998	1999	2000
Australia	15	23	25	23	19	46	22
Belgium	17	19	27	22	30	37	38
Canada	26	34	41	58	67	67	44
Finland	0	12	7	11	15	14	11
Germany	74	76	93	119	137	189	160
Japan	41	38	41	55	61	58	63
Netherlands	23	30	28	26	52	39	44
Norway	4	3	1	3	3	11	5
Spain	9	5	16	14	12	23	13
United Kingd	75	65	96	176	137	183	104
United States	210	243	292	395	406	413	355

Source: OECD, Patent Database, February 2003

With regard to the number of firms that have been created recently, Spain has registered an “explosion” of new small enterprises based on biotechnology, though there are evident barriers to their development. An outcome of the semistructured interviews carried out during the months of June and July 2003, where the businesses representatives were asked about the main hurdles faced by them for a positive evolution, gave some data on this issue. The salient features emerging from the responses were the high investments in equipment and technology; the increase in R&D activities in the last years; the small size of the Spanish NBF; the difficulties to obtain funding for their activities and the absence of the “researcher-entrepreneur” profile. The responses so obtained can be summarized with the following bullets:

Main entry barriers:

- The main one is the absence of products. To have one product requires several years of research, quite significant investments and the approval by the Ministry of Health and Consumption (MSYC).
- Difficulties to have access to the technology. The technology is pretty sophisticated and requires significant investments. The need for infrastructures is being attacked with the technological parks and bioincubators.
- High initial investment to begin with the activity
- High investments in equipment
- Difficulties to get good financing to carry out this type of projects
- Scarce participation of Spanish venture capital in this type of businesses. There is no a venture capital market with sufficient level of development
- The research (and finding) of an appropriate market "niche" where focus the activity
- Different regulatory requirements and every time more demanding (Europe differs from USA)
- The increasing costs in research for the last years
- The need to hire highly skilled personnel with a series of capabilities: networking, personal relations, strategic vision. This is a strong hurdle to the small companies, not so much for the big firms.
- The need to compete in a global market, inadequate size of the (Spanish) firms
- Absence of a blended profile like researcher-entrepreneur.
- Long lasting periods before recovering the investments. Industry with a long cycle whose returns take about 12 years before during to profit.
- Difficult forecasting for sales and returns
- Difficulties to assessing this type of projects
- Emergent market
- Insufficient size of the sector
- Technological and market uncertainty

On the other hand, two main barriers for the exit out from the sector were:

Main exit barriers

- High investments because the degree of sophistification and specialization of the technologies
- Long life cycle industry. The results take at least 12 years before giving returns. During this period it will difficult to get out from the sector owing to the difficulties to recover the high investments.

V. ROLE OF DEMAND SIDE ACTORS

Society and public opinion are factors intervening in the shaping and development of a biotechnology system. However, data obtained from different polls and surveys show differences in public acceptance depending on the biotechnology sub sector. The agro food sub sector is the one attracting more public interest and criticisms. The genetically modified plants and foods are generally poorly estimated as consumers do not see advantages in this type of products but are fearing risks for health and environment.

On the other hand, the Spanish organizations of consumers have not been very active in the social debate on biotechnology. One of the most relevant of such organizations is OCU (from its name in Spanish, Organización de Consumidores y Usuarios) that has been keeping a moderate position, asking for time to demonstrate the benefits and risks of this type of food, claiming for label to give consumers the opportunity to choose.

The main source of public information on the debate on biotechnology in Spain are the NGOs which hold in general strong critical positions on the biotechnology, in particular concerning its applications to agriculture and food. Two of them, Greenpeace and "Vida Sana" are among the most relevant, together with "Ecologistas en Acción" and "Amigos de la Tierra". Greenpeace holds the same position in Spain as it does in the global world. "Vida Sana" is a NGO very active in the field of agriculture as it is strong proponent of organic agriculture and livestock whose main objective is to convey information to the consumers about the contaminant and chemical products found in conventional food. This organization has the coordination of the "Platform against Genetic Manipulation". "Ecologistas en Acción" and "Amigos de la Tierra" are also holding critical positions on the use of biotechnology in agriculture, arguing on the (eventual) risks for the environment and also betting, in a more or less explicit manner, for the use of organic agriculture.

Two out of the three main farmers organizations in Spain, "Unión de Pequeños Agricultores" and "COAG", are also running against the use of agrobiotechnology, whereas the third one ASAJA ("Asociación de Jóvenes Agricultores") is supporting this type of biotechnological application. The organizations of cattle dealers have not expressed public opinions.

The biopharmaceutical subsector runs usually very well in the public opinion both in Europe and in Spain. Conflictive topics have to deal with ethical issues such as therapeutic cloning, use of embryos to obtain pluripotent cells, etc. The patients

associations have made public statements on their support to this type of applications, but some conservative organizations have shown positions against the use of embryos.

Role of socio – ethical debate

As general trend, it can be said that there is a gap between the interest of the lay population for the scientific topics, specially for those related to medicine, and the quality and quantity of the information provided by the mass media, which is assessed as scarce. Until recently, the majority of the scanty information and the debates started on the biotechnology have taken place either in the scientific publications and sections of conventional newspapers, or in specific sections of radio and TV programmes. The situation has changed with the introduction of topics such as "cloning" and the "Dolly sheep". The social debate centered basically in the ethical and legal aspects on the human genetics and on the assisted reproduction techniques, though this interest has not lasted for long time. Even if the interest for the transgenic good has declined, this topic has remained as a hot point in the social debate by the incorporation of some social scares related to food such as the case of dioxins, the clembuterol, etc. All this reflects last in a negative public opinion on the possible use of transgenic food for the eventual health risks.

The debate and exchange of information on biotechnology is gaining relevance among the journalists and conventional newspapers essentially because all the worries existing on the topics related to health. Within this context, two of the main newspapers of national edition such as "ABC" and "El Mundo" have a weekly supplement on science and health. Other monthly journals are popularizing topics related to science, environment, health, computers, natures, etc. such as Muy interesante, National Geographic, Quo, CNR, Más Allá de la Ciencia, Natura, Investigación y Ciencia, etc.

The Centro de Investigaciones Sociológicas (CIS) in its study "Opiniones y Actitudes de los españoles hacia la biotecnología" (Opinions and attitudes of Spaniards towards biotechnology) from year 2001, states that the Spanish public opinion asks for more and more clear information on biotechnology. According to CIS survey, 80% of the Spaniards declare that they have insufficient information. The main source for information in biotechnology is television.

It can be said that the positions of the public opinion are different depending on the topic. From the biotechnology applications, the Spanish citizens responding to the survey consider the most acceptable application of genetic engineering that of medical treatments with 8 points on 10, followed by the diagnostic of diseases. The less valued application is that of livestock fattening with 2 points on 10. A possible explanation to this data is that health is a common good highly valued for the public opinion for its direct implication on the wealth of individuals as compared to agriculture which is perceived as more distantly associated to the benefit of the individuals.

A worrying result from the CIS survey is that the 60% of the respondents consider the advances in biotechnology and genetic engineering as risky to some extent.

Role of demand side actors

A series of actors can be identified which to a greater or minor extent, are users of the health system and are directly involved in their processes of innovation. Among them: the patients association, medical or professional societies, foundations/non-profit organizations, etc.

Among the patients association, the most prominent are those of patients suffering from some diseases, though none of them has been playing a very active role according to the concept of innovation system. Their general mission is to give support to the patients as well as to their families providing advice on the disease, its potential treatments, secondary effects, initiatives to improve the quality of life concerning both the patients and their relatives. The associations with tighter links to the biopharmaceutical products are:

1.- SPANISH ASSOCIATION OF MULTIPLE ESCLEROSIS (AEDEM)

This association is a non-profit organization which gathers patients, relatives and other persons who feel sensible to this complex pathology.

The aim of AEDEM is to improve the quality of the persons who are affected by the disease: patients and their relatives. Specific objectives are:

- To provide information on the disease to the patients and relatives attempting to increase their knowledge about the symptoms, possible treatments, as well as some consequences and problems derived form suffering it.

- To increase the sensitiveness of the public opinion and the administration, as well as that of the socio-sanitary services in order to obtain a potential improvement of the prevention, treatment and cure. It also addresses the objective of a better medical, social, integral and multidisciplinary assistance, reducing and avoiding if possible any hurdles to the social integration.

- To promote the training of all the professionals involved in this type of disease.

- To foster the basic and clinical research, acting as support and financing agent for it.

Along its eighteen years of existence, AEDEM has brought about a significant number of projects and programmes, some of them of informative and popularizing character and others targeted to training. Among the first, the organization of

informative sessions on multiple sclerosis and the quarterly publication “Noticias EM” (News on MS). Among the second, it should be mentioned the organization of great number of training courses for the professionals involved in the care of this type of patients.

AEDEM also provides a series of services to their associates addressed all of them to the general objective of improving the quality of life. Among them, are worth to mention: the programme to provide help at home, a telephone line for juridical consultation on labour issues, centers for integral rehabilitation (with services of physiotherapy, logopedics, rehabilitating medical doctor, psychological orientation and support, etc.).

The multiple sclerosis is a disease that affect the central nervous system with a casual theory that there are tow possible causes that together may produce the pathological disorder. One of them rests on genetic factors, the other on environmental factors. There is no treatment driving to the cure of the disease by there are treatments that may alleviate the course of the disease, such it is the case of beta interferon.

2.- FOUNDATION ALZHEIMER ESPAÑA-FAE

This Foundation pursues the improvement of the quality of life of the patients, the caretakers and the families. For this, it undertakes a series of diverse activities from the information (telephone lines of support, interviews with caretakers and families, prospectus, guides, scientific conferences and seminars) until the assumption of the representation of the families in front of the socio-sanitary authorities. The FAE has designed a programme called Redafial (from its name in Spanish, “Red de Apoyo, Formación e Información Alzheimer”). This programme consists of the design, organization, development and maintenance of an interactive communication system which can effectively help both to Familial Associations of Alzheimer patients and to the professionals and the own familiars and patients caretaker, collaborating besides in the adequate sanitary training for each level and facilitating the appropriate information for each case.

At the scientific level, it is known that the Alzheimer of familial type is associated to three genes. The gene mutations can be detected by genetic tests. The members of a family inherit some of the genes which cause the disease. In the other type of Alzheimer, the sporadic one, there is a gene involved in the risk to suffer the disease. In this case, it is unlikely the prediction of a possible development of the disease. For it, the Foundation FAE does not promote the use of genetic tests for the sporadic disease.

There is also worth to mention, another organization, CEAFA – “Confederación Española de Familiares de Enfermos de Alzheimer y otras Demencias” – which is a non-profit organization with the recognition of public usefulness representing

thirteen federations and six associations form single provinces. It has the mission to improve the quality of life of the patients of dementia and the relatives as well.

3- FEDERACIÓN ESPAÑOLA DE ASOCIACIONES DE ENFERMEDADES RARAS-FEDER
("SPANISH FEDERATION OF ASSOCIATIONS OF RARE DISEASES")

FEDER was established the 17th of April of 1999 and is composed by non-profit associations and entities which take care of diseases with low incidence. It gathers the majority of associations of patients suffering from this type of diseases. It gathers the majority of associations of patients suffering form this type of diseases. According to European Legislation a "rare disease" is that affecting less that 5 individuals per 10,000 persons. The 80% of these diseases are of genetic origin. There are great hopes in the advances that may result from the sequence of the human genome for the eventual treatment of these diseases.

Among its objectives are:

1.- To support jointly the work and activities of the different associations acting under a common strategy in order to get the greater satisfaction as possible at the level of health and social policies.

2.- To promote and support initiatives which push to research with all the orientations: genetic, epidemio logical, clinical and therapeutic of these rare diseases.

3.- To support and monitor the implantation of the Regulation on Orphan Drugs which foresees incentives to the industry for developing treatments on the appropriate time. Without those incentives, such treatments shall not evolve because the low economic profitability.

4.- To sensitize and collaborate with the sanitary and scientific collectives, the administration and the industry, with the purpose of establishing specific working groups on the rare diseases, where it can be proposed viable projects and solutions for the safeguard of the affected persons.

5.- To improve the training of the family doctor on this type of diseases.

6.- To organize meetings with health professionals in order to improve the precocious detection, the recognition, the intervention and the prevention of rare diseases.

4.- FUNDACIÓN PARA LA DIABETES

(“DIABETES FOUNDATION”)

This Diabetes Foundation is a private, non-profit entity addressed to the general interest. Its objective is to contribute to the prevention and treatment of the diabetes and its consequences as well as to improve the quality of life of persons suffering form diabetes.

Among its specific objectives are:

1.- The promotion of educational activities related to diabetes for the patients and their familiar and social environment;

2.- To carry out technical training programmes targeted to professionals;

3.- To carry out programmes of sensitization to the society for the precocious detection of the disease;

4.- The development of pilot projects aimed to improve the quality of life of the persons with diabetes;

5.- The promotion of research projects on diabetes;

Diabetes is a chronic disease which handicaps the organism for using food adequately. The sick persons with diabetes do not produce enough insulin to metabolize the glucose or the insulin they produce does not work properly. By this deficit, the glucose is not transformed into energy what drives to its accumulation in blood at high, pathological, levels.

5.- ASOCIACIÓN PARA LOS ENFERMOS DE ATAXIA
(“ATAXIA PATIENTS ASSOCIATION”)

There are two associations of regional nature related to this pathological disorder: one from Andalucía and another from Madrid (“Asociación Andaluza” and “Asociación Madrileña de Ataxias Hereditarias”).

Their basic goal is to bring about the integration of all the persons suffering form these hereditary diseases into their social environment as well as to reach a better global care to this type of patients by the public administrations. Besides the general objective of attaining an improvement in the conditions of life of the affected collective, the Associations also pursue the promotion of research on this type of disease, the fostering of a specific legislation targeted to rule and promote the commercialization of orphan drugs, etc.

SCIENTIFIC AND MEDICAL SOCIETIES

On the other hand, the scientific and medical societies also play a role, albeit small, in the system by promoting the dissemination of scientific and technical knowledge through the organization of seminars, congresses, scientific meetings, publication of informative bulletins and reports.

Apart from the two biggest societies in the area of biological sciences which are: The Society for Biochemistry and Molecular Biology and the Society for Microbiology, the scientific and medical societies with greater relationship to the biopharmaceutical sector are:

1.- SOCIEDAD ESPAÑOLA DE BIOQUÍMICA CLÍNICA Y PATOLOGÍA MOLECULAR-SEQC
("SPANISH SOCIETY FOR CLINICAL BIOCHEMISTRY AND MOLECULAR PATHOLOGY")

It was founded in 1976 with the aim to gather all the scientists with interest in the field of clinical biochemistry. The specific objectives are those of a typical scientific society: promote the dissemination of scientific and technical publications, the organization of meetings, courses and congresses and to cooperate with other scientific societies as well.

2.- SOCIEDAD ESPAÑOLA DE CARDIOLOGÍA
("SPANISH SOCIETY FOR CARDIOLOGY")

It is constituted as a non-profit scientific and professional organization whose aim is to contribute to the advancement of knowledge on the heart and the circulatory system, to progress in the prevention and treatment of their pathological disorders, and to improve the survival and quality of life of the cardiac patients. One of the main concerns of this Society is the issue of communication which has been attacked by carrying out a great number of meetings, in the services for continuous training, etc. It organizes annually, since more than sixty years, a Congress on Cardiovascular Diseases and also holds a journal, "Revista Española de Cardiología" ("Spanish Journal on Cardiology")

3.- SOCIEDAD ESPAÑOLA DE GENÉTICA-SEG
("SPANISH SOCIETY FOR GENETICS")

It was established in 1972 with the objective of promoting the genetics development and the scientific knowledge around it in Spain through the following means:

a. The organization of scientific meetings (conferences, colloquia, seminars, congresses, etc.);
b. The publication of bulletins to convey specialized information as well as of monographs on specialized topics;

c. The promotion of the exchange between Spanish and Foreigners geneticists;
d. The dissemination of those social and scientific aspects which must present interest to the public and targeted to the Spanish society;
e. The diffusion of knowledge and education in genetics;
f. The collection of bibliographic and scientific resources;

To obtain this objectives, the SEG can establish and sign collaboration agreements with universities, public research centers, cultural entities and scientific societies both public or private, enterprises and other professional entities from the agrarian and health sectors.

4.- SOCIEDAD ESPAÑOLA DE INFORMÁTICA DE LA SALUD-SEIS ("SPANISH SOCIETY ON HEALTH INFORMATICS")

It is a scientific society, non-profit based, which is composed by a great number of sanitary technical professionals with the interest in improving and promoting the use of information and communications technologies in the health environment. It is evolving as a forum for the joint participation of professionals with different skills and qualifications: informatics, medicine, infirmary, veterinary, psychology and the remaining of health sciences, as well as for the students of related disciplines.

Among its objectives can be cited:

1.- The fitness of the society to the technological and professional reality in the health world;
2.- The promotion of the involvement of entities, scientific associations and interested professionals in this field;

Among the multiple activities and projects that this society has been developing along the last years, the following deserve a mention:

a. Organization of the National Congress on Health Informatics – INFORSALUD
b. Organization of the National Congresses on Internet and Health – INFORS@LUDNET
c. Organization of the National Congress of Informatics and Pharmacy – INFOR FARMA
d. Organization of the National Congress of Informatics and Infirmary
e. Organization of the National Symposium on Biocomputer, Genetic Information and Health.

5.- SOCIEDAD ESPAÑOLA DE INGENIERÍA BIOMÉDICA –SEIB ("SPANISH SOCIETY OF BIOMEDICAL ENGINEERING")

This Society has as objective the maintaining of contacts among professionals, researchers and students who develop activities in the field of bioengineering or who are attracted by this field.

The SEIB holds the mission of encouraging the study and research of diseases and to try the homologation of the clinical-therapeutic criteria in the diagnosis and treatment of cancer. To this end, the actions that have to be undertaken are:

a. To promote the development of the suitable therapeutic means in conjunction with the performance of research at all levels: basic, experimental and clinical;
b. To secure the coordination of all these instruments keeping harmony and complementary between them;
c. To encourage the infirmity of criteria for the treatment of cancer;

SEIB organizes an Annual Congress and an International Congress as vehicles for scientific dissemination.

6.- ASOCIACIÓN ESPAÑOLA DE BIOÉTICA Y ÉTICA MÉDICA-AEBI ("SPANISH ASSOCIATION OF BIOETHICS AND MEDICAL ETHICS")

This Association holds as mission the promotion of the ethical dimension in the medical practice and in the scientific research related to life and the human beings. AEBI has, among others, the following objectives:

a. To promote studies on the ethical values in research;
b. To inform and to educate the public opinion on the significance of bioethics;
c. To organize scientific events: meetings, courses, and congresses of multidisciplinary nature;
d. To promote publications and books on bioethics;

7.- ORGANIZACIÓN NACIONAL DE TRANSPLANTES-ONT ("NATIONAL ORGANIZATION ON TRANSPLANTS")

It is a technical organism ascribed to the Ministry of Health and Consumption whose mission is to promote, make easy and coordinate the process of donation and transplantation of all types of organs, tissues and bone marrow. The ONT performs as an agency of services for the whole of the National Health System, looking for the increase in the number of organs available for transplants.

Among its functions: the following can be emphasized:

a. The coordination of the processes of extraction and transport;
b. The promotion and coordination of multicenter studies and research projects;

c. The elaboration and diffusion of a set of materials: informative, didactic, on work field, among the professionals involved in the coordination and transplantation tasks;
d. The participation in courses on continuous training and postgraduate;
e. The promotion of specific training courses;

Around the issue of transplants, several Associations have emerged as for example:

1. Association “Virgen de la Paloma” of heart transplanted people from Madrid
2. Association of liver transplanted people and patients
3. Child’s oncological Association
4. Association of child’s oncological parents
5. Association from Madrid against cystic fibrosis
6. Kidney Association
7. Association of liver transplanted people from the Community of Madrid

8.- PRIVATE HEALTH COMPANIES

The companies involved in providing medical care are also worth to mention as they can play a role in the innovation system of the biopharmaceutical sector. The three most prominent insurance companies providing this type of services are:

a. Sanitas
b. Asisa
c. Adeslas

SANITAS was founded in 1956 and since 1989 it is part of the group BUPA, the greatest private company devoted to health care in the United Kingdom. It is one of the leading companies in Spain with 1.3 millions of associates to whom provide assistance 20,000 physicians in around 520 hospitals and clinics.

Sanitas also holds a Foundations which promotes research and medical and sanitary education. The charitable activities are carried out through a series of instruments like calls for prices, fellowships, grants in aid to research projects, seminars organization, conferences and congresses partnerships, publications, etc.

ASISA is owned by a Cooperative Society, Lavinia, which is constituted for more that 20,000 Spanish physicians. Its cooperative character allows to devote the benefits to the effective improvement of the medical care. It has 16 private hospitals, 6 medical association and agreements with more than 600 private clinics and medical centers.

ADESLAS has 1,700,000 associates what represents 25% of the Spanish market. Through its Foundation Agbar tries to promote and protect the environment.

9.- ASSOCIATIONS AND SOCIETIES RELATED TO BIOTECHNOLOGY

The Spanish Association of Biobusinesses (ASEBIO, from its name in Spanish, "Asociación Española de Bioempresas") was founded at the end of 1999 with the aim to promote and develop the industrial development of biotechnology in Spain. ASEBIO forms part of the European Association EuropaBio. ASEBIO and the Ministry of Science and Technology share the mutual compromise to foster the dissemination of biotechnological knowledge to the Spanish society and its eventual applications including advances, benefits and risks.

The Spanish Society for Biotechnology (SEBIOT from its name in Spanish, "Sociedad Española de Biotecnología") is far from being a conventional scientific study. It was created on 1989 and has at present 600 associates. One of the aims of this society is to foster and make easy the production of biotechnological knowledge and its eventual application to production and services. SEBIOT has been also responsible for organizing relevant events at national and international level, in relation to biotechnology. The Spanish scientific biotechnological community has international presence through the European Federation of Biotechnology (EFB) to whom SEBIOT belongs.

More recently, it has taken place the emergence of the "Fundación Genoma" a semi-public institution approved by the Spanish government in November 2001, with the essential objective of promoting research on genomics and proteomics in such a way that Spain had great involvement in the second phase of the genome project. This may drive to significant advances and applications in the health field as well as in the biotechnological processes and agrofood sectors.

Role of lead markets

From our point of view if we wish to become a lead market in biopharmaceutical, Spain must progress in the following circumstances:

1.- To develop a very significant effort on R & D activities;
2.- To have several important multinational companies;
3.- To dispose of a series of critical products;
4.- To have a good culture for exporting;
5.- To enjoy a satisfactory normative environment and a good social ambiance;

VI. COMPARISON OF SYSTEMIC FAILURES OF THE NATIONAL SYSTEMS

The main failures of the system can be gathered into four groups

1.- Misssing or inappropiate functions in the system of innovation, e.g. production, diffusion and application of new knowledge, demand articulation, education and training of skilled researchers, etc.

2.- Missing or inappropiate available actors in the system of innovation, e.g firms and research organizations, regulatory authorities, users/consumers, funding organizations, etc.

3.- Missing or inappropriate interactions in the innovation system, e.g. too much or too little interaction or coordination between the elements in the system of innovation.

4.- Missing or inappropriate institutions in the system of innovation, including framework conditions, e.g. set of laws and regulations, entrepreneurship, innovative climate, public policies, etc.

Possible interpretations to these failures are:

1.- The relative positive position of the Spanish subsystem of production of knowledge has been outlined previously but the difficulties to find a satisfactory application of the knowledge produced have been stressed. The number of researchers, an indicator that also presented deficits with regards to other countries, has undergone significant increments during the period 1990-2001. During this period, the number of R&D personnel (Full Time Equivalent) has rised by 80% to reach, in year 2001, a value close to 7% of the active population. More specifically, the number of FTE researchers has experienced an even more positive evolution with more than a doubling during the period under study to reach near 4.5% of the active population. In sum, there is a good scientific ground in Spain, though there are no satisfactory linkages to the application transfer of knowledge production to the business subsystem. Apart from the deficiencies of the business subsystem to explain these problems which are going to discussed below, there may be flows inherent to the scientific subsystem itself. This can be due to any of the following reasons:

- √ Spanish scientists are working with limited resources and infrastructures to compete in a highly competitive world;
- √ The lines and programmes of the Spanish teams may be either too conventional to reach international excellence or, alternatively, too sophisticated to be understood and applied by the Spanish subsystem;
- √ There may be a lack of “critical mass” in the Spanish teams to cope with the resolution of high level scientific problems;

2.- It is evident that the small size of the Spanish (bio)pharmaceutical sector represents a great handicap for its consolidation. As already stated, the Spanish system is formed by 50% of micro-firms and small companies, what implies a

strong need for financial, technological, human support to be able to carry out research in order to develop and consolidate satisfactorily. The financial support can be improved by specific public policies and programmes aiming to help in the high cost of the (bio)pharmaceutical R&D projects. The technological support could be improved by creating the adequate infrastructures. In this context, the establishments and development of technological parks and bioincubators may be an important asset for the creation and evolution of the innovation grounded enterprises. In relation with the critical issue of human resources and their availability for this type of firms, it should be emphasized that the small sized companies confront difficulties for hiring high level researchers by two main reason:

√ The so high salary cost for the company
√ The problems of compatibility between public research (civil servant statutes) and private activities

Some steps have been put forward to solve this problematic situation. Programme "Torres Quevedo" has been launched to promote the hiring of PhD researchers, through a contribution of the State Administration to the salary cost in order to reduce it for the company. A claim for a greater flexibility of the mechanisms of human resources transfer between public and private sectors has been installed in the Spanish society but the solution is not an easy one.

It is necessary to insist in the absence of entrepreneurial culture among the educated people in Spain. The Spanish society is "risk averse" and this conservative position is hard to change in view of the dominance of precarious employments in the labour market of Spain.

Obviously, the newness and smallness of the firms involved also hampers the degree of oppeness of the system. Taking into account the characteristics of the Spanish pharmaceutical and those of the (bio)pharmaceutical sector in particular, there are evident difficulties to foster the processes of internationalization and cooperation with foreigners. Efforts are being made at this respect by the Spanish Association of Biobusinesses (ASEBIO) and from the Fundación Genoma (a semipublic agency established recently by the Spanish Government to promote the development of biotechnology in Spain) and in collaboration with the Institute for Foreign Trade (ICEX), but continous efforts are needed on this direction.

3.- The failures associated to scarce links between the university and the entrepreneurial realm have been endemic to Spain. Programmes and schemes have been put into force since the last decades with partial successes. A continuous evaluation of these initiatives and their reshaping according to the outcomes of the process of evaluation seems pertinent.

4.- Within the policies side, Spain has made, during the two last decades significant efforts to establish policies and launch programmes to promote the development of the biotechnology sector in Spain. The national Plan for R&D&I with some specific

instruments like the National Programme for Biotechnology, the National Programme for Health, has contributed to the promotion of knowledge production in this sector. A fiscal policy aimed to allow tax deductions from the private investments in R&D&I activities that has been attracting the interest of the firms for increasing their efforts in the promotion of biotechnology is worth noting. On the other hand, the "Stability Agreement" signed in 2002 between Pharmaceutical sector and the Ministry of Health and Consumption (MSYC) has been an important asset for the generation of a trusty environment to fostering research and innovation. However, this good ambiance may be altered because the Spanish Government is actively involved in a policy addressed to reduce the public pharmaceutical expenditures, a movement that is rising controversies with the pharmaceutical industry. In any case, it seems evident that the positive evolution of the (bio)pharmaceutical industry requires the existence of an adequate environment built around three key factors:

√ Existence of an adequate and stable regulatory frame able to guarantee the investment in R&D;
√ Existence of a market with sustained growth;
√ The generation of an appropiate environment to foster innovation;

VII. CONCLUSIONS: IMPACT OF INNOVATION POLICIES

VII.1 CONCLUSIONS ABOUT THE STUDY ON THE NATIONAL SYSTEM OF INNOVATION

The concept of National Innovation Systems has been gaining support as an explanatory variable of the size, role and performance of innovation within the economy of each country or region. This concepts counts on the interplay between a series of actors whose actions and interactions are influenced by a set of factors: The financial subsystem, the business subsystem, the legal frame, the regulations, the skills of human resources, their mobility, the social relations and the negotiations practices.

The idea of National Innovation Systems relies in a view based on the complexity of the socio-economic activities.

Given the specific characteristics of the Spanish Innovation System in the Biopharmaceutical Sector that we have presently studied, it can be likely concluded that Spain does show indications from possessing a National Innovation System in Biopharmaceuticals but the country is still lacking a specifically built National System of Innovation shaped according to the main characteristics and specificities of the country.

If we keep in mind the three key factors that an authentic NSI demands it can be deduced that, in Spain, exists a National Innovation System in the Biopharmaceutical Sector because, first of all, exists a "culture of coordination" that

makes possible the collaboration between agents and institutions, though this behavior must be enhanced. Second, there is an interactive learning way of doing, that is, a system able to embody information and knowledge through a constant and permanent process, but it must be enhanced as well. Finally, there is some but yet unsatisfactory "entrepreneurial culture".

All the analysis, data and indicators support the contention that the efforts carried out in Spain along the last half of the twentieth century have led to the building of a National System with satisfactory scientific outputs. However its outcomes in relation to the building of innovation capacity in the biopharmaceutical sector have been rather limited. The Governmental and Research Subsystems and the Business Subsystem have followed separate path.

The analysis of the four subsystems reveals that in our country exist several mismatches between elements and actors of the system what are hampering the system's overall efficiency.

We can point out that:

1.- The Governmental and Research Subsystems do not function in a suitable way mainly because the small public investment in R&D, the small interaction between the public research subsystem and the business one, the lack of appropriate mechanism to protect that kind of innovations and the inadequate and insufficient innovation policy, basically;

The Spanish universities (we can include it in the research subsystem) could play a growing role in all this process. The NBF and the incumbents companies may make use of the basic knowledge essentially developed through interdisciplinary research going from molecular biology and gene sequencing to cell biology and biocomputers for identification of protein functions (proteomics) and development of cell engineering. The Spanish universities must be able to assume the complex roles requested to them. These roles can be summarized as follows:

b. To perform high quality research
c. To carry it out through new interdisciplinary and multidisciplinary approaches
d. To increase the effective links with biopharmaceutical industry

The Spanish Non-Universities Research Centers are comprised by multidisciplinary research organizations with a set of institutes performing basic and applied research. The CSIC institution is the principal actor involved in the national research . The frame is completed by a series of sector laboratories under the jurisdiction of the ministries with responsibilities for various areas. These institutions could play an important role in all this process, but are they able to do that? There exists three main factors that allow us to carry doubts about the capability of this type of organizations to accept the challenge:

a. The relationships with the University
b. The ability to modify the patterns of research imposed by the scientists themselves from their autonomy and self-compliance
c. The acceptance by the scientific personnel of changing their civil servant status to a contract-based system

2.- The Business Subsystem does not function in a right way due to the traditional lack of entrepreneurs, the risk perception associated with biotechnology, the small size of our NBF and their newness (risk of newness and smallness) as well as their difficulties to get funds for financing their activities; Needless to say that the Business Subsystem is a crucial actor in shaping the organization and performance of the National Innovation System in Biopharmaceuticals.

3.- The Financing Subsystem does not support pertinently these processes and companies. The absence of an adequate venture capital market makes difficult the viability of these companies;

We can conclude that flexibility and ability to adapt are critical assets in this emerging, highly dynamic area of research where the flows of knowledge, techniques and applications are running over the traditional slow pace of Academia – Research Institutions – Government – Business – Capital Markets.

VII.2 CONCLUSIONS ABOUT THE IMPACT ON INNOVATION POLICIES

For coping with the possible solutions to the detected flaws, it is essential to put into force mechanisms addressed to overcome them. The following ones offer a ground to advance in that direction:

1. A greater participation of the biopharmaceutical industry in joint projects with the Public Research Organisms;
2. Higher support from the Public Administrations by the increase in the financing resources aimed to fund the processes of innovation;
3. The development of a venture capital market which helps to face the high costs of research;
4. A clear governmental support to the creation of new companies based on biotechnology. Development of an ad-hoc regulation driven to foster and help the development of this industrial web;
5. The creation of appropriate necessary infrastructures for the expansion of this sector, that is for example, scientific parks and bioincubators;
6. The development of an adequate system for protecting the innovations;

7. The generation of an environment able to foster the innovation by means of a stable regulation frame which may allow to plan investments for a long term, what could favor a sustainable growth of the market and give rise to a general climate in supporting these processes.

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