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DOCUMENTED
BRIEFING

Health and Medical Research in Spain

Health Research Observatory

Fragiskos Archontakis

Prepared as part of RAND Europe's Health Research Observatory Documented Briefing series, funded by the UK Department of Health

RAND EUROPE

The research described in this report was prepared as part of RAND Europe's Health Research Observatory Documented Briefing series, funded by the UK Department of Health.

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Preface

This documented briefing provides an overview of health and medical research in Spain. The report is part of a series of country-specific reports available from RAND Europe's Health Research Observatory, funded by the Department of Health, England.

The report is divided into three parts. In the first part, the *Structure of the Spanish Health Research System*, funding sources, sectors performing health and medical research, and health research priority setting, is presented. The second part, *Processes and Performance of the Spanish Health Research System*, focuses on the types of funding available and how funding activities are conducted, and provides exemplars of the system's performance. The third part presents an *Outlook* and considers current and emerging health research issues in Spain.

The report is based on desk-based document review and will be updated on a regular basis. It does not attempt to discuss current policy options, or make recommendations for future strategy. The report will be of interest to government officials dealing with health and medical research policy, medical research councils, health and medical research charities, public and private institutions engaged in health research, and researchers.

The use of € throughout this report stands for euro, unless stated otherwise.

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Summary

Summary: Key Points

- Key funders of health R&D in Spain are industry, central government, and the local governments of the autonomous communities
- Important role of Carlos III Health Institute as a funds manager and of the Spanish National Research Council as a research driver
- R&D funding in Spain has increased year on year, and health R&D funding is also increasing as a percentage of total funding
- The INGENIO 2010 initiative includes a series of policies and strategic actions
- Research productivity (as measured by publications) has been increasing in biomedical sciences
- There are still some challenges for the future

This documented briefing provides an overview of health and medical research in Spain. It does so by providing an account of the main players, the funding flows within the research and development (R&D) system in general, and the health research system in particular, and various aspects of process and performance, including research priorities and evaluation of research.

The main funding sources of the Spanish health research system are industry (pharmaceutical and biomedical), central government (mostly through the Ministry of Health and the Ministry of Education and Science), and the local governments of the 17 autonomous communities.

The Carlos III Health Institute, under the aegis of Ministry of Health, was created in 1986 by the Health Law as a scientific and technical support body for the Spanish National Health System. This public research organisation is responsible for the funding and management of competitive health research calls, i.e. it is an intramural research centre and provides external competitive funding. The Spanish National Research Council is the main fund recipient for basic research in Spain, undertaking research for health and biomedical sciences (amongst other fields). University hospitals are also among the main fund recipients for research in health and biomedical sciences.

The INGENIO 2010 initiative is the main policy vehicle to shift "the policy mix" in Spain towards higher quality research and innovation in the business sector. In addition to introducing new measures, it intends to complement initiatives contemplated in the

Spanish National Research Plan approved in the past with an aim to improve Spanish competitiveness. Under INGENIO 2010, the central government has almost doubled public funds to support R&D and innovation. The government expects that general R&D expenditure will reach the 2 percent of gross domestic product (GDP) target by 2010. In practice, it proposes a number of instruments to increase the focus (via priority areas) and funding of government research, stimulate technology transfer by encouraging public–private partnerships and enhancing the incentives for private-sector research and diffusion of new technologies.

Research funding in Spain has been increasing in absolute terms and as a percentage of the country's GDP. In addition, health research funding has been increasing as a percentage of total R&D funding.

Spain has been doing relatively well in terms of research productivity during the past few years. Publications in international peer-reviewed journals have been rising and, in particular, publications in biomedical sciences have been rising as a percentage of total Spanish publications.

There are several challenging issues that can contribute to improvement of the Spanish health research system in the near future: to increase R&D funding, especially that coming from private initiative; to identify reasons of the so-called brain drain of young researchers; to consider the reform of university hospitals in Spain and increase the number of biomedical research institutions; to create a clear professional career for the biomedical researcher; and to increase the numbers of medical doctors who divide their activity between practice and research. In summary, there is a need for sufficient funding, a well-defined professional career structure for researchers, and an increase in the number of research institutions.

Acknowledgments

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Many thanks to Rosa de la Viesca of the *Centro de Información y Documentación Científica*, Madrid, Spain, for the useful material she has kindly provided.

Abbreviations and Terms

CÉNIT	*Consorcios Estratégicos Nacionales de Investigación Tecnológica* (National Strategic Technological Research Consortia)
CDTI	*Centro para el Desarrollo Tecnológico Industrial* (Centre for the Development of Industrial Technology)
CICYT	*Comisión Interministerial de Ciencia y Tecnología* (Interministerial Commission on Science and Technology)
CNIO	*Centro Nacional de Investigaciones Oncológicas* (Spanish National Cancer Centre)
CSIC	*Consejo Superior de Investigaciones Científicas* (Spanish National Research Council)
EU	European Union
EU15	The 15 member states of the EU (1995–2003)
EU25	The 25 member states of the EU (2004–2006)
FECYT	*Fundación Española para la Ciencia y la Tecnología* (Spanish Foundation for Science and Technology)
FUNCIS	*Fundación Canaria de Investigación y Salud* (Canary Islands Foundation for Research and Health)
GERD	gross domestic expenditure on R&D
GDP	gross domestic product
FIS	*Fondo de Investigaciones Sanitarias* (Health Research Fund)
IBIS	*Instituto de Biomedicina de Sevilla* (Biomedicine Institute of Seville)
IBV	Institute of Biomedicine of Valencia
IMI	Innovative Medicines Initiative
INE	*Instituto Nacional de Estadística* (National Statistical Institute)
ISCIII	*Instituto de Salud Carlos III* (Carlos III Health Institute)
MEC	*Ministerio de Educación y Ciencia* (Ministry of Education and Science)
MITYC	*Ministerio de Industria, Turismo y Comercio* (Ministry for Industry, Tourism, and Trade)

MSC	*Ministerio de Sanidad y Consumo* (Ministry of Health and Consumer Affairs)
NRP	National Research Plan
OECD	Organisation for Economic Cooperation and Development
PRBB	*Parc de Recerca Biomèdica de Barcelona* (Barcelona Biomedical Research Park)
R&D	research and development
SISE	*Sistema Integral de Seguimiento y Evaluación* (Integrated Monitoring and Evaluation System)
SNS	*Sistema Nacional de Salud* (Spanish National Health System)
TRIPS	Trade-Related aspects of Intellectual Property Rights

Introduction

Health and Medical Research in Spain

International Observatory on Health Research Systems

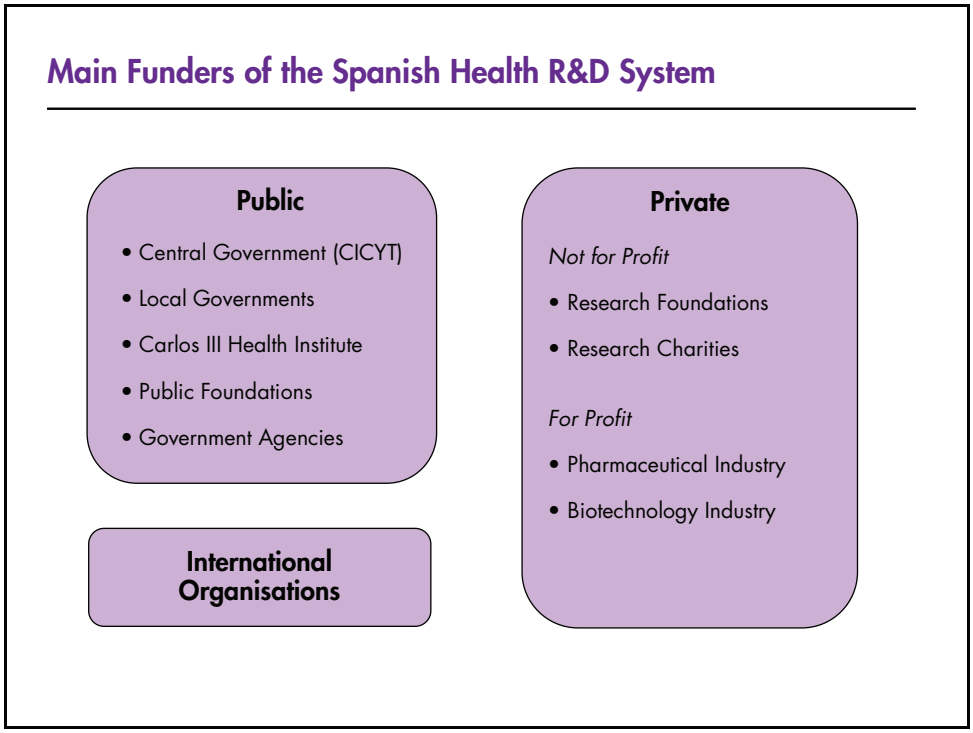
Fragiskos Archontakis

December 2008

The history of science in Spain has always been marked by a lack of continuity in scientific policies, which is one of the main aspects that differentiates it from other countries. Nevertheless, Spanish science has witnessed several important events, such as the big scientific leap at the end of the 19th century and the beginning of the 20th century, largely due to the awarding of the Nobel Prize in Medicine to Santiago Ramón y Cajal in 1906. In the 1930s, scientific progress in Spain slowed down because of the Civil War (1936–1939), although shortly afterwards some of the most important scientific institutions of the country would be established. In 1986, the Spanish government passed the Science Law and the Health Law, while in the same year Spain became a full member of the European Union (EU), coinciding with the approval of the Single European Act, which laid the basis for the European Framework Programme for Research and Development (R&D). Since then, and until today, the growth of scientific activity and financial investment in Spanish research, in general, and in biomedical research, in particular, has been substantial.

This documented briefing gives an overview of the Spanish health research system. In the first section it gives an overview of the structure and the main players within the Spanish health research system, including the funding mechanisms and funding flows within this system. The second section analyses the processes and performance of the Spanish health research system. The last section concludes with an overview of current and emerging issues and challenges in future health research policy in Spain.

Structure of the Spanish Health Research System

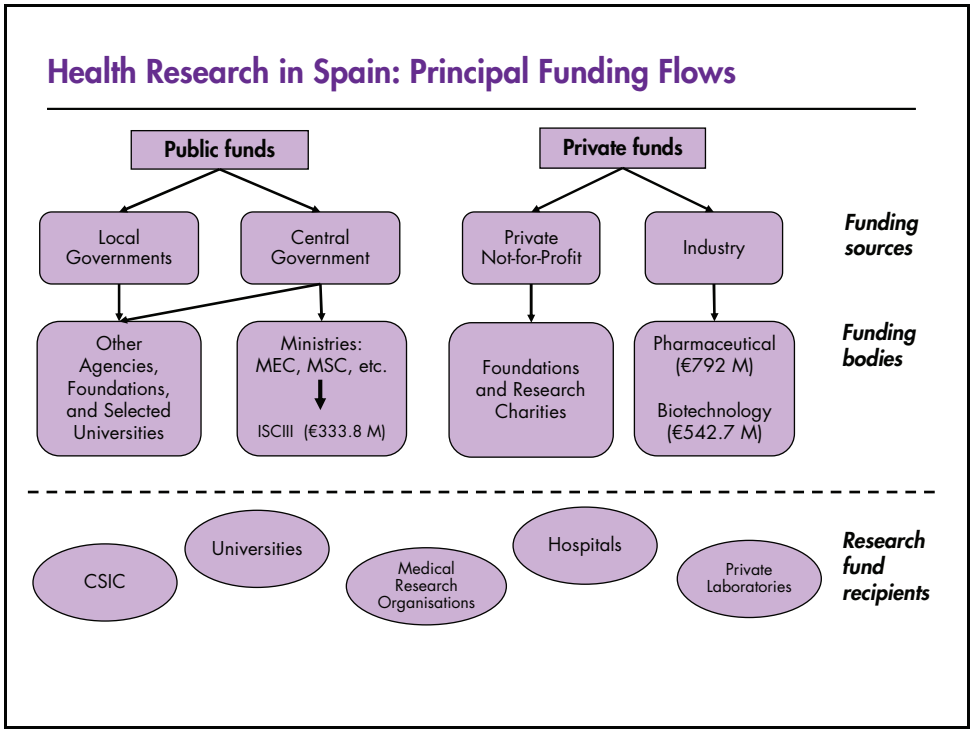


The Spanish health research system can be divided into three groups with respect to funding: public sector, private sector (private not-for-profit and private for profit), and international organisations. The main R&D funding bodies are government (central and local) and industry. Given the administrative structure of the country (Spain consists of 17 autonomous communities), public-sector funding is split between central and local government funds. The remaining funding is attributed to international funding sources, i.e. EU funds from the European Commission.

Historically, the policy mix for research, development, and innovation in Spain has been characterised by a disconnection between policies to support business innovation on the one hand and those to support the science base on the other. Part of this is related to the slow emergence of a coherent governance structure for innovation policy and weak coordination and cooperation between the main ministries responsible for science and technology. Until recently, the National Research Plan (NRP; i.e. the Spanish National Plan for Scientific Research, Development, and Technological Innovation) consisted of a vast range of programmes that were managed by various ministries. This was detrimental to the coordination of government measures, despite the efforts of the Interministerial Commission on Science and Technology (*Comisión Interministerial de Ciencia y Tecnología* [CICYT]), which designs and oversees the application of the NRP and the recent improvement in coordination in some areas (FECYT, 2007).

Furthermore, the link between the governance structure and funding for university research has been weak. Funding for university education comes from the regions, whereas funding for research projects comes mostly from the Ministry of Education and Science (*Ministerio de Educación y Ciencia* [MEC]) and the Ministry of Health and Consumer Affairs (*Ministerio de Sanidad y Consumo* [MSC]), with funding for health research in particular coming from regional governments and EU funds. In addition, funding for projects is based solely on the evaluation of projects and individual researchers' curricula, and not on the performance of institutions or research groups. Consequently, national and regional governments have not been able to sufficiently steer universities into focusing research funding and improving quality, and, up until now, most funding for research has been highly dispersed and research itself has been fragmented (FECYT, 2007).

Finally, the Spanish National Research Council (*Consejo Superior de Investigaciones Científicas* [CSIC]), public universities with medical schools, and the University of Navarra (a private institution) invest their own funds into biomedical research. However, this investment is part of a funding portfolio that includes investment from central government, local governments, industry, private foundations, and international organisations (e.g. the European Commission's Research Framework Programmes). Hence, these institutions are mostly fund recipients and thus will appear only in that category in this report.



The key funder in the public sector is the Carlos III Health Institute (*Instituto de Salud Carlos III* [ISCIII]), which is financially supported by central government through the MSC. In 2007, the research budget of ISCIII rose to €333.8 million. Public foundations and other government agencies play a minor part. Thus, although the natural candidate for public-funded research is the MEC, the MSC contributes most towards health research. Initially, funds were channelled through the Health Research Fund (*Fondo de Investigaciones Sanitarias* [FIS]), which has been active since 1980. In 1996, the FIS was incorporated within ISCIII's programmes (Campos Muñoz, 2002).

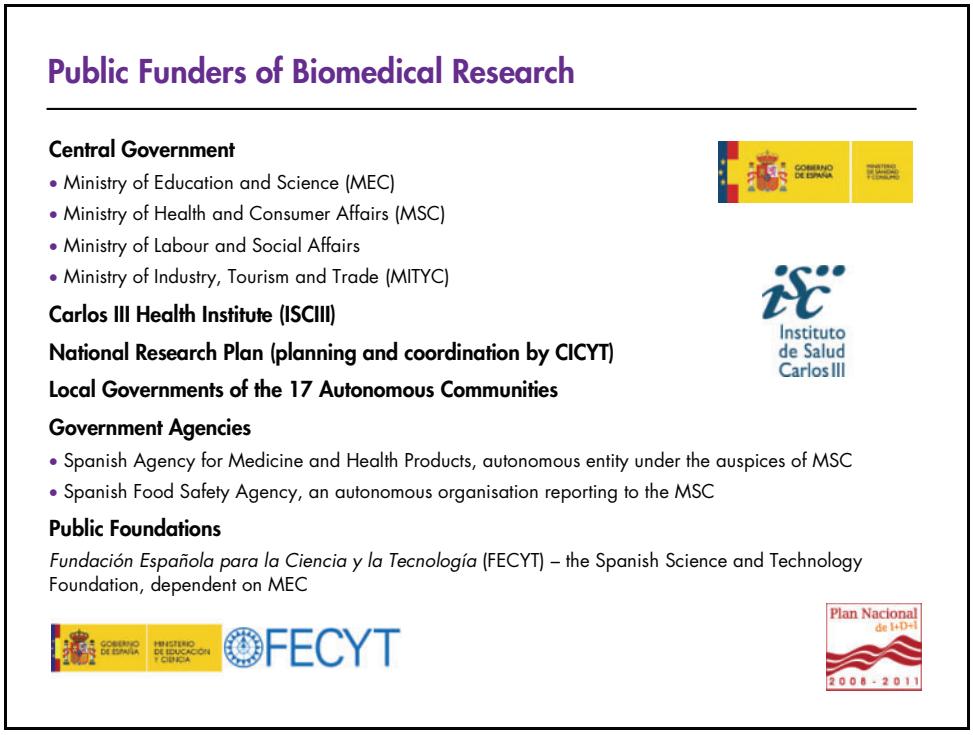
The ISCIII was created in 1986 as an autonomous public institution attached to the MSC. Its main objective is the promotion and support of research and technological development of health and biomedical research. ISCIII's general budget is revised annually by Spanish Parliament and was set at €333.8 million for 2007 and could reach €367 million for 2008. The total MSC budget for 2008 is over €1 billion with approximately €417 allocated to R&D, whereas €367 million will be going into research through ISCIII.[2]

The two key funding players in the private sector are the pharmaceutical and biotechnology industries. According to data from a survey undertaken by the pharmaceutical industry's association Farmaindustria, a total of €792 million was allocated to R&D in 2006 from the pharmaceutical companies (Farmaindustria, 2007). Furthermore, €542.7 million was the total R&D investment in the biotechnology industry sector in 2004 (March Chordà and Seoane Trigo, 2006). In the private not-for-profit

[2] MSC press communication (in Spanish), October 4, 2007: http://www.msc.es/gabinetePrensa/notaPrensa/desarrolloNotaPrensa.jsp?id=985 (as of September 26, 2008).

sector, many research foundations and a few research charities are sponsored by industry, although Spain does not have the same tradition as that found in other countries (i.e. United Kingdom) with regard to charities. Thus, data from this sector are sparse.

There are a number of research providers in Spain, including the CSIC, universities, medical research organizations, hospitals and private laboratories. These are discussed later in the report.



Most of public-funded research in Spain is allocated by the MEC. However, for health public-funded research, the MSC is the main funder via the ISCIII. Money distributed by the ISCIII is also incorporated within the NRP budget. Likewise, the Agency for Medicine and Health Products and the Food Safety Agency are autonomous entities under the auspices of the MSC and are of minor research importance compared to the ISCIII. The Ministry of Labour and Social Affairs and Ministry of Industry, Tourism, and Trade (*Ministerio de Industria, Turismo y Comercio* [MITYC]) also manage R&D projects with regard to biomedical research.

The NRP is implemented through more than 30 national R&D programmes and strategic actions managed by different ministerial departments or agencies (mainly MEC, MITYC, and MSC), which correspond to different thematic priority lines. It is presented around two axes: priority areas (thematic and horizontal areas) and actions (participation modes for the provision of financial support, mainly on a competitive basis through grants and interest-free loans). Responsible for its planning and coordination is the CICYT, which is chaired by the Prime Minister and has the formal objective of planning, coordinating, and monitoring the national R&D and innovation plan. It was created by the Science Act in 1986, and is dependent on support from the MEC (FECYT, 2007).

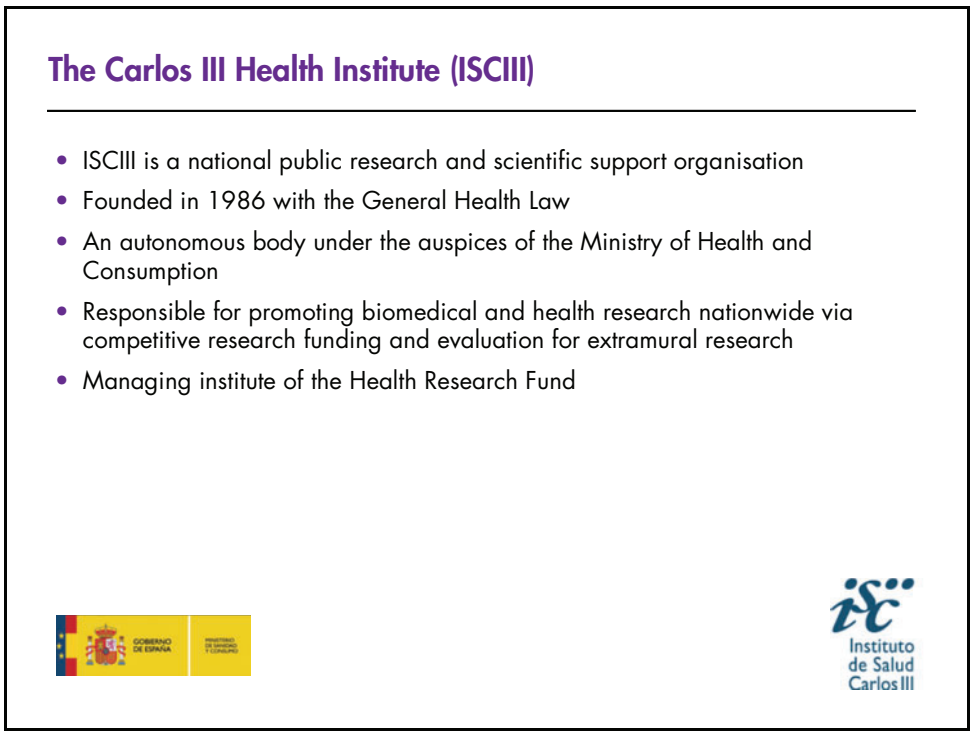
The local governments of the 17 Spanish autonomous communities are also health research funders at a lower level. For instance, *Generalitat de Catalunya* (Catalonia's local government) partially funds the private not-for-profit Catalan Foundation for Research and Innovation, which then distributes funds to research.

The Spanish Foundation for Science and Technology (*Fundación Española para la Ciencia y la Tecnología* [FECYT]), which is also dependent on the MEC, was founded in 2001 as a

tool of the national system of knowledge generation and technological transfer. The Foundation operates as a not-for-profit association and with functional autonomy, with the goal of rendering a continuous and flexible service to the Spanish system of science, technology, and enterprise. It helps to identify opportunities and needs, and proposes methods of action to agents of the scientific research and technological innovation system. Its strategic aims are (1) to promote activities of excellent technological research and development; (2) to favour collaboration between national and international agents of science and technology system; and (3) to promote the social spreading of the scientific culture, as a tool of competitiveness and improvement of the life quality of citizens.

There are other public foundations which fund biomedical research in Spain. However they are of much less significance compared to FECYT and they operate mostly at regional level[3].

[3] The Canary Islands' Foundation for Research and Health (*Fundación Canaria de Investigación y Salud* [FUNCIS]) is an example and is discussed later in this report.



The ISCIII is a national public research organisation, which was created in 1986.[4] It operates as an autonomous entity, governed by its own board of directors, under the aegis of the MSC. ISCIII is one of the few Spanish public research organisations[5] with intramural research centres and provision of external competitive funding, although ISCIII also maintains management functions as a research council, providing competitive research funds for extramural research in their budget.

The ISCIII employed 1054 staff in 2000 (Sanz Menéndez and Cruz Castro, 2003). The ISCIII is similar to organisations, such as the French *Institut National de la Santé et de la Recherche Médicale* (INSERM; National Institute for Health and Medical Research), *Deutsches Forschungszentrum für Gesundheit und Umwelt* (German National Research Centre for Environment and Health), the UK Medical Research Council, and *Istituto Superiore di Sanitá* (National Health Institute) in Italy (Sanz Menéndez and Cruz Castro, 2003).

Spanish public research institutions receive most of their funding from the annual budget through the particular ministry to which they are attached. Some of them, however, such as ISCIII, also receive public funds from other channels for other tasks not uniquely R&D related (intramural training, public health, and services). The FIS, managed by the ISCIII as its extramural funding branch, is responsible for providing funding (by means of public competitive calls) for most scientific research projects developed in hospitals, health centres, public research organisations, and universities, and for more than 15,000

[4] ISCIII was created under the General Health Law, 14/1986, enacted on April 25, 1986.

[5] There is also the National Institute for Agricultural and Food Research, under the aegis of the MEC.

researchers in the field of biomedicine, technologies for health and welfare, and other health sciences research in Spain. One of the objectives of the FIS is to link basic and clinical and public-health research and to promote cross-border research. It has also funded cooperative thematic networks on biomedical and other health sciences research (*Redes Temáticas de Investigación Cooperativa en Salud* [RETICS]) as well as research biomedical network centres with legal status (*Centros de Investigación Biomédica en Red* [CIBER]) (FECYT, 2007).

After the Spanish general elections in March 2008, the government created a new Ministry of Science and Innovation (Official Spanish Gazette, 2008b). Since then, many changes have been proposed in health and medical research. For example, ISCIII no longer belongs to the Ministry of Health but to the new Ministry of Science and Innovation.

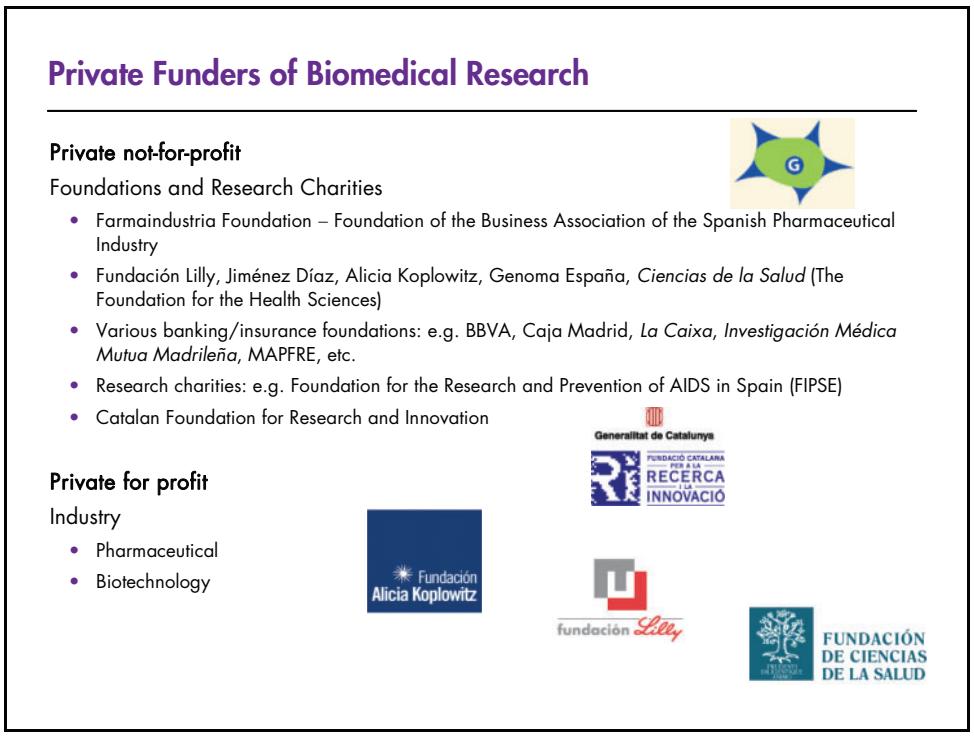
Canary Islands' Foundation of Research and Health (FUNCIS)

- A public, not-for-profit foundation established in 1990
- Main objective is to support health research and learning activities
- External funding mainly from private sector and the local government of the Canary Islands

An example of a public foundation at regional level is the Canary Islands' Foundation for Research and Health (*Fundación Canaria de Investigación y Salud* [FUNCIS]) is a foundation created within the regional law of the Canary Islands' foundations.[6] Thus, the regional law for the Canary Islands' foundations defines FUNCIS to be a public not-for-profit foundation, which has as beneficiaries all institutions, associations, or persons who are involved in research activities within the field of health in the Canary Islands. Accordingly, FUNCIS announces competitive calls for grants and research projects.

FUNCIS is funded through donations and subsidies that mainly come from the private companies based at the Canary Islands Autonomous Region (*Comunidad Autónoma*), from the Local Government of the Canary Islands (funds allocated to health research), and from other foundations and wealthy individuals. According to the Official Spanish Gazette (2007), the FUNCIS budget for the year 2007 amounted to €2.66 million.

[6] The regional law for Canary Islands' foundations: "Ley Territorial" 1/1990, enacted January 29, 1990: http://www.gobiernodecanarias.org/juriscan/ficha.jsp?id=282 (as of September 26, 2008).



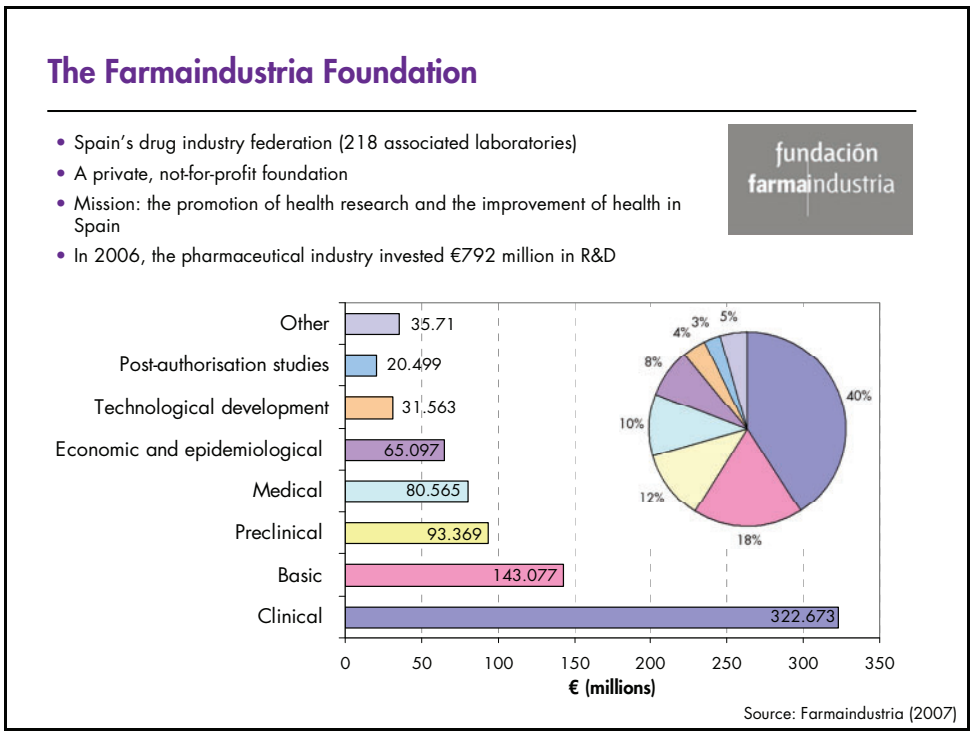
There are many private not-for-profit foundations and research charities that sponsor biomedical research in Spain, most of which are funded by the pharmaceutical industry. For the most part, their aims are similar: to bring together government, population, and industry to improve public health via better quality of medicine. Such foundations invest capital according to the priorities set by their governing boards. By default, the recipients are external research organisations, such as universities and medical research centres. However, there are some exceptions, such as the Jiménez Díaz Foundation, that operate their own biomedical research facilities.

For brevity we draw upon a few examples of private not-for-profit foundations. The Foundation for Health Sciences (*Fundación de Ciencias de la Salud*) is a private not-for-profit foundation, which was founded 1991 and is primarily sponsored by GlaxoSmithKline. Its mission is to bring closer the social sectors implicated in the world of health care: government authorities, civil society, and private enterprise. It encompasses three main institutions: the Bioethics Institute, the Biomedical Training Institute, and the Institute for Environmental Management and Protection.

In a similar fashion, the Lilly Foundation is a private not-for-profit foundation, created in April 2001 to channel and promote social and health collaboration initiatives in Spain. Its general objectives are to contribute to the development and improvement of the general public's health by undertaking research programmes and activities, training, information campaigns, prevention, consulting, technical assistance, and project development in the health field. The Lilly Foundation organises health research awards on a competitive basis.

Regional foundations aim to foster research at the autonomous community level. The Catalan Foundation for Research and Innovation is a private not-for-profit institution that

aims to coordinate Catalan research and innovation efforts and to increase the social awareness of the impact of science on society. One of its strategic aims is the improvement of health research, and it has contributed in the Barcelona Biomedical Alliance, a network of biomedical institutions (science parks).



The Farmaindustria Foundation is the National Association of the Pharmaceutical Industry in Spain,[7] and acts as the voice of the pharmaceutical industry. Founded on December 18, 2001, it is a private not-for-profit entity that aims to promote health research and the improvement of health in Spain. In particular, the Farmaindustria Foundation promotes biomedical and pharmaceutical research, training for health professionals, and health education for the wider public.

In 2006, Farmaindustria had some 218 members, which represent approximately 85 percent of prescription drug sales in Spain. The pharmaceutical industry invested a total of €792 million in R&D in 2006 (Farmaindustria, 2007). An overwhelming proportion of this investment (circa 40 percent or €323 million) was spent on clinical research (clinical trials), and approximately €143 million was spent on basic research.

Major foreign multinationals can be found in Spain, including Baxter, Bristol-Myers, Pfizer, Lilly, Merck Sharp & Dohme, Pharmacia & Upjohn, GlaxoSmithKline, Wyeth, Abbott Laboratories, Janssen-Cilag, Schering-Plough, Novartis, AstraZeneca, Roche, Solvay, Bayer, Boehringer Ingelheim, Ratiopharm, Merck, and Sanofi-Aventis.

[7] Equivalent to the Association of British Pharmaceutical Industry in the United Kingdom, or the European Federation of Pharmaceutical Industries and Associations.

R&D Personnel and Investment in Spain in 2005

Sector	Personnel in R&D (completed work days)	R&D Spending (€ millions)
Pharmaceutical	4365 (~11%)	763.84 (~17%)
Total	38,952 (100%)	4513.29 (100%)

Source: Farmaindustria (2007)

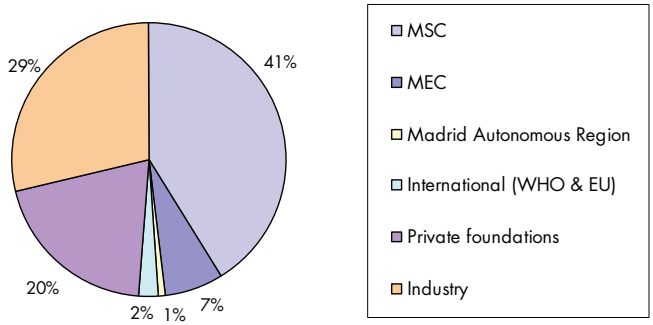
In 2005, the pharmaceutical sector invested €763 million in R&D, which is approximately 17 percent of all industry R&D investment in Spain (Farmaindustria, 2007). Furthermore, in 2005, it employed around 11 percent of the whole industry's R&D personnel.

In 2005, the European companies with the highest investments in R&D were GlaxoSmithKline, Sanofi-Aventis, and AstraZeneca, with Pfizer, Johnson & Johnson, and Novartis leading with R&D investments outside the EU.

To date, there are 218 laboratories associated with Farmaindustria. The leading Spanish laboratories in the pharmaceutical, chemical, and diagnostic sectors are Laboratorios Esteve, Grupo Uriach, and Almirall.

The Jiménez Díaz Foundation

- A Madrid-based hospital member of the international health group *Capio*
- A 70-year-old organization with the main objectives: quality health care, research, and teaching
- In 2006, external funding reached circa €2.68 million



Capio Fundación Jiménez Díaz

Source: http://www.capiosanidad.es/fjd/es/investigacion/proyectos.html

An interesting case of a private not-for-profit foundation is the Jiménez Díaz Foundation. This foundation has a long research experience in Spain, given that it introduced a new model of hospital in the country, integrating health care, teaching, and research (in a rich variety of health research fields) within its daily activities. Since 2003, it has been integrated into the international health group Capio.[8]

The Jiménez Díaz Foundation claims to be "one of the most efficient research hospitals, since it achieves the highest scientific production (publications) per economic expenditure unit".[9] Currently, it is ranked 10th in Spain in terms of research volume (Camí, Suñén-Piñol, and Méndez-Vasquez, 2005).

During 2006, the Jiménez Díaz Foundation's external funding, as generated by charities, subsidies, and contracts received by public and private entities, reached a total of €2.68 million distributed between €1.90 million in project funding and €0.78 million corresponding to income made from new clinical trials. Research funding was distributed as follows: 41 percent offered by the MSC, 7 percent by the MEC, 29 percent by industry, 20 percent by other private foundations, and the rest by the Madrid Autonomous Community and international funders (World Health Organization and the EU).

[8] Capio Sanidad is the leading private company in providing health-care services in Spain. Capio Sanidad became a part of the Capio Group (Sweden) in early 2005 through the acquisition of the IDC Grupo Sanitario. Capio Group is present in Sweden, Norway, France, Germany, Spain, and the United Kingdom (see http://www.capio.se/en/Capio-Presence/).

[9] Capio Fondacíon Jiménez Díaz, "Investigación," http://www.capiosanidad.es/fjd/es/investigacion/investigacion.html (as of September 26, 2008).

Research Charities: FIPSE

- The Foundation for the Research and Prevention of AIDS in Spain (FIPSE) is a private, not-for-profit entity.
- FIPSE is a fund for research projects, grants, and publications.
- Its objectives are to support Spanish research on the infection of HIV/AIDS, and to strengthen the link between research and evaluation with health-care policy.

One of the most important research charities is the Foundation for the Research and Prevention of AIDS in Spain (*Fundación para la Investigación y la Prevención del SIDA en España* [FIPSE]). FIPSE is private not-for-profit entity, with social and health-care priorities.

FIPSE was created in 1998 after an initiative by the MSC in collaboration with the pharmaceutical companies that carry out research on HIV/AIDS and produce antiretroviral drugs. It is basically a fund for research projects, grants, and publications. It is sponsored by the MSC, Abbott Laboratories, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, GlaxoSmithKline, Merck Sharp & Dohme, and Roche.

Its objectives are to unify public and private effort to support Spanish research on all aspects of HIV/AIDS (basic, clinical, epidemiological, preventive, economic, and social) and to strengthen the link between research and evaluation with health-care policy. For example, in 2007, FIPSE planned to invest €2.4 million in research and prevention activities of HIV/AIDS in Spain.[10]

[10] MSC press communication (in Spanish), December 19, 2006: http://www.msc.es/gabinetePrensa/notaPrensa/desarrolloNotaPrensa.jsp?id=765 (as of September 26, 2008).

Research Fund Recipients

- Spanish National Research Council (CSIC)
- Universities with Medical Schools
- Hospitals and Foundations
- Private Laboratories
- Medical Research Organisations (e.g. IBIS at Seville)

The main health research fund recipients in Spain are CSIC, universities with medical schools, hospitals and foundations, private laboratories, and medical research organisations. The contribution of public universities in health research is also substantial, and the University of Navarra, the only private university with a medical school and a university hospital, also provides a substantial contribution to health research.

In Spain, the main institutions performing public-health research are public universities and public research organisations, including CSIC, the main public research institution in the country. Public universities have a very important role in Spain, not only with regard to this research field, but also for clinical and medical training responsibilities. In a translational system, the job of the university hospitals has to be taken into account. In addition, several applied research institutes under the responsibility of different sectoral ministries (e.g. the MSC, the Ministry of the Environment, etc.) and the MEC have important roles.

For universities, funding for teaching and operations is the responsibility of the regions that allocate funding to them based mainly on the number of students and teachers and other related criteria. Because the regions provide little or no institutional funding for research (block grants), university faculties must apply and search for competitive funding available from national, regional, or European funding institutions. The law gives the national central government the facility to promote and coordinate research via competitive calls. However, researchers in one region cannot always apply for competitive research funds offered by another region because of various restrictions (e.g. location requirements), despite the fact that their proposal may fit into the policy objectives defined by the regional government or that they could work with a research team from that region. This policy goes against the objective of creating so-called "critical mass" (i.e. the size at

which a research group or department undergoes a fundamental change in regard to its sustainability and competitiveness within the research field it operates) in research and also limits cooperation (FECYT, 2007).

Spain spends around 1.1 percent of GDP on research and development (1.13 percent in 2005), significantly below the averages of the 25 member states of the EU (EU25; 1.8 percent) and the Organisation for Economic Cooperation and Development (OECD; 2.26 percent) (FECYT, 2007). The low level of funding for public research has prevented Spanish researchers from achieving the critical mass necessary to effectively compete for international research projects. Average total R&D expenditure per researcher in universities was 50 percent of the EU average in 2001 (EU15). This low level of support for research and the weak infrastructure has caused Spanish public research groups to focus their activities in fields of science that require fewer resources. This lack of critical mass is evident in the low impact of Spanish scientific production on the productive sector as measured by patenting or industry financing of university R&D, as well as the excessive fragmentation of research groups and limited participation in the European research programs (FECYT, 2007).

Another issue is the overlapping activity of research centres (e.g. Ricoy Campo, 1993). For instance, the Institute of Biomedicine of Valencia (IBV) is part of CSIC. The research activity of the groups working at IBV is carried out and financed competitively within the context of the NRP, local governments, EU framework programmes, and the funding initiatives of private charities. As an actor of research in the biomedical field, the IBV is a node of two networks of centres and of several networks of groups of ISCIII, and also has formal research and collaborative agreements with public hospitals, universities, and pharmaceutical/biotechnological companies. However, the Biomedicine Institute of Seville (*Instituto de Biomedicina de Sevilla* [IBIS]), was created on March 24, 2006, by virtue of an agreement signed by the Andalusian Local Government Health, Innovation, and Science, and Industry bodies (*Junta de Andalucía*: *Consejería de Salud*, *Consejería de Innovacióny Consejería de Ciencia y Empresa*), the Andalusian Health Service, the University of Seville, and CSIC. The mission of IBIS is to contribute and strengthen biomedical research in Spain, establishing itself as a national research centre for southern Europe. It is considered a multidisciplinary biomedical research space within the complex that hosts the Virgen del Rocío University Hospital. The Barcelona Biomedical Research Park (*Parc de Recerca Biomèdica de Barcelona* [PRBB]), one of the largest biomedical research clusters in southern Europe, joined IBV and IBIS in 2006. It is rather difficult to imagine that a perfect coordination between all these centres devoted to biotechnology research is possible (i.e. due to overlapping activities and policy mix of central and local governments). Moreover, it is difficult to evaluate the success of this system yet, since most of these centres are relatively new.

Catalonia BioCluster: Biotechnology and Life Sciences

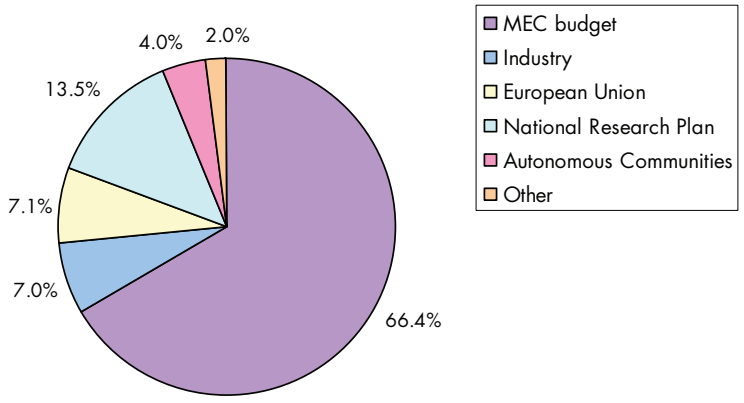
- Initiative of Catalan local government through the ministries (MEC, MSC, and Economy & Industry)
- 12 universities and 2 leading business schools
- Several science parks (biomedical, agro-food; e.g. Barcelona Biomedical Research Park)
- Networks of hospitals, centres of excellence, Technological Trampolines Network for technology transfer (entrepreneurial agencies linked to main universities and business schools)
- Home to the European Federation of Biotechnology

In 2003, the Barcelona Biomedical Alliance was launched. This initiative of several entities linked to biomedical research aims to organise and boost the quality and capacity of biomedical research performed by the public sector in Barcelona and its metropolitan area. The Alliance contributed towards the initiation of the Catalonia BioCluster Project in 2006, which aims to become a biocluster of reference for the international scientific community.

The cornerstone of this project is the PRBB, which is one of the largest biomedical research clusters in southern Europe. This research park, an initiative of the Government of Catalonia, the City Council of Barcelona, and the Pompeu Fabra University, is hosted in an impressive building co-financed by the MEC, the NRP, and the European Fund for Regional Development. This large scientific infrastructure is physically connected to the Hospital del Mar in Barcelona, which is the coordination centre for six public research centres. These are independent research centres focused on different aspects in biomedicine: Municipal Institute of Medical Research, Department of Experimental and Health Sciences at Pompeu Fabra University, Centre for Genomic Regulation, Centre of Regenerative Medicine in Barcelona, Centre for Research in Environmental Epidemiology, Institute of Advanced Technology, and the Hospital del Mar (which is also part of the *Institut Municipal d'Assistència Sanitària*). The following technology platforms are also involved: National Centre of Genotyping, National Institute of Bioinformatics, Catalonian Antidoping Laboratory (at the Municipal Institute of Medical Research), and National Institute of Proteomics (ProteoRed).

Spanish National Research Council (CSIC)

- CSIC is the largest public research body in Spain founded in 1939
- In 2006, CSIC had a research budget of €675.8 million
- The overwhelming majority of its funds comes from MEC



Source: CSIC (2007)

One of the most important fund recipients is CSIC, which was founded in 1939. Its aim is to promote and carry out scientific and technical research to serve Spain's science and technology policy, with the overall goal of contributing to the country's economic, social, and cultural development. CSIC carries out intramural research at its own institutes and does not fund extramural research at other research institutions (Martín-Sempere, Garzón-García, and Rey-Rocha, 2008).

CSIC is the largest public research body in Spain, with around 13,000 employees. Operating nationwide, it has research centres throughout most of the country's territory and plays an active part in the scientific policy of all 17 autonomous regions of Spain. CSIC is a multidisciplinary body and claims to cover all fields of knowledge, from basic research through to advanced technological development. CSIC is divided into eight science and technology areas, including biology and biomedicine, chemical sciences and technologies. It has 128 research centres and mixed institutes established in cooperation with universities, ten service centres, and 134 units associated with universities and other institutions (public research bodies, private companies, professional associations, foundations, autonomous regions, local authorities, and provincial councils).[11]

In terms of its legislative framework, CSIC is an autonomous public research body belonging to the MEC, to which it reports through the State Secretariat for Universities

[11] See CSIC's Web site: "CSIC Institutional Information," http://www.csic.es/quien_somos.do; and press communication, "Researcher Rafael Rodrigo Montero is named as new CSIC president [in Spanish]," April 25, 2008, http://www.csic.es/wi/VisualizarDocumento.jsp?id_object=0902bf8a800ad185&user=usuario-internet&docbase=CSIC_PROD (as of September 26, 2008).

and Research. It has its own legal identity, assets, and cash flow, and is independently managed.

In 2006, most of CSIC's funding (66.4 percent) came from the MEC. However, CSIC is also a Spanish leader in competitive funds capture from the NRP and the EU Research Framework Programmes.

As a result of the ministerial changes after the Spanish general elections in March 2008 (Official Spanish Gazette, 2008b), CSIC no longer belongs to the MEC but to the new Ministry of Science and Innovation.

The University of Navarra

- A private university, founded in 1952
- School of Medicine, Pharmacy, and University Hospital
- The only private university in Spain to have a university hospital
- Centre for Applied Medical Research

Among the private fund receivers of note is the private University of Navarra. The University of Navarra was founded in 1952 and the School of Medicine was founded in 1954. The University of Navarra's University Hospital is considered as one of the best in the country. Since its founding, the School of Medicine has been characterised by its incorporation of significant advances in medical education, placing special emphasis on practical instruction.

The University of Navarra's School of Medicine was the first Spanish School to create interdisciplinary departments, which provide instruction in the Schools of Science, Pharmacy and Medicine. It is a pioneer in the integration of medical-surgical programmes. It has incorporated the teaching of bioethics within the structure of its curriculum, developed multimedia techniques applied to medical instruction, and integrated its teaching with clinical practice.[12]

The University of Navarra's Centre for Applied Medical Research (*Centro de Investigación Médica Aplicada*) was inaugurated in 2004. It is financed by 15 companies and entities. The Centre's remit is to merge, develop, and emphasise those areas of research that have been done in the Schools of Medicine, Pharmacy, and Science, and in the University Hospital of the University of Navarra.

[12] See the University of Navarra's Web site: http://www.unav.es/medicina/lafacultad/

Processes and Performance of the Spanish Health Research System

The aim of CICYT is to safeguard an integral, coherent, and rigorous scientific policy at the planning, programming, execution, and monitoring levels to obtain the necessary increase in resources for research, and scientific, cultural, social, and economic returns, in line with needs and requirements. The Commission is entrusted with programming the research activities of the bodies that depend on state administration, and does so through the NRP, which enables more agile and effective programming. Modern methodology helps it to tackle the complex process of planning, coordination, and management.

The CICYT, in coordination with the state administration's economic planning bodies, draw up the NRP, submit it for review to advisory bodies who consider it and present it to the government for approval and subsequent referral to the Spanish National Parliament. Some of complementary functions of the CICYT include the following: proposing the allocation of public funds and agreed private funds earmarked for the different programmes that make up the NRP; conferring, where appropriate, the management and execution of these programmes and establishing their duration; evaluating compliance with the NRP and the corresponding budgetary programmes; and presenting an annual report to the government for submission to parliament on the implementation of the NRP, including, if necessary, any rectification proposals deemed necessary.

Policy Actions: Research Priorities in the Public Sector

- The government strategic initiative INGENIO 2010:
  - More funds
  - Focused on three strategic lines (CÉNIT, CONSOLIDER, AVANZ@)
  - Better managed and evaluated
- National Research Plan priorities for life sciences
- Research programmes (I3, Ramón y Cajal, etc.)
- CIBER and RETICS projects: to raise the quality of research in biomedicine and the health sciences by developing new research networks with a legal economic status
- The progressive Spanish legislation (ethical and fiscal)

The strategic initiative INGENIO 2010, launched in June 2005, made R&D and innovation policy an explicit part of the economic policy and objectives of the Spanish government. The programme sets the following objectives to be reached by 2010:

- To increase the ratio of R&D investment as a percentage of GDP (from 1.05 percent in 2003) to 1.6 percent in 2008, reaching 2 percent in 2010.
- To raise the private sector's contribution to R&D investment (from 48 percent in 2003) to 52.5 percent in 2008, reaching 55 percent in 2010.
- To reach the EU15 average in the percentage of GDP devoted to information and communication technologies (from 4.8 percent in 2004) to 6.4 percent in 2008, reaching 7 percent in 2010.

To comply with these ambitious objectives, the state's civil R&D and innovation budget increased by a staggering 21 percent in 2005, by 32 percent in 2006, and by 34 percent in 2007. In addition to this major increase in domestic funds, there will also be €2 billion from the European Technology Fund, obtained in the recent negotiation of the Financial Perspective 2007–2013, to finance research and development by and for companies.

The INGENIO 2010 programme aims to focus these resources gradually on strategic initiatives to meet the challenges faced by the Spanish science and technology system. This gradual focus will be achieved by allocating a significant portion of the minimum annual increase of 25 percent in the national R&D and innovation budget to strategic initiatives grouped in three major lines of action: the CÉNIT Programme (*Consorcios Estratégicos Nacionales de Investigación Tecnológica* [National Strategic Technological Research Consortia]) to stimulate R&D and innovation collaboration; the CONSOLIDER

Programme, to reach critical mass and research excellence; and the AVANZ@ Plan, to converge with Europe in the main information society indicators.

Within the NRP's priorities for life sciences, the fields of biomedicine, health and well-being technologies, biotechnology, and basic biology are also included. IBIS and PRBB exemplify best the strong state impetus towards this direction. Furthermore, in the past few years, the MSC through ISCIII has prioritised stem-cell research by means of the following initiatives:

- An increase of the budgets dedicated to the research in the field.
- Modification of the previous legal rules for authorising research concerned with human embryonic stem cells, and the elaboration of the Biomedical Research Law, which came into effect on July 4, 2007.
- Creation of a stem-cell bank for research purposes and creation of a dedicated Cooperative Research Network on Cell Therapy, with an independent budget.
- Financial agreements with several Spanish autonomous communities to boost the local initiatives on stem-cell research.
- Agreements with international institutions (Salk Institute and British Council) to allow the exchange of scientists doing research on stem cells, cell therapy, and regenerative medicine.

A rich variety of research programmes in the form of contracts and fellowships in human-resource development is funded by the public sector in Spain to train researchers. We shall refer to a selection of these research programmes in detail in the next section.

Spanish legislation on new technologies and their application to human reproduction and research has been significantly modified during the past few years (e.g. through the Biomedical Research Law). Spain is now one of the most advanced and permissive European countries on human transplantation, assisted human reproduction, and embryo research (Terribas, 2007).

The Spanish government has expanded the use of fiscal incentives to allow companies to choose between tax credits on profits and deductions for employer social security and other labour charges for hiring research personnel. These tax incentives should help support companies' investment in research at the earliest stage of the R&D process, when the risk of market failure is highest. This could be particularly attractive for small R&D companies that do not generate profits (FECYT, 2007).

The Minister of Science and Innovation has created a working group comprising 25 high-level scientists representative of all research fields who will write a new law for the National Strategy for Science and Technology (Official Spanish Gazette, 2008a). This new science law might bring some changes for the current running programmes within the Spanish research landscape.

General Research Programmes

- *Juan de la Cierva*: 3-year contracts for young postdoctorates
- *Ramón y Cajal*: 5-year contracts with possibility for tenure
- *I3*: Incentives, Incorporation, and Intensification of research
- *Torres Quevedo*: contracts for R&D personnel (postdoctorate researchers and technology management experts) at companies or technological centres

Various general research programmes exist to foster research in Spain. These programmes are announced on a competitive, yearly basis. Some of the most representative general research programmes are described below.

The Juan de la Cierva programme was launched in 2004 and is managed by MEC. It supports the recruitment of junior postdoctoral researchers by Spanish public research organisations on three-year contracts. It aims to increase the research capabilities of R&D groups and institutions through the recruitment of qualified researchers.

The Ramón y Cajal programme is also run by the MEC and its aim is to enhance the research capacity of R&D groups and institutions, both private and public, by hiring researchers who hold a Ph.D. and have presented a research topic to develop. The MEC's strategy is based on the provision of funding for the recruitment of these Ph.D. holders and co-funding from the institutions benefiting from the programme, which will be provided gradually. Resolution of the programme is based on a strict competitive process that guarantees objectivity, scientific quality, and the merits of the selected researchers. The grants are for the co-funding of five-year work contracts, for Ph.D. holders in all knowledge areas, by Spanish R&D centres.

The I3 programme (Incentives, Incorporation, and Intensification of research activity) is managed by both the MEC and the MSC through ISCIII, the latter for matters concerning the national health-research system.

The Torres Quevedo programme[13] offers money to private companies toward the cost of hiring young Ph.D. graduates to solve two problems: Spain's private sector is generally investing too little money in research and development (R&D), and their innovative capacity was limited as a consequence. In addition, the number of Ph.D. graduates had increased and it was impossible for academia alone to absorb them all. By encouraging companies to employ highly qualified personnel, the Torres Quevedo programme aims to invigorate private R&D in Spain while helping young scientists find a job after completing their Ph.D. The programme also offers researchers the possibility to negotiate a part-time position within a company while keeping a part-time research position in academia, an arrangement that demands hard work and flexibility, but allows the researcher to keep their options open as to which career they intend to pursue.[14] For 2008, the programme is co-financed by the European Social Fund.

[13] The Torres Quevedo Programme was introduced under the Spanish National Research Plan's 2000–2003 framework.

[14] Science, "Keeping both Academia and Industry on the go," http://sciencecareers.sciencemag.org/career_development/previous_issues/articles/3640/keeping_both_academia_and_industry_on_the_go (as of September 26, 2008).

Specific Health Programmes

- Pre- and postdoctoral fellowships for research management training
- Contracts for national health system researchers for a maximum of six years
- Researcher mobility for National Health System (SNS) personnel for scientific traineeships abroad
- Contracts for technical manpower for research support at the SNS shared-use research infrastructures

In addition to general programmes, there are also programmes that are specific to health research:

- Pre- and postdoctoral fellowships for research management training is an extramural programme managed by the MSC. This programme includes a mandatory one-year scientific traineeship abroad.
- The National Health System Researchers programme is a six-year job contract with a three-year research project, which is funded mainly by the MSC, although a small part of the funding also comes from the autonomous communities. It has been running since 1998. It also rewards the institutions (hospitals, universities, or public research organisations) that provide hired researchers with longer term or permanent job positions and employment security.
- Researcher Mobility for Personnel in the Spanish National Health System (*Sistema Nacional de Salud* [SNS]) is a programme managed by MSC–ISCIII and MEC. It promotes researcher mobility for SNS personnel for scientific traineeships abroad (MSC and ISCIII) and for projects (MEC).
- The programme for technical manpower for research support at SNS shared-use infrastructures is an extramural programme managed by MSC and ISCIII (since 2000) that offers technical manpower for research support contracts at SNS shared-use research infrastructures (e.g. SNS hospitals). Each contract lasts for three years and is co-funded by the recipient health institution, whose management is in turn carried out by the autonomous communities.

There are also other types of programmes, which include pre-doctoral fellowships for research management training (managed by MSC), and contracts for research training for health specialist trainees (managed by MSC and ISCIII since 2001). The latter are co-funded by recipient health institutions, which are in turn managed by the autonomous communities, with a mandatory one-year scientific traineeship abroad.

Research Policy in the Private Sector

- Disease-driven research and profit maximisation
- Research used for investment, visibility, and corporate social responsibility
- Spain in 2007: research funds on rare diseases are an instrument for a favourable modification of the legislation on intellectual property rights for drugs

As part of a typical free-market economy, the pharmaceutical and biotechnology industries tend to pursue research in the disease areas with the highest probability of profit for the companies. Various corporations have invested in biomedicine through, for instance, the Centre for Applied Medical Research at the University of Navarra. Furthermore, a company's visibility can be promoted better through research foundations or technological platforms (e.g. the Spanish Technological Platform for Innovative Medicine). Although Spain lags behind other countries in terms of corporate social responsibility, many companies have decided to catch up: Novartis now has an outstanding record of corporate social responsibility (Melé, 2004).

In fact, a platform named *Mesa Cuadrada* ("Square Table") was constituted in Spain to follow up on the programme of the United Nations' Global Compact Initiative launched under the auspices of the Secretary-General Kofi Annan in 1999 and has been in operation since 2000. *Mesa Cuadrada* brought together some 200 Spanish companies and its principle aim was to debate and investigate the issues related to Corporate Social Responsibility.

Another important factor is the work of various non-governmental organisations and study centres, mostly in collaboration with corporations and academic institutions. The earliest of these foundations goes back to the early 1990s and provides information and education on various levels.

As an example of national politics between the government and the private sector we note that during the past few years, there were two failed attempts by Farmaindustria to force the government to modify patent regulations. The attempts were supported by the

association's complaints because of a supposed lack of harmonisation with the TRIPS Agreement.[15] That, Farmaindustria says, has led to a so-called judicial war on patents of 20 drugs, which have an annual turnover of about €1.5–1.6 billion. In May 2007, Farmaindustria asked the Spanish government to achieve this harmonisation by using politics in return for the association investing a large amount of money (€300 million in 5 years) in research into the treatment of rare diseases. This controversy exists because Spain has a double intellectual property rights regulation: one terminated in 2006 and the other (same for whole EU) will not be fully enforced until 2012 when the conflict is expected to end.[16]

[15] From the various World Trade Organization agreements, the TRIPS (Trade-Related Aspects of Intellectual Property Rights) Agreement is expected to have the greatest impact on the pharmaceutical sector and access to medicines. The TRIPS Agreement has been in force since 1995 and is to date the most comprehensive multilateral agreement on intellectual property. The TRIPS Agreement introduced global minimum standards for protecting and enforcing nearly all forms of intellectual property rights, including those for patents. International conventions prior to TRIPS did not specify minimum standards for patents. At the time that negotiations began, over 40 countries in the world did not grant patent protection for pharmaceutical products. The TRIPS Agreement now requires all World Trade Organization members, with few exceptions, to adapt their laws to the minimum standards of intellectual property rights protection. In addition, the TRIPS Agreement also introduced detailed obligations for the enforcement of intellectual property rights. See: http://www.who.int/medicines/areas/policy/wto_trips/en/index.html (as of September 29, 2008).

[16] IPR Helpdesk Bulletin, No. 35, September–October 2007, "Drug Patents in India and Spain," http://www.ipr-helpdesk.org/newsletter/35/html/EN/editorial.html (as of September 29, 2008); and El País Newspaper, "Farmaindustria ofrece 300 millones a Sanidad para blindar les patentes," May 8, 2007, http://www.elpais.com/articulo/sociedad/Farmaindustria/ofrece/300/millones/Sanidad/blindar/patentes/elpepusoc/20070508elpepisoc_4/Tes (of September 30, 2008).

Public–Private Partnerships: INGENIO 2010

Health research has seen a shift in funding priorities:

- Public–private partnerships within the Strategic Action for Biotechnology of the National Research Plan
- Steering public research activities under public–private partnership arrangements

To focus resources on strategic actions, two new programmes have been launched: CÉNIT, managed by the Centre for the Development of Industrial Technology (*Centro para el Desarrollo Tecnológico Industrial* [CDTI]),[17] and the AVANZ@ Plan, which is managed by the Secretary of State for Telecommunications and the Information Society. Through the CÉNIT programme, the government also seeks to improve public support for business innovation. To this end, the government first identified broad priority areas, which included health and biomedicine.

Companies propose specific projects related to the above priorities identified by the government: a bottom-up approach whereby the selected projects are funded via grants. The projects must include at least six members in a consortium that must include at least two large private enterprises and an equal number of small and medium-sized enterprises. In addition, it should include two research centres associated with or subcontracted by participating companies that must make up 25 percent of the total budget. Finally, the companies must be able to provide half the funding necessary for the project. Proposals are evaluated on a competitive basis by the CDTI and the National Evaluation and Foresight Agency (*Agencia Nacional de Evaluación y Prospectiva*), with officials of the MEC and the MITYC. The first call for CÉNIT projects managed by CDTI approved €200 million to fund 16 large R&D and innovation consortia in strategic technology areas for four years (to be matched with €230 million from the private sector). The projects approved in the first round involved 178 companies (51 percent small-to-medium and 49 percent large

[17] The CDTI is a public corporate entity of the MITYC, but has a different role, mainly regarding the promotion of innovation and the technological development of companies located in Spain (Spanish or foreign based).

companies) and 208 research groups in universities, public research centres, and technology centres (FECYT, 2007).

There are several specific examples of public–private partnerships for health research in Spain that fall within the Strategic Action for Biotechnology of the NRP. On September 4, 2007, France, Germany, and Spain signed a Memorandum of Understanding to reinforce the strategy of public–private partnerships. The parties in this joint initiative are the *Ministère de l'Enseignement Supérieur et de la Recherche* (Ministry for Higher Education and Research; France), the *Agence Nationale de la Recherche* (National Research Agency; France), the *Bundesministerium für Bildung und Forschung* (Federal Ministry for Education and Research; Germany), and the MEC (Spain).

A call for research proposals (starting in early 2008 and until 2013), named "Scientific and Technological Cooperation in Plant Genome Research as basis of the Knowledge Based Bio-Economy" has been jointly implemented by the MEC in Spain, the *Bundesministerium für Bildung und Forschung* in Germany, and the *Agence Nationale de la Recherche* in France. It intends to further develop the former Trilateral Cooperation on Plant Genomics into a mutual research programme to support PLANT-KBBE (Transnational Plant Alliance for Novel Technologies towards implementing the Knowledge Based Bio-Economy in Europe). The MEC is attending the main objectives described in both the National Internationalization Program of R&D and the Strategic Action for Biotechnology of the National Plan 2008–2011. In this context, the reinforcement of public–private collaboration in research and the participation of Spanish groups in international cooperative research projects are among the most remarkable purposes of this action.[18]

In the mid-1990s, the CSIC and Pharmacia & Upjohn signed an agreement that allowed the pharmaceutical company to use the Department of Immunology and Cancer at the National Centre for Biotechnology as a corporate laboratory in exchange for contributing to finance the National Centre for Biotechnology with $55 million throughout the seven-year term of the agreement, which finished in 2000. This case is clearly the result of key role of scientific entrepreneurs matching private needs and public infrastructures (Sanz Menéndez, 2003).

Another example of public–private partnership is the creation of the new Spanish National Cancer Centre (*Centro Nacional de Investigaciones Oncológicas* [CNIO]), which was founded in 1998 by the ISCIII, and is dependent on the MSC. The CNIO is one of the few European cancer centres to allocate resources to both basic and applied research in an integrated fashion, thus supporting the interaction of basic research programmes with those of molecular diagnostics and drug discovery. The CNIO is managed through its foundation (*Fundación Centro Nacional de Investigaciones Oncológicas Carlos III*), which was created at the same time as the CNIO. This not-for-profit foundation receives block grant funding, competes for public funding, and gets additional support for private

[18] ERA-NET Plant Genomics, "News items 2008," February 11, 2008, http://www.erapg.org/everyone/17134/19059 (as of September 30, 2008); and Ministry of Science and Innovation, "Scientific and Technological Cooperation in Plant Genome Research as Basis of the 'Knowledge-Based Bio-Economy'. 3rd Call for Proposals (2008)," http://www.micinn.es/ciencia/eranets/files/2008-call-text-plant-kbbe.pdf (as of September 26, 2008).

industry through collaboration agreements and sponsorship. The way in which the CNIO operates reflects the flexibility associated with a private organisation, with such freedom resulting from the creation of the foundation, along with the accountability expected of public organisational status, which translates into the strict vigilance of all public funds received. For example, Pfizer, Microsoft, and Hewlett Packard have become permanent sponsors of the CNIO. The director of the centre played a key role in the raising of new funding for their scientific plans (Sanz Menéndez, 2003).[19]

Another implementation under the principle of public–private partnership was the agreement between the MSC and Farmaindustria. The agreement is part of the regulatory environment on prices of pharmaceutical products to be bought by the SNS. The pharmaceutical industry agreed to increase R&D investment to €1.35 million for 2002–2004, with a third to be spent in non-company laboratories. In addition, industry was going to provide €150–300 million to finance special R&D projects in the SNS. The fund will be managed with the MSC's regular competitive funding mechanism (i.e. the FIS). This is an example of a private financial contribution, with public management, to finance public-sector research (Sanz Menéndez, 2003).

[19] CNIO, "About the CNIO," http://www.cnio.es/ing/about/antecedentes.asp (as of September 26, 2008).

The Innovative Medicines Initiative (IMI) is a unique public–private partnership between the pharmaceutical industry (represented by the European Federation of Pharmaceutical Industries and Associations) and the European Community (represented by the European Commission). IMI's overall goal is to make Europe the world leader in pharmaceutical research for the benefit of the economy and society, by removing research bottlenecks in the current drug development process. The IMI was formally adopted by the Council of the EU in December 2007, and has a budget of €2 billion to fund pan-European public–private partnerships in pharmaceuticals.[20] Historically, IMI grew out of the European Technology Platform on Innovative Medicines. The platform was launched under the 6th Framework Program for Research as a gathering of stakeholders, led by the pharmaceutical industry.

The Spanish Technological Platform for Innovative Medicines is supported by Farmaindustria, which aims to encourage biomedical research into new medicines through the cooperation of all agents: industry, regulators from the various public administrations, health managers, basic and clinical researchers, scientific societies, patients and their associations, and suppliers of goods and services related to research.

[20] See also IMI's Web site: http://imi.europa.eu/index_en.html and http://imi.europa.eu/docs/imi-factsheet_en.pdf (as of September 26, 2008).

Research Evaluation

Challenge I: Barriers for career advancement in science

Challenge II: Coordination of National Strategies with the autonomous communities' regional policies.

Autonomous communities are growing R&D policy players
(e.g. by setting regional agencies duplicating the national one).

Important points for health research

- ISCIII to become an agency both funding and performing research
- CSIC also to be converted to a national agency improving both research and fund management

The perceived lack of meritocracy or competitive funding and the endemic nepotism that is a feature of Spanish academia is a challenge for the whole Spanish research landscape. Indeed, Schiermeier (2004) notes that, "traditionally, Spain has been a difficult place to start a career in science—especially for non-natives. The civil-servant status of most faculty staff makes the system hard for foreigners to penetrate." He continues, "requirements for obtaining grants keep changing."

In a similar fashion, "the main barrier for career advancement is the transition from a temporary to a permanent position," and "internal promotion is also normal in Spanish academia and for many advertised positions the candidate has been chosen beforehand. Professors often handpick their students for research posts. It can thus be crucial to have a network to help kick-start the career. It has been noted that in Spanish academia one needs very stable relations with one's nearest academic environment in order to have the opportunity to be promoted."[21] Unfortunately, this situation has all characteristics of a vicious circle: poor research spending and inefficient funding due to lack of competition leads to nepotism or endogamic university departments, and vice versa.

Another challenge that Spain faces with respect to R&D and innovation policy is the need to clarify the role of the regions in the national strategy and to ensure that institutional coordination and planning work to serve the national interest. Although coordination has improved in several areas, there is still a certain risk of wasteful duplication, lack of synergy, and overlap or even conflict of objectives. Each region has its own universities, its

[21] European University Institute, "Spain – Academic Career Structure," http://www.iue.it/MaxWeberProgramme/AcademicCareers/Spain.shtml (as of September 26, 2008).

own science parks, and its own innovation agency. The Spanish government envisages a new structure to promote cooperation between regional governments to develop joint approaches to the same problems, as opposed to the duplication of initiatives. Indeed, the commitment of regional authorities is necessary even if the main role lies with the national government. However, regional political interests are very often becoming a serious burden for the continuity of the national strategy.

Indeed, regions have strengthened their role as institutional players in science and technology policy and performance. Apart from the national evaluation bodies (e.g. CDTI for technical research, National Evaluation and Foresight Agency for scientific research, ISCIII for biomedical and health sciences), and the SNS research body set up for university quality and accreditation (National Agency for Quality Assessment and Accreditation), several autonomous communities have created their own agencies for the assessment of the quality of research and universities (e.g. Andalusia, Catalonia, Madrid, and Valencia).

The Spanish government, in the context of the development of a new Public Agencies Act, has already approved the creation of new agencies related to R&D funding and promotion. The MEC will transfer some of the traditional units that manage support directly from the Ministry into an Agency of Public Support for R&D, whereas the MSC will change the status of the ISCIII into an agency that both funds and does research. The proposed transformation of the CSIC is also covered by the new Act. The new regulation should increase flexibility in the management of public funds, improving efficiency in the use of resources and improve the quality of implementation of R&D funding and promotion (FECYT, 2007).

Research Evaluation within the INGENIO 2010 initiative

- The government has introduced a new mechanism for monitoring and evaluating the National Research Plan
- Implementation of the Integrated Monitoring and Evaluation System (SISE) for retrospective assessments of the results of R&D programmes
- Until now, the ex-post evaluation of R&D programmes has been rare and non-systematic
- Continuous evaluation is fundamental to revise and correct current actions and identify new ones

An integrated monitoring and evaluation system (*Sistema Integral de Seguimiento y Evaluación* [SISE]) has been defined for the evaluation of the INGENIO 2010 strategic initiative. This standard system is used for the evaluation of the main policies and programmes related to R&D at a national level.

The SISE instruments are the collection of documents and information that must be produced regularly by the units and agencies with managerial responsibility regarding the progress of the programmes and actions, as well as on the R&D system or the diverse fields of science and technology. The SISE instruments shall include, for example, follow-up reports, reports monitoring R&D, and innovation indicators and evaluation reports. The analysis process will be as follows: programmes will be evaluated by groups of experts, who will then produce an annual report with their recommendations; these programmes will then be reviewed and approved by the CICYT.[22]

[22] ERAWATCH, "Ingenio 2010 Programme," http://cordis.europa.eu/erawatch/index.cfm?fuseaction=prog.document&uuid=7D87B2C4-B1DB-D569-419CB0503278006E (as of September 26, 2008).

Spanish Achievements in Health R&D

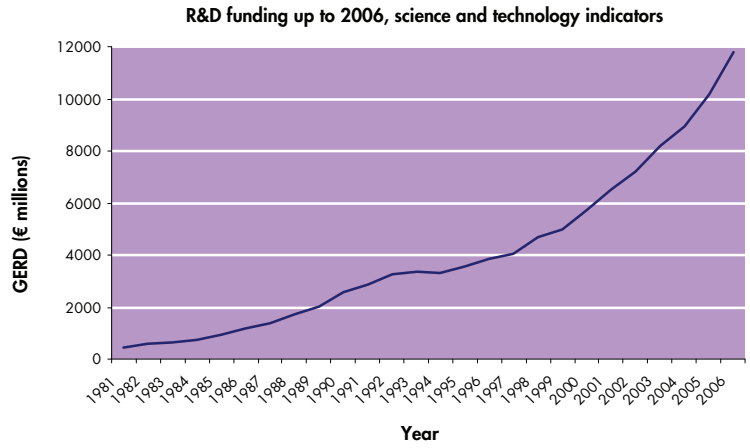
- Spain has a long history in health research including two Nobel laureates: Santiago Ramón y Cajal (1852–1934) won the Medicine Prize in 1906, Severo Ochoa (1905–1993) won the Medicine Prize in 1959
- An increasing number of publications in Science Citation Index journals in recent years
- An established trend of R&D funds greater than1% GDP during recent years and an increasing percentage for health and biomedical sciences research

Spain has a long history of health research. Santiago Ramón y Cajal, jointly with Camillo Golgi, won the Nobel Prize for Medicine in 1906 for recognition of their work on the structure of the nervous system. Severo Ochoa, jointly with Arthur Kornberg, won the Nobel Prize for Medicine in 1959 for their discovery of the mechanisms in the biological synthesis of RNA and DNA. Although, it should be noted that Severo Ochoa was also a U.S. citizen (he had an American passport) and carried out his research almost exclusively in Europe and the United States since emigrating from Spain in 1936.[23]

[23] See Nobelprize.org, "Severo Ochoa," http://nobelprize.org/nobel_prizes/medicine/laureates/1959/ochoa-bio.html (as of September 24, 2008).

Gross Domestic Expenditure on R&D

R&D funding in Spain is increasing on yearly basis



Source: INE (http://www.ine.es/en/inebmenu/indice_en.htm)

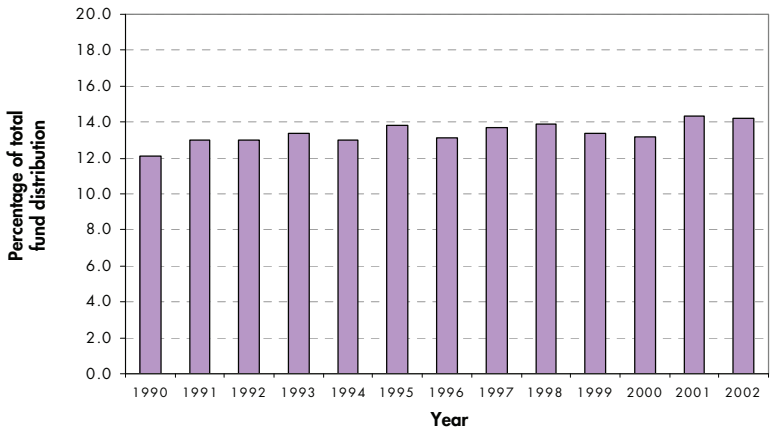
The total gross domestic expenditure on R&D (GERD)[24] in Spain has increased from 0.79 percent of GDP in 1995 to 1.12–1.13 percent of GDP in 2005, reaching well over €10 billion in 2005 and close to €12 billion in 2006 (OECD, 2007; and data from the National Statistical Institute [*Instituto Nacional de Estadística* (INE)]). Under the National Plan for R&D and Innovation 2008–2011, GERD investment is predicted to rise by up to 2 percent by 2010 (Presidencia del Gobierno, 2007).

During the past few years, Spain has achieved R&D funds that are consistently greater than 1 percent of GDP and are heading towards the 2 percent objective. At the same time, R&D funding in health research has been increasing on a yearly basis, reaching approximately 14 percent of total R&D funds. At present, Spain spends around 1.1–1.2 percent of GDP on R&D, which is significantly below the EU25 (1.8 percent) and OECD (2.26 percent) averages. Nevertheless, this current level represents a substantial increase from the levels of the previous decades. The share of total GERD financed by the business sector is 48 percent, whereas that financed by government is 41 percent, with 6.2 percent financed from abroad and 4.8 percent from other national sources. This distribution of the sources of financing for R&D, by contrast, has remained more or less stable since the mid-1990s. In terms of performance of GERD, the business sector contributes 54 percent, whereas the higher education sector provides 29.5 percent, and the government sector provides 16 percent of GERD. The government has pledged to increase R&D expenditure in the health sector as it seeks to restore Spain's competitiveness in this area.

[24] Total intramural expenditure on R&D performed on the national territory during a given period. It includes R&D performed within a country and funded from abroad but excludes payments made abroad for R&D.

Public Budget Spending for Health R&D

Health R&D funding is increasing as a percentage of total R&D funding in Spain. In 2001 it reached 14.3%.

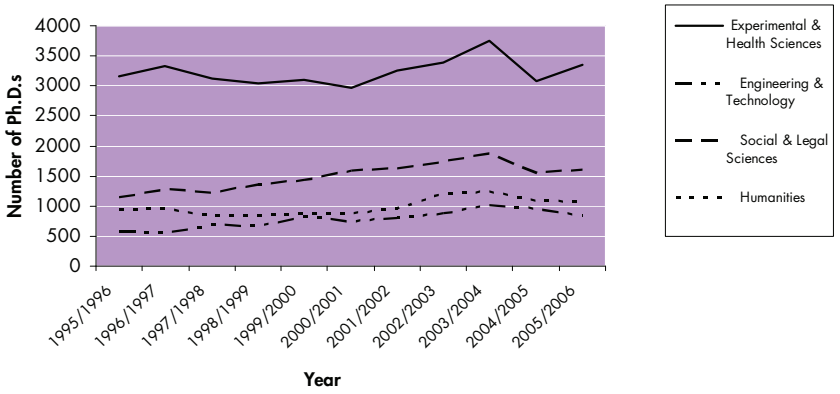


Source: MEC (2004), INE (http://www.ine.es/en/inebmenu/indice_en.htm)

During the past few years, total R&D funding in Spain is increasing steadily as a percentage of GDP. In addition, Spanish spending on health R&D is increasing as a percentage of the total distribution of funds. Indeed, data from the INE indicate that, whereas in 1990 the health R&D funding as a percentage of total R&D funding in Spain was approximately 12 percent, in 2001 and 2002 it reached well over 14 percent.

Ph.D. Awards in Spain by Research Area

The majority of the new Ph.D.s awarded in Spain are within the fields of Experimental and Health Sciences

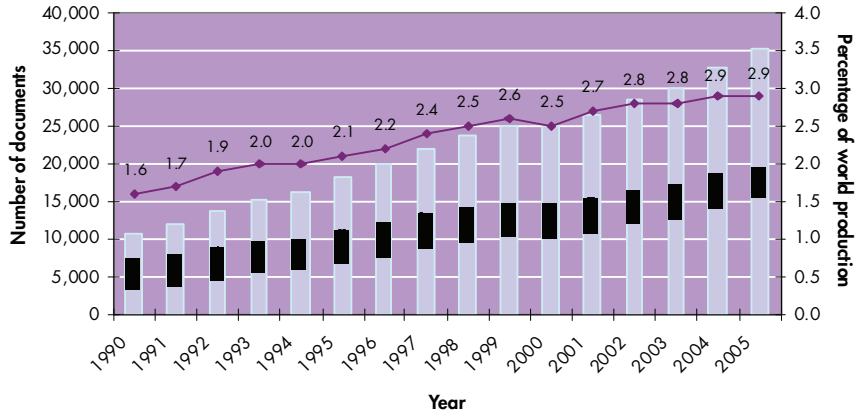


Source: INE (http://www.ine.es/en/inebmenu/indice_en.htm)

In Spain, the number of Ph.D. awards by research area is indicating a strong preference by young researchers for what is classified as "experimental and health sciences" by the INE. Indeed, data from the INE indicate that, in year 2005–2006, 3358 of 7159 Ph.D.s were from this class. In particular, there were 814 Ph.D.s in medicine (11.4 percent), 688 in biological sciences (9.6 percent), 583 in chemistry (8.1 percent), and 247 in pharmacy (3.5 percent). These four categories account for over 30 percent of the total number of Ph.D. awards in Spain for 2005–2006.

Number of Publications in International Scientific Journals

Research productivity has been increasing in Spain.



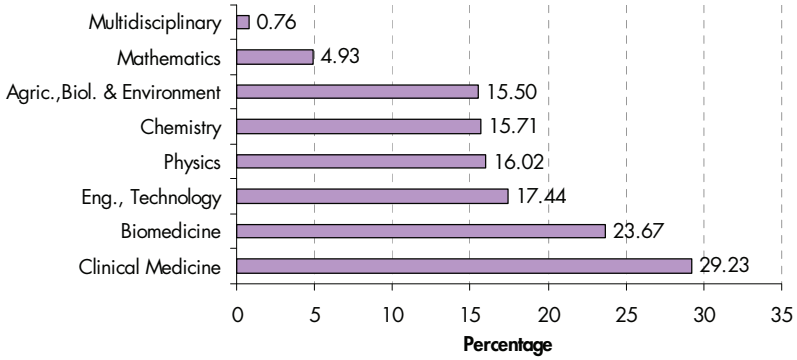
Source: COTEC (2007)

The number of publications in international journals has increased rapidly, from 10,688 in 1990 to 35,191 in 2005, indicating a trebling of scientific production. Furthermore, this significant growth in publications implies that the Spanish scientific production amounts to 2.9 percent of the world production in 2005, compared to a mere 1.6 percent in 1990.

Bibliometric analysis shows that after sustainable growth in research activity, Spain occupies the eleventh position in the world and seventh among the European countries in biomedical research production (i.e. publications in international peer-reviewed journals). Although Spanish contribution to world biomedical research production is 2.4 percent, it only accounts for 1.8 percent of the total number of citations. The Spanish health sector is responsible for nearly the half of the total biomedical output.

Publications by Field in Spain

Distribution by field of research productivity in international scientific journals as a percentage of total (2001–2005).



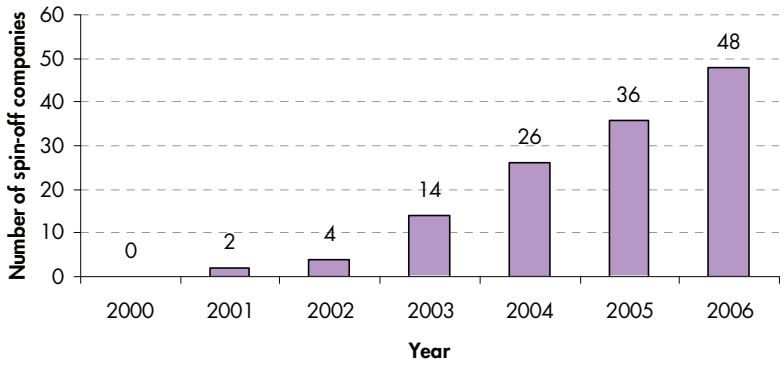
Note that Biomedicine and Clinical Medicine accounts for more than 50% of total.

Source: COTEC (2007)

Data from the COTEC Foundation's Annual Report (2007) indicate that, for the years 2001–2005, the distribution by field of research productivity (publications in international journals) has been particularly favourable for the biomedical sciences (23.67 percent of the total) and clinical medicine (29.23 percent of total) in Spain. Indeed, these two categories account for more than 50 percent of the total number of publications in this period in Spain (Camí, Suñén-Piñol, and Méndez-Vasquez [2005] provide a more detailed bibliometric map in biomedical sciences for Spain for 1994–2002).

Biotechnology Spin-off Companies

Evolution of new spin-off companies created by Spanish universities since 2000.



Source: Genoma España (2007)

Although R&D in Spain has traditionally followed an unstructured path built around regional locations and driven by factors and influences external to the country, the emergence of a fast-growing sector of spin-off companies (created from public institutions involved in R&D activities) from the public research system (especially in the biopharmaceutical sector), points to a change of model of development of the industry, on the national as well as the regional level (Todt et al., 2004).

Between 2000 and 2006, the biotechnology industry in Spain experienced an astonishing growth in the number of spin-off companies, 200 percent increase in turnover, and 750 percent increase in numbers of employees. Spain is a key player in R&D, spin-off companies, research, and collaboration. Additionally, the biomedicine field is one in which Spanish industries particularly excel, being ranked fourth in the EU15 in terms of scientific production, lagging only behind Germany, United Kingdom, and France. The increase in the number of spin-off companies is particularly important. Since 2003, approximately ten to twelve biotechnology spin-off companies have been created by the Spanish public universities each year.

Finally, the macroeconomic impact of biotechnology is approximately 0.6 percent of the Spanish GDP and is a rapidly growing field with respect to the average EU15 growth (Genoma España, 2007).

Outlook

Outlook: Future Policy Challenges

- Keep up with increasing number of publications/patents
- Keep up with established trend of GERD funds, from >1% of GDP to reach 2% by 2010
- Identify reasons for brain drain of young researchers
- Lack of private initiative (funding) compared to countries like United Kingdom or France
- Reform of university hospitals in Spain and increase the number of biomedical research institutions
- Create a clear professional career for the biomedical researcher
- Increase the numbers of medical doctors who divide their activity between practice and research

As we have seen in the previous sections, health and medical research in Spain has experienced a substantial growth during the past 15 years. However, there are several challenging issues that could contribute to the improvement of the Spanish health research system in the near future.

For example, Spain needs to keep up with the increasing number of publications and patents to close the gap on the leading countries in the health research field and to achieve the INGENIO 2010 strategic initiative's objectives, such as GERD reaching 2% of GDP by 2010.

Furthermore, Spain has to cope with the brain drain of young researchers who move abroad towards better laboratories and a more secure professional career as a biomedical researcher. The lack of private funding compared to other European countries (i.e. United Kingdom, France) is one reason. Identifying more specific reasons, apart from the financial ones, is imperative for the continuous growth of this research field.

Another important step that has to be taken is the reform of the institution of the university hospital, in addition to an increase in the number of biomedical research institutions and in the numbers of medical doctors who divide their activity between practice and research. These last actions have to be taken conditionally on the capacity of coordination and organisation of the Spanish research system from a country perspective (with other research centres and departments and autonomous regions) and internationally

(particularly within the EU), and by setting objectives and establishing the means to achieve these targets.

In summary, there is a need for sufficient funding, a well-defined professional research career structure, and an increase in the number of research institutions (Universia, 2007).[25]

[25] Universia, "Especial—Investigación en Medicina Clínica en España: panorama de luces y sombras," http://investigacion.universia.es/seccionEspecial.jsp?idEspecial=40&idSeccion=4674&title=INVESTIGACION-MEDICINA-CLINICA-ESPAÑA-PANORAMA-LUCES-SOMBRAS&idSeccionAd=8 (as of September 11, 2008).

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