ANNUAL REPORT 2000

Farmaindustria

ANNUAL REPORT

2000

Farmaindustria

Contents

Message from the President

In view of the profound changes FARMAINDUSTRIA underwent in 2000, it may safely be said that our Association has reached a crossroads. On 25th October 2000, the General Assembly elected new governing bodies for the coming two years and, for the first time in FARMAINDUSTRIA'S long history, a representative from a foreign-owned company took office as President. There could be no clearer sign of our Association's maturity.

A new course naturally entails fresh challenges and a shift in our objectives. Early efforts have centred on ensuring a rational, well-organised transition, resolving outstanding issues with the Health Authorities, and setting in motion a process of internal change by recruiting new staff. Having successfully completed this initial stage, we can now move forward to focus on the Association's strategic activities for the next two years.

For the first time, FARMAINDUSTRIA'S has drawn up, debated and approved a strategic plan which defines our main priorities. Four guiding principles will set the tone of our actions henceforth: (1) a pro-active approach in dealings with Government to help generate a climate of regulatory predictability and certainty; (2) interaction with society, stressing the social value of medicines and the sector's contribution to the economy and to industry; (3) service to members, increasing their involvement in the life of the Association; and (4) internal organisation, based on the modernisation and adaptation of our structures to achieve maximum efficiency.

Let us not suppose, however, that FARMAINDUSTRIA'S activity in 2000 has been confined to organisational issues. Throughout the year, the Association has carried on an intense activity, producing the results in the scientific and technical, economic and international fields that are described later in this annual report. It is enough here to mention FARMAINDUSTRIA'S participation in numerous Spanish and international committees, and the reports and position papers it has issued as the representative of the pharmaceutical industry.

One of the year's main achievements was the successful conclusion of arduous negotiations with the Ministry of Health and Consumer Affairs in the agreement signed on 8th March 2001. This marked the end of a prolonged dispute with the Health Authorities in connection with the pharmaceutical industry's mandatory contributions to the containment of State pharmaceutical expenditure and the funding of public biomedical research in Spain.

Throughout this process, the industry has shown itself open to dialogue and conciliation with a view to reaching solutions that will ensure the sustainability of the National Health System in Spain. FARMAINDUSTRIA will maintain this attitude in the negotiations for the pharmaceutical expenditure Stability Pact, which the Administration needs to close with all interested parties during 2001. The pharmaceutical industry is more than willing to respect the State's budgetary concerns, but considers that these must be made compatible with the health care, economic and industrial interests which underlie pharmaceutical expenditure and are at the root of its natural tendency to grow. The industry's aspirations in this area are crystal clear in light of the complexity of the market and the high level of State intervention, factors which generate considerable insecurity.

Nonetheless, we should not obsession with pharmaceutical expenditure to blind us to the overall concept of health care and related issues. It is a little remembered fact that access to medicines in Spain is among the best in the developed countries, and at a cost which is lower than in most European countries. Thus, public health care expenditure, which is frequently linked with spending on medicines, is almost 50% below the European average, even as growth in the numbers of protected patients, the introduction of new treatments and the decline in patient responsibility for health care funding push up public spending. In the last analysis, the advanced societies have made health care a top priority, and the pharmaceutical industry will need to respond this demand in a climate of increasing globalisation and international competition.

Access to medicines in Spain is among the best in the developed countries, and at a cost which is lower than in most European countries

Despite the strong performance of the industrialised economies —including Spain— in 2000, the pace of growth has slowed, especially in Europe due to the budget control commitments made by the EMU member States. The Spanish pharmaceutical market (retail pharmacies) was not immune to these pressures, with growth of only 8.8% in 2000, the lowest since 1994. The Government's latest raft of measures have already had an impact and will continue to affect the industry for some time to come. This cannot be ignored if and when new demands are made of the pharmaceutical industry.

In a high-tech industry such as pharmaceuticals, R&D is a key business driver, yet it is becoming ever more costly and demanding. In view of the contribution made by medicinal and pharmaceutical research to the well-being of citizens and to the economy in general, society needs to recognise that it represents a strategic asset, whose importance outweighs short-term budgetary considerations. In this context, FARMAINDUSTRIA's mission is to achieve convergence with Europe in the future, progressively narrowing Spain's continuing structural deficit within a framework of co-responsibility for funding, regulatory certainty, growth and business stability.

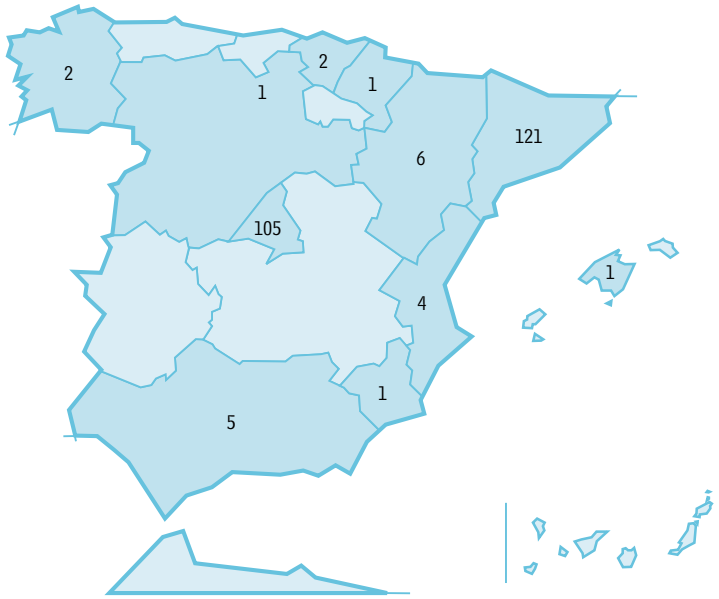
Jesús Acebillo Marín President of FARMAINDUSTRIA

The year 2000 saw a turning point for Farmaindustria as we entered a new stage which will bring new challenges, opportunities and new goals.

1 FARMAINDUSTRIA in 2000

1.1 Membership

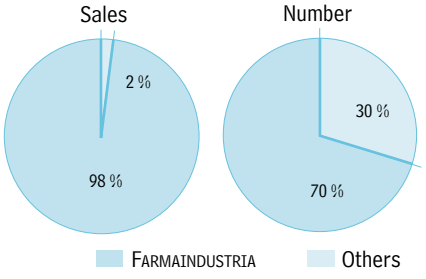
At 31 December 2000, the membership FARMAINDUSTRIA comprised 249 pharmaceutical companies, 9 more than the previous year. The geographical distribution of member companies was as follows:



FARMAINDUSTRIA members represent 70% of the pharmaceutical companies operating in Spain (i.e. total manufacturing and/or marketing companies making sales through retail pharmacies), which account of 98% of sales.

Classification of pharmaceutical companies

SPANISH	123	INTERNATIONAL	126
Majors	10	Majors	26
Mid-size	8	Mid-size	31
SMEs	105	SMEs	69
TOTAL 249			



1.2 Organisation

In October 2000 elections were held for the Association's governing bodies. The General Assembly ratified the appointment of the new Board and Steering Committee, and Jesús Acebillo took office as the new President of FARMAINDUSTRIA in place of Enrique González Hervada. The Association wishes to express its gratitude to Mr. González Hervada for all his efforts on our behalf.

Meeting of the Steering Committee, May 2001

The members of the Association's governing bodies to date (May 2001) are:

STEERING COMMITTEE

PRESIDENT

D. Jesús Acebillo Marín NOVARTIS FARMACEUTICA, S.A.

VICE-PRESIDENTS

D. Rafael Foguet Ambrós FERRER INTERNACIONAL, S.A.
D. Manuel García Garrido BOEHRINGER INGELHEIM, S.A.
D. Jorge Gallardo Ballart ALMIRALL PRODESFARMA, S.A.
D. Javier Urcelay Alonso DU PONT PHARMA, S.A.

DIRECTORS

D. José Miguel Colldefors Martínez* GLAXO WELLCOME, S.A.
D. Rafael Giménez Cuesta FARMA LEPORI, S.A.
D. Rafael Juste Sesé JUSTE, S.A. QCO. FCA.
D. Javier Peris Musso S.A.L.V.A.T., S.A., LABORATORIO
D. Albert Esteve Cruella DR. ESTEVE, S.A., LABORATORIOS
D. Peter Hug** ROCHE FARMA, S.A.
D. John A. Keeler SANOFI-SYNTHELABO, S.A.
D. Juan Uriach Torelló J. URIACH & CIA., S.A.

ADVISERS

D. Javier Ellena Aramburu LILLY, S.A.
D. Javier Font Salgado FARDI LBO.DE APLIC. FARMACODINÁMICAS, S.A.

*Since 17/01/01, replacing Carlos Galdón Cabrera

** Since 18/04/01, replacing Klaus P. Ringer

General Assembly, October 2000

From left to right: Javier Urcelay Alonso, Manuel García Garrido, Jesús Acebillo Marín, Rafael Foguet Ambrós and Jorge Gallardo Ballart

BOARD OF GOVERNORS

Chairman

D. Jesús Acebillo Marín NOVARTIS FARMACÉUTICA, S.A.

Vice-chairmen

ALMIRALL PRODESFARMA, S.A. **D. Jorge Gallardo Ballart**
DU PONT PHARMA, S.A. **D. Javier Urcelay Alonso**
BOEHRINGER INGELHEIM, S.A. **D. Manuel García Garrido**
FERRER INTERNACIONAL, S.A. **D. Rafael Foguet Ambrós**

Committee members

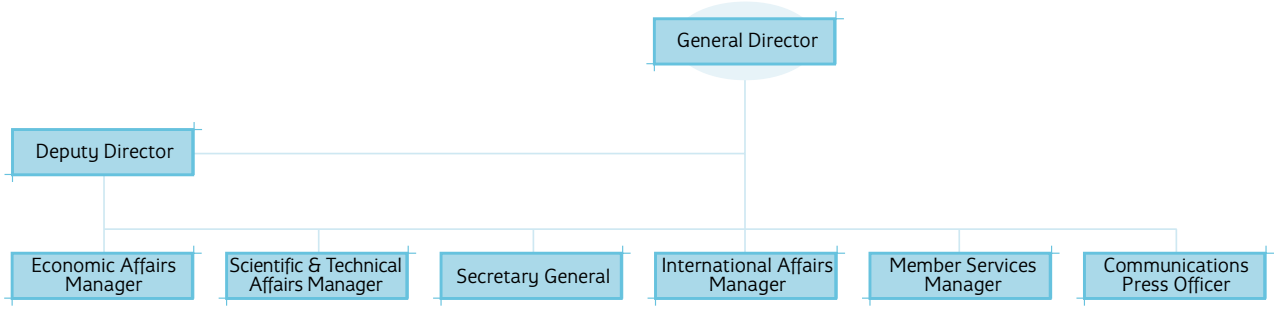
AMGEN, S.A. **D. Ramón A. Limiñana Soler**
ASTRA ESPAÑA, S.A., LABORATORIO **D. Carlos Trias Vidal**
DR. ESTEVE, S.A., LABORATORIOS **D. Albert Esteve Cruella**
FARMA LEPORI, S.A. **D. Rafael Giménez Cuesta**
J. URIACH & CIA., S.A. **D. Juan Uriach Torelló**
LESVI, S.A., LABORATORIOS **D. Enric Vallés Rodoreda**
MENARINI, S.A., LABORATORIOS **D. Joaquín Puig Corcoy**
PFIZER, S.A. **D. Emilio Moraleda Martínez**
S.A.L.V.A.T., S.A., LABORATORIO **D. Javier Peris Musso**
VIÑAS, S.A., LABORATORIOS **D. Antonio Buxadé Viñas**
LBO.DE APLIC. FARMACODINÁMICAS, S.A. FARDI **D. Javier Font Salgado**
CEPA SCHWARZ PHARMA, S.L. **D. Antonio Martín García**
FAES, S.A. **D. Eduardo Fernández de Valderrama**
GLAXO WELLCOME, S.A. **D. José Miguel Colldefors Martínez**
JUSTE, S.A. QCO. FCA. **D. Rafael Juste Sesé**
LILLY, S.A. **D. Javier Ellena Aramburu**
NORMON, S.A., LABORATORIOS **D. Jesús Govantes Esteso**
ROCHE FARMA, S.A. **D. Peter Hug** **
SANOFI-SYNTHELABO, S.A. **D. John A. Keeler**
ZAMBON, S.A. **D. Davide Sirtoli Lovati**

* Since 17/01/01. Previously Carlos Galdón Cabrera

** Since 18/04/01. Previously Klaus P. Ringer

EXECUTIVE ORGANISATION

In February 2001, Humberto Arnés Corellano took office as FARMAINDUSTRIA'S Director General. New blood has been brought into the Association's management team during the first half of 2001 and services have been reorganised in the following departmental structure:



Humberto Arnés Corellano	General Director
José María Hernández Vicente	Deputy Director General and Economic Affairs Manager
Emili Esteve Sala	Scientific and Technical Affairs Manager
Alberto Ferreiro Delgado	Secretary General
Javier Urzay Ramírez	Member Services Manager
Icíar Sanz de Madrid Ibrán	International Affairs Manager
Alfredo del Campo Martín	Communications. Project Manager
Julián Zabala Pino	Communications Press Officer

Humberto Arnés Corellano

At the beginning of 2001, FARMAINDUSTRIA moved to new offices at Calle Serrano 116 in Madrid.

1.3 Technical Activities

1.3.1. CODEM

The Committee for the Evaluation of Medicinal Products for Human Use (Comité de Evaluación de Medicamentos de Uso Humano – CODEM) is the associate body of the Spanish Medicinal Evaluation Agency responsible for advising on the technical and scientific affairs of the Agency's activities in connection with new drugs and other medicinal products.

Royal Decree 520/199 issued of 26th March 1999, by which the statutes of the Spanish Medicinal Evaluation Agency were approved, provides the appointment of one CODEM committee member by the Ministry of Health and Consumer Affairs, at the proposal of the pharmaceutical industry association.

CODEM obviously plays a key role in the authorisation process for new drugs and medicinal products, and it is therefore a invaluable for member companies to have a voice on the Committee through FARMAINDUSTRIA.

Accordingly, one of FARMAINDUSTRIA's main activities has been to prepare CODEM meetings thoroughly in order to secure positive evaluations for the new drugs and therapies brought before the Committee for examination. During the year 73 product referrals from the Medicinal Products Agency were reviewed and 38 reports were issued, while some twenty preparatory meetings were held with FARMAINDUSTRIA member companies.

1.3.2. Clinical Trials Advisory Committee

Together with other institutions involved in performance of clinical trials, FARMAINDUSTRIA participates in the analysis of the factors and conditions affecting the quality of clinical drugs research from the standpoint of all those parties involved in the develpment of these clinical trials. The Association also supports activities designed to maintain and promote first class practice and procedure in this area. These activities have been carried out in Catalonia.

A wide range of policy and position papers were issued and debated at the meetings of the Committee, outstanding the technical draft for the amendment of the Department for Health and Social Security Order dated 22 October 1992 concerning the accreditation of Ethical Committees for Clinical Research. This document, prepared by the Department of Health and Social Security, contains the proposed rewording of the Order in order to align requirements for existing Ethical Committee for Clinical Research and those that will be set up pursuant to the new international guidelines for good clinical practice agreed at the International Conference on Harmonisation. (ICH).

1.3.3. Good Laboratory Practice

Good Laboratory Practice (GLP) refers to the managerial organisation and conditions under which pre-clinical studies are planned, performed, monitored, recorded and reported. Application of GLP provides quality assurance, permitting government agencies to use study data and results in their assessment of the potential risks of chemical substances.

The principles of good laboratory practice and the rules for their application in pre-clinical trials on chemical substances and agents have been transposed into Spanish legislation through Royal Decree 1369/2000, which amends Royal Decree 822/1993 of 23 May 1993.
The quality and reliability of the pre-clinical health and environmental safety studies used as the basis for risk evaluation is an issue of singular concern both to the Health Authorities and to the pharmaceutical industry, and the reason why the OECD member States drew up the principles for the conduct of testing procedures.
With the objective of preventing disharmonies in data acceptance programmes from affecting international trade in chemical substances, the OECD member States have sought to ensure international harmonisation of testing methods and good laboratory practice. Thus, an international panel of experts was set up under the special programme for the control of chemicals in the early 1980s to draw up the "OECD Principles of Good Laboratory Practice" based on the management and scientific practices and experiences of the different countries. These principles were then adopted by the OECD Council. In 1995, a new panel was set up to review and update the principles and, since then, FARMAINDUSTRIA has worked closely with the competent Spanish health authorities on the design and implementation of compliance programmes.

1.3.4. Pharmacovigilance

Pharmacovigilance is concerned with the identification, assessment and prevention of risks associated with drugs once they are brought on the market. The scientific basis for this public health activity is pharmacoepidemiology, which may be defined as the science which studies the utilisation and effects of drugs in large number of people using epidemiological techniques, methodology and reasoning.
The pharmaceutical industry was originally placed under a legal obligation to participate in pharmacovigilance activities in Spain by the General Health Act, 1986. Subsequently, article 57.2 of the Medicinal Law Act, 1990 (Law 25/1990) established a compulsory reporting requirement for manufacturers and marketing authorisation holders, who must inform the health authorities of any unforeseen or toxic side-effects of the drugs they produce or sell wherever such circumstances come to their attention.
In 1990 a working group was set up between FARMAINDUSTRIA and the Spanish Health Authorities to address the issue of adverse reactions and frame rules and regulations for their reporting. This working group, which comprises pharmaceutical industry experts appointed by FARMAINDUSTRIA and Health Ministry representatives, continues with its task nowdays and is an outstanding example of ongoing collaboration. The group drew up a

number of documents to create a regulatory framework for pharmacovigilance activities, including the *Guide for the Pharmaceutical Industry: Pharmacovigilance in the New European System* issued in 1995. The objective of this document was to adapt the new European guidelines set out in Chapter V of the NOTICE TO APPLICANTS to the particularities of the Spanish market. Intended as a temporary guide, its aim was to prepare the ground for the new regulatory scenario was established with the publication by EMEA of new European pharmacovigilance guidelines in the *Notice to Marketing Authorisation Holders,* the reference document detailing all of the industry's pharmacovigilance tasks and responsibilities.

In April 2000, the Spanish Medicinal Evaluation Agency published Circular 4/2000 concerning Pharmacovigilance reporting procedures between the pharmaceutical industry and the Spanish Medicinal Products Agency in connection with medicinal products for human use. This Circular contains the latest European recommendations and updates the 1995 Guide, which has until now been the reference document for pharmacovigilance matters.

1.3.5. Biological Weapons

FARMAINDUSTRIA first contacted the Spanish Foreign Ministry's Department for the United Nations, Security and Disarmament in connection with the foreseeable ratification of the Convention on the Prohibition of Bacteriological and Toxin Weapons Verification Protocol in 1998.

The terms and conditions of the Protocol will become applicable in Spain upon ratification. Accordingly, any life sciences industries working with listed biological agents, as well as companies equipped with fermentation capacity exceeding the defined limits or have level 3 and 4 laboratories will be required to report on the nature of their facilities. These companies may also be subject to on-site inspection and investigation by international agencies.

With the aim of protecting the industry's interests, FARMAINDUSTRIA maintains close contact with the working group on the prohibition of biological weapons (GRUPABI) set up by the Foreign, Health, Education, Agriculture and Defence Ministries .

During 2000, the European, American and Japanese pharmaceutical industries agreed a common position in support not only of the objectives of the Convention on the Prohibition of Biological Weapons, which has been in force since 1975, but also of any additional enforcement and compliance measures designed to reduce the potential risk of deviation of any biological agents could be used in armed conflicts.

1.3.6. Royal Pharmacopoeia

The Pharmacopoeia codifies the specifications which drugs and the raw materials used in their manufacture must comply with. As an official document, it is therefore of prime importance for quality assurance in the manufacture and sale of drugs and for the protection of consumer health. FARMAINDUSTRIA through its representative on the National Commission for the Royal Pharmacopoeia, took part during 2000 FARMAINDUSTRIA in the

preparation of Spanish monograph studies of European scope as in the framing of the draft Royal Decree amending Royal Decree 294/1995.
The new legislation will transfer responsibility for preparing, updating and publishing the National Formulary and the Royal Pharmacopoeia from the Directorate General for Pharmacy and Health Products to the Spanish Medicinal Evaluation Agency.
The Royal Pharmacopoeia supplement for 2000 was published and preparatory work started on the supplement for 2001, which is scheduled to come into force in May of the current year.

1.3.7. Advertising standards commissions

The provision for the promotion of medicines in Spain is regulated basically through Royal Decree 1416/1994, which governs advertising of medicinal products for human use, transposing Directive 92/28/EEC of 31 March 1992 into Spanish Law.
The Royal Decree defines two types of advertising:

- Information on prescription medicines targeting health care professionals, which might be exercised via the distribution of free samples, sponsorship of scientific events, advertisements in professional journals, and so on. These activities must be reported to the regional health authorities.
- Information targeting the general public. Advertising in this category is restricted to over-the-counter medicinal products for the treatment of minor symptoms and ailments. National campaigns must be authorised by the Directorate General for Pharmacy and Health Products and local campaigns by the relevant Regional Government health authorities.

Advertising campaigns are initially considered by the Committee for Preliminary Advertising Control. FARMAINDUSTRIA represents and defends the interests of member companies seeking the go-ahead for campaigns (CPS number) on this joint committee
FARMAINDUSTRIA also works closely with ANEFP (the Spanish OTC Association) through its Advertising Self-Regulation Committee to examine and supervise campaigns and make recommendations to companies seeking Government authorisation for advertising.

1.3.8. Regulatory matters

The regulations drafted by the various tiers of Government in Spain can have a major impact on the activities of the pharmaceutical industry. FARMAINDUSTRIA channels members' opinion on the issues at stake and presents a common position for the Association as a whole. During 2000, FARMAINDUSTRIA published positions in relation to 21 proposals for new regulations.

1.3.9. Working Group on Internet Advertising

FARMAINDUSTRIA participates in the working group on internet advertising set up by the International Federation of Pharmaceutical Manufacturers Associations (IFPMA) in view of growing public interest in health care issues and, specifically, patients' desire to learn about new treatments and therapeutic innovations. In this context, direct to consumer

advertising has become a priority issue for the pharmaceutical industry. This concern should not, however, be viewed as a matter of pure commercial interest, since it is consumers and patients' associations themselves who have taken up the demand for consolidation of the right to know. The industry is decisively in favour of using the internet to deliver information on medicinal products to the benefit of both patients and health care professionals. The potential benefits, in terms of providing consumers with access to previously unavailable information, outweigh the risks, although the industry is, naturally, concerned about the quality of information from uncontrolled and ill-informed sources operating outside the limits imposed by codes of ethics. Because of this, IFPMA and its member associations have insisted that proper mechanisms be established to ensure that the information made available to patients is factual and reliable.

The current regulatory framework in Europe prohibits the pharmaceutical industry from providing consumers with information on prescription medicines.

It is therefore the industry's position that the Advertising Directive (Directive 92/28/EEC) should be interpreted in a more liberal sense in order to achieve the very flexibility in the regulations recommended by the European Commission, which is currently debating the issue in its pharmaceutical Committee. The industry is in favour of self-regulation for internet information, since it already has a long history of successfully applying codes of good practice to commercial and promotional activities, as well as framing guidelines and standards for product information.

The industry has proposed measures to ensure that information published on the internet is truthful, factual and reliable, while supporting regulatory harmonisation in accordance with the principle of proportionality with the aim of regulating responsible direct to consumer communications.

1.3.10. FORCEM (Spanish Continuous Training Foundation)

The 2nd National Continuous Training Agreement signed in 1996 assigned a key role in the collective management, monitoring and control of State-sponsored continuous training activities to sector and regional Parity Committees formed by representative business and trade union organisations. These Committees are created ad hoc for each industry and region with the mission of optimising the implementation of the Agreement.

As the main pharmaceuticals industry association, FARMAINDUSTRIA forms part of the chemicals sector Parity Committee, in which it defends member companies' interests in relation to training programmes, reporting on implementation and advancing proposals within the wide scope of the Committee's responsibilities.

In connection with the financial awards programme for 2000, FARMAINDUSTRIA channelled information on the terms and conditions of grants and subsidies to target organisations, providing them with orientation regarding priorities and the requirements of application procedures. The basic objective of this work was to ensure that the Association's members would have full access to State funding for their training plans.

1.3.11. On-the-job training in the pharmaceutical industry

As a member State of the European Community, Spain is bound by the terms of Directives 432/85/EEC and 433/85/EEC, which refer to the syllabus and requirements for graduate qualifications in Pharmacy. Pursuant to the legislation, all undergraduates must undergo six months' laboratory practicals, which may be carried out in the pharmaceutical industry.
Once the Directives were transposed into Spanish Law by Royal Decree 1607/1989, a number of universities contacted FARMAINDUSTRIA with a view to reaching enabling agreements allowing students to undertake their traineeships in pharmaceutical laboratories in Spain.
The first such framework agreement was made between FARMAINDUSTRIA and the Universidad Complutense de Madrid in 1991 to set up a specific training programme for students covering all aspects of drugs research and development, as well as production, quality control and marketing of medicinal products.
The enthusiasm this scheme has generated for both parties has prompted FARMAINDUSTRIA to make further agreements with the Universidad Complutense de Madrid and with the Universidad San Pablo-CEU (Madrid) in connection with integrated training of future pharmacy graduates.
During 2000, a total of 19 companies accepted 61 students for the on-the-job training programmes announced, supervised and co-ordinated by FARMAINDUSTRIA.

1.3.12. Scientific conferences and seminars

Scientific courses are a necessary part of the Association's activities. During 2000, FARMAINDUSTRIA sponsored the organisation of the five-day seminar *Clinical Trials in Spain* held between 21st and 25th August at the Menéndez Pelayo International University in Santander. Also, the Association once again sponsored the annual conference in La Granda (Asturias), which was this year entitled *The 21st century: Scientific and social challenges*.
Conference activities will continue in 2001 with the objective of promoting and maintaining the pharmaceutical industry's reputation for excellence in the professional circles at the forefront of medical and scientific innovation and its standing with the general public.

Palacio de la Magdalena, Santander, headquarters of the Menéndez Pelayo International University.

1.4 Activities in the European Federation of Pharmaceutical Industries and Associations

FARMAINDUSTRIA's international activities in 2000 mainly relates to the European Federation of Pharmaceutical Industry Associations (EFPIA). FARMAINDUSTRIA is a permanent member of EFPIA, and belongs to the first group of countries, together with the German, British, French, Swiss and Italian associations.

As a member of the EFPIA Board, which includes representatives from the other 10 national associations and 11 pharmaceutical companies (of the Federation's 45 member companies), FARMAINDUSTRIA contributes actively to the furtherance of priority areas defined by the General Assembly.

FARMAINDUSTRIA also participates in the formulation of recommendations and policy positions by the three Policy Committees at the heart of EFPIA: the Economic and Social Policy Committee, the Intellectual Property Policy Committee and the Scientific, Technical and Regulatory Policy Committee.

1.4.1. Economic and Social Policy

The mission of the Economic and Social Policy Committee is:

- To plan strategy for economic and health issues affecting the pharmaceutical industry as a result of the policies adopted and proposed by the EU and individual member States.
- To prepare position papers and make recommendations to the Board in order to implement the priorities established in EFPIA's operating plan.

This year, the Committee has focused on:

TRIPARTITE PROCESS

The tripartite discussions between the European Commission, member States and industry were resumed through two ad hoc Working Groups. The first of these was set up to design an experimental model for price deregulation of new medicines in 2 or 3 countries where price controls are applied. The team includes a representative from FARMAINDUSTRIA as well as one from the Spanish Ministry of Health. The mission of the second working group is to examine the scope and limitations of health outcomes research as a method for assessing the value of innovation in connection with reimbursement decisions.

Industry concerns about economic evolution of medicines were voiced in a joint paper issued in 2000 by EFPIA and the International Federation of Pharmaceutical Manufacturers Associations (IFPMA), which included contributions from FARMAINDUSTRIA and other national associations. This document sets out the principles that should guide industry practice in connection with pharmaco-economics.

Briefly, these principles are as follows:

- Marketing authorisation decisions must be based strictly on an evaluation of quality, safety and efficacy.

- Opposition to the mandatory application of economic evaluation of new drugs as a prerequisite for reimbursement decisions.
- Health care provision and costs vary from country to country. Because of this, the results obtained from the economic evaluation of medicines must be considered locally and not extrapolated across borders. The industry is therefore absolutely opposed to any pan-European directive for the economic evaluation of medicinal products.

FARMAINDUSTRIA and, indeed, the European industry as a whole represented by EFPIA are actively seeking price de-regulation and long-term reimbursement solutions. Progress has, however, been disappointing, at least partly because the member States remain convinced that deregulation will inevitably entail uncontrolled pharmaceutical expenditure, while the European institutions appear to lack the necessary political will. Nevertheless, both FARMAINDUSTRIA and EFPIA believe that the discussions held with the EU member States and the Commission have served to improve understanding of the pharmaceutical industry's needs.

In this context, the President of EFPIA, Jorge Gallardo, took part in the Symposium organised by Commissioner Liikanen on 11th December 2000 on the subject of Global Competitiveness in the Pharmaceutical Industry in support of the conclusions set out in the report on Global Competitiveness in Pharmaceuticals prepared by the European Commission's Directorate General for Enterprise. This report confirms the findings of other studies pointing to declining competitiveness in the European pharmaceutical industry compared with the United States. It relates this diagnosis partly to the impact of measures taken to contain pharmaceutical expenditure in the context of market fragmentation due to the existence of multiple institutions and differences in legislation. The diversity of European health systems thus represents a serious obstacle to the creation of a single market. The report recommends strengthening industry R&D, as well as advocating the introduction of mechanisms to boost market competition.

"FUTURES" PROJECT

In parallel with European-level tripartite discussions, EFPIA Board set up the so called Futures Project to stimulate national initiatives to progress towards long-term industry goals, such as price de-regulation, increased health care / pharmaceutical expenditure, greater recognition of innovation, and increased patient responsibility for health care funding. Italy, Netherlands, Switzerland and the United Kingdom were selected as the pilot countries for the project. In 2000 Germany and France joined as observers. For the moment, FARMAINDUSTRIA, as the representative of the Spanish pharmaceutical industry, has opted not to participate in the project, while keeping a close watch on developments through its involvement in the Economic and Social Policy Committee and other economic forums.

NATIONAL PRICING AND REIMBURSEMENT POLICIES

During the 1990s the member States of the European Union individually adopted a series of pharmaceutical price control measures and reimbursement policies with the aim of

containing expenditure. An overview of the situation as it stands in 2000 is as follows:

- General price cuts and/or freezes in 12 member States.
- Price-fixing systems in 11 member States by reference to prices in other European countries.
- Over the past two years, 5 countries formally adopted pharmaco-economic evaluation of medicines either as a mandatory part of the price-fixing mechanism (Finland) or as one of the reimbursement criteria (Holland, Norway, Portugal and the United Kingdom).
- Reference price systems in 6 countries (Denmark, Germany, Holland, Norway, Spain and Sweden), which resulted in an overall drop in prices when introduced.
- Fixed growth targets for pharmaceutical expenditure. These systems make the industry responsible (either individually or collectively) for budget overruns either through pay-back mechanisms or direct tax on sales.
- Extensive delisting (Belgium, Greece, Italy and Spain) and changes in co-payment rules (Denmark, Finland, Germany, Italy and Sweden).
- Compulsory prescribing practices to contain pharmaceutical demand, either through the allocation of indicative prescribing budgets, or through the implementation of guidelines or surveillance systems to identify excessive prescribers.
- Generic substitution (Denmark, Finland, Sweden, France and Switzerland).

The agenda of the Economic and Social Policy Committee has been marked not only by the task of monitoring expenditure controls, but also by two significant trends:

- Market access delays affecting medicinal products and increasing use of pharmaco-economic evaluation criteria.
- The increased parallel trend due to the downward spiral of pharmaceutical prices in some countries, with price-fixing based on the lowest European price.

1.4.2. Intellectual Property Policy

The Intellectual Property Policy Committee has a three-fold mission:

- To defend high levels of intellectual property protection for the pharmaceutical industry both in Europe and worldwide.
- To work towards the recognition of IP rights in all agreements the EU makes with third parties.
- To co-ordinate actions in defence of IP rights with non-governmental organisations.

COMMUNITY PATENT

In July 2000, the European Commission approved the proposal for a Regulation creating a Community patent. Key aspects are as follows:

- The European Patent Office will issue the Community patent.
- European and national patents will co-exist with the Community patent system.
- The Community patent system will aim to reduce costs, fees and translations.
- Litigation concerning breaches and validation of Community patents will be resolved by a new, centralised and specialised Community tribunal.

INTERNATIONAL INTELLECTUAL PROPERTY ISSUES

Since the Ministerial Conference of the World Trade Organisation (WTO) in Seattle and the entry into force of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPs) for developing countries on 1st January 2000, one of EFPIA's main priorities has been to obtain EU support for full and timely TRIPs implementation.

The highly competitive international environment makes essential that the EU authorities support the European pharmaceutical industry's capacity to perform R&D activities by enhancing their ability to operate and compete in foreign markets. In this regard, the TRIPs agreement, which establishes minimum standards for intellectual property rights, was one of the outstanding achievements of the Uruguay Round.

The Intellectual Property Policy Committee, with the help of FARMAINDUSTRIA and other national associations, has worked closely with EU institutions to ensure that the provisions of the TRIPs agreement are properly implemented. The European pharmaceutical industry welcomes the European Commission's commitment of principle that in any new round of WTO negotiations it will oppose any lowering of existing standards, seek further progress with TRIPs implementation and resist any proposals to alter the transition timetable.

EXHAUSTION OF TRADEMARK RIGHTS

In February 1999, a report on the economic consequences of international exhaustion in the area of trademarks was prepared for the European Commission. This report concentrated on consumer goods, excluding pharmaceutical products because of the complex implications of price intervention in the member States. As the number of member States calling for a change of regime from Community exhaustion of trademark rights to international exhaustion grew (the original group formed by Sweden, Finland, Denmark and Netherlands were soon followed by the United Kingdom and Ireland), the national associations, co-ordinated by EFPIA designed an action plan to oppose the proposed move.

Following the Internal Market Council of 25th May 2000, EFPIA supplemented its original position paper on the issue with an economic study showing that up to 20% of the total European pharmaceutical market could be vulnerable to parallel imports as a result of international exhaustion.

The co-ordinated action taken by the industry as a whole was successful in persuading the European Commission not to propose a change in the current system. The Commission in fact adopted the industry's arguments, stressing that a change to international exhaustion would not significantly reduce prices for most consumer goods.

WORKING GROUP ON GENERICS

In view of the increasing activity of EFPIA's corporate members in the generic medicines market, the EFPIA Board approved the setting up of a working group to deal specifically with the related issues.

The working group comprises representatives of both research-driven companies that also have generics divisions and of national associations, including FARMAINDUSTRIA. Its mandate is to work in tandem with European institutions and health authorities to promote balanced growth in the market for generic drugs without discouraging medicines research

and innovation, thereby contributing to the development of a strong European pharmaceutical industry, in which generics have an important role to play. The group also aims to promote a high level of quality for the generic medicines produced in all the EU member States and to achieve a better balance in the pharmaceutical market as a whole. In the course of 2000, the working group produced two position papers, the first of which addresses the issue of generic substitution and the second regulatory data protection, an area in which the current situation favours the interests of neither generics manufacturers nor research-driven companies.

1.4.3. Scientific, Technical and Regulatory Policy

The mission of the Scientific, Technical and Regulatory Policy Committee is:

- To guarantee that marketing authorisation procedures provide the fastest and most effective access to market, based on a pragmatic approach according to with the needs of the pharmaceutical companies.
- To uphold the highest possible standards for the evaluation of marketing authorisation and ensure continued international recognition for pharmaceutical assessments and authorisations obtained in Europe.
- To ensure that technical and regulatory requirements do not restrict growth in the pharmaceutical industry.

ORPHAN DRUGS

In mid-1996, the European Commission first presented a draft Regulation to encourage the development in the EU of pharmaceuticals for the treatment of approximately 5,000 diseases classified as "rare". The draft has since passed through the whole of the European legislative procedure and was formally adopted by the Council and the European Parliament in December 1999.

FARMAINDUSTRIA welcomes the final text because it places pharmaceutical companies operating in Europe on an equal footing with companies in the US and Japan, where orphan drug laws have been in effect for over eight years now.

EUROPEAN REGISTRATION PROCEDURE

FARMAINDUSTRIA, like other associations in the European Federation, regularly collects data for the joint survey on the performance of the centralised registration procedure undertaken by the European agency for the Evaluation of Medicinal Products (EMEA) and EFPIA. These data are used to build up a picture of the situation of the centralised procedure on the basis of performance indicators. Despite a gradual improvement, a series of worrying issues for the pharmaceutical industry remain, such as the increasing number of market withdrawals and negative opinions, as well as the length of the European Commission's decision-making process.

Special workshops have been held on the basis of the findings from the survey in order to develop concrete proposals to improve weaknesses in the procedure. These Efpia-Info workshops, the most recent of which was held on 20th November 2000, also contribute to the improvement of the European registration procedure as a whole.

In March 2000 it was decided to carry out a similar survey on the Performance of the Mutual Recognition Procedure (decentralised procedure) for applications filed after January 1998. The results of this survey were published at the end of August 2000. Among other issues, it was noted that the mutual recognition procedure had failed to progress due to poor co-ordination and interaction between the member States, lack of transparence and the scarcity of resources.

FARMAINDUSTRIA and the other national associations have been active in the search for solutions to certain specific issues: how to facilitate the repeat use of MRP, encourage multiple applications, eliminate additional national requirements, obtain true mutual recognition of assessments between member States, reduce unilateral withdrawals and, finally, avoid delays in national marketing authorisations.

EVOLUTION OF REGULATORY STANDARDS

There is a growing move among some EU authorities to call for data evaluating the benefits of new drugs in relation to existing products. This would add to the traditional criteria of quality, safety and efficacy an additional, consideration depending not on the nature of the innovative product as such but on the market environment. In order to forestall untoward developments in this regard, the EFPIA Board decided to set up a task force to examine the issue in detail.

In considering relative benefit assessment as an additional requirement to gaining marketing authorisation for new products over and above the standard criteria of quality, security and efficacy, the competent authorities are changing the rules governing the registration of medicinal products in the EU. Such a move could have a negative impact on the research and development of new therapies, resulting in damage to public health over the long term.

INTERNATIONAL CONFERENCE ON HARMONISATION (ICH)

In its ten years of operation the ICH has brought together scientific experts from the pharmaceutical industries and health authorities from Japan, the US and Europe to harmonise global technical standards for the development and registration of new medicinal products.

The work of the ICH has been oriented towards the formulation of a common technical information package suitable for submission in any of the three ICH regions: the Common Technical Document (CTD) for new product applications.

A major tripartite consensus on several modules of the three parts of the CTD (quality, safety and efficacy) was reached at the end of 1999, and the CTD was completed towards the end of 2000. All of the national associations including FARMAINDUSTRIA have continued to lend their support to the activities of the ICH following the 5th International Conference on Harmonisation, which took place in San Diego, USA, in 1999.

1.4.4. Priority Action Teams

In addition to its work in the EFPIA Policy Committees, FARMAINDUSTRIA also participates in and collaborates at the Priority Action Teams (PATs) created ad hoc to consider critical issues related with the Federation's objectives.

EU ENLARGEMENT

At the beginning of 2000, accession negotiations were in progress with twelve countries (Cyprus, the Czech Republic, Estonia, Hungary and Poland in the leading group, with Bulgaria, Latvia, Lithuania, Rumania and Slovakia included as newcomers at the end of 1999).

Throughout the accession process, FARMAINDUSTRIA has input its opinions in areas of concern to the pharmaceutical industry, in particular advocating the need to:

- Align the levels of intellectual property protection in the candidate countries.
- Address the economic and social imbalances to avoid market distortions.

FARMAINDUSTRIA and the other national associations have worked hard within EFPIA over the year to facilitate the Collaboration Agreement between Drug Regulatory Authorities in European Union Association Countries (CADREAC). This agreement is based on a simplified procedure for authorising in accession countries those medicines that have already been approved in the EU via the centralised procedure.

REGULATION 2000

The priority action team was set up in anticipation of the review of the Community pharmaceutical regulatory system scheduled for 2001. From the outset FARMAINDUSTRIA has been represented in the PAT, whose mission is to form an industry consensus on long-term strategic issues for the European regulatory system in the authorisation of medicinal products (centralised procedure, mutual recognition procedure, pharmacovigilance and information technology).

The PAT's findings were presented to the Spanish Medical Products Agency in May 2000 aiming at sharing with the authorities proposals for modifications to the European system in order to guarantee the highest quality standards, optimise the use of resources and free the decision-making process of delays. In particular, FARMAINDUSTRIA has insisted that the system must operate without imposing restrictions on companies' freedom to enter into licensing agreements, defending the possibility that more than one tradename may exist for an active agent approved in the centralised procedure.

REGULATORY DATA PROTECTION

The ambiguities and concerns raised by the lack of regulatory data protection harmonisation in the member States led to the creation of this PAT, stablished was set up to achieve three objectives:

- A single 10-years of protection throughout the EU in the decentralised procedure consistent with the term already applicable in the centralised procedure.

- Autonomous protection for new batches of data in order to avoid discouraging research into new treatments using existing active substances.
- Improved definition of the concept of "essential similarity" in order to avoid any risks for patients in cases where the efficacy of medicines is supported by reference to data for other innovative products based on a different composition of active substances.

FARMAINDUSTRIA has been at great pains to raise the protection to 10 years, stressing this message both to the Spanish health authorities and to MEPs, with the result that a Resolution has been adopted recommending a change in EU legislation in this area.

CLINICAL TRIALS

Discussion of clinical trials issues between the Scientific, Technical and Regulatory Policy Committee and the European Commission began as far back as 1991. Since then, FARMAINDUSTRIA, as a member of the Committee and with the feedback of its members, has consistently communicated to Brussels its support for the idea of technical harmonisation, while stressing the need to avoid any requirements that could be detrimental to Europe's attraction as a location from which to carry out clinical trials, since this would deny patients fast access to innovative treatments.

In May 2000 the European Council of Ministers adopted a common position, reflecting a compromise with the fifteen member States, which are in principle rather reluctant to change their own systems. The text establishes an "optional" system to start clinical trials, giving individual countries the flexibility to transpose this solution into their national legislation over a period of three years. The main features of this proposal are:

- Maximum waiting periods of 60 days for the delivery of an opinion by the ethics committee, as well as for the competent authorities to complete the procedure for the commencement of clinical trials.
- Optional written authorisation for biotechnology products and "other products with special characteristics" to be further defined by the Commission.
- Absence of time limits for gene and cell therapy, and for all medicinal products containing genetically modified organisms.

The Directive was finally approved on 14th December 2000.

ACCESS TO MEDICINES IN THE THIRD WORLD

The issue of access to medicines in Third World countries continues to be hotly debated in the international arena. At the European level, EFPIA and its national member associations have taken part in the discussions with all stakeholders organised by the European Commission to seek possible ways of improving access to new drugs and treatments in developing countries.

The pharmaceutical industry can contribute to this global issue in various ways:

- By continuing with actions and initiatives to combat health problems in the developing world.
- Through a strong commitment to research into the major diseases that have such devastating effects in the Third World (AIDS, malaria, tuberculosis and other infectious diseases).

n Where possible, on an individual company basis, by addressing medicines' affordability taking into account the different existing health systems, government policies and pharmaceutical markets existing in different countries.

1.4.5. EFPIA 2000 Annual Meeting

EFPIA held its Annual Meeting for 2000 in Venice on 21st to 23rd June. At the proposal of the Board, the General Assembly extended Jorge Gallardo's mandate as President of the Federation. In January 2001, the Extraordinary General Assembly appointed Jean-François Dehercq, PDG of Sanofi, as the new President of EFPIA.
The Annual Meeting brought together over 400 representatives from the pharmaceutical industry and competent health authorities at EU and national level, who were honoured by the presence of Romano Prodi, the President of the European Commission. Jorge Gallardo asked Mr. Prodi for his support in attaining priority goals for the industry in areas of intellectual property, EU applications and the completion of the simple market for pharmaceutics.

Jorge Gallardo with Romano Prodi at the Annual General meeting of EFPIA, held in Venice in June 2000.

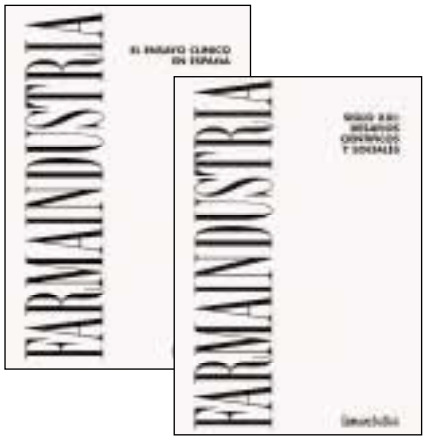
1.5 Communication and publications

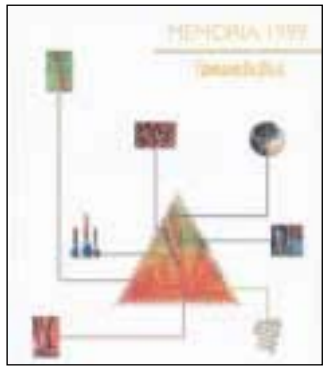
FARMAINDUSTRIA's activity in the field of communications involved close collaboration with the media, numerous press articles, the organisation of seminars and conferences, and publishing.

Among these, there are two relevant issues of the *Indufarma* magazine: nº 37 focused on science and technology, and nº 38 centred on the Association's internal changes.

During the year the Association published its Annual Report for 1999 and a new edition of the statistical review *La Industria Farmacéutica en Cifras*, both of them essential references for anybody interested in learning about the situation and outlook of the pharmaceutical industry in Spain. Both are also available to members in digital format (Lotus Notes) through the FARMAINDUSTRIA communications system. Another document of great interest, which is sponsored by FARMAINDUSTRIA and published by SANED, is the *Anuario de la Sanidad y del Medicamento en España* (Spanish Health and Medicines Yearbook). In line with previous years, the 246 pages of the 2000 edition offer a wealth of statistical data on health care in Spain.

Finally, the science list will shortly publish the papers given at the *Clinical Trials in Spain* seminar organised by FARMAINDUSTRIA at the Menéndez Pelayo International University in August 2000 and at the La Granda (Asturias) conference on the subject of *The 21st century: Scientific and social challenges*.





1.6 Integrated waste management: SIGRE, S.L.

During 2000 and the current year to date, *Sistema Integrado de Gestión y Recogida de Envases,* S.L. (SIGRE), a not-for-profit company incorporated in accordance with the provisions of Article 7 of the enabling Regulations for the Packaging and Waste Packaging Act, 1997 (Law 11/97), has been awarded licences to operate as an Integrated Waste Management System in the Self-Governing Regions of Castille-La Mancha, Andalusia, Catalonia, Murcia, Melilla, Galicia and Asturias. The licences awarded will, however, remain provisional until all conditions are met on a case-by-case basis. This will require, inter alia, the arrangement of the relevant guarantees, and the submission of collaboration agreements with retail pharmacies, distributors, waste management companies, materials associations and so on in each of the respective Regions. It will also be necessary to commission the communications campaign.

In order to start up the system, an agreement, forming part of the conditions for the award of the definitive licence, was made with the Galicia Regional Government to carry out a pilot test in 150 regional pharmacies. The four-month pilot test, which will commence in the province of Orense in June 2001, will be SIGRE's first operational experience as a waste management system. It is therefore of the utmost importance to demonstrate that the system functions properly and to establish the waste classification and management criteria, as well as analysing costs.

Key activities carried out by SIGRE in 2000 include framing Prevention Plans for Business, which are aimed at pharmaceutical companies as a whole (Industry Plan) and were presented to Regional Governments on 22nd December 2000.

The Prevention Plan for Businesses comprises the programme proposed by the company in connection with the objectives established in the Packaging and Waste Packaging Act, 1997. It must therefore set out quantifiable prevention targets, concrete measures to achieve them and the control procedures designed to measure performance. Though SIGRE is responsible for the design and monitoring of the Industry Plans, the pharmaceutical companies are individually liable for compliance.

At the end of March 2001, SIGRE prepared and filed its annual packaging report, which details the packaging released through retail pharmacies during 2000 by the pharmaceutical companies adhering to the system. Pursuant to prevailing regulations, this

report must be presented in each of the Self-Governing Regions. Its main purpose is to form the basis for the calculation of the contributions payable on account by each of the companies participating in SIGRE to fund the integrated waste management system.

A total of 1,050 units were sold, representing a volume by weight of the packaging materials used (cardboard, glass, metals, plastics, etc.) of 47,000 metric tons.

Key issues that will be addressed in 2001 include commissioning the communication campaign, the design and manufacture of containers, and the design, start-up and live operation of the Information and Control System. Adhesion and Logo Licensing Agreements must also be formalised with all of the participating companies, as well as Agreements with the General Council of Spanish Colleges of Pharmacists, FEDIFAR, the Spanish Federation of Municipalities and Provinces, waste management companies and Materials Associations. In addition, SIGRE has yet to comply with its obligations under the licences awarded by the Regional Governments, as explained above, and to complete the process of obtaining the remaining licences needed for it to operate as an integrated waste management system throughout Spain.

SIGRE thus has a busy schedule ahead of it in order to start up its operations and complete the selective medicine packaging and packaging waste collection system so as to cover every home in Spain, which is no less than the undertaking given by the pharmaceutical companies adhering to SIGRE through FARMAINDUSTRIA. In view of this, the company's management team has been thoroughly renewed with the recruitment of a new General Manager and the appointment of the new Director General of FARMAINDUSTRIA as Chairman of SIGRE.

Four principles set the tone for Farmaindustria's action: proactive approach to Goverment, communications with society, service to members and internal organization.

2 The Strategic Plan and new projects

At their meetings in December 2000 the Board and Steering Committee approved a concept paper entitled Commencing a New Cycle in the Association: Innovation and Sustainability. This document reflects the new strategic guidelines adopted by the governing bodies for the further development of FARMAINDUSTRIA.

Over the coming two years, the Association will need to seize the opportunities offered by the new cycle to reshape itself internally in order to improve the services provided to members, become more pro-active in its dealings with Government and adopt a more open stance to society in general and priority stakeholders in particular in order to deliver the message that the medicines and the pharmaceutical sector are a major source of added value.

The document sets out the following strategic guidelines:

A) Government: a pro-active approach must be taken to close outstanding issues successfully and establish a permanent basis for dialogue in order to reach stable agreements that are acceptable to the pharmaceutical industry.

B) Society: the industry needs to improve its image in society, deploying an effective communication policy to deliver the message that medicines have social value and the pharmaceutical sector economic value, both industrially and in terms of research, development and innovation.

C) Members: our members deserve enhanced service and openness and must be involved in the life of the Association. Only in this way will FARMAINDUSTRIA generate value for its stakeholders.

D) Organisation: progressive modernisation of internal structures is critical to the effective implementation of the other guiding principles in the context of the strategic plan defined by the Board and the Steering Committee.

The implementation of the strategic guidelines is critical to the whole of the Association. Because of this, a brief sketch of the first steps taken in the new direction during the early months of the year 2001 has been included in the following pages, even though the Annual Report deals essentially with FARMAINDUSTRIA's activity during 2000.

2.1 A new scenario for relations with Government. Towards a Stability Pact

Relations between the pharmaceutical industry and Government must be defined by a climate of concord, if agreements and pacts are to be made to the benefit of society as a whole. It is therefore critical to combine the need for certainty to encourage future investment by industry with the need to achieve sustainability in the health care system. The readiness of both parties to negotiate and seek consensus will make this possible.

The Agreement of 22nd January 1998 between FARMAINDUSTRIA and the Ministry of Health and Consumer Affairs was initially made for a term of two years with a view to meeting the Government's demands industry participation in health care funding. The total pharmaceutical industry contribution agreed was 65,145 million pesetas, payable in accordance with the terms of the Annex to the Agreement.

In July 1999, however, the General Assembly of FARMAINDUSTRIA resolved to repudiate the Agreement, in accordance with the recommendation of the Board, because the Association understood that the regulatory framework under which it was negotiated and approved had changed. Furthermore, FARMAINDUSTRIA considered that the Spanish Health Authorities had repeatedly failed to abide by their commitments in the period since the Agreement took effect.

As a result of the repudiation of the Agreement, the pharmaceutical companies withheld the sums claimed by the Social Security Treasury Office, while the Government countered with a Royal Decree slashing the prices of medicinal products. The whole situation was thus left to await a firm ruling from the courts.

In order to remedy matters, the new Health Authority representatives and the pharmaceutical industry agreed to draw a line under the dispute as a first step towards finding a full and lasting solution. On 8th March 2001, the Ministry of Health and Consumer Affairs entered into a Collaboration Agreement with FARMAINDUSTRIA to promote and develop scientific and technical research in the field of health care, which closed the dispute arising in connection with the ill-fated Agreement of 2nd January 1998.

The new climate of relations with government is a clear sign of the pharmaceutical industry's willingness to debate the key issues of stability in the National Health System and seek compromise wherever possible. This approach has and will continue to underlie our relations with the Ministry of Health and Consumer Affairs. In view of the realities and regulatory framework of the Spanish health care industry, the Agreement signed on 8th March 2001 is of enormous importance and has various decisive effects. Firstly, it closes the rift over the interpretation of the commitments made in accordance with the Agreement of 22nd January 1998, opening the way to discussions and the search for a consensus response to the challenges and problems faced by both industry and Government, which are essentially similar.

Secondly, the new approach taken by the industry in March 2001 represents a direct and meaningful contribution to Spanish biomedical research. The industry contribution of 5,500 million pesetas provided for under the Agreement is, more or less, twice the annual budget of the National Health Care Research Fund.

The pharmaceutical industry's whole raison d' être is to respond to society's demands for improvements in health care through research and innovation. This is best achieved within a stable regulatory framework, conducive to long-term research planning and investment. This is because a predictable climate for management decisions allows the research arm to concetrate on producing tangible results.

An understanding has thus been reached between FARMAINDUSTRIA and the Ministry of Health and Consumer Affairs, which allows us to look ahead in a new and constructive mood defined rather by willingness to discuss the issues than to fight our separate corners. This understanding aims to achieve a critical, dual objective for all health stakeholders: the stability of the pharmaceutical industry and the National Health System.

In addition to these matters, upcoming administrative and economic issues will substantially modify the existing structure of health care in Spain:

- Forthcoming completion of the process by which responsibility for medicines provision will be transferred to the Self-Governing Regions.
- Negotiation of new health care funding arrangements (including the funding of medicines) for the period from 2002 until 2004.
- New budget targets to be set by the State with the specific objective of achieving a zero deficit throughout the administration.

In view of this new situation, the Health Authorities are pressing for a stability pact for public pharmaceutical expenditure to be reached with all stakeholders. In the Spanish Parliament, Coalición Canaria (a small regional party) tabled a motion urging the Government to close the relevant agreements before 30th June 2001, which was unanimously approved by the House.

FARMAINDUSTRIA is optimistic about this emerging scenario, despite concerns that the Government may be tempted to impose further sacrifices on the industry without asking other stakeholders to shoulder a fair share of the burden. This is because the pharmaceutical industry has historically had to make more than proportional contributions to the containment of public health care spending.

Aside from the potential consequences for health care, such a scenario could have a severe economic impact, because it would accelerate and heighten the strains that are already being felt as a result of the ongoing process of globalisation in the pharmaceutical industry. Spain could find itself forced out of the circles in which the major international drugs companies decide on investments in both production and R&D. Meanwhile, the domestic sector, which is mainly made up of small and medium-sized companies could fall prey to a ferocious restructuring, causing job cuts and loss of local market share.

As discussion of the proposed stability pact gets under way with the Ministry of Health, FARMAINDUSTRIA has drawn up a list of key negotiating points:

- Stability must be addressed not only as a budgetary issue but also in terms of its health, economic and industrial effects, taking into consideration the interests of all stakeholders.
- The growth in spending required to achieve stability in the system must be established objectively in light of both domestic and international review criteria.
- All stakeholders in the pharmaceutical process (health authorities, doctors, wholesalers, retail pharmacies and industry) must be involved in negotiations and take their share of the burden.
- A climate of certainty must be generated, ruling out the possibility that additional measures may be taken at a later date to modify the status quo established in the stability pact, since this would cause legal unpredictability.

Only if burdens are shared in a climate of certainty will the pharmaceutical industry be able to contribute to stabilising public pharmaceutical expenditure without putting its own health at risk.

2.2 Social perceptions of medicine and the pharmaceutical industry

One of the strategic priorities established for the new cycle in the Association is to deliver the message that medicine has a social value in order to improve public perception of the pharmaceutical industry.

SOCIAL VALUE OF MEDICINES

Consideration of the social role played by medicines and the pharmaceutical industry in Spain in recent years brings to light a perceptual paradox unparalleled in any other economic activity. On the one hand, nobody doubts that medicinal products are good, at least generally in terms of their contribution to the well-being of the citizen. On the other, it seems that society subconsciously measures the social value of the pharmaceutical industry by a different yardstick to other sectors. Suffice it to say that social perceptions of our industry in no way match its enterprise, commitment and drive. The explanation for this is clear: our activity links the concepts of health and sickness, which have very different emotional connotations to other consumer goods and services marketed without more ado.

The industry is keenly aware of this situation and is determined to change its relationship with society, Government, public opinion and the media. We have much in our favour.

Firstly, the product. Drugs are the basis of medical therapy. They cure, prevent, alleviate and transform diseases, afflictions and situations that would otherwise cause great suffering and unhappiness. The advances made by pharmaceutical research and innovation have led to the development of new and increasingly effective medicines and treatments for cancer, HIV infection, mental illness, heart disease, asthma, allergic and respiratory complaints and other infectious diseases. The extraordinary efficacy of medicines is neither heaven sent nor a coincidence, but the fruit of years of painstaking research, co-operation with scientists, testing and evaluation culminating in a positive impact on disease. Such an outcome could not be achieved without a first class medical system and the labour of a host of health care professionals including doctors, nurses, pharmacists and medical researchers to name but a few. And this implies spending on health.

In this context, it is not enough simply to point out the efficacy of different medicines. The benefits must also be considered in light of the economic savings they product. A paradox? Yet the medium and long-term savings generated from the use of innovative medicines are rarely considered. Countless clinical trials and pharmaco-economic studies show and document how medicines:

- contribute to lower mortality rates and thereby to reducing the phenomenon defined by economists as "years of life lost";
- reduce the need for surgical operations and hospitalisation, even making these measures unnecessary at times;
- prevent or moderate clinical complications, which also require treatment;

- prevent or delay the onset of disease;
- prevent disabilities;
- lower absenteeism and poor productivity in the workplace; and
- generate innumerable positive side-effects that can never be appropriately valued from a purely economic standpoint.

The true value of medicines to the citizen and society in general is, however, to be found in their intangible effects of reducing suffering and generating well-being and greater happiness, which are less visible and more sensitive to emotional responses. Pharmaceutical products contribute to medical science and their application in the health services saves lives, alleviates pain and the physical and mental suffering of patients and their families, enabling personal development and social integration. Medicines thus make it possible to "add years to life and life to years".

Contrary to popular belief, new active substances capable of revolutionising therapy are largely not discovered and developed in publicly funded research centres but by industry. The manufacture of medicines, and thus the creation of added value (in conditions of quality, efficacy and safety), is the exclusive concern of industry. It is industry that provides doctors with information on prescribing and dosage. Finally, industry bears the brunt of the costs incurred in pharmacovigilance activities to track the efficacy and safety of medicines.

Medicines are not, however, just another consumer good, but rather a response to the demands of the scientific community, citizens and government. Because of this, the pharmaceutical industry must remain committed and participate actively in health care decisions. In this light, it is essential that medicines should be recognised as an essential facet of the effort to improve citizens' health and quality of life.

ECONOMIC AND INDUSTRIAL VALUE OF THE PHARMACEUTICAL SECTOR

It will not be enough, however, simply to explain and underline the value of medicines in themselves. As an industry, the pharmaceutical sector has immense economic value, and its contribution to wealth creation needs to be made clear and used as an argument.

The Spanish pharmaceutical sector is important from an economic and industrial standpoint not only in terms of its percentage contribution to GDP but also qualitatively as a source of

value added, driver of research and development, and provider of skilled jobs. The key figures and discussion of the pharmaceutical sector presented in Chapter 3 of this Annual Report provide an accurate snapshot of the industry and its contribution to the Spanish economy.

PERCEPTIONS OF PUBLIC PHARMACEUTICAL SPENDING

Public Pharmaceutical expenditure in Spain, which in 1999 totalled 1,016 billion pesetas at retail prices (i.e. Social Security spending via retail pharmacies) is frequently portrayed as excessive and unsustainable for a society such as ours, while the industry is singled out as the main cause of cost overruns. This opinion is backed up by two trite and simplistic arguments: (1) pharmaceutical spending accounts for 22.5% of total public outlay on health care, which is 9 points more than the European average; and (2) annual growth in public pharmaceutical expenditure is faster than nominal GDP growth (averaging between 2 and 3 points in recent years).

Nobody, however, seems to have factored the cost of public pharmaceutical provision, an area where Spain is at the head of the developed countries, into the equation. All drugs are prescribed in Spain, the entire population is eligible for protection and the level of public coverage is the highest in Europe. Spain's level of co-payment (7.4%) is the lowest on the Continent (average 15.2%), while public pharmaceutical expenditure as a percentage of total spending on drugs is the highest (72.2% compared to 63.4%). Furthermore, it is absolutely misleading to point to the high percentage of total health outlay represented by pharmaceutical expenditure for two reasons:

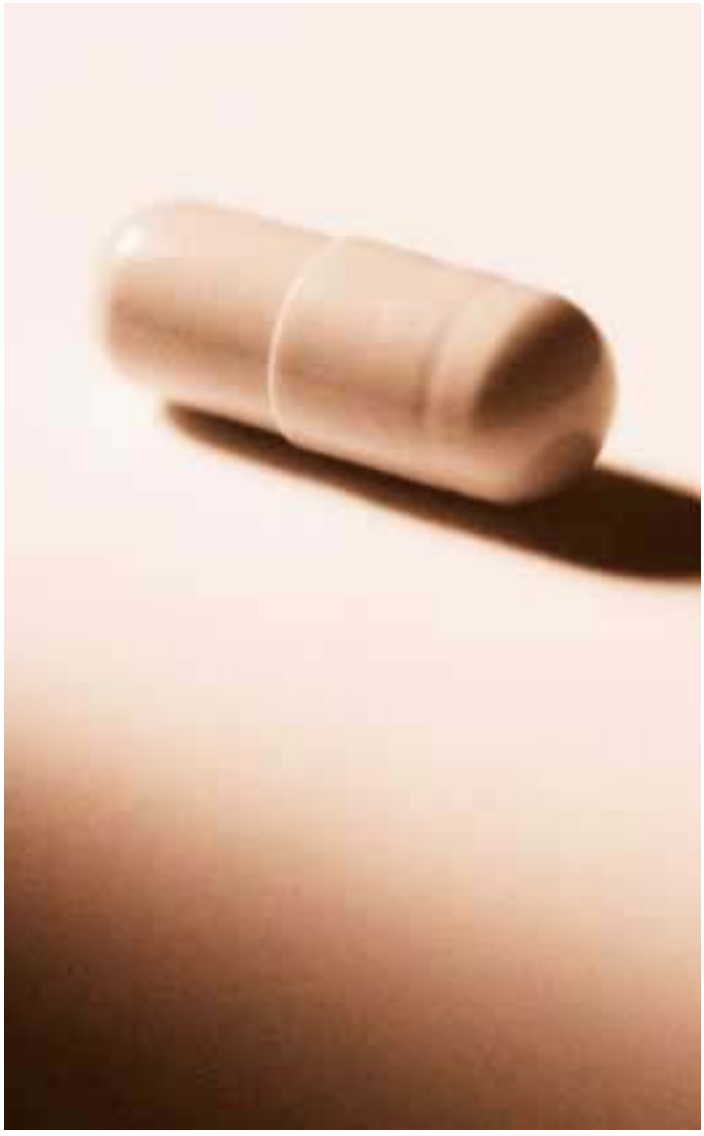
- While health care spending is directly related with the levels of development reached in a given country, and therefore on the existing infrastructure, this is not so with pharmaceutical expenditure, which may even offset certain weaknesses in the health system.
- Spanish public health care expenditure is among the lowest in Europe at just 5.4% of GDP compared to an average of 6.6%, almost 20% less. In per capita terms, Spain spends an annual 119,809 pesetas per person, just under half of the average 233,168 pesetas spent

in Europe. Starting from such a low base for the comparative calculation of pharmaceutical expenditure, it is hardly to be wondered at if the resulting percentage is high.

The second of these arguments (fast growth in spending) can also be answered from the standpoint that this trend has been common to all advanced countries in recent years and is as a consequence of numerous overlapping factors connected with higher levels of development, public health care provision and social demand. The rising numbers protected, ageing of the population, absorption of new communities (immigrants), declining levels of co-payment, treatment of chronic ailments, and the development of new treatments for formerly incurable diseases are all excellent examples of the causes underlying growth in public spending.

Furthermore, the rise in the average cost of medicines has had no inflationary effects, because it is due to the launch of new products, which are not included in the consumer price index for conceptual and methodological reasons. In fact, the index of pharmaceutical prices increased by just 8.5% between 1992 and 2000, compared to 30.4% for the general CPI (Consumer Price Index).

A look at other measures puts public pharmaceutical expenditure into a clearer light compared to the situation in other European countries. The per capita cost to the Spanish public purse is currently 27,006 pesetas per year compared to 30,486 pesetas in Europe. However, total pharmaceutical spending (i.e. public and private) in Spain is 37,410 pesetas per head compared to 48,071 per head in Europe. Moreover, the weighted average price of drugs in Spain (i.e. manufacturer's price) is 912 pesetas compared to a European average of 1,174 pesetas.



Pharmaceutical Market: Structural differences between Spain and the EU

Comparative Structure	Units	Europe	Spain	Difference
Total health care expenditure in Spain	Pta/Capita	295,196	155,872	-47%
is lower than in the EU	GDP (%)	8.7	7.1	-1.7 p
Public health care expenditure in Spain	Pta/Capita	233,168	119,809	-49%
is lower than in the EU	GDP (%)	6.6	5.4	-1.2 p
Total pharmaceutical expenditure (TPE)	Pta/Capita	48,072	37,410	-22%
is lower in Spain than in the EU				
Public pharmaceutical expenditure (PPE)	Pta/Capita	30,486	27,006	-11%
is lower in Spain than in the EU				
PPE represents a higher percentage of TPE	%	63.4	72.2	8.8 p
in Spain than in the EU				
Co-payment as a percentage of TPE	%	15.2	7.4	-7.8 p
is much lower in Spain than in the EU				
The **average price** of medicines	Pta/Unit	1,174	912	-22%
is lower in Spain than in the EU				
The **volume of medicines consumed**	Units per	26	27	3%
is similar in Spain to the EU	head			
Purchases of **OTC medicines** as a percentage	%	29.4	13.6	-15.8 p
of TPE are lower in Spain than in the EU				
Purchases of **generic medicines** as a percentage	%	15.0	1.7	-13.3 p
of TPE are lower in Spain than in the EU				
Distribution and dispensing costs	% /RRP	33.6	35.6	2.0 p
are higher in Spain than in the EU	% /RRP+VAT	30.8	34.3	3.5 p
Growth in the pharmaceutical market	% 1997-00	7.7	10.2	2.5 p
is higher in Spain than in the EU (IMS)	% 1998-00	8.1	9.9	1.9 p
Nominal GDP growth in Spain	% 1999	5.0	7.8	2.8 p
has been higher than in the EU				

Sources: OECD, IMS, Farmaindustria data

Contradictory though it may seem, Spain at once has the highest levels of public pharmaceutical cover and some of the lowest costs to be found anywhere in the EU. The reason is pricing policy historically followed by the Spanish Government, whereby new product prices have been fixed at lower levels than in Europe and the prices of existing products have been held down, at the same time as the industry has been obliged to accept general price cuts and agreed discounts in order to avoid incurring more severe penalties.

2.3 Member services

A new Member Services office has been created as part of the Association's internal reorganisation. However, member services should be understood rather as a mindset than merely another department. The Member Services office has a three-fold mission:

1. To develop and grow a member-oriented culture within the organisation.
2. To propose and implement new services and improve those that already provide added value to members.
3. To stimulate members' active involvement in affairs of the Association.

To achieve these objectives, the new department has taken a leading role in the internal reorganisation process, as well as undertaking the projects described in the following pages:

BARCELONA OFFICE

FARMAINDUSTRIA'S Barcelona office is set to become a key element in member relations, gradually enhancing the range of services provided. The first priority is to modernise technological infrastructure, enabling a quantum leap in the technical support that the office will be able to offer members.

The office forms part of the Technical Secretariat that has recently been created to provide support to the Association's working groups, sections and functional areas. This will enable the Barcelona office to take a more pro-active stance towards member concerns, acting in concert with the Madrid head office and providing an effective response to the requirements of pharmaceutical companies.

MEMBER RELATIONSHIPS TECHNOLOGY PLATFORM

The Association's Communications System has become an indispensable documentation resource for the pharmaceutical industry both as regards legal texts, and for economic and scientific papers, press and journals, and general information.

The quality of content, which is updated on an ongoing basis, and the diversity of the information available have encouraged increasing numbers of members to sign up for the service. The improvements made to the service in 2000 both extended the use of data bases within companies, and simultaneously achieved a reduction in document search and loading times. The 114 member companies currently connected to the system represent 87% of the total market. These figures include not only the vast majority of large companies but an increasingly significant number of small and medium-sized members.

Evolution of companies connecting to the system

	JANUARY-1998	JANUARY-1999	JANUARY-2000	JANUARY-2001
Member companies connected	28	69	109	114
Percentage of total market	29%	63%	82%	87%

The most frequently used data bases are Circulars, Press, *The Pharmaceutical Industry in Figures* (IFC) and the daily *New documents bulletin* listing newly loaded items. *The Spanish Medicines Legislation*, *Information Flash* and daily news bulletin FARMAINDUSTRIA *Day-by-Day* also receive frequent consultations.

Logically, most hits are in data bases loading daily information and those that are either highly specialised or contain quality content that is unavailable elsewhere (e.g. IFC and Legislation).

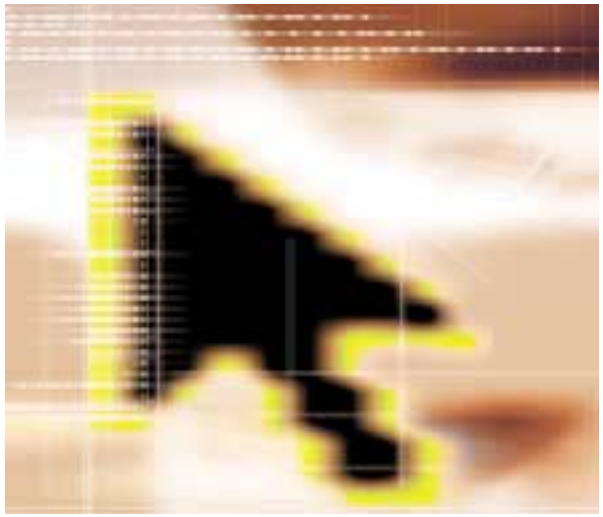
Percentage use of data bases

NAME	NUMBER OF DOCUMENTS	%
Circulars	1,010	24
Notes e-mail addresses	67	2
FARMAINDUSTRIA Day-by-Day	412	8
Information Flash	1,352	7
The Pharmaceutical Industry in Figures	454	12
Spanish Medicines Legislation	367	8
FARMAINDUSTRIA Annual Report	22	4
New Documents	808	11
Press	7,315	19
Publications	6	1
Indufarma magazine	174	3
Data bases (administration)	14	1
TOTAL	**12,001**	**100**

Daily full-text updates are performed that are easily accessible using standard applications (e.g. word processors and spread sheets), requiring only a simple "cut and paste" operation. The data is stored to the user's hard disk, which provides multiple advantages:

- The information is independent of telephone infrastructures (only updates require on-line connection).
- Consultations can be carried out locally via the laboratory LAN, resulting in minimal access times.
- Information can be distributed to various offices throughout a company via a single connection.

Permanent growth in the use of the data base by the companies connected entails ever rising demand for improvements to the service. FARMAINDUSTRIA therefore regularly reviews the system to anticipate the need for new data bases and upgrades to enhance analysis capability, as well as scaling up to accommodate potential new users. Work is currently under way to develop a new internet communications technology platform, which will make user access to data bases even easier from any connection and provide the Association with a general communications channel reaching health care professionals and society in general.



NEW SERVICES

Work has started on the preparation of a catalogue of FARMAINDUSTRIA'S services with the identification of areas for improvement and proposals for new services in the areas of: (1) data bases —feasibility analyses for registration data, European legislation and a directory of members; (2) publications —new lay-out for Indufarma and monograph studies; (3) member consultations —functional organisation, and response time and quality measures; (4) training —workshops and seminars, and student traineships; (5) communications with members —press service, information flash, etc. Special attention has also been given to developing and upgrading telematic systems.

WORKING GROUPS, SECTIONS AND FUNCTIONAL AREAS

Working groups, sections and functional areas represent a new departure in FARMAINDUSTRIA's working practices and are a response to the need to encourage members' active involvement in the Association's affairs.

The smooth functioning of these groups will tie the strategy of the Association more closely to the needs and concerns of members.

The working groups have already started work, following the guidelines laid down by FARMAINDUSTRIA's governing bodies. At present, working groups have been set up to address the issues of parallel trade, communications, reference prices, sustainable growth and promotion regulations. Special sections have also been created for SMEs, generics, hospital supplies, biotechnology and R&D. A working group on international issues is also planned.

The Member Services office with function as a technical secretariat for the working groups, sections and functional areas with the dual objective of providing support to co-ordinators in order to ensure that projects run smoothly, and maintaining co-ordination between the activities of each group and the various operational departments of FARMAINDUSTRIA.

Price cuts in 1999 and the implementation of the reference price system in year 2000 held market growth down to 8,8%, the lowest rate since 1994.

3 The pharmaceutical industry in Spain and worldwide

3.1 The international context

3.1.1. World economy

The main macro-economic indicators for the world economy were exceptionally good in 2000, with the majority of developed countries enjoying exceptionally strong growth.

Economic growth in the major economies (2000)

COUNTRY	GPD GROWTH FOR 2000	LAST YEAR OF COMPARABLE GROWTH
Germany	3.1	1991
France	3.2	1989
Italy	2.9	1995
United Kingdom	3.0	1997
SPAIN	**4.1**	**1989**
Total EU	3.4	1989
United States	5.0	1984

Source: FARMAINDUSTRIA based on OECD data.

Despite strong growth in the world economy, two contrary trends became apparent over the course of the year. The first half was marked by the optimism generated by strong profits from business and the only concern was inflation. As a result, the Central Banks raised interest rates to moderate both consumer spending (the main component of GDP) and investment (highly active due to the buoyant business outlook). After the summer, however, the climate changed sharply for a number of reasons:

- Already high oil prices not only failed to fall, but a series of continual price hikes began, basically caused by rising world demand, restriction in supply by the oil producing countries and refining problems.

- The effects of high energy costs were translated into other prices as rising production costs were passed on to consumers.
- Workers began to claim larger wage rises to offset fears of a loss of purchasing power.

This new situation implies a scenario of lower growth and higher inflation rate. As a result, the Central Banks faced a dilemma in their management of monetary policy. They could either cut interest rates in order to boost growth, thereby risking higher inflation, or they could maintain high rates to control inflation, despite the impact this would have on economic growth.

The change in the trend of the economic cycle had a radical effect on the confidence of both business and consumers, resulting in a stock market crisis, which initially shook technology companies and later became general as the contagion spread to other stocks following profit warnings from certain major corporations.

As explained below, the attitudes of the US Federal Reserve and the European Central Bank (ECB) differed markedly because the growth cycles of the American and European economies do not move in step.

UNITED STATES

As mentioned at the beginning of this Section, the US economy achieved overall growth of 5.0% in 2000, well ahead of the 3.5% growth in the European economy.

The US economy not only reported strong growth, but almost all indicators were positive. Thus, production rose by 5.7%, employment grew by 1.3%, cutting the unemployment rate to 4.0%, and inflation was held down to 3.4%. However, analysis of quarterly growth rates compared to the prior year's shows a sharp slowdown in the second half of the year: Q1: 5.3%, Q2: 6.1%, Q3: 5.2% and Q4: 3.4%.

This slowdown has been confirmed in the first quarter of 2001 and, since inflation seems to be under control, the Federal Reserve, whose philosophy towards monetary policy differs from that of the ECB, decided to cut interest rates sharply. As a result, US interest rates at the date of writing (may 2001) are 4.5%, equal to the levels prevailing in the euro zone, a circumstance unheard of since 1995.

JAPAN

With GDP expanding by only 1.7%, Japan was the only exception to the generally fast growth enjoyed worldwide in 2000. The country has still not been able to shake off the crisis that began in 1992 and has yet to hit upon the right formula. The Japanese Government has tried to reactivate public and private spending, and investment by boosting public expenditure, while following a policy of ultra-low interest rates (real interest rates are close to zero), but the strategy has failed. The Japanese economy is in need of sweeping restructuring in the banking sector and a far-reaching reform of the tax system. The major banks are labouring under piles of bad debt, a situation which is reinforced by the structure of the large Japanese conglomerates. The government intends to approve a restructuring plan for the country's financial institutions.

EUROPEAN UNION

Overall growth in the member States of the European Union was the fastest for ten years (3.3% for the EU as a whole and 3.4% for the euro zone) with Germany and France (growth

of 3.1% and 3.2%, respectively) acting as the main motors. This growth was achieved despite the slowdown experienced by the European economy from the third quarter of 2000 onwards. In these circumstances, the ECB remained determined not to cut interest rates, which it held steady at 4.75%, since its priority is to keep inflation below a threshold of 2%, while average inflation for the euro zone was 2.7% in the last quarter (only France had lower than threshold inflation). Nevertheless, the slowdown was less pronounced than in the United States, mainly because dwindling domestic demand was offset by a rise in exports on the back of the weak euro.

The public accounts of the euro zone as a whole were favoured by fast economic growth and closed with a surplus of 0.3% of GDP, which was largely due to the revenues generated by the auctions of 3G mobile telephony spectrums in some countries (the deficit excluding such extraordinary items would be 0.8%).

Employment also continued to rise at an encouraging rate (2.0%) and the euro zone rate of unemployment in December was 9.1%.

SPAIN

Spain continues to grow faster than the average for the EU countries (Spain grew by 4.1% compared to 3.4% for the EU as a whole). It is, of course, critical to maintain this gap if the process of real convergence is to continue, which is one of the present Government's main campaign promises. Nevertheless, the last quarter of 2000 also saw a sharp slowdown in Spain due to shrinking consumer spending and investment, though this was partially offset by a rise in exports.

In 2000 the Spanish economy created 4.7% more jobs than in the previous year, as a result of which the rate of unemployment at the year end was 14.1%, or 1.6 million unemployed according to the National Employment Institute (INEM).

The expansion in the Spanish economy, together with the high rate of job creation, led to a quick rise in tax receipts. As a consequence, the year closed with a deficit of 0.3% of GDP.

The Government's objective for 2001 is to achieve a zero deficit, though tax receipts are likely to stagnate in view of slower growth and job creation, which will make it necessary to apply a restrictive fiscal policy if this target is to be met.

Without doubt, the worst performing indicator was inflation. Spain remains one of the countries that suffers most from inflationary pressures and at December 2000 the rate was 4.0%. It seems that the effects of the BSE crisis on food prices and traditional dependence on oil imports have joined forces to push up our already high rate of inflation. It is critical that Spain control prices in order to close the gap with the rest of the EU and maintain the competitiveness of our industries.

In this context, the controversial monetary policy of the ECB may help to relieve inflationary pressures in Spain, although it will be necessary to keep a careful watch on growth to prevent any excessive decline.

Main macro-economic indicators in the EU countries (2000)

Country	GDP (billion euros)	Population (1) (thousands)	Inflation (2)	Inflation (3)	Unemploy. rate	Balance of trade (billion euros)		C. ratio	Interest rate	
						Imports	Exports		Short term (4)	Long term (5)
Austria	205	8,114	2.3	1.8	3.7	74,026	68,961	93	4.39	5.56
Belgium	246	10,214	2.5	3.0	7.0	185,584	200,130	108	4.39	5.57
Denmark	174	5,319	2.9	2.3	4.7	47,532	51,688	109	4.99	5.62
Finland	132	5,171	3.3	2.9	9.8	36,623	49,221	134	4.39	5.48
France	1,397	59,099	1.6	1.7	9.5	320,649	322,338	101	4.39	5.89
Germany	2,027	82,087	2.0	2.3	8.1	539,610	595,325	110	4.39	5.30
Greece	121	10,553	3.1	3.7	n.a.	26,679(1)	9,906(1)	37	7.90	n.d.
Ireland	102	3,745	5.6	4.6	4.2	54,935	82,987	151	4.39	5.48
Italy	1,162	57,078	2.6	2.8	10.5	252,078	253,766	101	4.39	5.58
Netherlands	397	15,808	2.6	2.9	2.8	212,597	228,571	108	4.39	5.40
Portugal	113	9,983	2.9	3.8	4.2	41,299	25,195	61	4.39	5.60
Spain	**601**	**39,418**	**3.5**	**4.0**	**14.1**	**165,714**	**122,727**	**74**	**4.39**	**5.36**
Sweden	247	8.858	0.3(1)	1,3	5,9	78.961	94.286	119	3,95	5,37
U. K.	1,532	59.333	2.9	0,9	5,5	364.156	307.013	84	6,10	5,31

(1) Data corresponding to 1999. (2) Annual average. (3) CPI harmonised to December 2000. (4) 3-months interbank rates. (5) Long term bond yields.
Sources: OECD (Main Economic Indicators) – April 2000 and INE (CPI harmonised)

3.1.2. The pharmaceutical industry

The evolution of the European pharmaceutical industry during 2000 has once again been conditioned by the government imperative to hold down public deficits, due to the budgetary constraints imposed on the EMU States. In the area of pharmaceutical provision, this has translated into the adoption of health policies that prioritise the objective of containing pharmaceutical expenditure while trying to meet rising social health demand and maintain minimum levels of quality and coverage for developed countries with the available funds.

As a result, national governments have continued to implement special measures in the area of health care spending, since the markets have gradually eliminated the reducing effects of policies adopted in earlier years.

The range of actions taken is wide, as regards both the nature of the measures and their impact on expenditure, industrial activity and public pharmaceutical coverage of the population. The main such measures were as follows:

n Price reductions and / or freezes in virtually all of the EU member States, with a growing trend towards referencing the fixed / authorised launch prices of new products to levels prevailing in other European countries. There is some diversity in the price referencing methods applied, as shown in the following chart:

Notification of prices of similar products applicable in other EU member States	Austria, Belgium, Finland, France, Spain and Sweden
Calculation of the average European price for identical products marketed in other European countries	Denmark and Italy
Comparison against the lowest priced equivalent products in Europe	Greece
Reference to prevailing prices for the same product in a number of other European countries	Ireland, Netherlands, Norway, Portugal and Switzerland

- Changes in co-payment rules and/or the amounts of co-payment, as well as reimbursement criteria. These measures have in some cases included delisting of medicines and in other restrictions on the indications qualifying for public funding
- Generic substitution and a greater use of the reference price systems in the Mediterranean countries, where public intervention in prices and markets is already considerable, traditionally applied in northern Europe to control pharmaceutical expenditure.
- Fixing growth targets for public pharmaceutical spending, while seeking to make the industry (mainly) responsible for budget overruns through pay-back systems applied either to individual companies or collectively, sales taxes, price cuts or delisting of the products commercialised.
- Adoption of cost/effectiveness criteria for the evaluation of new products as a part of the price fixing mechanism, admission to reimbursement or in prescribing guidance issued to doctors.
- Surveillance of doctors' prescribing and other measures to encourage rationalisation.

Consideration of the evolution of annual sales over the past four years provides an approximate picture of the effects of the measures referred to above in the five largest European markets.

Annual percentage change in pharmaceutical sales by retail pharmacies at manufacturer's prices

	1997/96	1998/97	1999/98	2000/99	MAG 2001/96	% SALES/TOTAL 5 MARKETS 1996	2000
France	5	8	9	10	8.3	17.1	17.7
Germany	2	6	6	6	5.4	31.5	28.3
Italy	4	4	5	9	5.3	28.7	26.1
SPAIN	**10**	**11**	**11**	**9**	**10.2**	**9.7**	**10.4**
United Kingdom	7	8	10	6	7.7	13.0	17.5

MAG: Mean annual growth rate.

Source: FARMAINDUSTRIA on the basis of IMS data.

To concentrate on the events of 2000, the first point of note is that Spain recorded the second highest growth, after France, in sales through retail pharmacies, reversing the trend of the preceding years. Specifically, growth for 2000 slipped to 9%, though Spain remained in pole position for the period from 1996 to 2000 with cumulative annual growth of 10.2% .
The slowdown in our domestic market was caused by the price cuts which took effect in the last quarter of 1999, the full impact of which was felt in 2000. This has put the brakes on the process of convergence of Spanish with European prices for new medicines observed in recent years. The entry into force of the reference price system in December also caused prices to fall faster and more generally than had initially been expected. In this light, we may expect a further deceleration of the Spanish market in 2001.
Turning to other European countries, the stable and moderate evolution of sales in Germany is due to the greater use of generics and more rational prescribing by doctors in accordance with the guidelines established in the Agreement made between the medical practitioners and the health authorities.
The French market has recovered well, although the Government announced a series of measures intended to hold growth in public pharmaceutical expenditure down to a target rate of 2%. These measures included reductions in both prices and reimbursement levels for certain medicines, as well as promoting the substitution of generics for prescription drugs in dispensing.
The Italian market grew fastest in the last year of the series, largely because of the application of a new price adjustment for pharmaceuticals already on the market to align prices with the European average. This measure was in line with the policy followed since 1998, the year in which the Decree establishing this price referencing method was approved.
Finally, the sustained growth in the United Kingdom slowed brusquely after a general tightening of public spending policy, which resulted in price cuts and freezes in medicine prices, as well as caps on the prices of generics.

General EU pharmaceutical industry figures (1999)

Country	Nº of Laboratories (*)	Production (euro million)	Employment	Domestic Sales (euro million)	Exports at manufacturer's prices (euro million)	
					Imports	Exports
Austria	107	1,311	9,000	1,660	2,228	1,662
Belgium	142	4,247	21,817	2,576	4,718	6,046
Denmark	45	3,040	17,574	810	877	2,764
Finland	61	610	6,016	1,068	667	222
France	249	23,391	92,200	15,916	5,184	8,190
Germany	327	18,331	112,996	17,380	8,142	14,070
Greece	64	438(1)	7,800(1)	1,543	1,040	159
Ireland	58	5,071	14,000	608	1,122	4,830
Italy	222	13,514	69,970	10,529	6,138	5,523
Netherlands	59	4,548	12,800	2,350	3,997	4,026
Portugal	126	396(2)	9,650	2,103	953	229
Spain	**240**	**6,776**	**38,600**	**6,607**	**3,216**	**1,810**
Sweden	64	5,313(1)	16,300	2,103	1,347	3,762
United Kingdom	75	18,478	59,500	11,850	6,484	9,608
Total	**1,839**	**105,464**	**488,223**	**77,103**	**46,113**	**62,901**

Note: Figures refer to production of medicinal products and raw materials for human and veterinary use, except Spain, where the data refers exclusively to medicinal products for human use. (Pharmaceutical production in Spain is defined as the apparent production of medicinal products and raw materials for human use.)

(*) Pharmaceutical companies forming part of EFPIA member Associations.

(1)1998 data. (2) 1995 data.

Source: Farmaindustria on the basis of EFPIA data and information furnished by national pharmaceutical associations

3.2 The pharmaceutical industry in Spain

3.2.1. Companies

The continuing trend towards concentration in the industry, which has been going on for some years now, combined with a move by some companies to spin off generics and raw materials divisions resulted in zero growth in the number of manufacturing companies in Spain. The number of sales and marketing companies has, however, increase. These companies basically operate in the emerging generics market, though some were set up by their parent pharmaceutical companies with the mission of targeting medicine sales in specific segments of the market.

3.2.2. Jobs

The total workforce of the manufacturing companies has remained steady with a slight increase in job creation by sales networks associated with the increase in sales and marketing operations referred to above. The final result is a small rise in the overall level of employment in the sector.

Companies and employment

	Companies with Manufacturing Facilities	Marketing Companies (1)	Employment in Manufacturing	Total Employment
1998	266	361	34,200	38,400
1999	270	351	34,500	38,600
2000	270	359	34,500	38,700

(1) Revised series

Source: Own estimates based on the Spanish Statistical Institute's Survey of Industry and Companies and data from the General Board of the Spanish Colleges of Pharmacists (Catalogue of Medicinal Products)

3.2.3. Manufacturing

The latest estimates place the value of pharmaceutical products for human use manufactured in Spain during 2000 at 1,211,725 million pesetas at ex-factory prices. This is 7.2% more than the final figure for 1999.

Manufacturing in 2000 has continued to slow, in line with the trend beginning in 1996. Pharmaceutical specialities, which represent the greater part of output, continue to condition overall performance in manufacturing, which is still feeling the effects of the delistings decreed in 1998, the general price cut in 1999 and, more recently, the entry into force of the reference price system.

Pharmaceutical production for human use
(pesetas millions)

	Raw Materials (e)	Δ %	Pharmaceutical Specialities (1)	Δ %	Total (2)	Δ %
1998	225,000	2.0	824,200	8.4	1,049,200	7.0
1999	225,044	0.0	904,794	9.8	1,129,838	7.7
2000 (p)	226,000	0.4	985,725	8.9	1,211,725	7.2

(e) Estimated figures

(p) Provisional figures

(1) Apparent production = Domestic sales at ex-factory prices + Net exports of finished medicines

(2) Recorded production of raw materials + Apparent production of medicinal products

Source: Farmaindustria on the basis of IMS and Directorate General of Customs and Excise data

The contraction cuased by containment measures in manufacturing has been partially offset by buoyant direct sales to hospitals, which grew by 16% in 2000.

3.2.4. R&D&I

One of the key differentiating factors for pharmaceutical companies, which operate in a highly competitive market, is their capacity to launch new products to improve existing therapies or meet demand for new drugs to cure or alleviate previously untreatable diseases. These objectives require major investment, which does not always generate a return. Even so, the pharmaceutical industry has continually demonstrated its leadership in research over the years, despite occasionally disappointing financial returns on investments, as was the case in 1999, the last year for which data from the Spanish Statistical Institute's R&D Survey are available, when the Government applied an average 6% across-the-board price cut. There can be no doubt that such measures influence pharmaceutical companies' future research decisions . Nevertheless, total pharmaceutical R&D outlay (in-house and contracted research) totalled 61,554 million pesetas in 1999, according to the R&D Survey.

R&D activity in Spanish companies (1999)

	Employment in R&D	% Change since 1997	R&D Expenditure (pesetas millions)			
			In House	Contracted	Total	% Change since 1997
Total business sectors	38,323	27.6	432,121	131,087	563,207	37.1
Aerospace	2,339	2.9	33,160	3,389	36,549	18.0
Motor vehicles	3,354	9.6	40,584	42,762	83,346	49.6
Pharmaceuticals	3,351	9.8	41,113	20,441	61,554	15.5
Radio, TV and Communications	2,935	10.6	34,068	2,891	36,959	12.1

Source: Farmaindustria based on Spanish Statistical Institute data (R&D Surveys for 1999 and 1997).

The importance of R&D to the pharmaceutical industry cannot be understated:

- It is the absolute leader in terms of in-house research.
- R&D expenditure by the pharmaceutical industry represents 10.9% of the total amount by all industrial sectors, whereas pharmaceutical sales are only 2% of the total for Spanish industry.
- Pharmaceutical innovation is almost entirely based on R&D work. This clearly differentiates it from other industries.

Most innovative industries (1998)

Industry	Total Companies in the sector	% of Innovative companies	% Companies with R&D activity	Total expenditure on innovation
Motor vehicles	1,670	27.1	9.5	167,251
Pharmaceuticals	336	46.1	41.1	73,251
Radio, TV and Communications	219	44.3	38.4	53,274
Chemicals (excl. pharmaceuticals)	3,227	25.6	19.1	47,797
Aeroespace	44	27.6	20.5	49,697
Total industry	**160,359**	**10.0**	**3.0**	**1,010,671**

Source: Farmaindustria based on Spanish Statistical Institute data (Survey of Technological Innovation in companies. 1998 results).

Although the industry has not yet lost its leading position in industrial R&D&I, there has been a decline in the rate at which pharmaceutical industry spending on these activities has grown. In the main, this slowdown has been caused by a combination of the risks inherent in research activities and those provoked by the health authorities through the repeated application of measures to hold down public pharmaceutical expenditure to the maximum in order to ensure that it does not outstrip available budgets in the National Health System. This policy is absolutely incompatible with the market growth scenarios needed to assure returns on costly R&D investments.

The environment in which the pharmaceutical industry operates is heavily influenced by the demand channelled through the National Health System and is therefore prey to pressures on revenues and uncertainty caused by Government regulatory and budget control policies. This disincentive for R&D is in stark contrast to the political will that exists in Spain to foment R&D&I, which recently crystallised in the most significant legislation to date in this area —Law 55 of 29th December 1999, providing for a considerable increase in the R&D&I expenses allowable for corporate income tax purposes. The legislation establishes a general deduction up to 30% from gross taxable income in respect of expenses incurred in R&D expenses and, in cases where expenses exceed the average outlay for the preceding two fiscal years, the 30% deduction is applicable to the limit of average expenditure with an additional 50% deduction on the surplus. Moreover, an additional 10% deduction is provided for personnel expenses incurred in respect of employees assigned full-time to research and development projects and the cost of R&D&I work contracted out to universities, public research centres and technology and innovation centres.

A further measure specifically to encourage R&D in the pharmaceutical industry is the "Profarma" Plan, with which the industry is now thoroughly familiar. The results of this Plan are consistent with those obtained from the National R&D Survey (1999) carried out by the Spanish Statistical Institute, and complete the picture of research carried out by the pharmaceutical companies operating in Spain.

Profarma Plan, 1999 awards (1998 data)

Company ratings	Number	R&D Expenses	Total Sales	Sales of Medicinal Products	% R&D/Sales of Medicinal Products
Excellent	7	15,803	258,981	181,049	8.7
Very good	8	10,368	230,360	129,451	8.0
Good	11	7,114	144,730	77,080	9.2
Acceptable	10	6,431	215,604	129,202	5.0
Technological development and industrial plant	11	2,216	49,576	28,558	7.8
Research activity without industrial plant	5	4,490	89,459	58,861	7.6
Total	**52**	**46,422**	**988,710**	**604,201**	**7.7**

Figures in millions of pesetas. Source: Farmaindustria on the basis of MINER data.

The pharmaceutical industry's innovative drive and long-standing commitment to research extend beyond the narrow bounds of its own specialist fields, as demonstrated by the Collaboration Agreement recently made with the Ministry of Health to encourage and conduct scientific and technical research in the whole area of health and the life sciences. Under this agreement the industry has contributed 5,500 million pesetas to promote and undertake plans, programmes and other activities in support of scientific research through the Instituto de Salud Carlos III.

3.2.5. Domestic Market

Sales of medicinal products through retail pharmacies in the Spanish market totalled 953,108 million pesetas in 2000. Annual growth in the pharmacies channel was 8.8%, the lowest figure since 1994 when sales were squeezed by a general 3% price cut for all medicinal products with an ex-factory price of over 300 pesetas. Once again in 2000, the deceleration was due to a price cut, imposed by decree in 1999, as well as the implementation of the reference price system. Although reference prices did not come into force until 1st December, the effects were anticipated in the market and the prices of numerous products were lowered at mid-year, as soon as the list of medicines affected by the new system became known.

Direct sales by manufacturers to hospitals added a total 260,617 million pesetas to the domestic pharmaceuticals market, which was worth slightly over 1.2 billion pesetas at manufacturer's prices.

Hospital sales continue to grow faster than the pharmacies channel, increasing their share of the total market to 21.5% this year.

Closer analysis of the pharmacies channel reveals that prescription products accounted for 94.5% of the total market by value, but only 85.3% of unit sales.

Domestic market for medicinal products

	Retail Pharmacies	% change	Hospitals	% change	Total	% change
1999	875,212	11.3	224,670	13.0	1,099,882	11.7
2000	953,108	8.8	260,617	16.0	1,213,725	10.4

(Values at manufacturer's prices). Source: Farmaindustria using IMS data

Sales of medicinal products through retail pharmacies
(figures for 2000, expressed in millions)

	Total	% change	Prescript. products	% change	Other products	% change
Units	1,045.7	1.7	892,3	2.9	153.4	0.3
Pesetas	953,108	8.8	900,689	9.3	52,419	7.0

Source: Farmaindustria using IMS data

Average Price (pesetas)

	Total	% change	Prescript. products	% change	Other products	% change
1999	851	8.5	944	8.2	321	6.9
2000	911	7.0	1,009	6.9	342	6.5

Source: Farmaindustria using IMS data

The fastest growing treatments by therapeutic class were musculoskeletal systems, up 26% mainly due to the strong growth of anti-inflammatory and anti-rheumatic drugs (40%), followed by GU systems and sex hormones (21%) and blood and blood forming organs (18%).

The following table shows the relative share of each therapeutic class by units and value of sales.

Pharmacy sales of medicinal products by therapeutic class (2000)

Therapeutic class	Units (Thousands)	(%)	Value (Pesetas million)	(%)	Average ex-factory price
A. Alimentary tract and metabolism	158,471	15.2	143,468	15.1	905
B. Blood and blood forming organs	26,982	2.6	27,952	2.9	1,036
C. Cardiovascular system	144,492	13.8	216,880	22.8	1,501
D. Dermatologicals	62,450	6.0	34,855	3.7	558
G. GU systems and sex hormones	40,508	3.9	47,641	5.0	1,176
H. Systemic hormonal preparations (exc. sex hormones)	13,885	1.3	26,046	2.7	1,876
J. Systemic anti-infectives	73,528	7.0	74,780	7.8	1,017
K. Hospital solutions	2,056	0.2	420	0.0	204
L. Citostatic products	4,673	0.4	39,918	4.2	8,542
M. Musculoskeletal system	65,185	6.2	50,597	5.3	776
N. Central nervous system	261,027	25.0	167,502	17.6	642
P. Antiparasitic agents	985	0.1	340	0.0	345
R. Respiratory system	151,006	14.4	102,116	10.7	676
S. Sensory organs	39,442	3.8	19,661	2.1	498
T. Diagnostic products	217	0.0	310	0.0	1,431
V. Others products	830	0.1	620	0.1	747
Total	**1,045,737**	**100.0**	**953,108**	**100.0**	**911**

Source: IMS

New products launched in 2000 accounted for 3.2% of the total market, selling at an average manufacturer's price of 2,269 million pesetas, two and a half times the average for the market as a whole. Nevertheless, the large numbers of generic drug launches has caused an 18% fall in the average price of new products (i.e. those brought to market within the last 12 months) compared to 1999 (2,782 pesetas). Meanwhile, the emergence of generic products has increased the number of products on the market by 10% since 1995, with a total 8.735 pharmaceutical presentations marketed in 2000.
As in other sectors of the economy, the pharmaceutical sector continues to see intensive M&A activity, which has increasingly concentrated sales in a shrinking number of companies. Even so, concentration in the pharmaceutical industry remains far behind other high technology manufacturing sectors. By way of illustration, 64% of car sales were made by just five major groups in 2000, while the five largest pharmaceutical concerns accounted for only 28% of the total market.

3.2.6. International Trade

Once again in 2000, the balance of international trade in pharmaceutical products resulted in a deficit for Spain, which this year totalled –236,436 million pesetas, 13.5% more than in 1999.
The performance of raw materials and finished medicinal products, the key components of the balance of pharmaceutical trade, was as follows:

Total pharmaceutical trade in 2000 (pesetas millions)

	Imports	Exports	Balance	% change
Raw materials	66,447	74,387	7,940	320.0
Pharmaceutical Products	592,009	300,632	-291,377	-18.4
Total	**658,455**	**375,019**	**–283,436**	**–13.5**

Source: Directorate General of Customs (monthly data)

The pharmaceutical industry's international trade cover rate (i.e. exports / imports) for 2000 was 57.0%, a slight improvement on the rate for 1999 (54.3%). This was largely because raw materials trade returned to surplus after the deficit of 1999. Nevertheless, the coverage rate for pharmaceutical trade is still far from closing the gap with the balance of trade for total industrial sectors, which was 77.9%.
Pharmaceutical trade in 2000 continued to be concentrated in Europe, with 76.9% of imports originating in the EU and 74.2% of exports going to our European partners. The pharmaceutical's sectors intra-EU trade is considerably higher than that of other industrial sectors, representing 71.9% of imports and 70.1% of exports.

International trade in pharmaceuticals by region in 2000
(pesetas millions)

	European Union			Rest of World		
	Imports	Exports	Balance	Imports	Exports	Balance
Raw materials	36,020	36,591	571	30,427	37,796	7,369
Pharmaceutical Products	470,273	241,741	-228,532	121,736	58,891	-62,845
Total	**506,293**	**278,332**	**-227,961**	**152,163**	**96,687**	**-55,476**

Source: Directorate General of Customs and Excise (monthly data)

As in previous years, the main components of trade in raw materials and medicinal products were, respectively, antibiotics (item 29.42) and retail medicines (item 30.04). A breakdown for 2000 based on the customs classification of products is as follows:

Structure of international trade in pharmaceutical products for 2000
(% of total and balance in pesetas millions)

	Imports	Exports	Balance
Raw materials	**10.1**	**19.8**	**7,940**
29.35 Sulphonamides	0.8	0.9	-1,813
29.36 Vitamins and Pro-vitamins	2.1	0.9	-10,598
29.37 Hormones	1.1	1.7	-599
29.38 Heterosides Alkaloids	0,4	0.8	-560
29.39 Vegetable alcaloids	1.1	1.3	-2,338
29.41 Antibiotics	4.6	14.2	22,729
Medicinal products	**89.9**	**80.2**	**-291,377**
30.01 Glands and other organs	1.1	0.6	-4,919
30.02 Blood, antisera and Vaccines	9.7	8.2	-32,699
30.03 Bulk medicines	2.5	2.1	-8,908
30.04 Medicines	71.6	64.9	-227,694
30.05 Gauzes and bandages	2.6	1.7	-10,687
30.06 Other products	2.5	2.6	-6,469
Total	**100.0**	**100.0**	**-283,436**

Source: Directorate General of Customs (monthly data)

On the basis of these figures, which show a particularly large deficit in retail medicines for 2000, and the evolution of trade in recent years, imports of pharmaceuticals are among the highest for industrial products. In accordance with customs data, imports of pharmaceutical raw materials and finished products were sixth out of all imports by value and third in terms of year-on-year growth (20.5%). In the ranking of exports, on the other hand, pharmaceutical products fanked ninth, showing an increase of 26.4% compared to 1999.

In qualitative terms, international trade in pharmaceuticals has varied little in recent years, with a continued surplus in raw materials due to higher export than import prices, and a widening deficit in finished products, despite the positive balance in terms of volumes. This is because export prices are low compared to the cost of imports.

3.2.7. Social Security consumption

Some 597 million prescriptions were written by Social Security doctors and dispensed by pharmacies in 2000, particularly in the areas of prescription drugs, formulas and therapeutic products, for a total value of 1,215,807 million pesetas.

The relatively slow growth in public costs was influenced by the across-the-board cuts in the authorised manufacturer's prices of reimbursed drugs imposed at the end of 1999. As was only to be expected, the impact was felt as a deceleration in the rate of growth in spending per prescription in 2000. This low growth is not, however, attributable solely to price reductions, as might appear to be the case at first sight, but is also a consequence of the sharp increase in the number of prescriptions, particularly formulas and stamped prescriptions (+16.0%) and prescription drugs (+4.7%), which represented 97% of the total.

Social Security market. Prescriptions dispensed through retail pharmacies (1)

	Total Prescriptions (RRP + VAT in millions pesetas)	Δ %	Number of Prescriptions (Millions)	Δ %	Cost per prescription (Pesetas)	Δ %
1999	1,123,722	9.5	569.5	1.4	1,973	8.0
2000	1,215,807	8.2	596.8	4.8	2,037	3.3

(1) Includes all prescription billings: prescription drugs, formulas and therapeutic devices.
Source: Ministry of Health and Consumer Affairs (Summary of medical prescriptions turnover, December 1999 and 2000).

Two further factors affected the evolution of public spending on medicinal products in 2000. Firstly, Royal Decree Law 5/2000, which came into force during the year, established new margins for pharmaceutical distribution, as well as a volume rebate for sales to retail pharmacies. Secondly, the reference pricing system took effect in December, resulting in the inclusion of new items in overall pharmaceutical spending in Spain, as shown in the following chart:

Breakdown of billings for medical prescriptions

	2000	1999	% 2000/1999
Total sales	1,215,806,841	1,123,721,697	8.19
General contribution	86,615,529	82,686,608	4.75
Reference price contribution	75,672	-	-
Gross expenditure	1,129,191,313	1,041,035,089	8.47
Discounts and rebates	10,483,769	-	-
NET EXPENDITURE	**1,118,707,544**	**1,041,035,089**	**7.46**

Figures in thousands of pesetas. Notes: Total sales: billings at mandatory pharmacy prices for medicinal products, which may either be RRP plus VAT or the reference price. General contribution: the traditional contribution made by the patient (40% in general; 10%, to a maximum of 439 pesetas, for certain chronic ailments; 0% for pensioners, victims of workplace accidents, toxin syndrome patients, and patients suffering from work-related diseases). Reference price contribution: amount payable by the patient in addition to the reference price to cover the difference between the sale price of the drug prescribed and the reference price, where the patient prefers not to substitute the prescribed drug with a generic product at a price equal to or lower than the reference price. Gross expenditure: cost billed by retail pharmacies before application of the discounts and rebates established by Royal Decree 5/2000. Net expenditure: expenditure net of discounts and rebates pursuant to Royal Decree 5/2000. Source: Ministry of Health and Consumer Affairs (Summary of medical prescriptions turnover, December 1999 and 2000).

There are significant differences in the spending of the Regional Health Services in Spain. The Regions where health provision is managed directly by the Insalud have played a leading role in containment, since they simultaneously represent a high proportion of total spending (35%) and have held growth down to almost 1 point below the increment for the Spanish National Health System as a whole. The Canary Islands saw the fastest expenditure growth, although per capita spending by the Region's independent health service is the second lowest out of the Regions where responsibility for health provision has been transferred to the second tier of government. Pharmaceutical expenditure also expanded notably in Andalusia, a Region that has traditionally lagged behind the national average in absolute terms and per capita. In 2000, the Region's spending was close to the average.

Breakdown of Regional pharmaceutical expenditure (2000)

	PERCENTAGE OF TOTAL SPENDING	PER CAPITA SPENDING (PESETAS)	% CHANGE 1999
Regions under direct Management by Insalud	34.8	22,613	6.3
Andalusia	18.4	25,506	7.3
Catalonia	17.6	28,761	7.6
Canary Islands	3.8	23,438	9.3
Galicia	7.3	27,046	7.3
Navarre	1.3	24,383	5.3
Valencian Region	12.0	29,968	7.3
Basque Country	4.8	22,984	8.1
TOTAL	**100.0**	**25,211**	**7.1**

Note: Expenditure net of discounts and rebates established under Royal Decree Law 5/2000.
Source: Ministry of Health and Consumer Affairs (Summary of medical prescriptions turnover, December 1999 and 2000).

3.3 Medicines prices

The prices of pharmaceutical products in Spain continued to be low compared to other EU markets.

This is certainly because of government intervention to hold down prices, a policy which, with minor differences, has historically been applied particularly strictly in the Mediterranean countries.

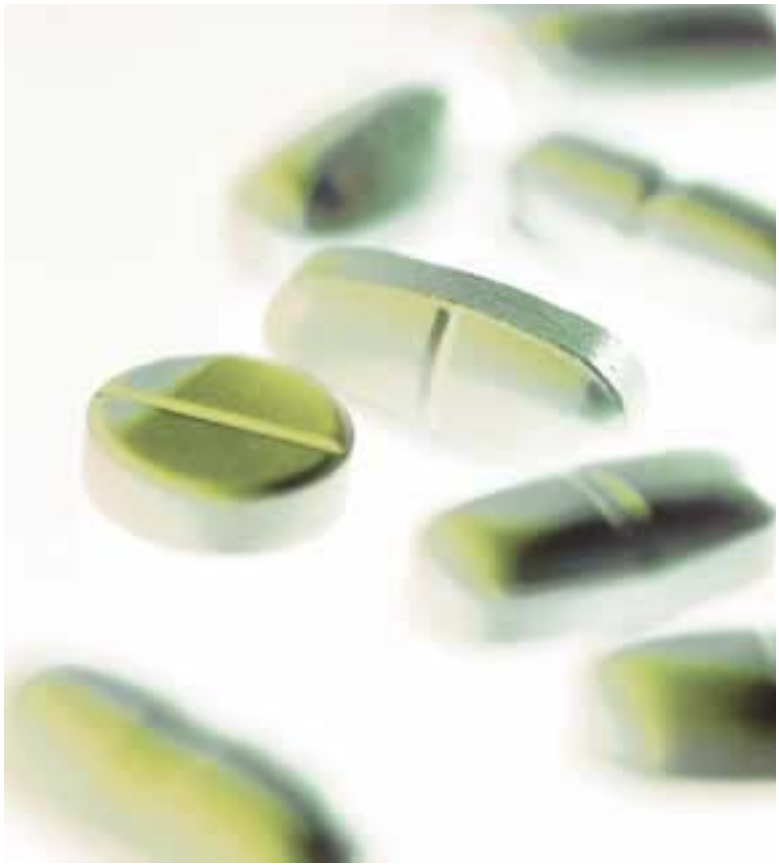
The briefest analysis of the situation in the EU clearly shows how policy differences with regard to pharmaceutical expenditure have created two main price blocs, which roughly comprise the northern and southern countries in what is supposed to be a single market.

In the area formed by Sweden, Denmark, Finland, the Netherlands, Germany and the United Kingdom, the average market price of medicinal products (ex factory price) is 1,735 pesetas, whereas in the southern area, comprising Portugal, Spain, France, Italy and Greece, it is 898 pesetas, practically half the average for the northern bloc.

Curiously, both areas have a similar population size, with the northern bloc containing 47.1% of the EU's total inhabitants and the southern countries 47.0%. Given the difference in prices, therefore, this translates into much higher consumption of units or packages of medicines in the Mediterranean area (62.9%) compared to the northern countries (32.2%).

Though it would be simplistic to claim that higher prices in the northern countries explain their leadership in European pharmaceutical research, it is undeniable that price controls have at least not hindered R&D investment, thereby enabling pharmaceutical companies to increase their presence in other markets.

A further group formed by Belgium, Austria and Ireland can also be made out in an intermediate position between the northern and Mediterranean blocs, which, for the sake of argument, we shall call the "central" bloc. In these countries the average price of pharmaceutical products is 1,330 pesetas. In percentage terms, the central bloc represents only a small part of the EU's population (5.9%) and consumption of pharmaceutical products (5.5% of the total market by volume and 4.9% by units).



EU medicine prices (weighted average market price, ex-factory prices)

		Price in pesetas	Index (EU 14 = 100)
NORTH	Sweden	2,791	238
	Denmark	2,305	196
	Netherlands	1,659	141
	Finland	1,650	141
	Germany	1,636	139
	United Kingdom	1,597	136
CENTRE	Belgium	1,393	119
	Ireland	1,316	112
	Austria	1,244	106
	UE 14 (excl. Luxembourg)	1,174	100
SOUTH	Portugal	1,168	99
	Italy	1,051	90
	Spain	911	78
	France	807	69
	Greece	734	63

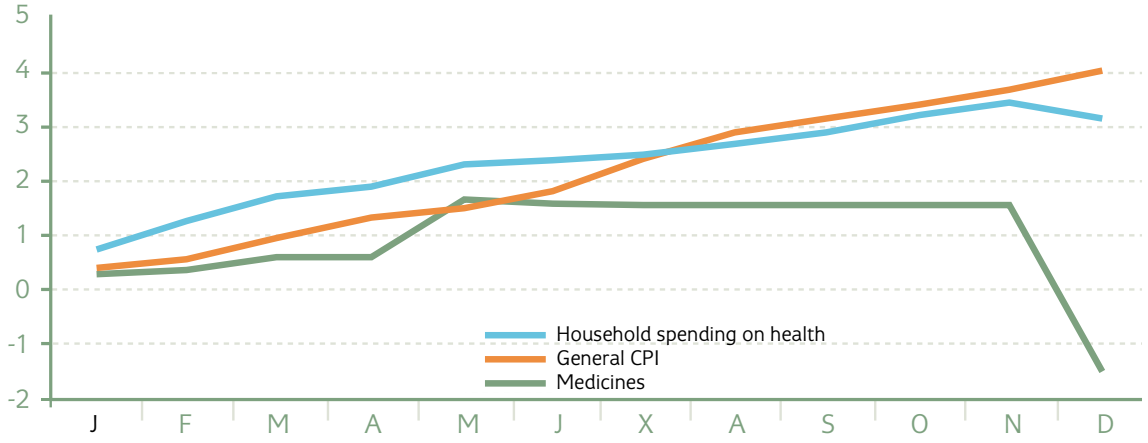
AREA	Price in pesetas	Index (UE14=100)	% EU population	EU market share (5%) ex-factory prices	EU market share (5%) Units
NORTH	1,735	148	47.1	46.3	32.2
CENTRE	1,330	113	5.9	5.5	4.9
SOUTH	898	76	47.0	48.2	62.9

Source: Own compilation from IMS data.

The average ex-manufacturer's price in Spain is only 911 pesetas, higher only than in France and Greece. The average price for the EU as a whole is 28% higher than in Spain, while average prices in the northern bloc of countries are 90% above ours, and those of the central group of countries 46%.

With regard to the evolution of prices, Spain saw a 6.9% increase compared to 5.8% for the EU as a whole. Nevertheless, the CPI for medicines was actually negative (1.46%) for reasons that are explained in detail in the FARMAINDUSTRIA Annual Report for 1999. In this light, rising inflation in Spain, which reached 3.95% in 2000, can in no wise be blamed upon pharmaceutical prices.

Consumer price index (CPI). Cumulative monthly rate of inflation for 2000



Source: Own compilation from INE data.

The above chart of cumulative monthly inflation for 2000 shows the CPI for medicines running clearly below those for household spending on health-related goods and services for each month in the year. Meanwhile, increases in medicine prices overtook the general rate of inflation in only one month (May). This spike (1.07%) could only have been due to price rises for certain freely priced medicines (i.e. medicines that do not qualify for Social Security reimbursement) with a relatively high weighting in the basket of medicines used for indexing purposes, since there were no interventions from the government that might have implied a general shift in pharmaceutical prices.

The most striking feature of the medicines CPI, however, is the steep, general fall in prices in December (2.9% compared to November), as a result of which the cumulative change in prices switched from +1.49% in November to –1.46% at the end of the year. This is explained quite simply by the impact of the new reference price system on 1st December, which provoked sharp cuts in the prices of numerous medicines accounting for a significant portion of the overall basket of medicines (established in 1992), due to their long periods of commercialisation and widespread consumption.

The impact of these price cuts on the CPI was further amplified because household spending on the medicines affected by the reference price system in the National Health System (i.e. co-payment) also declined, since it is established as a percentage of the price. It is necessary to take into account here that the CPI measures changes in household spending in relation to a basket of goods and services established in the base year of the index. The change in this spending therefore coincides with the variation in the prices of goods that are not subsidised out of the public purse, but this need not be the case for publicly funded goods, such as the majority of medicines. If co-payment were established as a fixed charge for each package rather than a percentage of the price, the reference price system would have had a smaller impact on the pharmaceutical CPI, which would only have reflected the decline in household spending on pharmaceutical products in the private market, but not National Health System prescriptions, which would not have undergone any change.

3.4 Reference prices

The Ministry of Health and Consumer Affairs Order published in the Official State Gazette on 13th July 2000 by way of secondary legislation implementing Royal Decree 1035 of 18th June 1999. This order establishes homogeneous groups of presentations for medicinal products and approves references prices.

The initial implementation of the reference price system affected 593 pharmaceutical presentations for formulas containing 42 active substances, while 114 homogeneous groups, and consequently reference prices, were defined.

FARMAINDUSTRIA's estimates of the impact on the pharmaceuticals market at manufacturer's prices in view of the Ministerial Order were close to Health Ministry calculations. On the assumption that prices for all medicines priced above the reference price would fall to the levels established, the overall impact was estimated at 16,000 million pesetas at ex-factory prices (total market) and around 21,000 million in terms of social Security pharmaceutical expenditure.

The application of the system for the purposes of Social Security billings was scheduled for 1st December 2000. However, from the moment the Ministerial Order was published,

prices of numerous presentations started to fall. In fact, such strategic price cuts had already begun some months previously. Furthermore, the reference prices were calculated on the basis of authorised manufacter's prices at 31st December 1999, and in the interim between that date and the final entry into force of the system eleven months later, some pharmaceutical companies had registered generic products at ex-factory sales that were significantly lower than existing ones and, naturally, far below the reference prices.

In this initial scenario for reference pricing, the scope of substitution of prescription drugs with generics has been much wider than initially expected, largely because tensions between the doctor and the pharmacist in this regard have not yet been clearly resolved. In some cases, branded generics that are already more economical than the reference price are even substituted with other, cheaper products. As a consequence, in a sizeable number of homogeneous groups the reference prices fixed in the Ministerial Order have in fact been pruned back even further due to the fierce price competition unleashed by the system.

The economic consequences for the industry as a whole and for the Social Security system have marked an even greater fall in revenues on the one hand, and expenditure on the other than had initially been foreseen on the basis of theoretical estimates.

The results of a direct survey carried out by FARMAINDUSTRIA among all of its members show that the companies affected by reference pricing have suffered losses due to price cuts and falling unit sales for a total of 6,579 million pesetas compared to 1999 in the first three months since the implementation of the system (from 1st December 2000 until 28th February 2001). Annualising this estimate, the loss would be some 26,316 million pesetas, though even this figure could easily be superseded given the faster than expected incidence of price cutting following the introduction of reference prices, as noted above. In terms of Social Security expenditure on prescriptions, savings could top 37,000 million pesetas in the first year of the reference price system.

The behaviour of pharmacists with regard to substitutions could, however, lead to a reaction from doctors wishing to ensure that the prescribed medicine is actually dispensed in cases where they hold it necessary in their professional judgement, and all the more so where the doctor does not know exactly what substitute product will be given to the patient. In this context, it is possible that medical practitioners will opt to prescribe alternative active principles or pharmaceutical presentations that are not included in the reference price system and are therefore more expensive. This would reduce the savings the system is designed to produce.

4 Appendix: new legislation

New legislation has been approved during 2000 and up to the date of writing as follows (may 2001) :

ANTI-DOPING

SPORTS COUNCIL RESOLUTION OF 21ST MARCH 2000 approving the list of banned substances and pharmacological groups, as well as illicit doping methods.

CHEMICAL WEAPONS

FOREIGN TRADE BOARD CIRCULAR OF 2ND FEBRUARY 2000 concerning prohibitions on imports and of certain toxins and chemical precursors from and to certain countries.

GOOD LABORATORY PRACTICE

MINISTERIAL ORDER OF 14TH APRIL 2000 amending the annexes to Royal Decree 2043 of 14th October 1994 concerning Good Laboratory Practice inspections and verification procedures in view of the effect of technical developments.

ROYAL DECREE 1369 OF 19TH JULY 2000 amending Royal Decree 822 of 28th May 1993, which established the principles of Good Laboratory Practice and required the application thereof to non-clinical trials of chemical substances and products.

PARALLEL TRADE

ROYAL DECREE 1785 OF 27TH OCTOBER 2000 governing intra-EU trade in medicines for human use.

RESIDUAL SOLVENTS

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 5 OF 28TH MARCH 2001 concerning residual solvents in authorised pharmaceutical products.

EURO

ROYAL DECREE 286 OF 16TH MARCH 2001 regulating dual pricing for pharmaceutical products and devices in pesetas and euros.

DIRECTORATE GENERAL OF PHARMACY AND HEALTH PRODUCTS CIRCULAR 4 OF 6TH APRIL 2001. The Circular sets out instructions for the application of Royal Decree 286 of 16th March 2001 regulating dual pricing for pharmaceutical products and devices in pesetas and euros.

TRANSMISSIBLE SPONGIFORM ENCEPHALITIS

MINISTERIAL ORDER OF 3RD MARCH 2000 updating annex II of Royal Decree 767 dated 21st May 1993, which regulates the evaluation, authorisation, and dispensing conditions of industrially manufactured medicinal products and other medicines for human use.

ROYAL DECREE 1911 OF 24TH NOVEMBER 2000 regulating the destruction of specific materials representing a risk in relation to transmissible spongiform encephalitis.

SUB-SECRETARIAT FOR AGRICULTURE, FISHERIES AND FOOD RESOLUTION OF 1ST DECEMBER 2000 authorising the publication of the Agreement of the Council of Ministers of the Spanish Government of 1st December 2000. This Agreement established general criteria for the negotiation and closure of specific Collaboration Agreements with Regional Governments and other measures concerning the instrumentation of anti-BSE measures.

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 15/2000 concerning the minimisation of the risk of transmission of animal spongiform encephalitis agents via medicines.

ROYAL DECREE 3454 OF 22ND DECEMBER 2000 establishing and regulating the integrated co-ordination Program for transmissible animal spongiform encephalitis oversight and control.

SPANISH MEDICINAL PRODUCTS AGENCY NOTE DATED 12TH JANUARY 2001. Clarification for compliance with Spanish Medicinal Products Agency Circular 15/2000 concerning the minimisation of the risk of transmission of animal spongiform encephalitis agents via medicines.

MINISTERIAL ORDER OF 21ST FEBRUARY 2001 regulating the National Epidemiological Oversight Network in relation with transmissible human spongiform encephalitis.

ROYAL DECREE 221 OF 2ND MARCH 2001 amending Royal Decree 1911 of 24th November 2000, which governs the destruction of materials specified as constituting a risk in relation with transmissible spongiform encephalitis.

BIO-EQUIVALENT MEDICINAL PRODUCTS

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 1 OF 12TH JANUARY 2001. Instructions relating to the definition of products as bio-equivalents in accordance with the provisions of Royal Decree 1035/1999.

OTC MEDICINES SUITABLE FOR ADVERTISING

MINISTERIAL ORDER OF 28TH SEPTEMBER 2000 amending the contents of the annex to the Ministerial Order of 17th September 1982, which implements Royal Decree 2730/1981

governing the registration of over-the-counter medicines suitable for advertising.

ILLEGAL DRUGS AND PSYCHOTROPIC SUBSTANCES

MINISTERIAL ORDER OF 31ST JANUARY 2000 listing the substance 4methyltioamphetamine (4MTA) in annex I of Royal Decree 2829 of 6th October 1977, which governs psychotropic substances and products.

MINISTERIAL ORDER OF 7TH FEBRUARY 2000 which lists certain active substances in annex I of the 1961 Convention on illegal drugs.

LABELS AND PROSPECTUS PILS (PACIENT INFORMATION LEAFLETS)

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 2/2000. Directive concerning the legibility of labelling materials and prospectuses, and ANNEXES.

SPANISH PHARMACOPOEIA

MINISTERIAL ORDER OF 17TH FEBRUARY 2000 approving additions and updates to the Royal Pharmacopoeia.

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 3 OF 15TH JANUARY 2001 concerning the Project for the Royal Pharmacopoeia Guide.

ROYAL DECREE 249 OF 9TH MARCH amending Royal Decree 294 of 24th February 19995, which regulates the Spanish Pharmacopoeia, the Technical Document and the consultative bodies of the Ministry of Health and Consumer Affairs.

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 8 OF 28TH MARCH 2001. Project for a Royal Pharmacopoeia Guide concerning "In vitro erythrocite marking using 99mTc".

EUROPEAN PHARMACOPOEIA

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULARS 5 OF 6TH APRIL 2000, 9 OF 18TH MAY 2000, 14 OF 20TH NOVEMBER 2000, 2 OF 15TH JANUARY 2001 and 4 OF 15TH JANUARY 2001. These Circulars refer to the urgent procedure to bring monographs and texts from the European Pharmacopoeia into effect.

PHARMACOVIGILANCE

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 4/2000. Pharmacovigilance reporting procedure between the Pharmaceutical Industry and the Spanish Medicinal Products Agency for medicines for human use.

MEDICAL FORMULAS AND PHARMACY PREPARATIONS, ROYAL DECREE 175 OF 23RD FEBRUARY 2001 approving the regulations for the proper preparation and quality assurance of medical formulas and pharmacy preparations.

PUBLIC HEALTH FOUNDATIONS

ROYAL DECREE 29 OF 14TH JANUARY 2000 concerning new management methods for the National Health Institute (Insalud).

PHARMACEUTICAL EXPENDITURE

ROYAL DECREE LAW 5 OF 23RD JUNE 2000 establishing urgent measures for the containment of public pharmaceutical expenditure and rationalisation of the use of medicines, and DIRECTORATE GENERAL OF PHARMACY AND HEALTH PRODUCTS INFORMATION CIRCULAR of 265th June concerning the application of the aforementioned Royal Decree.

BLOOD PRODUCTS

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 13 OF 14TH JULY 2000. Information governing viral safety in the technical files and prospectus of medicinal products containing any human plasma derivatives as an active substance.

INSALUD

ROYAL DECREE 29 OF 14TH JANUARY 2000 concerning new management methods for the National Health Institute (Insalud).

MINISTRY OF HEALTH AND CONSUMER AFFAIRS

ROYAL DECREE 809 OF 19TH MAY and ROYAL DECREE 1450 OF 28TH JULY 2000 implementing the basic structure of the Ministry of Health and Consumer Affairs.

PRICES

MINISTERIAL ORDER OF 13TH JULY 2000 establishing homogeneous groups of pharmaceutical presentations and products and fixing reference prices.

HEALTH PRODUCTS

ROYAL DECREE 1662 OF 29TH SEPTEMBER 2000 concerning health products for in vitro diagnosis.

WASTE PRODUCTS

SPANISH ENVIRONMENT BOARD RESOLUTION OF 13TH JANUARY 2000 authorising the publication of the Spanish Government Council of Ministers Agreement dated 7th January 2000, which approves the National Plan for Urban Waste.