Farmaindustria

ANNUAL REPORT

2002

Contents

Message from the President

The publication of the FARMAINDUSTRIA Annual Report is always a good ocasi n to take stock of the year and look towards the immediate future. This year is also special in that I share the responsibility for explaining the association's activities in 2002 with my predecessor, Jes s Acebillo Marín, from whom I took over the office of President of the General Assembly last October.

I believe it is only right and proper to recognise at this point the distance we have travelled over the past two years. We have recovered a good level of dialogue with Government at all levels, culminating with the signing of the Pact, and this would not have been possible without the credibility we have earned in this new stage thanks to the endeavour of our members, the leadership of the Governing Bodies and the work of the Association's management team. The renewal and implementation of the new Ethics Code would also have been impossible without the firm commitment of the Association to respond as a whole to the demands of these changing times.

Upon taking office I already explained the major issues that will concern us as priorities and which have,indeed, defined the work of the Association in recent months.

Our first priority, for obvious reasons, has been to update the Stability and Innovation Pact made with the Spanish Ministry of Health and Consumer Affairs. This will serve as an instrument to ensure a stable regulatory framework providing the context for sustainable growth in public expenditure on pharmaceuticals. At the closing date of this annual report, we are in fact discussing the contents of an addendum to update the Pact in view of the reform of the Reference Pricing System implemented by the Government through the amendment of article 94.6 of the Medicines Act, 1990 (Law 25/1990) via the National Health System Cohesion and Quality Act.

Despite the major impact of this modification to the Reference Pricing System, FARMAINDUSTRIA understands Government's need to control growth in expenditure, which is already reaching levels that are close to unsustainable for the National Health System. We also recognise that this falls within the scope of structural measures aimed at harmonisation with Europe as provided for in the Pact, at least insofar as regulatory developments also respect the sustainability of business activities.

The second major issue, which is also greatly affected by the above, is the increasingly complex scenario in which we find ourselves due to the completion of the devolution process and changes in the funding system for the Regions. The main challenge in this area is

to promote continued unity in the market and a harmonious regulatory structure. These are key factors for the framework of the pharmaceutical industry's activities.

The third key issue is our objective of preserving the internal cohesion of the Association, ensuring that we reach solutions that provide appropriate representation of all interests involved. At the same time, we intend to continue driving the involvement of members in the Association's working groups and sections, which have so far generated excellent results, improving information flows and communication between members on an ongoing basis. I am certain that we will continue to strengthen united action by our industry in a time of change and uncertainty in the environment.

This uncertain climate is a result not only of the devolution of healthcare powers to the Regions but also of the intense process of change in the international scene, which is the fourth major area for our activities. We must remain alert to various major issues that are currently taking shape on the European scene and are likely to condition our activity in Spain to a considerable degree. These are: i) the implementation of the G-10 recommendations both at the level of the European Commission and in each Member State; ii) the review process for European pharmaceutical legislation, which among other matters will affect registration procedures, the protection of innovations, licensing policy, and advertising and promotional activities; and iii) the EU enlargement process, which will result in the accession of countries that will compete directly with us.

Finally, let me briefly mention certain areas where the Association continues to work and intensify its activity. We must persist with our efforts to communicate the value that our Industry provides to society and our country. This will mean dedicating further resources to communication in order to strengthen public awareness of medicines and our industry. In this field we need to uphold the banner of Research, Development and Innovation in Spain, a country which dearly needs to upgrade its scientific and technology base and therefore requires sectors such as ours to act as a driver. We must seize these opportunities and, in all probability, we will have to make a qualitative leap in this area, making the best use of the funding we contribute through the Pact and emphasising the Industry's commitment to Spain's scientific and healthcare future.

To conclude,it may seem that the list of issues and priorities is always the same, but the truth is that both the form and content of these matters are subject to continual changes over time. We must, therefore, constantly renew our methods and think ahead, anticipating the future in order successfully to take up the new challenges arising from perennial problems.

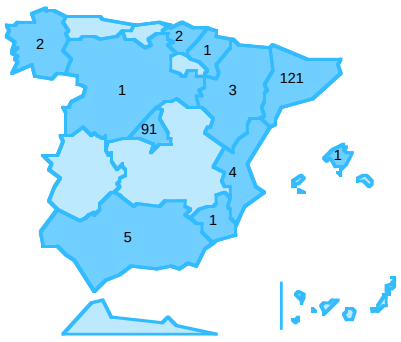
JORGE GALLARDO BALLART
President of FARMAINDUSTRIA

FARMAINDUSTRIA in 2002

1 Membership

At 31 December 2002 FARMAINDUSTRIA's membership comprises a total of 232 pharmaceutical companies. The geographical distribution of member companies is as follows:

FARMAINDUSTRIA's members represent 67% of the pharmaceutical companies operating in Spain (i.e. total manufacturing and/or marketing companies, and making sales through retail pharmacies), which account for 92% of sales.



CLASSIFICATION OF PHARMACEUTICAL COMPANIES

DOMESTIC	118	INTERNATIONAL	114
Major	9	Major	23
Medium-size	10	Medium-size	30
Small	99	Small	61

TOTAL 232

2 Organisation

2.1. Governing Bodies

The General Assembly of members is the supreme governing body of the Association and expresses their collective will.
The governance of the Association is the responsibility of the Board of Governors, which comprises the President and 24 representatives of member companies, and the Steering Committee formed by the President, six Vice-Presidents and eight members appointed by the Board of Governors from among its own members.

FARMAINDUSTRIA General Assembly, October 2002

Elections were held in October 2002 to renew the Association's Governing Bodies. In accordance with the statutory provision requiring the appointment of a new President every two years, Jorge Gallardo Ballart was chosen to take office as the representative of the Domestic Group of member companies, taking over from Jes s Acebillo Marín, who held the Presidency until October representing the International Group.
As a result of these elections, the Governing Bodies of the Association are now as follows:

STEERING COMMITTEE

PRESIDENT

D. Jorge Gallardo Ballart ALMIRALL PRODESFARMA, S.A.

VICE-PRESIDENTS

D. Jesús Acebillo Marín NOVARTIS FARMAC UTICA, S.A.
D. Albert Esteve Cruella DR. ESTEVE, S.A., LABORATORIOS
D. Rafael Juste Sesé JUSTE, S.A. QCO. FCA.
D. Javier Ellena Aramburu DISTA, S.A.
D. Rafael Foguet Ambrós FERRER INTERNACIONAL, S.A.
D. Carlos Trías Vidal de Llobatera ASTRAZENECA FCA. SPAIN, S.A.

MEMBERS

D. Helmut Andress LACER, S.A.
D. Manuel García Garrido BOEHRINGER INGELHEIM, S.A.
D. John A. Keeler SANOFI-SYNTHELABO, S.A.
D. Javier Peris Musso S.A.L.V.A.T., S.A., LABORATORIO
D. Javier Font Salgado FARDI LBO.DE APLIC. FARMACODIN MICAS, S.A.
D. Rafael Giménez Cuesta FARMA LEPORI, S.A.
D. Emilio Moraleda Martínez PFIZER, S.A.
D. Juan Uriach Torelló J. URIACH & CIA., S.A.

BOARD OF GOVERNORS

President

D. Jorge Gallardo Ballart ALMIRALL PRODESFARMA, S.A.

Vice-Presidents

ASTRAZENECA FCA. SPAIN, S.A. **D. C. Trías Vidal de Llobatera**
DR. ESTEVE, S.A., LABORATORIOS **D. Albert Esteve Cruella**
JUSTE, S.A. QCO. FCA. **D. Rafael Juste Sesé**
DISTA, S.A. **D. Javier Ellena Aramburu**
FERRER INTERNACIONAL, S.A. **D. Rafael Foguet Ambrós**
NOVARTIS FARMAC UTICA, S.A. **D. Jesús Acebillo Marín**

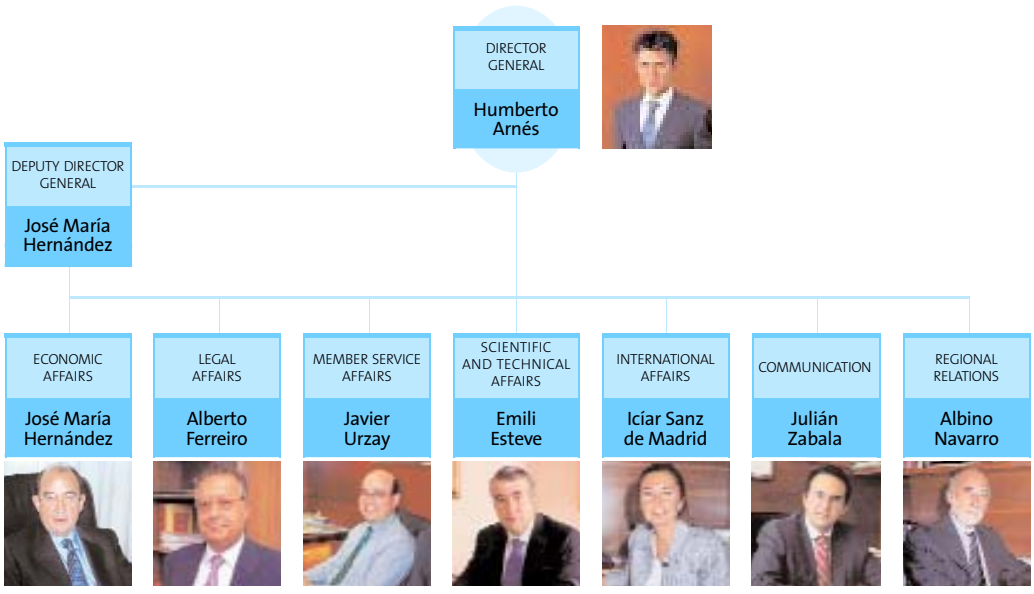
Member Company Representatives

ABBOTT CIENTÍFICA, S.A.-Div. Ross Lbo. **D. R. Zafra Roldán**
BOEHRINGER INGELHEIM, S.A. **D. Manuel García Garrido**
FAES PHARMA, S.L. **D. Eduardo Fernández de Valderrama**
FARMA LEPORI, S.A. **D. Rafael Giménez Cuesta**
JANSSEN CILAG, S.A. **D. José Luis Sotoca Santos**
LESVI, S.A., LABORATORIOS **D. Enric Vallés Rodoreda**
MERCK, SHARP & DOHME DE ESPAÑA, S.A. **D. A. Pérez Mosquera**
PFIZER., S.A. **D. Emilio Moraleda Martínez**
S.A.L.V.A.T., S.A., LABORATORIO **D. Javier Peris Musso**
ALTER, S.A., LABORATORIOS **D. Antonio Alonso Aventín**
CEPA SCHWARZ PHARMA S.L., **D. Antonio Martín García**
LBO.DE APLIC. FARMACODIN MICAS, S.A. FARDI **D. Javier Font Salgado**
J. URIACH & CIA., S.A. **D. Juan Uriach Torelló**
LACER, S.A. **D. Helmut Andress**
MENARINI, S.A., LABORATORIOS **D. Joan Puig Corcoy***
NORMON, S.A., LABORATORIOS **D. Jesús Govantes Esteso**
PHARMAZAM, S.A., **D. Davide Sirtoli Lovati**
SANOFI-SYNTHELABO, S.A. **D. John A. Keeler**

* As from 17/12/02. Formerly represented by Joaquín Puig Corcoy

2.2 Executive

Farmaindustria's executive is headed by the Director General. The executive is, in turn, structured through seven functional departments. The Association's head office is in Madrid, and it also has an Office in Barcelona.
The resulting functional organisation is as follows:



3 Activities in context

The medicines produced by the pharmaceutical industry are not only enormously valuable in themselves but also contribute more than any goods to the well-being and health of the citizen. The industry researches, manufactures and brings to market pharmaceutical products that alleviate suffering and cure disease.

At the same time, medicines are probably the most regulated products in any market, precisely to safeguard the health of the citizen. Not only does the State foot a large part of the bill for the medicines consumed in the country, but it decides what medicines may be sold through what channels, how products are manufactured and dispensed, and when they are paid for.

In this context, FARMAINDUSTRIA's mission has the following objectives:

- Co-operating with Government to establish a stable regulatory and economic framework that is conducive to balanced growth in the market, the expansion of R&D activities and the development of the Spanish pharmaceutical industry.
- Improving public perceptions of the pharmaceutical industry and medicines by raising awareness among citizens, opinion formers and politicians of the added value that therapeutic products provide for social progress and the quality of our lives.
- Offering value added services to member pharmaceutical companies by providing information, business advice and a joint approach to the issues.
- Representing the Spanish pharmaceutical industry both nationally and internationally.

FARMAINDUSTRIA's mission thus involves activities in four different contexts, each of which is discussed in detail in the following sections.

3.1. Relations with Government

3.1.1. The first year of the Pact, 2002-04

FARMAINDUSTRIA's corporate activity over the past year has been deeply marked by the Stability and Innovation Pact made with the Ministry of Health and Consumer Affairs on 31 October 2001. As a consequence, a large part of the activity of the Association's staff has centred on participation in mixed working groups set up to build upon the commitments made by the Ministry of Health and Consumer Affairs in the Pact. These commitments concern the issues of parallel trade, the extension of the data protection period and more favourable treatment of the R&D costs incurred by the pharmaceutical industry.

At the same time, the Association has closely tracked and analysed the evolution of Spanish National Health System spending on medicines, in view of its impact on the finances of Regional healthcare services and the ongoing political disputes surrounding this item of the public healthcare budget. This arguments could indeed jeopardize the continuation of the Pact if the reasons for and meaning of the changes observed in recent months are not properly explained.

The close of 2002, the first year of the Pact, is thus an appropriate moment to take stock of its results in terms of the level of compliance with the objectives established.

An analysis of the strengths and weaknesses arising from the practical implementation of the institutions and mechanisms provided for in the Pact will furnish the basis for possible consensus-based modifications or changes by the parties in order to ensure that it runs for the whole of the original three-year term.

An analysis of compliance with commitments that are the sole responsibility of the pharmaceutical industry should begin with reference to appropriations to the public health research Fund. These amounts are channelled through the new FARMAINDUSTRIA FOUNDATION, the creation of which was provided for in the Pact, via the Carlos III Health Institute in order to fund flagship projects in the field of oncology, the cardiovascular system, neuro-

logy and genomics. Given that growth in pharmaceutical expenditure has outpaced the three percent excess over adjusted nominal GDP, reaching 6.5%, the industry has been obliged to contribute a total of e99.16 million for these purposes. Of this total, the pharmaceutical companies disbursed payments on account of e76.5 million during 2002.
This overall total for the industry will be further increased by around e13 million because pharmaceutical expenditure in 2002 exceeded the ceiling of 9.5% maximum growth allowed in the Pact by 0.4 points. in accordance with the Pact, then, the industry has or will be required to contribute e112 million in respect of 2002.
The following data give some idea of the importance of these contributions in the context of public health research:

- Of the total funding for the bio-medical research programme over the period 2002-2005, 56% will be provided by the pharmaceutical industry, a significantly higher contribution than that of the FIS (Fondo de Investigaci n Sanitaria or Health Research Fund), the second major source of funding (29%).
- The e112 million contributed by the industry in 2002 by way of appropriations to the public health research Fund channelled through the Carlos III Health Institute represent 57% of the Institute's budget for 2003.
- Key fields financed by the Carlos III Health Institute via cooperative research networks using pharmaceutical industry funds are as follows (amounts approved for the first year): oncology e9.8 million; neurology e9.4 million; cardiovascular system e6.2 million; rare diseases e5.2 million; public health e4.7 million; infectious diseases e6.7 million; and transplants e3.8 million.

To resume our examination of the industry's commitments, we have accepted the obligation to apply a total of e1,352 million to R&D over the three-year term of the Pact, with annual appropriations rising at a faster rate than GDP. One third of this amount must be directed to external collaboration projects. Assuming rises of 6.5% in GDP for each of the years 2002, 2003 and 2004, R&D commitments (expressed in millions of euros) would be as follows:

R&D expenditure commiments per Pact

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

According to a FARMAINDUSTRIA survey of R&D outlay, however, the industry has applied almost e110 million more than the commitment for 2002, spending a total of e532 million, of which e201 million, or 38%, were invested in external R&D instrumented through research agreements with hospitals, universities and other public institutes.
In short, the industry has more than fulfilled its commitments the area of R&D expenditure, in terms both of contributions to public health research managed by the Ministry of Health and Consumer Affairs and projects directed by its own laboratories and undertaken either internally or externally in collaboration with other institutions.

Let us now turn to the shared goal of the Pact to restrain growth in pharmaceutical expenditure and ensure that it remains acceptable in terms of the public purse.

The target growth threshold established in this area was adjusted nominal GDP, which was 6.5% in 2002.

However, expenditure growth rose to 9.9%, slightly higher than the estimates considered by FARMAINDUSTRIA in the course of negotiations prior to the Pact. These estimates were based on hypotheses and assumptions that have since been confirmed by the empirical evidence and were related with the demographic ageing, the expansion of the eligible population, demand for ever higher levels of quality in healthcare services, and innovation (see the NERA paper published by FARMAINDUSTRIA under the title *Diagnóstico y perspectiva del gasto farmacéutico en España).*

It is clear that the measures and mechanisms provided for in the Pact to narrow the gap between target expenditure growth (6.5%) and the maximum ceiling (9.5%) have failed to produce the expected results. These instruments comprised the reference pricing system and measures to foster the generics market, and they were considered appropriate for the stable scenario the industry sought to establish through the Pact in view of their structural nature and predictability, and because they were in harmony with similar policies implemented in other EU countries.

To conclude this brief review of the Pact in 2002 let us summarise strengths and weaknesses with regard to the goals sought:

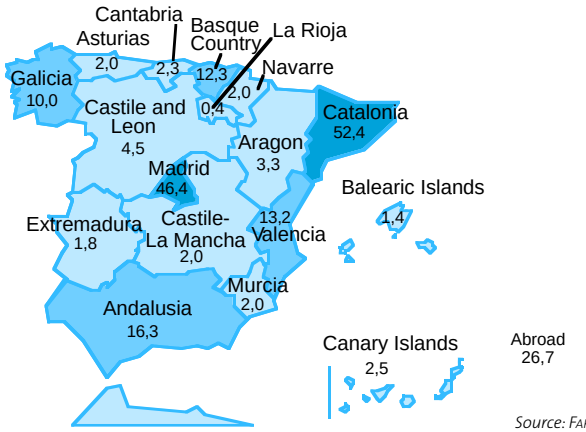
Strengths:

- The Pact has been a powerful instrument for stimulating investment in pharmaceutical R&D in Spain, offering a credible framework of regulatory stability which has allowed the Spanish affiliates of multinational concerns to compete with other countries for research funding and resources.

- The Pact has been confirmed as a decisive and key driver of public health research, channelling funding to the public institutions responsible for fostering, coordinating and carrying out these activities.
- Both the health research carried out through Field Networks promoted by the Carlos III Health Institute and external pharmaceutical expenditure, basically applied to clinical trials, have contributed to the spread of scientific knowledge throughout Spain. These measures have thus benefited both hospitals in the various Autonomous Communities and their medical and scientific staff, not to mention society in general, whose health is the ultimate objective of the whole system.
- The industry has made a very significant financial effort to deliver on its commitments in the Pact, having directly or indirectly applied over e600 million to research in 2002. This is equivalent to 12% of revenues from the sale of medicines to the National Health System.

External pharmaceutical industry R&D (millions of euros)

External R&D spending in 2002 e**201,5** million



Source: FARMAINDUSTRIA.

Weaknesses:

- Although expenditure growth was held down to a level close to the maximum ceiling (9.9% as compared to 9.5%), it is clear that the reference pricing system has not been as successful a moderating mechanism as had been hoped.
- It will be necessary to analyse the reasons for this failure and push ahead with the relevant changes to ensure that the system contributes as expected to holding down costs, thereby relieving the pressure on Regional health budgets.
- It should not be forgotten that significant certain drivers of pharmaceutical expenditure remain and that their impact is particularly acute in some regions. Specifically, these include the immigration boom, which, in conjunction with other structural factors such as the continued ageing of the Spanish population and innovation, is likely to put further upward pressure on pharmaceutical spending and hinder efforts to bring it into line with GDP, which is the objective in this area.
- Similarly, the generic medicines has failed to achieve the hoped for share of the total market. There can be no doubt that the existence side by side of copycat medicines, generics and patented originals is one cause of the limited growth of generic products.

3.1.2 Relations with Regions

The devolution of healthcare powers and the funding model approved at the end of 2001 have redrawn the map of Spanish health politics. Though it is still too soon to evaluate all of these effects, it is already clear that the first year of the new system has not served to lower the risks of fragmentation and the breakdown of the National Health System in view of the very minor role played by the Inter-regional Council during 2002 and political impediments to the search for solutions. The situation is such that there are those who now believe that the external structures (i.e. professional and business organisations) in fact contributed more to keeping the System together.

It is logical to assume that a decentralised model will, at least in the early days, involve certain inefficiencies and additional costs, which should in principle be offset by improvements in the healthcare service provided because the new system is closer to the citizen. In the absence of an appropriate structure and some degree of uniformity, however, fragmentation not only worsens problems but brings with it two major risks, one for the citizen, since equal access to healthcare provision may be affected, and the other for the industry, if the unity of the market nationwide is broken up.

In the specific case of pharmaceutical provision to the citizen, the situation could arise where two patients living in different Regions do not have access to the same medicines. Similarly, time lags could occur with access to innovations, or medicines may be sold at different prices or under varying reimbursement conditions. At present, supply restrictions have occurred in certain Regions and a patient holding a prescription for a given medicine issued in one Region could face dispensing problems in another.

There is also the paradox that some Regions are prepared to pay for products that are not on the list of financed medicines, despite their protestations of budgetary constraints.

The wording of the National Health System Cohesion and Quality Act should prevent discriminatory situations, since it guarantees that "citizens shall be dispensed medicines under equal conditions nationwide, regardless of the Region in which they may reside".

With regard to the industry, it should not be forgotten that the Spanish pharmaceutical market is the fifth largest in the European Union and the seventh worldwide. It is in large part thanks to the size of the market that the Spanish pharmaceutical industry has increasingly strengthened R&D and is an active participant in the country's scientific and professional standing.

The collapse of this unified market would not only have an adverse impact on the industrial fabric, and therefore on jobs, but also on the research investments made in Spain, which would in all likelihood be channelled towards more favourable environments. This would also affect the ongoing flow of knowledge from the industry to public research facilities and health professionals throughout the country.

The signs of this lack of cohesion and diversity of policy have been clear throughout 2002. For example: (1) invasion of regulatory competences by certain Regions (implementation of health visas, active-agent based prescribing, double reference pricing); (2) inharmonious regulation by some Regions establishing very radical positions in certain areas (doctor's visits); (3) systematic attacks on the Pact made between FARMAINDUSTRIA and the Ministry of Health and Consumer Affairs by a group of Regions with no consideration of outcomes; and (4) obstacles to the passage of the Cohesion Act, which have only been overcome in the spring of 2003.

These practices, which have obliged the industry to multiply institutional activities, not only put the unity of the market at risk, but also generate a climate of uncertainty and unpredictability in the industry that runs counter to the stability sought by the pharmaceuticals sector, which operates over a long business cycle and depends on innovation. This situation has been further aggravated by the scant realism and venomous effects of some of the measures taken by more than one Region during the year.

In the first place, then, the scope of State and Regional powers should be clearly defined and any conflicts arising should be resolved in accordance with the existing status quo in order to ensure the stability of the system and maintain an appropriate framework in the future. Central government is not only responsible for defining common health provision, but should be for the supply of medicinal products, which is to say for the approval and registration of medicines, price setting and financing conditions. Without excluding regional governments from cooperation in the powers assigned to the State, the Regions should concentrate on structuring demand, taking responsibility for the management of pharmaceutical provision and thus for the processes of prescription, dispensing and billing medicines.

A more detailed discussion of some of the measures taken in 2002 that go beyond the limits of regional government powers will highlight the twin problems of inequality and fragmentation of the market:

- In practice, the application of medical visas and other restrictions on various products within certain Regions, depending on the specific objectives of the regional governments in question, selectively excludes medicines from the provision approved at the national level. This situation has health consequences for the patient in the Regions affected and impacts on the commercial activities of the industry researching, producing and marketing medicines.
- Active-agent prescribing and reimbursement only of the cheapest products has similar consequences, even in the case of generics. Furthermore, where this practice is extended

to products that are not bio-equivalents and are protected by patents in the innovating countries, it not only produces potential health risks, but also runs counter to the principles of industrial property protection.

It is at least a hopeful sign that the Cohesion Act clearly empowers the Ministry of Health and Consumer Affairs to establish the specific conditions for the prescription and dispensing of medicinal products in the National Health System.

In the second place, it is essential that regulations governing matters that are the competence of regional government be drawn up on the one hand in accordance with common criteria and, on the other, on the basis of an overall view of health and industrial realities throughout Spain. Budgetary pressures in some of the Regions due to growth in pharmaceutical expenditure should not lead regional governments unilaterally to impose individual measures, and still less to take action that is contrary to the interests of the sector as a whole.

Two examples will clearly illustrate the risks and harm caused to the industry, the overall economic interest of the country and to the patient:

- Inharmonious regulation of visits to doctors would affect the availability of similar information to health professionals in the Regions, making it necessary to design individual promotional and information policies in each, thereby creating difference frameworks for employment relations between the industry and their representatives. Also, highly restrictive regulation, such as the measures recently implemented in Madrid, would: (1) cause significant job losses; (2) hinder the industry's legitimate promotional activities; and (3) restrict the access of innovations to the market.
- Inharmonious regulation of clinical trials would have a tremendous impact on research at the national level and would put the development of research networks at risk, since it would be necessary to adapt the same trial to a plethora of regulations. Spain would lose its chance in the area of research to neighbouring countries with a unified regulatory framework. If the single nationwide market were to break up, the impact on post-authorisation studies would be similar and pharmacovigilance activities would be jeopardised. Such measures therefore clearly involve an additional risk for patients.

In short, the situation is replete with uncertainties both for the citizen and for the pharmaceutical industry. These need to be resolved as soon as possible. The risk is there that citizens' equality of access to the healthcare system may be disturbed, and we may even reach the point where the medicinal products prescription/dispensing process becomes an obstacle to the free flow of pharmaceuticals throughout Spain. At the same time, the Spanish State could fragment into 17 different micro-markets, a situation that would be difficult to justify in a scenario of increasing European integration. Such an outcome would clearly put at risk the progress achieved in Spanish public and private bio-medical research in recent years.

It is easy enough to envisage a pendulum effect in this first phase of devolution, confusion and budgetary pressures, and to conclude that the regions, while seeking to implement the full range of their regulatory competences, have taken matters too far, encroaching on the powers of the State. It is also to be hoped that it will become easier to establish dialogue and reach understandings with regional government as the process of devolution settles into its definitive shape and a balance is struck, providing common ground.

FARMAINDUSTRIA's stance in this situation is to seek clarification of the limits on the powers of the various administrations involved, without neglecting to impose a degree of rationality on its actions and using all available means (political, health-related, economic, media,

etc.). The Association will also undertake systematic legal action against all and any measures that infringe its legitimate rights.
Another priority in dealings with the Regions is the matter of late payment of invoices for hospital supplies. In the course of its ongoing relations with regional authorities, FARMAINDUSTRIA has stressed the danger of allowing arrears interest to mount up following the European directive on late payment, which took effect in August 2002 and establishes arrears interest of Euribor plus 7%. This should have the effect of encouraging payment within a reasonable period. At the same time, the Association has consistently underscored the severe financial and even viability problems affecting some companies in the industry as a result of payment periods that may at times exceed 600 days.

3.1.3. Regulatory Framework

The considerable degree to which the pharmaceutical sector is regulated is a determining factor behind FARMAINDUSTRIA's active participation in prior hearings for new legislation and its ongoing dialogue with the relevant national and regional authorities.
In many cases the Association also draws on the invaluable assistance of experts from member pharmaceutical companies, who participate in the work of establishing a representative industry position that reflects key concerns.
In the course of public hearings held during 2002, FARMAINDUSTRIA expressed positions on the following regulatory changes:

Regulatory changes examined by FARMAINDUSTRIA in 2002:

- *Draft order including certain active substances in Annex I of Royal Decree 2829 dated 6th October 1977 governing psychotropic substances and drugs.*
- *Draft Decree governing medical ethics and research bodies and clinical trials in the Andalusia public health system.*
- *Draft Order amending the Annex to the Order dated 17 September 1982 implementing Royal Decree 2730/1981 governing the registration of over-the-counter drugs.*
- *Draft Circular 8/2002, which replaces Circular 22/2001 concerning the Manufacture of unregistered Medicines and the Export of Medicines.*
- *Edict dated 25 February 2002 making public the Draft Decree on the accreditation of Ethics Committees in Clinical Trials.*
- *Draft Decree regulating the Basque Region's pharmacovigilance system.*
- *Draft Order including paramethoxymethylamphetamine (PMMA) as an active substance in list 1 of Annex I to Royal Decree 2829/1977 governing psychotropic substances and drugs.*
- *Draft Order approving the second edition of the Spanish Royal Pharmacopoeia.*
- *Proposal for Spanish Medicinal Products Agency Circular 01/2002 concerning "Amendments to Circular 2/2000, which establishes guidelines for the readability of packaging materials and prospectuses".*
- *Text of the Draft Order defining new standard groups of medicine presentations and approving the related reference prices.*
- *Draft Spanish Medicinal Products Agency Circular 15/2002 concerning "reporting procedures between the pharmaceutical industry and the Spanish Pharmacovigilance System in the area of pharmacovigilance of medicines for human use".*
- *Draft Royal Decree establishing Regulations governing the processing and award of aid for haemophiliacs and other persons suffering congenital blood coagulation diseases who have contracted hepatitis C due to Public Health System treatments using concentrated coagulation agents.*
- *Draft Royal Decree implementing certain aspects of article 100 of the Medicinal Products Act, 1990 (Law 25 of 20 December 1990).*
- *Draft Order adapting the annexes to Royal Decree 1599 dated 17 October 1997 governing cosmetic products to scientific and technical advances for the fourth time.*
- *Proposal for Circular 21/2002 concerning the "Format of Applications for the authorisation of medicines for human use".*
- *Draft Decree governing the performance of post-authorisation studies on medicinal products (Regional Government of Catalonia).*
- *Draft Directorate General for Pharmacy and Health Products Circular concerning the "Regulation of certain medicine promotion activities in the Region of Madrid's Single Public Health Network".*

Of the above, statutory changes referring to the implementation of article 100 of the Medicinal Products Act, 1990 and the regulation of visits to doctors in the Region of Madrid are of particular importance. Key regulations approved include the Royal Decree concerning pharmacovigilance and provisions governing clinical trials. We shall also briefly refer to the review process affecting European pharmaceutical legislation, although a more detailed discussion is provided below in the section on international relations.

➜ **Draft Royal Decree for the implementation of article 100 of the Medicinal Products Act.** The draft Royal Decree is a necessary step in the basic regulation of medicinal products in Spain, as it provides for the coherent implementation of the Spanish price control system, which will permit its application on an appropriate basis.
The system for the regulation of medicine prices in Spain as established in article 100 of the Medicinal Products Act is restricted to medicinal products dispensed within the country, which are financed out of Social Security or other State healthcare funds. Thus, the provisions of article 100 are only applicable if the medicine can be shown to have been dispensed in Spain, and this information has until now been available to the retailer alone.
To date, the Spanish Council of State's preliminary report on the Royal Decree is pending.

➜ **Medical visit in Madrid.** Circular 1/2002 of 25 November 2002 concerning the regulation of visits to doctors and other medicine promotion activities in the Region of Madrid's Single Public Health Network was published in the Region's Official Gazette on 2 December.
This Circular has enormous implications due to the extent and negative impact of the restrictions it imposes on the pharmaceutical industry's promotional activities in the Region of Madrid. In this light, FARMAINDUSTRIA has appealed to the Administrative Disputes Division of the Madrid High Court of Justice.
FARMAINDUSTRIA concurs with health professionals and managers that what is needed is a new regulatory approach to doctor visits in order to improve quality while respecting the industry's legitimate interests. To achieve this, it is essential that a standard regulatory framework be established nationwide, while legislation such as the Madrid Circular should be strenuously avoided.

➜ **Pharmacovigilance and post-authorisation studies.** Royal Decree 711/2002 dated 19 July 2002 governing pharmacovigilance of medicines for human use has now been published. This secondary legislation finally implements chapter six of Title II to the Medicinal Products Act, 1990 (Law 25/1990), as well as transposing Commission Directive 2000/38/EC into Spanish Law. The new Commission Directive amends Chapter V (ii), "Pharmacovigilance" of Council Directive 75/319/EC.
Royal Decree 711/2002 shares responsibility for pharmacovigilance between the Spanish Medicinal Products Agency and the relevant regional government agencies. Supplementary to the new legislation, the Spanish Medicinal Products Agency issued Circular 15/2002, which governs certain practicalities of reporting procedures for pharmacovigilance of medicines for human use affecting communication between the pharmaceutical industry and the Spanish Pharmacovigilance System.

At the same time, Royal Decree 711/2002 regulates post-authorisation studies in Spain, approval of which is reserved for the Regions. Circular 15/2002 establishes the frame of reference for secondary legislation by the Regions, but the final regulation of these matters is the province of each regional government, which have so far established widely differing requirements. This is likely to hinder the performance of post-authorisation studies resulting in the loss of information concerning individual medicinal products after their commercial launch.

➜ **Clinical trials.** Following the publication of the clinical trials Directive in 2001, regulatory activity has concentrated on the technical rules for implementation, which will permit the application of the Directive in the various EU member States.
In Spain, Circular 15/2001 concerning clinical trials on medicinal products was published on 23 April 2002. The Circular, which the Spanish Medicinal Products Agency has been translated into English with the collaboration of FARMAINDUSTRIA, brings together in a single text a series of practical issues concerning application procedures for the authorisation of clinical trials in Spain. The regulation of these matters was formerly scattered throughout a range of different norms.
At the level of the Regions, a key event has been the creation of the Regional Clinical Trials Committee in Andalusia with the objective of simplifying and standardising evaluation and administration criteria concerning clinical trials, at the same time. The Committee will also ensure that a single opinion is issued in multi-centre trials carried out in Andalusia, thus regulating the work of Local Clinical Trials Committees.

➜ **Future European medicines legislation**
During 2002, the review of pharmaceutical legislation proposed by the Commission has been the subject of intense debate in the European Council and the Parliament. This will lead to changes in some of the ground rules in areas such as data protection, manufacturing, registration, dispensing conditions and medicines advertising.
The EFPIA set up the FML Group (Future Medicines Legislation Working Group) with the mission of examining drafts and preparing a variety of position papers. FARMAINDUSTRIA forms a part of the FML Group.
In October 2002, the European Parliament issued its first reading report, as a result of which the Commission decided to include certain amendments. The Commission's latest text presented for debate in the Council has not achieved a common position, although this appears likely in 2003.
Overall, the Commission's current legislative proposal presents a number of positive aspects for the industry, such as the harmonisation of the registration data protection for a period of ten years (with the possibility of a one-year extension if significant new treatments are found), the elimination of the requirement to renew marketing authorisation every five years and the creation of a fast-track registration process in the interest of the health system.
However, the industry does not favour the amendments decided by the Parliament in support of the Commission's proposal to require mandatory registration of any new chemical entity through the centralised procedure, nor is it in conformity with the limitation of registration data protection periods.
Over the year FARMAINDUSTRIA has been at pains to make the sector's position clear to the representatives of the Spanish Ministry of Health and Consumer Affairs, the European Commission and various members of the European Parliament.

3.1.4. Technical Committees

Medicines are highly complex, and because of this permanent scientific and technical monitoring is necessary starting in the early stages before the commercial launch of a product (clinical and manufacturing trials), continuing through authorisation (evaluation and registration) and, finally, after the launch when it becomes available to patients (pharmacovigilance and environmental monitoring). For this reason, FARMAINDUSTRIA participates in numerous technical committees created by the authorities.

➜ **CODEM.** The Committee for the Evaluation of Medicinal Products for Human Use (Comit de Evaluaci n de Medicamentos de Uso Humano–CODEM) is the associate body of the Spanish Medicinal Products Agency responsible for advising on the technical and scientific issues involved in the authorisation of new medicines. One of the members of CODEM is appointed at the proposal of the Pharmaceutical Industry Association, providing FARMAINDUSTRIA with a permanent presence on the Committee.

Applications handled by CODEM in 2002

Meetings held	10
Issues raised	**1.083**
New applications accepted	**647**
* Mutual recognition	199
* Domestic	125
* Generics	282
* Medical plants	0
* OTC	41
* Homeopathic products	0
New applications turned down	**319**
* Mutual recognition	35
* Domestic	57
* Generics	185
* Medical plants	6
* OTC	36
* Homeopathic products	0
Modifications accepted	**81**
Modifications turned down	**19**
Reports on centralised product applications	**17**

Source: Spanish Medicinal Products Agency.

➜ **Directorate General of Health Resources of the Regional Government of Catalonia Advisory Committee on Clinical Trials.** FARMAINDUSTRIA has once again played an active role as a member of the Advisory Committee on Clinical Trials set up by the Catalonia Regional Government's Directorate General of Health Resource in 1997. During the year the Committee worked together with FARMAINDUSTRIA on the Draft Decree on the accreditation of ethics committees in clinical trials prepared by the Regional Government Health and Social Security Department and on the Draft Decree establishing technical and health requirements for units carrying out clinical trials on medicaments without therapeutic use for participating subjects. Both drafts were awaiting publication at the end of 2002.

➜ **Catalonia Regional Government Pharmacovigilance Group.** FARMAINDUSTRIA formed a part of the Pharmacovigilance Group created by the Directorate General of Health Resources of the Catalonia Regional Government Health and Social Security Department. This was set up as a multi-disciplinary group to prepare a Report on Best Practice in Pharmacovigilance for the pharmaceutical industry. This report was finally approved by the Technical Inspection Committee on 19 June 2002 and its findings were included in Royal Decree 711/2002 governing pharmacovigilance in Spain.

➜ **Advisory Commission on the Reporting of Risks to the Citizen.** Towards the end of 2002 the Spanish Medicinal Products Agency set up the Advisory Commission on the Reporting of Risks to the Citizen, which is formed by various interested parties, including FARMAINDUSTRIA. The Commission reports to the Committee on the Safety of Medicines and its mission is to prepare a report on the most appropriate methods of disclosing information on the potential risks inherent in medicines to the citizen.

➜ **Committee on the Readability of Patient Information Leaflets.** The Spanish Medicinal Products Agency created the Committee on the Readability of Patient Information Leaflets in 2001. FARMAINDUSTRIA joined this body in 2002. Its mission is to review the contents of certain medicine prospectuses in depth in order to ensure that they effectively perform their primary function of providing the patient/consumer with accurate, appropriate and understandable information.

➜ **Committee on the inclusion of active substances in OTC products.** Over-the-counter medicines contain certain listed active substances, which are updated on a regular basis via Ministerial Orders. Proposals for the inclusion of new active substances in the list, modifications and the information required for the technical specifications of OTC products are handled, among other tasks, by this multi-disciplinary group set up under the aegis of the Spanish Medicinal Products Agency.

Advertising control and OTC self-regulatory committees. Advertising of medicinal products in Spain is regulated by Royal Decree 1416/1994, which defines two forms of advertising, the first aimed at health professionals, containing information on prescription products, which must be reported to the health authorities, and messages targeting the general public, which are only permitted for products expressly classified as over-the-counter medicines. Nationwide advertising campaigns of this kind must be authorised by the Directorate General for Pharmacy and Health Products and regional campaigns by the relevant Region.
FARMAINDUSTRIA participates in the Committee for Preliminary Advertising Control, together with representatives of ANEFP (Spanish OTC Products Association), the Directorate General for Pharmacy and Health Products and the Spanish Medicinal Products Agency. The committee examines the advertising campaigns for over-the-counter products submitted for approval to the authorities.

Good Laboratory Practice. The principles of Good Laboratory Practice (GLP) are enshrined in Royal Decree 1369/2000, which amends Royal Decree 822/1993. The same legislation governs the application of the principles in pre-clinical trials on chemical substances and agents.
The GLP principles refer to organisation systems and the conditions under which trials are planned, performed, registered and presented. Oversight of compliance with GLP ensures that trials are properly planned and appropriate resources assigned to complete the work. This aids the conduct of the work and completion of scientific studies, as well as encouraging precise reporting of results and the provision of resources to verify their integrity.
In 2001 the Spanish Medicinal Products Agency set up the Technical Inspection Committee (TIC), creating a number of working groups to cover the different facets of pharmaceutical inspection, including scrutiny of Good Laboratory Practice. The CIT is formed by inspectors from the Spanish Medicinal Products Agency and the Regional agencies for Catalonia, Madrid, Navarre and Valencia, as well as FARMAINDUSTRIA experts.
During the year, this GLP group has concentrated on reviewing and approving OECD GLP principles Nº. 3 The Research Director in GLP and Nº. 5 GLP in the analysis of drugs and metabolites in biological specimens, as well as the guidelines for the validation of IT systems and the records and main researcher in multi-centre studies.

3.2. Communication

In line with the strategic priorities established by the Association, FARMAINDUSTRIA consolidated its communication activities during 2002 as regards both its institutional presence and relations with the media, and actions designed to improve public perceptions of the pharmaceutical industry, which are closely associated with the image of drugs.
Internal structures have been strengthened over the year to ensure that FARMAINDUSTRIA is able to progress with a twofold programme of work involving, on the one hand, the development of a series of initiatives to transmit strategic messages concerning the pharmaceutical industry and, on the other, improving effective access to the press and media.
The Association made excellent progress in both areas, producing numerous publications, creating publicity and organising events, as well as raising its profile and influence with the media. It has also planned a number of innovative projects for 2003.

3.2.1. FARMAINDUSTRIA in the media

During the first six months of the year, FARMAINDUSTRIA's media presence was mainly associated with the Stability Pact, campaigns to foster the rational use of medicines (2nd campaign, *Dont't play with antibiotics)*, the Code of Best Practice for the promotion of medicinal products, price control legislation (article 100 of the Medical Products Act), inspection certificates, the book presentation for the title *Medicines in the world,* and the presentation of the report entitled *Mental illness. The contribution of drugs to the treatment of depression.*
Other matters reported in the press in connection with FARMAINDUSTRIA included news items on the roll-out of the SIGRE project, meetings with Government representatives and the first payment to the Biomedical Research Fund created under the Stability Pact.

Presentation of the FARMAINDUSTRIA FOUNDATION, July 2002

In June the press also picked up on EFPIA's annual general meeting in Bruges (following a FARMAINDUSTRIA press release) and the presentation of the Delphi Report on Future scenarios for medicines in Spain. The media also showed considerable interest in the launch of the Code of Best Practice in the Promotion of Medicines and the presentation of the FARMAINDUSTRIA FOUNDATION on 23 July 2002.

At the same time, a systematic policy was established to communicate FARMAINDUSTRIA's positions on matters related with its activities. Specifically, this policy covered the evolution of pharmaceutical expenditure in the first six months of the year, the appointment of the new Minister of Health and the planned reform of regulations governing doctor visits in the Region of Madrid. All of these issues were widely reported in the national, regional and specialised press.

The media also gave considerable space to the change in the presidency of the Association at the General Assembly held in October.

November was a particularly intense month in the communications area. A number of press conferences were held at the Association's head offices and numerous press releases were issued, generating a considerable media impact. FARMAINDUSTRIA publicly announced its decision to take legal action against regional government resolutions in Andalusia, Extremadura and Madrid in connection with active substance prescribing. The Association also presented a new report forming part of the *Value of medicine* series and addressed issues such as the implementation of article 100 of the Medicinal Products Act, the use of pharmacy formulas in hospitals, the late payments directive and patent protection.

In addition, FARMAINDUSTRIA representatives took part in a variety of debating and other forums, and both the President and the Director General of the Association gave numerous interviews in different media (general and specialised press, radio and so on).

In general, FARMAINDUSTRIA succeeded in projecting a highly positive image (over 70% of cases) in the press throughout 2002. The year was also notable for the rise in the number of press items featuring or mentioning the Association, a clear indication of its commitment to the media.

FARMAINDUSTRIA has undertaken an unprecedented activity in the area of communication in order to build bridges with society, which has until now been largely unaware of the role and contribution of the pharmaceutical industry to health and well-being. This has been

an ongoing project in which FARMAINDUSTRIA has at all times pursued the goals of openness, objectivity and rigour, seeking to respond to the concerns of the media while keeping the initiative in the area of communication and establishing itself as a creator of opinion.

3.2.2 Publicity Campaigns

The *Value of medicine* campaign launched in 2001 has been kept going through the insertion of reminder advertising in the specialist media and original features on new patholo-

gies. Insertions were planned in view of their topicality (e.g. asthma in spring and HIV at the time of the International AIDS Congress).
A Rational Use of Medicines Campaign was also carried out on the theme *For your own good and the good of others*. This campaign, designed in June, was more intensive than its predecessor in terms of both presence and content, with full-page, colour insertions in all general national newspapers over period of three weeks.
The campaign aimed to reach a double audience comprising the population in general and health professionals, resulting in a dual focus for creative work. It also included references to the implementation of the Spanish Code of Best Practice in the Promotion of Medicines.

3.2.3. Studies and publications

Following on the work carried out in 2001 to update FARMAINDUSTRIA's institutional publications on the basis of a common style, the Association this year launched an ambitious publishing programme including the following key documents (all available in PDF format at *www.farmaindustria.es*):

➜ Annual Report y *The pharmaceutical industry in figures*

The English-language version of the Association's Annual Report has been published for the second time with the same format and features as the original in Spanish. This widens the scope of information concerning the industry in Spain at the same time as providing a useful communication tool for the Spanish affiliates of international companies.

➜ *The Value of Medicines* Series

Mental illness. The contribution of drugs to the treatment of depression. The presentation of the report was attended by its author, Doctor Xavier Badía and by Doctor Enrique Rojas Marcos, an excellent speaker who gave a short talk on the history of mental illness and its treatment. The report highlights the prevalence of mental illness in Spanish society and the undeniable relief afforded to patients through advances in anti-depressant drungs. The report also discusses the financial implications of the progress made, particularly stressing the savings generated by avoiding hospitalisation.

The value of medicines: realities and hope for the future. This report was issued at the presentation of the FARMAINDUSTRIA FOUNDATION in July 2002. It examines a number of different pathologies, illustrated with actual examples of patient cases, and underlines the key role of research and development of new drugs to combat diseases such as diabetes, cancer, multiple sclerosis and AIDS. In the same vein, the report stresses the need to provide incentives for research and innovation if new and better medicines are to be developed in ever shorter periods.

The role of medicines in the treatment of high blood pressure and the prevention of cardiovascular risks. This report highlights the contribution made by new drugs to the treatment of diseases that are the leading cause of death of the developed world. It also discusses the high therapeutic failure rate for the condition and the problem of inadequate diagnosis, both matters that entail significant social and economic costs.

The contribution of chemotherapy drugs to the treatment of cancer. The progress of pharmacological research and the growing importance of cancer prevention, diagnosis and early treatment have led to some success in changing the outcome of cancer, with the result that many patients now survive and are able to lead a normal and fulfilling life. This transformation has been nothing short of spectacular with child cancer. Mortality has declined in Spain by 36% for boys and 45% for girls over the last decade.

➜ Studies

Prospective Delphi Study of Future Scenarios for Medicines in Spain. The report uses the Delphi methodology to examine over 130 variables, realities and factors, projecting probabilities for their occurrence over a variety of time horizons. On the basis of this study, it seems clear that expected changes in the world of pharmaceuticals will have far-reaching social consequences in the medium term. The development of medicines will result, for example, in rising life expectancies and, particularly, improved quality of life from 2010 onwards.

➜ Technical Series

Spanish Medicinal Products Agency Circular 15/2001 concerning clinical trials on medicines. This is a bi-lingual publication in Spanish and English containing the relevant legal texts and was produced in association with the Spanish Medicinal Products Agency.

➜ Scientific Series

The Frontiers of Alzheimer's Disease. This book contains a collection of the lectures given at the Men ndez Pelayo International University (UIMP) course on this subject held in August 2002. The course was organised by the Te filo Hernando School of Pharmacology.

3.2.4. Events and sponsorship

FARMAINDUSTRIA organised and sponsored a series of events connected with medicines and the pharmaceutical industry during 2002.

Presentation of the FARMAINDUSTRIA FOUNDATION. This event took place at the Hotel Ritz in Madrid on 23 July 2002. It was attended by the new Minister of Health and Consumer Affairs, Ana Pastor, as her first public appearance in office, and by Dr. Valentín Fuster, who gave a master class on networked bio-medical research.

Second Meeting of the Pharmaceutical and Drugs Industry and the Regions organised by the UIMP. Discussions were aimed at reaching a common stance on matters of concern arising from the recent devolution of healthcare powers to the Regions and their impact on the pharmaceutical industry, particularly with regard to legal and financial outcomes.
Teófilo Hernando School of Pharmacology. Alzheimer's Disease. This course was also held at the Men ndez Pelayo University in Santander from 26 to 30 August 2002. Course content included the presentation of the V School specialising in Alzheimer's disease and, in particular, the search for and development of medicines to prevent, alleviate or cure the condition.
Bio-medicine Seminar organised by the Asturias School of Hispanic Studies at La Granda.
Second National Don't Play with Antibiotics Campaign. The campaign was conducted between 15 February and 9 May 2002. This initiative was launched in Madrid, Castile and Le n, Cantabria, Extremadura, Catalonia, Navarre, Aragon, Murcia, the Region of Valencia, Castile-La Mancha, Andalusia, Galicia and Asturias with the objective of encouraging people to make use antibiotics properly.
It succeeded in mobilising the population as a whole and health professionals to take part in a nationwide scheme promoted by FARMAINDUSTRIA with the involvement of the Ministry of Health and Consumer Affairs, the Spanish Medical Associations and the General Council of Official Pharmacists' Associations, as well as relevant scientific societies and consumer organisations. The campaign achieved over 400 impacts in Spain's national and regional media, reporting data from the Don't Play with Antibiotics survey of user practices with these medicines.

3.3. Member services

FARMAINDUSTRIA's raison d'être as an Association is to provide services to its members either in fields where the individual company has no access (e.g. institutional dialogue at the sector level) or where the costs involved prohibit independent action. Indeed, the whole of FARMAINDUSTRIA's activity may be viewed as a service to its members. Thus, the Association carries on a dialogue with Government and monitors the regulation of the industry as its basic functions, while communication actions undertaken to enhance the public image of the pharmaceutical industry may also be understood as a value added service for members.

Having made this general point, this section will concentrate on specific services aimed at FARMAINDUSTRIA members. These are related to the technological platform used to communicate with the affiliated pharmaceutical companies and provide them with online access to the Association's data bases and information sources, the working

groups, sections and functional areas, which are responsible for channelling involvement in day-to-day affairs, the activities of the Barcelona Office, and the employment issues affecting companies. The section ends with a wide-ranging discussion of the self-regulation system for promotional activities implemented by the Association in 2002 through the new Ethical Code.

3.3.1. www.farmaindustria.es

In 2001 the Association made a qualitative leap in terms of technology culminating in the launch of the FARMAINDUSTRIA *website (www.farmaindustria.es)* on 1 February 2002.

The site comprises a public access area where any visitor can obtain a wide range of information concerning our Association and its publications, as well as other services such as a daily press review, events programme and links, and a press area, where media professionals can find all of the information distributed by FARMAINDUSTRIA.
However, the material providing the greatest interest and added value is reserved for member pharmaceutical companies and access is restricted by passwords. This reserved area provides access to all of the services formerly provided over the Lotus Notes connection, in addition to new facilities that have gradually been incorporated into the site.
Perhaps the key point is the excellent response to the FARMAINDUSTRIA website and the number of consultations made with an average of 4,500 page visits per day. Of these 4,500 hits in FARMAINDUSTRIA pages, around 700 represent on-line document consultations by member companies, a clear indication of the site's utility as a tool for the pharmaceutical industry.

3.3.2. Working Groups, Sections and Functional Groups

The Working Groups, Sections and Functional Groups play a key role in FARMAINDUSTRIA's working methods, drawing on the active participation of its members. A brief description of each is as follows:

- **Working Groups:** formed on the initiative of the Governing Bodies, they address explicit concerns for a specified period of time. The Groups main task is to establish industry positions and analyse high-impact regulatory proposals.
- **Sections:** formed by groups of pharmaceutical companies with common concerns, the sections meet on a regular basis to discuss the issues and table proposals. Sections are created on a permanent basis while relevant concerns requiring debate and a common approach continue to exist.
- **Functional Groups:** bringing together managers from various pharmaceutical companies by functional group, these clusters examine specialist issues and provide support to the FARMAINDUSTRIA departments responsible for framing proposals and sector positions in their Groups of interest. The Functional Areas sometimes also set up ad hoc working Groups or committees for specific issues.

The Member Services Department has a Technical Office for Working Groups and Sections. This office coordinates the various groups both among themselves and with the Association's other departments, as well as providing logistical support for meetings. The Functional Areas are coordinated by the relevant FARMAINDUSTRIA Departments.
The membership of the various groups and sections reflects the

Association's plural nature, encouraging involvement by senior officers from the member companies in its work. Thus, five Working Groups, five Sections and seven Functional Groups, one of which included three ad hoc groups, were active in 2002, involving 86 member pharmaceutical companies.
The following pages briefly describe the main activities of these groups during 2002.

➜ **Working Group on Business Flexibility.** This group, which is formed by 12 pharmaceutical companies, was created to monitor the review of European pharmaceutical legislation. Its two main objectives are to keep options open in the area of registration procedures and to defend business flexibility.
The group meets whenever new developments occur in the Community's arduous legislative process, which involves the Council, the Commission and the European Parliament.

➜ **Working Group on the implementation of article 100 of the Medicinal Products Act.**
The system for the regulation of medicine prices in Spain as established in article 100 of the Medicinal Products Act, 1990 (Law 25 of 20 December 1990) is restricted to medicinal products dispensed within the country, which are financed out of Social Security or other State healthcare funds.
The mission of this Working Group is to monitor secondary legislation related with this article, which the Government intends to enact through a Royal Decree.
On the one hand, the implementation of article 100 will give practical form to G-10 Recommendation VI in a manner that fully respects Community Law. Thus, the Royal Decree will align Spanish legislation with regulatory processes under way in other member States in order to give effect to the Recommendation, which restricts price controls on medicines throughout the European Union to products purchased or reimbursed by National Health Systems.
Indeed, there would be little sense in extending price controls, which are a response to public financing of medicines, to trading in medicinal products between intermediaries for purposes other than dispensing funded out of the Spanish public purse. Such a move would only foment speculative trading by intermediaries and this would have a severe impact on the legitimate interests of the pharmaceutical industry, removing the incentive to invest in R&D, without in any benefiting the Spanish consumer, whether it be the patient or the State, which reimburses a significant part of the cost of medicaments.
On the other hand, the development of this legislation should produce positive public health outcomes, because it will facilitate compliance by the pharmaceutical companies, wholesalers and pharmacies with their legal obligation to supply the market on a permanent basis, which is a basic guarantee

for Spanish patients. There is ample evidence that price differentials result in occasional medicine stock-outs, which harm the interest of the consumer who is unable easily to obtain the required products, despite more than sufficient deliveries to supply the domestic market on a regular basis.
In short, these necessary regulatory developments should foster collaboration between the various agents involved in the medicinal products supply chain in order to attain the main objective, which is quite simply to ensure that citizens have access to medicine under optimum financial, technical and health conditions.

➜ **Working Group on Active Substance Prescribing.** This Group has prepared a position paper concerning the practice of promoting active-substance based prescribing that has emerged in some Regions, as a result of which the medicaments dispensed are the cheapest of those authorised for a given composition. These actions could have grave healthcare and financial/industrial implications in Spain given the special nature of medicines provision, in which patented, licensed, copycat and generic products exist side by side.
These measures are also debatable from the legal standpoint. In the first place, the agreements entered into by the Regions with the Pharmacists' Associations in order to implement the policy exceed the bounds of regional government powers, since changes in price and reimbursement conditions represent an invasion of the central government's exclusive competence in these areas. Secondly, interference in the market by excluding some products on the supply side has a major impact on competitive conditions.

➜ **Working Group on Industrial Property.** The position paper prepared by this Group in June 2002 forms the basis for the approach defended by FARMAINDUSTRIA with regard to monitoring of the Stability Pact, which contains a commitment to harmonise Spanish

data protection legislation with that of other European countries. In fact, the protection of registration data currently provided for as of right in European legislation has been shown to be a very efficient measure (frequently acting as a supplement to patents) to prevent businesses that have not been authorised by the innovator benefiting from the research of others by using protected data as the scientific basis for the registration of products.

FARMAINDUSTRIA has presented proposals to the Spanish Ministry of Health and Consumer Affairs with the aims: 1) of extending the registration data protection period to 10 years in Spain; 2) of classifying any medicament submitted an abbreviated application based on a patented product as a generic drug when the industrial property rights in force in any EU country lapse; and 3) establishing notification of the company responsible for the original medicament as a requirement for generics applications.

➜ **Working Group on Promotional Regulation.** The Working Group on Promotional Regulation concentrated on two key tasks in 2002: a) completion of the new Ethical Code; and b) the regulation of doctor visits in the Region of Madrid.

The finalised texts of the new Code of Ethics and its accompanying regulations were presented and approved by the Governing Bodies of FARMAINDUSTRIA in February 2002, and ratified by the General Assembly in March. The Code took effect on 1 July 2002 after the collaboration agreement was signed with the AUTOCONTROL organisation, whose Jury has been entrusted with resolving disputes under the Code where it is not possible to reconcile the parties.

The regulation of visits to doctors in the Region of Madrid kept Working Group very busy in the second half of the year. The numerous meetings held produced a range of position

papers, which have formed the basis for discussions with the Regional Government. Following the publication of the restrictive Circular on visits to doctors in December 2002, the Group drew up a proposal in early 2003 advocating an alternative nationwide platform for the organisation of doctor visits, which would be based on realistic premises and include a wide-ranging and ambitious programme to improve the scientific and ethical quality of visits to physicians.

➜ **Biotechnology and Vaccines Section. Vaccines Group.** The Vaccines Group was set up in September 2002, its members being drawn from the FARMAINDUSTRIA associates manufacturing and/or supplying human vaccines in Spain.
The objectives of this Group include, inter alia, promotion of the advantages of vaccination as a public health strategy; preparation of proposals for action by the Governing Bodies of the Association in connection with the issues dealt with by the Group; creation of an open dialogue with vaccines opinion leaders to enable pharmaceutical companies to adjust their R&D work on the basis of proposed policies for new vaccines; organisation of mechanisms for the exchange of information and opinions between member companies in line with Spanish and EU legislation; and cooperation in relations with the relevant authorities and the resolution of common problems emerging in the vaccines world.

➜ **Innovation Section.** The Section was formed at the end of 2002 with three main issues on the agenda: 1) monitoring of pricing policy in Spain to ensure that innovative products are accorded fair treatment and assigned prices in line with European levels in short periods; 2) fostering public support for R&D, especially as regards taxation and the link between research and healthcare policies; and 3) boosting the communications policies of both the Association and the pharmaceutical companies themselves with a view to highlighting the social and economic value of innovation.

➜ **SME's Section.** The SME's Section is formed by the statutory Spanish-owned SME group, which for some years now has come together following the regular meetings of the Board. The information provided by the representatives of the Board is accompanied by presentations made by FARMAINDUSTRIA's departmental managers.

➜ **Hospital Supplies Section.** This Section met six times in 2002. The main issues dealt with were as follows: 1) the financial crisis at the Jim nez Díaz Foundation, which was not resolved until the spring of 2003, when an out-of-court settlement was reached; 2) the 2% discount on hospital supplies which, aside from legal discussions concerning its enforceability until 1 January 2003, ceased to be applicable as of that date following the repudiation of the agreement by FARMAINDUSTRIA as duly notified to the interested parties; 3) the transposition, foreseeably in the summer of 2003 (one year behind schedule), of Directive 35/2000 dated 29 June 2000, which establishes anti-late payment measures in commercial operations (Official Bulletin of the European Community, 8 August 2000); and 4) hospital debt, which exceeds e1,200 million and has continued to deteriorate, particularly in the Valencia Region, where payments were delayed by 649 days at 31 August 2002 (404 days in Andalusia, and 347 days in the Canary Islands).

Generics Section. The objective of this section is to promote a quality generics market capable of generating reasonable margins for the companies involved. Sufficient industrial margins would encourage promotion among physicians and, in the judgment of the Section, would ensure that effective therapeutic molecules would remain on the market longer at lower cost to the National Health System. The Section believes that policies to promote active substance prescribing and agreements between the Regions and the Pharmacists' Associations to dispense the cheapest products for prescriptions of this nature are detrimental to the development of a quality generics market, since they accelerate the downward price spiral and negate the effect of promotional activities undertaken by generics companies with doctors.

The Section's commitment to a quality generics market as opposed to a mere commodities market are based, aside from the above, on other arguments, such as the continuity of treatment, the quality of generic products and concerns about bureaucratic impediments to flexible competition on prices.

Legal Services Group. The legal services area brings together the legal affairs officers of the member companies and holds an six-monthly seminar on current issues. The two seminars held in 2002 examined major issues including, inter alia, the financial crisis in the Jim nez Díaz Foundation; the repudiation of the former INSALUD agreement, which provided for a discount on hospital supplies; the application of the new Ethical Code; new pharmacovigilance and clinical trials legislation; a review of European pharmaceutical legislation, the Madrid Regional Government's circular on visits to doctors; personal data protection in the pharmaceutical industry; regulations governing rebates; and the regulation of post-authorisation studies.

Registration Group. Various *ad hoc* groups were formed in the Registration area in 2002. The ad hoc group on changes examined, assessed and reported on the new proposals made by the Committee for the Review of Regulations 541/95 and 542/95, working closely with the Spanish Medicinal Products Agency and EFPIA to obtain a hearing for the Spanish pharmaceutical industry's opinions in connection with these projects.

The group set up to examine the CTD (Common Technical Document), a new dossier unifying the requirements of the three regions (the United States, Japan and Europe) involved in the International Conference on Harmonisation (ICH) that is expected to replace the current format for the presentation of registration applications in July 2003, prepared an initial report on the translation of the official data required for the registration application. A mixed working group was created with the Spanish Medicinal Products Agency to

reach a consensus and the document was finally approved as the official text for use in registration applications under the Spanish and EU procedures. The Group continued its activity with the translation of the whole of the CTD, which the Spanish Medicinal Products Agency expects to publish some time in 2003. The Agency is currently examining the possibility of preparing a handbook describing differences between the traditional format and the CTD.

The other *ad hoc* group created in the Registration Group during 2002 was entrusted with the task of studying future pharmaceutical legislation, analysing proposals for the amendment of Directive 2001/83/EEC and Regulation 2309/93. After identifying key areas of concern for the sector (scope of application, business flexibility, data protection, pharmacovigilance, compassionate use, etc.), the group has followed up in each phase of the passage of the draft legislation.

➜ **Technical Operations Group.** Since its creation in 2001 this Group has met on a quarterly basis to discuss major emerging issues for the sector from a technical standpoint.

Together with the Spanish Committee of Representatives of the Disabled (CERMI) and the National Association of the Blind, the group has continued to examine the possibility of including the name of medicaments in Braille on the packaging. The State Budget Act passed in December 2002 amended article 24 of the Medicinal Products Act, exempting the inclusion of Braille descriptors on packaging materials from tax, which should facilitate progressive implementation of the initiative.

Other issues dealt with by the Group include the impact of reference prices, personalised dosing systems, the single dose pilot project, new coding systems, transportation of medicinal products, childproof packaging and pharmacy formulas, as well as evaluation of the impact of a variety of regulatory proposals such as the amendment of article 100 of the Medicinal Products Act with reference to logistics operations and environmental projects.

➜ **Environment Group.** The activity of the Environment Group in 2002 centred on monitoring regulatory and legislative changes and tracking environmental matters concerning the pharmaceutical industry (e.g. waste products, dumping and emissions)-

With the collaboration of SIGRE, the Environment Group has continued to represent FARMAINDUSTRIA on the Environmental Committee of the Spanish Chemicals Industry Federation (FEIQUE) as well as establishing closer ties with the Environment Ministry in connection with matters affecting the sector.

The main environmental matters emerging in 2002 include the European Parliament and Council proposals for a Directive on environmental liability in connection with the prevention and repair of environmental damage; the draft Royal Decree on the restriction of volatile organic compounds due to the use of solvents in certain activities; the Directive on Integrated Pollution Prevention and Control (IPPC) –Law 16/2002 governing integrated prevention and control; and the European Pollutant Emission Register (EPER) for Spain.

➜ **Pharmacovigilance Group.** Responsibility for pharmacovigilance is shared between the authorities, the holders of marketing authorisation and health professionals. As explained above, 2002 saw the publication of Royal Decree 711/2002 concerning pharmacovigilance,

Circular 15/2002 and the report on Best Practice for Pharmacovigilance in the pharmaceutical industry. The Pharmacovigilance area main work during the year involved examining and commenting on these documents, maintaining constant contact with the health authorities with regard to this matter.

As things stand, these new provisions would create uncertainty and reflect a lack of common criteria among Region requirements for the presentation and authorisation of post-authorisation studies. It seems clear that excessive controls over post-authorisation research and the failure to take the pharmaceutical industry into consideration could cause a sharp decline in such studies. The multiple levels of official control that would be involved in the registration and control of post-authorisation studies should be a matter of concern for the health authorities if activities are not to be duplicated and harmonious procedures are to be established to avoid any loss of the scientific and educational benefits derived from such work.

The area has also been involved in tracking the development of the European clinical trials directive as regards safety issues, as well as the implementation of electronic pharmacovigilance reporting.

➜ **Clinical Trials Group.** The transposition of the new clinical trials Directive into domestic legislation has the potential to attract numerous research projects to Spain given the country's capacity to perform biomedical research, particularly if administrative processes are simplified and regional requirements brought into line. However, the contrary effect could also be produced, with other member States winning clinical research projects, unless more favourable conditions are offered. During the year the clinical trials area has held various meetings with Spanish Medicinal Products Agency officers responsible for clinical trials in order to inform them of the pharmaceutical industry's standpoint with regard to the effective adaptation of the European Directive on clinical trials, 2001/20/CE. These meetings succeeded in creating significant common ground.

➜ **Orphan Drugs Group.** The Functional Area for Rare Diseases and Orphan Drugs was created during 2002 with the aim of examining current issues, establishing possible objectives and seeking appropriate contacts among the health authorities and associations. The question of orphan drugs covers a range of issues that converge on the industry's need for incentives to develop therapies that are at once expensive and aimed at a very small number of patients. This group will contribute the sector's response to the initiatives taken by public and private institutions.

3.3.3. Barcelona Office

During 2002 FARMAINDUSTRIA's Barcelona Office has consolidated its position as an permanent forum for our members, becoming an active instrument for serving their needs. The Office's main activities were as follows:

➜ **Consultative functions.** The Office receives and resolves the queries raised by pharmaceutical companies in the course of its daily activities, which are carried out under the principles of immediacy and speed of response. In terms of subject matter, the majority of queries handled during 2002 were technical (42%), followed by legal and employment matters (20%), financial issues (16%), international affairs (8%) and sundry questions (14%).

➜ **Technical office for Working Groups and Sections.** The Association's Working Groups and Sections held numerous meetings in Barcelona last year, in the course of which the Office performed the functions of the Member Services Department Technical Office.

➜ **R&D cooperation.** Various events were organised in 2002 to foster R&D cooperation between the industry and universities, public research institutions and private associations and institutes, the most significant of which were as follows:

- Universidad Aut noma de Barcelona (UAB): Second R&D Cooperation Seminar held jointly with the Universidad Aut noma de Barcelona (UAB). The seminar was attended by over twenty representatives of pharmaceutical companies and a similar number of university researchers and teachers. Sixteen lines of research and scientific services currently under way in the UAB (biochemical pharmacology, molecular biology and biotechnology, in vivo metabolic studies and models for in vitro and animal experiments, and drug delivery vehicles: liposomes).

- High Technology Institute (IAT): Presentation of the project for the creation of the High Technology Institute, an R&D facility that will be located in the Barcelona Biomedical Research Park. The Institute's mission will be to apply new positron technologies in the field of clinical diagnosis, basic biomedical research and advanced clinical trials. The event was held at the facilities future buildings and was attended by over twenty-five member companies.

➜ **Relations with regional institutions.** The Barcelona Office held a series of meetings with a range of regional institutions in 2002, both to promote the exchange of information between them and the pharmaceutical industry (as in the case of CIDEM, Foment de Treball, the Royal Academy of Pharmacy in Catalonia, and the Fundaci Robert) and to engage actively in their work in the pharmaceutical sector (among others the Fedequim Mixed Commission and the Les Heures Pharmaceutical Sector Advisory Committee of the Fundaci Bosch i Gimpera).

➜ **Logistical support and coordination with the head office.** As usual, the Barcelona Office has provided logistical support in connection with the regular meetings held by associated companies, government agencies and other pharmaceutical sector institutions (SIGRE, Coashiq, ANEFP and others). The Office also functions as a permanent instrument providing support and coordination to all head office departments of FARMAINDUSTRIA.

3.3.4. Spanish Code of Best Practice in the Promotion of Medicines

The Spanish Code of Best Practice in the Promotion of Medicines, known as the Ethical Code, was approved at the Board Meeting held on 12 February 2002 and unanimously ratified at the General Assembly held on 12 March 2002.

In response to the increasing demands and requirements of modern society, and as a tangible example of the pharmaceutical companies' commitment to effective self-regulation and respect for the rules established in the new Code, the Association opted to entrust oversight and compliance functions to the Spanish Pharmaceutical Industry's Ethics Commission and to the AUTOCONTROL Advertising Jury. This independent dispute resolution agency enjoys high standing and a proven track record in advertising matters. It was co-opted to perform the jury role through the Agreement entered into by the two Associations on 18 April 2002.

The intention of the Governing Bodies of FARMAINDUSTRIA was to bear witness in this way to the pharmaceutical industry's responsible attitude to the health authorities and society in general. The Code came into effect on 1 July 2002, the same date as the official formation of the Ethics Committee, which is formed by three members of good standing in the pharmaceutical sector and will act as a conciliator in all disputes brought in connection with infractions. The Committee members are Dr. Juan Manuel Reol Tejada, Dr. Josep Torrent i Farnell and Dr. Miguel Vilardell Tarr s.

During 2002 FARMAINDUSTRIA worked intensely to organise conferences and promote campaigns in favour of the rational use of medicines, driving a range of initiatives aimed at explaining and clarifying the new Code to physicians through Medical Associations and scientific societies.

➜ **Adhesions to the Code.** The system is voluntary for all companies that are not members of FARMAINDUSTRIA. Between 1 July 2002 and 31 March 2003 a total of 22 non-member pharmaceutical companies have sought adhesion to the Ethical Code, as follows: Bexal Farmac utica, S.A.; Binesa 2.000, S.L.; Centro Pet Complutense; Davis Medica, S.L.; Davur, S.L., Laboratorios; Ercros Industrial, S.A.; Grapa, S.L., Laboratorios; Invicta Farma, S.A.; Litaphar, S.A., Laboratorios; Laboratorios Farmac uticos Logogen, S.A.; Laboratorios Farmac uticos Valomed, S.A.; Mabo-Pharma, S.A., Laboratorios; Narval Pharma, S.A., Laboratorio; Nefox Farma, S.A.; Nostrum Farma, S.A.; Parke Davis, S.L.; Pliva Pharma Iberica, S.A.; Química Sintetica, S.A.; Sumol Pharma, S.A.; Uquifa, S.A.; Vegal Farmac utica, S.A.; and Vinci Farma, S.A.

➜ **Activities of the Ethics Committee.** In this first phase of the Code's application (1 July 2002 until 31 March 2003), the Ethics Committee has held six mediation meetings.
During this period, the Committee also received three queries connected with the interpretation of the Code's provisions concerning the nursing community and hospitality at meetings.
A total of 28 complaints were brought for purported violations of the Code:

- 19 related with the contents of promotional materials for medicinal products.
- 4 concerning promotional activities in connection with hospitality at meetings.
- 4 in connection with incentives practices. Two of these complaints were turned away for lack of capacity to act because the companies concerned were not FARMAINDUSTRIA members and had not adhered to the Code, and one was dismissed.
- 1 complaint concerned illicit advertising.

Proceedings were heard and resolved by the Ethics Committee within a period of 28 days.
The companies that brought most complaints, defined according to size as required by FARMAINDUSTRIA's Statutes, were the majors (i.e. those with sales exceeding e100 million). Foreign-owned companies brought more complaints than Spanish undertakings.
Once again as defined by size, more complaints were brought against the major companies and among these foreign-owned concerns were prevalent.

	COMPLAINANTS	DEFENDANT COMPANIES
Size		
Majors	51.7%	53.8%
Others	48.3%	46.2%
Ownership		
USA	41%	50%
EU	31%	30.8%
Spanish	28%	19.2%

The following table reflects the total number of complaints, the nature of the parties and the actions taken by the bodies responsible for oversight of the Code (i.e. the Ethics Committee and the AUTOCONTROL Jury).

Total complaints		28
Upheld	21	
Turned away	2	
Other proceedings	5	
Complainants		34
Member companies	25	
Adherent non-member companies	4	
Third parties	5	
Defendant companies		29
Member companies	24	
Adherent companies	2	
Non-member companies not adhering to the Code	3	
Actions of the Ethics Committee		
Complains resolved through mediation	8	
In Committee hearings	6	
Actions of the AUTOCONTROL Jury		
Referred to the Jury	8	
In Jury hearings	2	
Resolved by the Jury	6	
Other proceedings		4

In the cases amicably resolved by the Ethics Committee, the agreements reached consisted basically of the withdrawal or rectification of the promotional materials concerned. Meanwhile, the AUTOCONTROL Jury imposed fines totalling e6,000 and e9,000 on the companies found to be at fault.

3.3.5. Employment issues

Continuous Training. FARMAINDUSTRIA holds a seat on the Chemical Sector Commission formed by the most representative employers' and trade union organisations, in accordance with the Third National Agreement on Continuous Training. The Commission's duties include, inter alia, overseeing compliance with the Agreement in the sector, reporting on training plans to the State Mixed Commission for Continuous Training, helping to moni-

tor the execution of the training plans approved within its remit, acting as a mediator to resolve discrepancies arising in Company Training Plans and issued raised by the legal representatives of the employees, establishing priorities for continuous training initiatives, and agreeing proposals for approval purposes.
In 2002 FARMAINDUSTRIA actively publicised training programme financial awards processes (comprising grants and subsidies for continuous training, individual training plans, and supplementary or accompanying measures), as well as providing details of the objectives of awards made to the various interested parties, priority criteria, and application requirements.

➜ **On-the-job training in the pharmaceutical industry.** European legislation provides for a mandatory six months practical training for the award of Pharmacy degrees. FARMAINDUSTRIA has entered into agreements with the Universidad Complutense de Madrid and Universidad San Pablo-CEU which provide for the training of students in all areas related with the research and development of medicaments, as well as manufacturing processes, quality control and marketing. During 2002 a total of 16 companies accepted 71 students for on-the-job training.

➜ **Agreement with the University of Barcelona.** In April 2002 the University of Barcelona and FARMAINDUSTRIA entered into an agreement governing collaboration to facilitate access to the practical training required for post-graduates studying Industrial Pharmacy and Galenics to obtain the Specialist Pharmacist diploma in this discipline.

3.4. International Relations: involvement in EFPIA

In the field of international relations in 2002 FARMAINDUSTRIA has concentrated on promoting the industry's priorities within the European Federation of Pharmaceutical Industries and Associations (EFPIA), which seeks to build a favourable business framework in Europe that would:
- enable the pharmaceutical industry to lead the field in scientific and technological development (R&D);
- foster the global competitiveness of the European pharmaceutical industry.

In parallel to its involvement in EFPIA, FARMAINDUSTRIA has prioritised Community initiatives for future legislation and the G-10 process in the international field.

3.4.1. Promotion and protection of R&D activities

The economic cycle of investment and innovation is the engine of the pharmaceutical sector, but it can only be set rolling within a regulatory framework that strongly protects intellectual property. For this reason, FARMAINDUSTRIA has focused a large part of its efforts on persuading the Spanish Government to support existing initiatives for Community legislation favouring innovation.

➜ **Regulatory data protection.** As a part of the legislative package related with the review of European Pharmaceutical Legislation, the European Commission has proposed a har-

monised protection period of ten years to reinforce the protection of regulatory data, with an additional year's protection for potential new therapies using products that are already on the market.
FARMAINDUSTRIA has repeatedly brought up the importance of supporting the Commission's proposal with the Spanish health authorities, since this measure responds to the need to improve conditions for innovative medicines, as established in G-10 Recommendation IV.

Paediatric medicines. In line with G-10 Recommendation IX, FARMAINDUSTRIA supports the creation of Regulations that would pick up on the Commission's consultative paper of March 2002, which calls for regulatory action to foster paediatric research.

Protection of biotechnology innovations. Directive 98/44/EEC concerning protection of biotechnological innovations is a crucial document in that it provides a favourable climate for R&D investment in the biotechnology area. Nonetheless, the Directive has been transposed into the national legislation of only four member States (including Spain, Law 10 of 29 April 2002), even though the deadline was 30 June 2002.

Intellectual property and access to medicines in the Third World. There is a clear need to safeguard appropriate levels of intellectual property protection and, in parallel with Community initiatives, FARMAINDUSTRIA has been in constant contact with the Spanish Ministry of the Economy in this regard. Our objective is to ensure that the EU authorities guarantee strict application of the TRIPS agreement (Trade-related Aspects of Intellectual Property Rights) by all of the member States of the World Trade Organisation (WTO).
Since the Declaration made at the WTO Conference in Doha in November 2001 in connection with TRIPS and public health, which requested that the TRIPS Council take immediate action to eradicate public health problems in less developed countries, FARMAINDUSTRIA has cooperated with the Spanish authorities and the European Commission's Committee on article 133 in the quest for solutions that would not affect intellectual property rights.
The outcome of this search is based on the possibility of authorising the export of mandatory licences in order to meet demand for medicines in countries that lack sufficient (or indeed any) manufacturing capacity. Negotiations in this regard continued throughout 2002. However, a deadlock was reached on 20 December because of the lack of agreement as to the definition of countries permitted to import under the immediate solution and the diseases for which production of medicines under mandatory licences would be allowed.

The dialogue will be maintained in the coming months in order to ensure that less favoured countries are able to address public health emergencies not only through donations and collaboration programmes established by the industry with third world governments, but also through the avenues established in paragraph 6 without infringing on intellectual property rights, which are vital to scientific innovation. We should, however, remind ourselves that this avenue will not produce results unless we also address the underlying problems of poverty, deficient infrastructure and the lack of political will to tackle the public health crisis at the root.

At the same time, and also within the ambit of intellectual property rights and public health, the Commission announced its proposed Regulation concerning the diversion of medicines from the Third World to the EU on 30 October 2002.

This proposed Regulation provides for an action plan to be managed by the Commission to strengthen controls over the illegal re-importing of medicines acquired at differential prices in the Third World. Medicines for the three target pathologies (AIDS, malaria and tuberculosis) may benefit from enhanced protection measures provided their prices are 80% lower than those applied in OECD markets or are not more than 10% higher than production cost. The Regulation also proposes a list of 72 countries for inclusion in this system for the supply of medicinal products.

Despite the positive intentions of this proposal, it is important the final version of the Regulation also provide for private initiatives in collaboration with the Third World, establishing a flexible framework capable of integrating all avenues of cooperation.

➜ Faster access to new medicines for European patients

It is not sufficient for innovation to be recognised solely through the protection of intellectual property rights. Innovation also requires the commercial launch of new medicines in all European markets without delay, and this implies the need to accelerate patient access.

Consequently, the industry favours the proposals contained in the legislative package arising from the review of European Pharmaceutical Legislation in connection with shorter registration periods in the harmonisation of this process (basically the periods involved in purely administrative processes), as well as the reduction of the periods established for setting prices and reimbursement conditions.

The proposal for the creation of a fast track registration procedure will also facilitate patient access to innovative medicines that are of interest from a healthcare standpoint.

It is to be hoped in this regard that G-10 Recommendations II and III will shortly be trans-

lated into policy action to promote a quick market response to innovations to the benefit of European patients.

3.4.2. Promoting the competitiveness of the European pharmaceutical industry

The deterioration of the European pharmaceutical industry's competitive position was already noted by the European Commission in its Communication of March 1994 on Industrial Policy for the Pharmaceutical Industry in Europe. A subsequent report prepared at the behest of the Commission and published in November 2002 observed that there was a relationship between the industry's loss of competitiveness and national cost control policies in a fragmented and overregulated market.

In order to restore lost competitiveness, Commissioners Liikanen and Byrne set up the High Level Group on Innovation and the Provision of Medicines (G-10 Group) in March 2001, bringing together the different stakeholders –industry, the Commission, representatives of member States, patients and healthcare providers.

The final report, which was officially presented on 7 May 2002, underlines the need to find the right balance between fostering R&D, making Europe a more attractive locus for investment and, in this context, developing a generics policy.

The result of numerous meetings held in the first half of 2002, the report contains XIV Recommendations, some of which are particularly relevant to the issue of European competitiveness and may contribute to improving the framework within which the pharmaceutical industry operates in Europe.

The Recommendations reflect the G-10's consensus view that action is needed in four key areas in order to stimulate R&D and innovation, strengthen European medicines legislation, promote better access to therapeutic innovations and address the matter of national cost control policies.

The industry's response to the G-10 report has been highly positive, since it represents a first step in the right direction. However, a great deal of work remains to be done in the

coming months. All of the stakeholders will have work to do to develop the XIV Recommendations, translating them into concrete measures with the final aim of restoring the lost competitiveness of the European pharmaceutical industry.
In this light, some of the reports recommendations have been given absolute priority in the work and at the meetings of the Economic Policy and Intellectual Policy Committee, on which FARMAINDUSTRIA holds a permanent seat. In particular, work in 2002 centred on addressing and seeking solutions to the problems of fragmentation of the European pharmaceutical market Recommendation VI), EU enlargement (Recommendation XIV) and patient information (Recommendation X).

➜ **Fragmentation of the market.** The fragmentation of the EU market is a result of different market structures (currently 15 and soon to be 28 separate markets following the enlargement of the Union) and legislation governing pricing and reimbursement. The combination of this segmentation with the principle of free flows of products has resulted in the artificial flow of parallel trade between the member States, which takes advantage of differentials in controlled prices. This trade is one of several factors behind the loss of the pharmaceutical industry's competitiveness.
G-10 Recommendation VI (lifting price controls over non-reimbursable or OTC products) would be a first step towards the clarification of the market. Like all of the recommendations, however, VI is only a policy guideline. Thus, the G-10 may put forward ideas, but it is the national governments of the member States who are responsible for implementing specific measures in line with the Recommendations. To date, Spain and France are the only countries to have taken the initiative. In Spain this has involved using the possibilities offered by article 100 of the Medicinal Products Act and in France through the face price.

EU enlargement. The G-10 is aware that the enlargement of the EU will only accentuate the problems of fragmentation in the European markets and parallel trade. In Recommendation XIV it therefore calls for the derogation of the principle of the free flow of products in the accession treaties with the candidate countries. The derogation, which has been negotiated in the treaties, will apply only to those medicines for which a differential in intellectual property protection exists between the 15 current member States of the EU and the candidates. Accordingly, Recommendation XIV recognises that the derogation provided for in the terms of the treaties is not sufficient and paves the way for an additional protocol to cover differences in public health and market conditions between the two regions.
The issue of EU enlargement has been jointly analysed by FARMAINDUSTRIA, the Ministry of Health and Consumer Affairs and the Spanish Medicinal Products Agency. Numerous meetings have been held throughout the year to seek a mechanism to make the proposed derogation effective.

Patient information. FARMAINDUSTRIA has worked closely with other national associations in Brussels to promote the deregulation of patient information. The industry unconditionally supports the principle enshrined in G-10 Recommendation X, which notes the increasing demand from patients for information on which to base decisions regarding their health and the treatments available. This implies the possibility to request and receive accurate, balanced, quality information concerning medicines from the pharmaceutical industry itself.
At the same time, the European Commission has proposed the amendment of Directive 92/28/EEC on the advertising of medicinal products as part of the review of Pharmaceutical Legislation. In the opinion of both the industry and the European Parliament, this proposal should be reconsidered. In the terms proposed (a pilot phase for only three pathologies, with further confusion of the concepts of advertising and information) such an amendment

would be a step back and would hinder the application of the principle enshrined in Recommendation X.

3.4.3. New President of EFPIA

The General Assembly of the European Federation of Pharmaceutical Industry Associations held in Bruges (Belgium) on 24 June 2002 unanimously ratified the appointment of Sir Tom McKillop (AstraZeneca) as the new President. Sir Tom takes over from Jean-François Dehecq (Sanofi-Synth labo) and will hold the office for the period 2002-2004. The new President expressed his determination to proceed with the policy approved by the Board with the aim of restoring and strengthening the international competitiveness of the European pharmaceutical industry.
Franz B. Humer (Roche) was also confirmed as Vice-President of the Federation for the same period, replacing Jorge Gallardo (Almirall-Prodesfarma).

3.4.4. EU health policy during the Spanish Presidency

Spain held the Presidency of the EU during the first half of 2002. The Ministry of Health's programme in health matters rested on the following four planks:

- Harmonisation of health systems, an issue of increasing importance in order to provide for the free movement of patients.
- The repercussions of various rulings by the European Court concerning reimbursements to patients treated outside their countries of origin.
- Various technical issues such as the appropriate coordination of health information networks and systems required for the preparation of analyse and programmes for action.
- Consolidation of a single European market based on the harmonisation of consumption with a higher level of protection for consumers.

FARMAINDUSTRIA remained in permanent contact with the Ministry of Health and Consumer Affairs, seeking to contribute to the success of its programme for the Spanish Presidency.
One of the highpoints of the Presidency for FARMAINDUSTRIA was its intervention at the Symposium on Research in EU health systems held in Granada in May, which discussed progress with the implementation of EU's the VI Framework Programme in depth and considered the need to optimise coordination between the various authorities responsible for the preparation of research and health policy and programmes.
FARMAINDUSTRIA also played an active role in various events organised in connection with Malaga meetings of the Committee for Proprietary Medicinal Products (CPMP/EMEA), the Orphan Drugs Committee, the Mutual Recognition Group and the Pharmacovigilance Group.
Last but not least, FARMAINDUSTRIA organised a high level meeting in Madrid on 12 February 2002 attended by the leading Health Ministry officials and EFPI with the objective of conveying to the Ministry the pharmaceutical industry's concerns in the face of European legislative initiatives and challenges. In particular, the industry representatives concentrated on the G-10 process, stressing the importance of Recommendation VI and the need to maintain a permanent dialogue in order to prevent the emergence of unilateral national measures that might upset the stable framework for operations needed by the European pharmaceutical industry. At the same time, progress was made in the matter of price convergence and measures to ensure similar levels of intellectual property protection.

4 FARMAINDUSTRIA FOUNDATION

The FARMAINDUSTRIA FOUNDATION was created in Madrid on 18 December 2001. Its main objectives are to encourage scientific research and contribute to the development of healthcare in Spain, in particular by promoting biomedical and pharmaceutical research, training health professionals and fostering health awareness among the population. The FOUNDATION's financial resources basically comprise the funds assigned in accordance with the terms of an Agreement entered into between the Ministry of Health and Consumer Affairs and FARMAINDUSTRIA on 31 October 2001, as well as private donations.

The public presentation of the FOUNDATION was held in Madrid on 23 July 2002 and attended by Ana Pastor, the Spanish Minister for Health and Consumer Affairs and Dr. Valentín Fuster, director of the Mount Sinai Institute in New York and President of the American Heart Association. Dr. Fuster gave a talk on the subject of Networked biomedical research in the cardiovascular field.

In its first year the FARMAINDUSTRIA FOUNDATION has undertaken a number of projects, including activities carried out using the contributions made to the Carlos III Health Institute to fund public R&D projects for the furtherance of social healthcare.

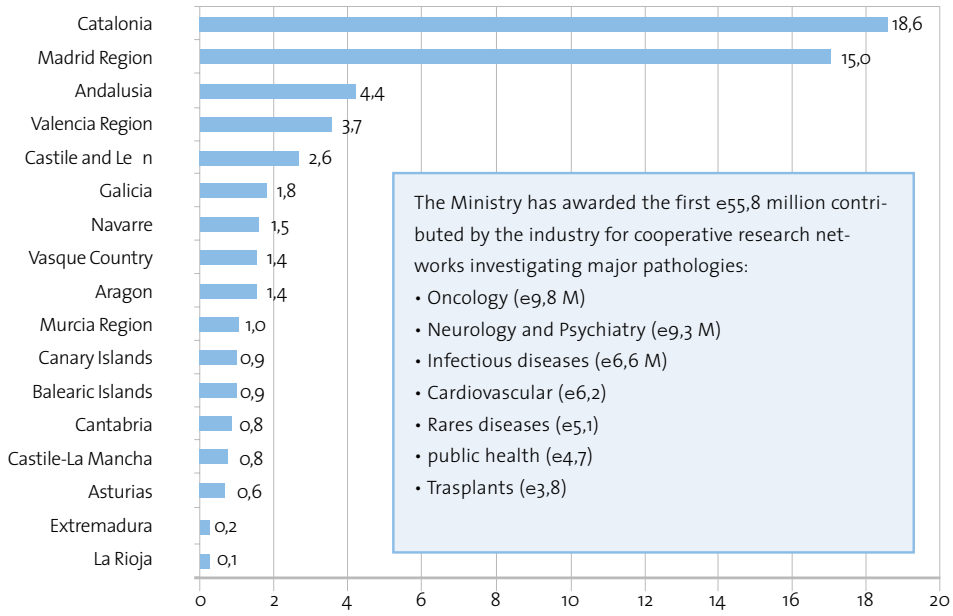
The Agreement made with the Ministry of Health requires that the funding of projects be instrumented through the Carlos III Health Institute, which was the organisation chosen to provide scientific and technical support to the Ministry of Health and Consumer Affairs and Region Health Services. The Institute is also responsible for managing and tracking projects.

On 30 December 2002 the first annual aid award was approved for Cooperative Research Field Networks in accordance with the criteria established in the fourteenth and fifteenth provisions of Order SCO709/2002 dated 22 March 2002 (Official Gazette of the Spanish State of 3 April) after the examination of the definitive proposal by the Inter-Regional Council's Scientific and Technical Committee, which acts as the Selection Board.

Funding has been approved for 69 networks, of which 13 are Centre Networks and the remaining 56 are Group Networks. The funding awarded for this project totals e55.8 million.

The FARMAINDUSTRIA FOUNDATION also sponsored a series of publications, events and symposia, which are described in more detail in this Annual Report's chapter on Communications.

➜ Application of the Biomedical Research fund (millions of euros)



Source: Carlos III Health Institute. Amount of the first annual award (2003) for funded Centres and Groups.

5 The Integrated Waste Management System (SIGRE)

SIGRE is an environmental initiative designed and implemented by FARMAINDUSTRIA to help the Spanish pharmaceutical industry comply with its obligations under European Union Directive 94/62, which was transposed by the Spanish Parliament by means of the prevailing Packaging and Waste Packaging Act, 1997 (Law 11/97).

By creating its own Integrated Waste Management System, the industry has in fact gone further than required by the Act, taking responsibility not only for packaging but also for any discarded medicines.

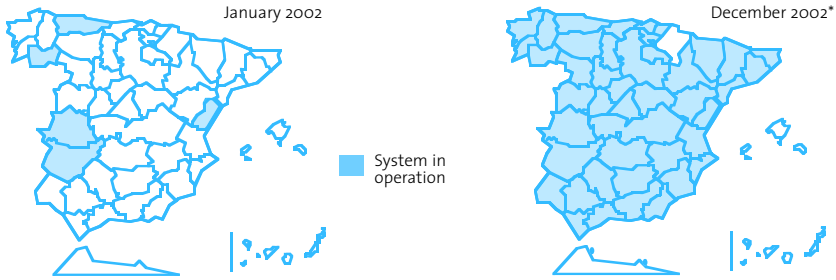
The pharmaceutical industry's Integrated Waste Management System has been implemented in most of Spain during 2002.

With the participation of all of the agents operating in the sector, the pharmaceutical industry has decisively pushed this initiative, enabling Spanish citizens to contribute to the defence of the environment through selective collection of waste packaging and discarded medicines. Key quality indicators are as follows:

- The system embraces 213 pharmaceutical companies, representing 95% of medicine sales in Spain.
- SIGRE's logistics are handled by 100 marketing companies, representing almost all of those operating in Spain.

- 92% of Spanish pharmacies are involved in the collection of packaging and discarded medicines.
- The system is operational in 14 Regions and 2 Autonomous Cities (nationwide in May 2003).
- 38 million Spanish citizens contribute to this environmental initiative.
- Over 900 tonnes of packaging and discarded medicines have already been collected.

SIGRE Implementation



** In May 2003 the SIGRE waste management system has been implemented throughout Spain.*
Source: SIGRE.

The SIGRE Separation and Classification plant located in Cerceda (Province of La Corunna) started up its operations in the autumn of 2002. This plant is the first and only one of its kind in Spain. It was officially opened by the Minister for Health and Consumer Affairs, Ana Pastor, in April 2003.
At the plant, medicine packaging materials picked up from the SIGRE Collection Points at pharmacies throughout Spain are separated and classified fro subsequent delivery to recyclers. Discarded medicines are evaluated for use in the production of power. This separation and classification system thus ensures the reuse of materials (paper, cardboard, plastic, glass, etc.) while at the same time exploiting discarded medicines to generate power, resulting in fuel savings.

Concern for the environment. SIGRE has been implemented under the motto Por la salud de la naturaleza *(For the good health of nature),* which reflects the spirit in which this not-for-profit corporation was founded. It is thus a reflection of the pharmaceutical industry's environmental commitment and concern.
From the outset, the implementation of SIGRE has met with an enthusiastic response and high levels of participation, as revealed by the various surveys carried out. According to these surveys, almost 100% of consumers believe the initiative is either positive or very positive and affirm their willingness to take part. They also define the System as easy to use and flexible.
Since the citizen, and thus society in general, is the main beneficiary of this pharmaceutical industry environmental initiative, SIGRE has worked hard to launch intensive campaigns in the Regions where it operates in order to create and foster the environmental of society and greater concern for the use of medicines.

SIGRE has carried out this task with the support and cooperation of the agents operating in the sector, as well as other social and institutional partners, under the direction of Regional Government Environment Departments, which are also responsible for oversight and the verification of the System.
SIGRE also received considerable media attention in 2002, with 70 appearances and interviews in national, regional and local television stations, features on its implementation and operations in at least 95 radio stations and over 360 mentions in the press and on-line.

➜ **Towards tomorrow's environment.** In addition to collecting and managing medicine packaging materials, SIGRE also does important preventive work, preparing Business Prevention Plans for the pharmaceutical sector. These plans provide for the adoption of measures in the medicine production and packaging processes with a view to reducing the weight and volume of packaging and the use of environmentally friendly materials.
As the integrated waste management system for the pharmaceutical industry, SIGRE has so far drawn up a three-year Business Prevention Plan, which was presented in March 2000, as well as two annual monitoring reports for 2001 and 2002. These reports describe the proposed prevention measures and the results achieved.
In the presentation of its Business Prevention Plan for the period 2003-2005 to the Regions, SIGRE has put forward the main guidelines for member companies with regard to the design of more environmentally friendly packaging in the coming years. These activities are of particular importance in that they demonstrate the pharmaceutical industry's concern in an area where it is subject to numerous restrictions because of its obligation to guarantee the protection and safety of medicinal products at all times.

The pharmaceutical industry in Spain and Worldwide

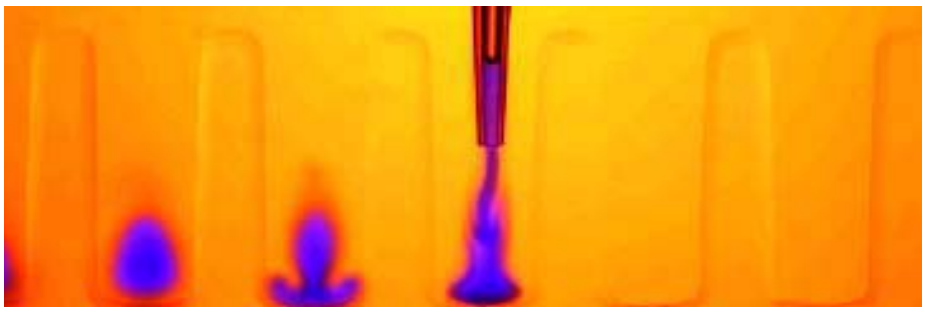
1 The international context

The worsening situation of the world economy has created increased budgetary pressures in the majority of countries. Falling revenues, mainly from indirect taxes due to the decline in business activity, have made it ever more difficult to keep up with the continual growth of social expenditure. This effect is reflected with peculiar intensity in European countries, which provide public health coverage. Rising demand for health provision is directly apparent in pharmaceutical expenditure, which is subject to additional upward pressure resulting from the inclusion of innovative medicines to meet needs that are insufficiently covered at present. Because of this, European governments have had little option but to take a firm line, implementing a galaxy of measures in a determined effort to constrain public spending on medicines.

The main measures taken to restrain pharmaceutical expenditure in European countries in 2002 have been as follows:

- Policies aimed at increasing the use of generic drugs.
- Use of pharmaco-economic studies in reimbursement decisions.
- Control of the pharmaceutical industry's promotional and marketing expenditure.
- Greater responsibility of the regions for the provision and funding of medicines (Spain, Italy and the United Kingdom).

The evolution of the retail drugs market (i.e. medicines sold through pharmacies) in the five main European markets in 2002 reveals the scope of the measures imposed in these countries.



Percentage annual change in the retail pharmacies drugs market

	Change (%) 2002/01	% of total sales in all 5 countries 2002
France	2	24.6
Germany	8	29.1
Italy	3	17.3
Spain	**10**	**10.9**
United Kingdom	10	18.0

Sources: FARMAINDUSTRIA based on IMS data.

The starting point for an analysis of the main European markets is Germany, where the pharmaceutical market grew by 8%. The Federal Republic is also, together with the United Kingdom,the European country that is quickest to make innovative therapies available to its citizens.Over the pastfive years, pharmaceutical expenditure has grown at a rate of over 10%, and concerns about this trend have recently led to the adoption of new measures to restrain the spending. These include a financial contribution from the industry to avoid the need to impose price cuts on medicines that are outside the scope of the reference pricing system, a review of the levels of reference prices, publication of a new list of exclusions, incentives for parallel imports, active substance prescribing and economic evaluation of new products.

France recorded the lowest growth in the pharmaceuticals market among the five major European countries. Without doubt, this was partly a consequence of the Guigou Plan (July, 2001), which is based on price cutting and the exclusion of medicines from the reimbursement system. However, the French government does not consider that the Plan exhausts containment measures, and is currently preparing new ones such as reference prices, active substance prescribing and further exclusions from publicly funded medicines. In order to compensate the pharmaceutical companies for the pressure that these measure have put on profits, the government intends to accelerate the inclusion of therapeutic innovations in the market.

Italy saw growth of only 3% in 2002, as a result of an across-the-board cut in medicine prices and restrictions on the promotional activities of the pharmaceutical companies imposed through a Decree Law enacted in mid-2002. It should be remembered, moreover, that Italy is currently in the midst of a far-reaching decentralisation process affecting the funding and provision of healthcare.

At 10% the growth rate in the United Kingdom reached double figures.However, the British government has not taken any significant measures to contain pharmaceutical spending during the year. Also, the country has traditionally fostered R&D and facilitated market access for therapeutic innovations.
Finally, growth in the retail pharmaceutical market in Spain has been at the head of the main European countries, alongside the United Kingdom. The evolution of spending has confirmed the forecasts made before 31 October 2001, when the Pact between the Ministry of Health and Consumer Affairs and FARMAINDUSTRIA was signed, as well as the inability of the reference pricing system to generate the savings provided for in the Pact. This matter is discussed in more detail in other sections of this Annual Report.

The EU pharmaceutical industry in figures, 2000

Country	Companies (*)	Production (_ million)	Jobs	Domestic sales (_ million)	Foreing trade at laboratory prices (_ million)	
					Imports	Exports
Austria	42	1,548	9,200	1,648	2,141	1,982
Belgium	146	4,203	22,713	2,667	6,038	7,431
Denmark	44	3,609	17,574 (2)	1,031	1,031	3,242
Finland	66	600	6,544	1,142	746	285
France	264	25,174	95,300	17,263	5,662	9,621
Germany	333	18,558	114,581	18,375	10,254	14,890
Greece	61	438 (1)	11,500	1,804	1,190	256
Ireland	56	5,657	16,000	719	1,560	5,388
Italy	221	14,668	72,559	11,479	7,076	7,587
Netherlands	57	5.013	13,200	2,555	4,432	4,996
Portugal	129	752	9,388	2,142	1,008	305
Spain	**249**	**7,283**	**38,700**	**7,295**	**3,957**	**2,254**
Sweden	61	5,295 (2)	118,700	2,398	1,448	4,233
United Kingdom	73	19,755	65,000	13,282	8,153	11,936
Total	**1.839**	**130,104**	**560,665**	**89,679**	**63,789**	**88,987**

Note: Figures refer to the production of proprietary medicines and raw materials for human and veterinary use, except in Spain, where they reflect only activities for human use (in Spain, pharmaceutical production is defined as apparent production of proprietary medicines and raw materials for human use).

(*) Member companies of EFPIA Associations.

(1) 1998 data.

(2) 1999 data.

Sources: FARMAINDUSTRIA based on data from EFPIA and country Pharmaceutical Industry Associations.

2 The pharmaceutical industry in Spain

2.1. R&D

Cutbacks in expenses that are not related with short-term revenue generation are one of the main consequences for business of the loss of confidence in the future evolution of the economy. This being the case, R&D investment is always an item that may be reduced at times of economic uncertainty. Indeed, recent statistics on scientific research and technological development reveal that R&D expenditure has stagnated throughout manufacturing industry compared to 1999 figures. This effect is clearly evident in the most innovative sectors, where expenditure earmarked for R&D has fallen sharply, with the sole exception of the pharmaceutical industry,

R&D activity in Spanish companies, 2001

	R%D staff	% change since 1999	R&D expenditure (_ million)			
			Internal	External	Total	% change since 1999
Total industry	29,266	-5.9	1,995.34	717.31	2,712.64	0.2
Aerospace	1,909	-18.4	170.12	43.90	214.40	-2.4
Automotive	4,014	19.7	253.87	192.69	446.56	-10.9
Pharmaceutical Industry	3,620	8.7	320.08	166.36	486.44	31.5
Radio, TV and communications	2,467	-15.9	167.12	14.77	181.89	-30.6

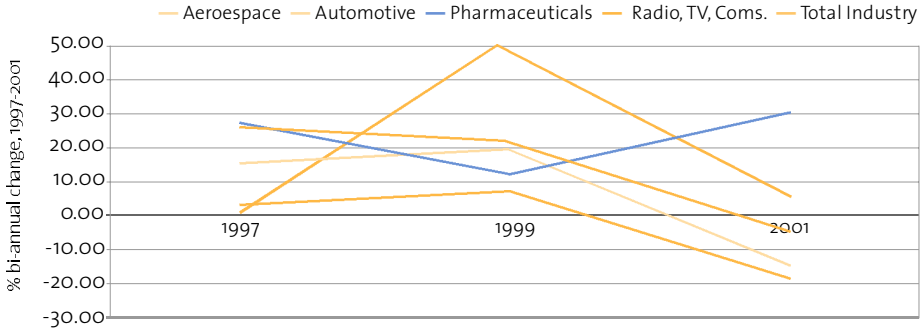
Source: FARMAINDUSTRIA based on National Statistical Institute data (R&D Surveys, 2001 and 1999).

The pharmaceutical industry is thus the exception to the general trend, with a 31.5% increase in R&D expenditure since 1999. As a result, the sector's share of the total R&D outlay in manufacturing industry has risen from 13.7% to 17.9% over this period. Taking into consideration that projects designed to obtain innovative new products require investment plans with a time horizon of various years, there can be no doubt that the intensification of the Spanish pharmaceutical industry's research effort have been considerably influenced by two factors that have generated an outlook for business stability:

- At the beginning of 2001, litigation with the health authorities in connection with the 1998 Pact was settled.
- The new Pact signed in October 2001 established the basis for consensus in the implementation and application of measures designed to contain pharmaceutical expenditure without destabilising the structural framework for the industry's activities.

The rapid growth in the pharmaceutical industry's internal R&D expenditure between 1999 and 2001 is evident from a comparison of R&D investment in the most innovative sectors over the period 1997-2001 (see chart).

Evolution of internal R&D expenses in innovative sectors Growth rates for 2001/99 and 1999/97



Source: FARMAINDUSTRIA based on National Statistical Institute data (R&D Surveys, 1997, 1999 and 2001).

With regard to jobs in research in 2001, the pharmaceutical industry employed approximately 9% of its headcount in full-time R&D activities, compared to just 1% of employees in manufacturing industry as a whole. It is because of this that the pharmaceutical industry represents 12.4% of the total research employees of industrial companies (excluding construction, agriculture and services), although in terms of revenues its share is just 2.3%.

The pharmaceutical industry's internal R&D expenses in 2001 comprised 84% operating expenses in respect of wages and salaries paid to researchers, technicians and ancillary staff and other expenses, while the remaining 16% was capital expenditure, mainly earmarked for the purchase of equipment and instruments. This breakdown is very similar to industry as a whole.

Once again,it is necessary to stress the firm commitment to society that the pharmaceutical industry's research activities represents. Although the sector accounts for just 2.3% of total industrial revenues, as mentioned above, it nevertheless contributes 17.9% of the research performed by privately owned industrial firms in Spain. These figures appear even more significant in terms of the average rates of change in revenues and R&D expenditure for the most innovative sectors between 1995 and 2001.

Average Annual Change (%), 1995-2001

Average Annual Change (%)	Revenues	R&D expenditure
Total Industry	8.1	7.3
Aerospace	14.1	3.2
Automotive	8.8	8.5
Pharmaceutical Industry	7.4	12.4
Radio, TV, Communications	10.7	-0.6

Source: FARMAINDUSTRIA based on National Statistical Institute data (Survey of Industrial Companies and R&D Statistics).

The pharmaceutical industry has been the only one to sustain faster growth in R&D investment than in revenues. It was thus not only Spain's leading research industry in quantitative terms in 2001, but also increased its R&D expenditure.

In view of the pharmaceutical industry's commitments to R&D investment under the October 2001 Pact with the Ministry of Health and Consumer Affairs, and assuming that these can be maintained until it expires in 2004, it is to be expected that the growth trend in pharmaceutical research seen in recent years will continue to be considerably higher than that of other industries.

The ratio of R&D expenditure to gross value added (R&D/GVA) clearly reflects the importance to the pharmaceutical industry of obtaining therapeutic innovations compared to the situation in other industrial sectors.

Gross Value Added (GVA) is calculated by subtracting total intermediate costs from final production. This measure is of interest because it reveals the value actually created in any given sector, or by industry as a whole, in the Spanish economy or, in other words, the contribution made to GDP. On the basis of the National Institute of Statistics' R&D and Industrial Surveys, we may analyse the proportional evolution of resources applied to R&D by companies compared to annual value creation (i.e. R&D as a percentage of GVA for the pharmaceutical industry) in 2001 compared to the rest of manufacturing industry.

Evolution of R&D expenses/GVA,1995-2001

	Pharmaceutical Industry	Total industry
1995	10.9%	2.1%
1997	13.3%	2.3%
1999	14.8%	2.6%
2001	16.1%	2.3%

Source: FARMAINDUSTRIA based on National Statistical Institute data (Survey of Industrial Companies and R&D Statistics).

Unquestionably, then, the Spanish pharmaceutical sector is the spearhead of business research activities in Spain.

2.2. Domestic market

Estimated sales of proprietary medicines at laboratory prices increased by 9.6% in 2002 to a total of €8,845 million, of which €6,934 (78.4%) were sold through retail pharmacies and €1,910 million (21.6%) through hospitals. Growth was 9.8% compared to the prior year in the retail pharmacies channel and 8.9% in the hospital channel.

In the retail pharmacies market, sales of prescription products (95.5% by value) grew by 10.2%,driven by the two main segments of low-reimbursement products (growth of 13.1%) and generics (21.5%). Sales of generic products totalled €249.03 million, representing a 3.8% share by value of the prescriptions market, and 48.35 million units (5.1% of the prescriptions market).

The over-the-counter (OTC) segment represents only 4.5% of the total market. Sales grew

by 1.9% in cash terms compared to 2001, which is significantly slower than the growth of the market as a whole.
A total of 185 new products were launched in 2002, of which 55% were generic medicines, representing 1.2% of the total market. The average price of therapeutic innovations coming to market in 2002 was €13.72. This is very considerably higher than the average price of existing medicines, which was €6.43. New product launches mainly comprised cardiovascular, antineoplasic and central nervous system therapies, which accounted for 60% of sales of new medicines.

Domestic market for medicinal products (laboratory prices, € million), 2001-2002

	Retail pharmacies	% Change	Hospitals	% Change	Total	% Change
2001	6,315.59	10.5	1,754.30	12.0	8,069.89	10.6
2002	6,934.14	9.8	1,910.40	8.9	8,844.57	9.6

Source: FARMAINDUSTRIA based on IMS data.

Sales of medical products through retail pharmacies (laboratory prices), 2002

	Total	% Change	Prescription	% Change	Others	% Change
Units (million)	1,078	2.2	945	3.1	133	-3.9
Value at laboratory (€ million)	6,934.14	9.8	6,621.62	10.2	312.52	1.9

Source: FARMAINDUSTRIA based on IMS data.

As shown in the following chart, the therapeutic classes making the greatest contribution to growth in the market were Blood and Blood Forming Organs (up 18%), Antineoplasic products (17%), Central Nervous System (16%), GU Systems and Sex Hormones (16%) and Cardiovascular System products. This growth is in large part a consequence of the performance of a series of therapeutic sub-classes such as Plaque Aggregation Inhibitors (Blood and Blood Forming Organs), Citostatic products (Antineoplasic products), Atypical Anti-Psychotic and Anti-Alzheimer products (Central Nervous System), Other Sex Hormones and Gonadotropins (GU products) and Angiotensin II Antagonists (Cardiovascular system).

Pharmacy sales of medicinal products by therapeutic class (2002)

Therapeutic class	Units (Thousand)	Units (%)	% change	Value (e Million)	Value (%)	Incr. (%) change	Average price (LSP)
A Alimentary tract and metab.	155,779	14.5	0.8	917.96	13.2	3.0	5.89
B Blood and blood forming organs	38,049	3.5	7.3	247.19	3.6	18.1	6.50
C Cardiovascular system	165,637	15.4	5.6	1,605.86	23.2	10.7	9.70
D Dermatologicals	62,543	5.8	-3.0	236.20	3.4	2.6	3.78
G GU systems and sex hormones	45,899	4.3	4.2	414.65	6.0	15.5	9.03
H Systemic hormonal preparations	14,942	1.4	4.1	171.09	2.5	3.3	11.45
J Systemic anti-infectives	65,946	6.1	-5.2	439.23	6.3	1.8	6.66
K Hospital solutions	2,224	0.2	2.9	2.65	0.0	0,8	1.19
L Citostatic and immunol. prod.	4,859	0.5	4.1	299.30	4.3	16.8	61.60
MMusculoskeletal system	72,032	6.7	4.1	382.02	5.5	4.7	5.30
N Central nervous system	268,036	24.9	2.9	1,347.38	19.4	16.0	5.03
P Parasitology	997	0.1	3.4	3.06	0.0	33.4	3.07
R Respiratory system	137,525	12.8	1.1	695.20	10.0	8.0	5.06
S Sensory organs	42,790	4.0	3.5	163.12	2.4	15.8	3.81
T Diagnostic products	177	0.0	-12.3	1.54	0.0	-11.2	8.70
V Other products	579	0.1	3.9	7.69	0.1	86.7	13.28
Total	**1,078,014**	**100.0**	**2.2**	**6,934.14**	**100.0**	**9.8**	**6.43**

Note: LSP = Laboratory Sale Price.

Source:IMS.

2.3. International trade

Spain's GDP grew at a rate of 2% in 2002, slightly higher than the average rate of 1.5% for the OECD countries. Slack economic activity during the year resulted in a slowdown in international trade. As a result, Spanish exports of goods, which totalled €130,814.2 million grew by 1.4% in real terms compared to 2001, while imports increased 3.8% (also in real terms) to €172,788.8 million. Accordingly, the trade deficit narrowed by 2.4% in 2002 to €41,974.6 million. The coverage rate was 75.7%. Pharmaceutical imports represented 3.5% of total trade and exports 2.7%.

As has traditionally been the case, trade in pharmaceutical products were less affected than other goods by ups and downs in the economy, since they are less dependent on the general economic situation. As a result,pharmaceutical imports, including both raw materials and finished products, totalled €6,059 million, growing by 21.8% compared to 2001. Meanwhile, Spain exported pharmaceutical goods worth €3,568, 30.3% more than in the prior year. On this basis, the trade deficit in pharmaceuticals was €2,491.41 million, an 11.46% increase compared to 2001.

Taking into consideration only caption 30 —pharmaceutical products (excluding raw materials)— was the sixth largest item of trade by volume in the Spanish economy in relation with the situation in 2001. Furthermore,it saw the fastest growth compared to the prior year (28%) out of the 20 captions with the highest volume of trade in 2002.

Total foreign trade in pharmaceutical products in 2002 (_ million)

	Imports	Exports	Balance
Raw materials	500.87	523.31	22.44
Pharmaceutical products	5,558.21	3,044.36	-2,513.85
TOTAL	**6,059.08**	**3,567.67**	**-2,491.41**

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

The rate of cover in 2002 (i.e. exports / imports) for the total pharmaceutical balance was 58.9%, a slight improvement compared to 2001 (55.1%), although still significantly lower than the coverage rate for goods and services as a whole (75.7%). The coverage varies very significantly when broken down, however, with raw materials at 104.5% and pharmaceutical products at 54.8%. This situation is a major improvement on the prior year, when the coverage rates for raw materials and pharmaceutical products were respectively 97.6% and 50.5%.

The geographical distribution of Spanish pharmaceutical trade appears to have experienced a sharp shift in the process of concentration in favour of cross-border trade with other EU countries. In fact, the EU now accounts for 81.7% of imports in the period considered compared to 77.9% in 2001, and 77.6% of exports compared to 74.5% in the prior year.

International trade in pharmaceutical products by region, 2002 (_ million)

	European Union			Rest of World		
	Imports	Exports	Balance	Imports	Exports	Balance
Raw materials	259.88	267.27	7.40	240.99	256.04	15.05
Pharmaceutical products	4,688.44	2,501.32	-2,187.13	869.77	543.04	-326.72
Total	**4,948.32**	**2,768.59**	**-2,179.73**	**1,110.76**	**799.08**	**-311.68**

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

Analysis of itemised foreign trade data reveals that item 30.04 (Medicines packaged for retail sale) has further increased its share, representing 73.4% of total pharmaceutical imports and 71.6% of exports in 2002. On this basis, imports have increased by 0.5% compared to the prior year and exports by 4%. The most significant component of raw materials is line 29.41 "Antibiotics", which accounts for 10.7% of Spanish pharmaceutical exports.

Structure of international trade in pharmaceutical products, 2002 (% of total)

	Imports	Exports
Raw materials	**8,3**	**14,7**
29.35 Sulphamides	0,9	0,6
29.36 Vitamins and pro-vitamins	2,2	0,6
29.37 Hormones	0,8	1,1
29.38 Heteroxides	0,4	0,6
29.39 Vegetable alkaloids	1,1	1,1
29.41 Antibiotics	2,9	10,7
Pharmaceutical products	**91,7**	**85,3**
30.01 Glands and other organs	1,4	0,5
30.02 Drips and vaccines	9,6	7,5
30.03 Bulk medicines	2,9	2,3
30.04 Retail medicines	73,4	71,6
30.05 Gauzes and bandages	2,0	1,2
30.06 Other products	2,5	2,3
TOTAL	**100,0**	**100,0**

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

Estimates for 2003 suggest growth of between 6 and 7% in world trade as a consequence of the reactivation of the international economcy. Trade in pharmaceuticals, which has been among the most dynamic sectors in recent years, is expected to keep to trend, continuing to increase as a proportion of total Spanish trade with the rest of the world. However, the traditional imbalances of a small surplus in raw materials and an increasing deficit in finished pharmaceuticals will remain. The outlook by region is for faster growth in trade in transitional economies, which are more dynamic. Specifically, the future enlargement of the Europe of 15 is likely to lead to an increase in trade within the zone.

2.4. Social Security pharmaceutical expenditure

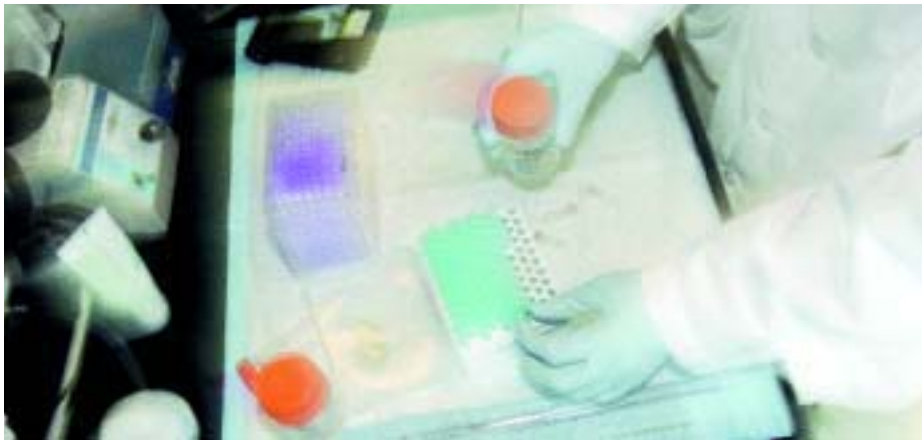
During 2002 a total of 661.1 million Social Security financed prescriptions were dispensed at Spanish pharmacies. This represents an increase of 6.4% compared to 2001 and generated expenditure of €7,972.33, 9.9% more than in the prior year.

Social Security market. Prescriptions dispensed through retail pharmacies (1), 2001-2002

	Expense (2) (RRP+VAT in Mill. €)	% change	Total prescription (Million)	% change	Costper prescription (€)	% change
2001	7,256.48	7.9	621.4	4.1	11.68	3.7
2002	7,972.33	9.9	661.1	6.4	12.06	3.3

(1) Includes all prescription expenditure items: prescription drugs, formulas and therapeutic devices.
(2) Final expenditure after subtracting payments to pharmacies in accordance with Royal Decree Law 5/2000.
Source:Ministry of Health and Consumer Affairs (Summaries of expenditure on prescription medicines).

In recent years, and especially in 2002, there has been a gradual but significant change in the reasons behind the number of prescriptions and their average cost in proportion to final pharmaceutical expenditure. Historically, the increase in the number of prescriptions was between 2 and 3% and the rise in the average cost per prescription was between 5 and



7%. In 2002, however, this trend has been reversed, and the final growth of 9.9% in expenditure was the result of 6.4% growth in the number of prescriptions and an increment of 3.3% in the average cost per prescription.

Almost one point of the increase in the number of prescriptions is attributable to growth in the protected population as a consequence of more intense migratory flows together with traditional factors pushing up demand / expense.

In accordance with FARMAINDUSTRIA's analyses, 0.9% of the total 6.4% rise in the number of prescriptions dispensed nationwide are attributable to the increase in the protected population; 0.8% to impact of the flu epidemic at the beginning of the year; 1% to the treatment of certain pathologies identified as a result of preventive health campaigns; and a final 3.2 are associated with the ageing of the Spanish population. The remaining 0.5% making up the total 6.4% are due to unidentifiable factors.

The distribution and evolution of expenditure in the Regions, except the two cities of Ceuta and Melilla where healthcare management continues to be centralised and which are in any case of little relevance to the overall picture, reveals that Andalusia, Catalonia, and the Regions of Valencia and Madrid account for over 56% of total expenditure. This is very similar to the proportion of Spain's population living in these regions.

In *per capita* terms, the highest expenditure was in the Region of Valencia (€225.2), followed by Galicia (€217.5) and Asturias (€213.1). In apparent contradiction with the image sometimes projected by pharmaceutical provision data released on a periodic basis by the Ministry of Health and Consumer Affairs, the Region of Madrid appears at the other extreme (€145), followed by the Balearic Islands (€147.8) and the Canary Islands (€172.6).

The fastest *per capita* growth in expenditure occurred in Extremadura, Castile and Le n, Asturias and Navarre, while the lowest growth was in La Rioja, the Basque Country and the Region of Valencia.

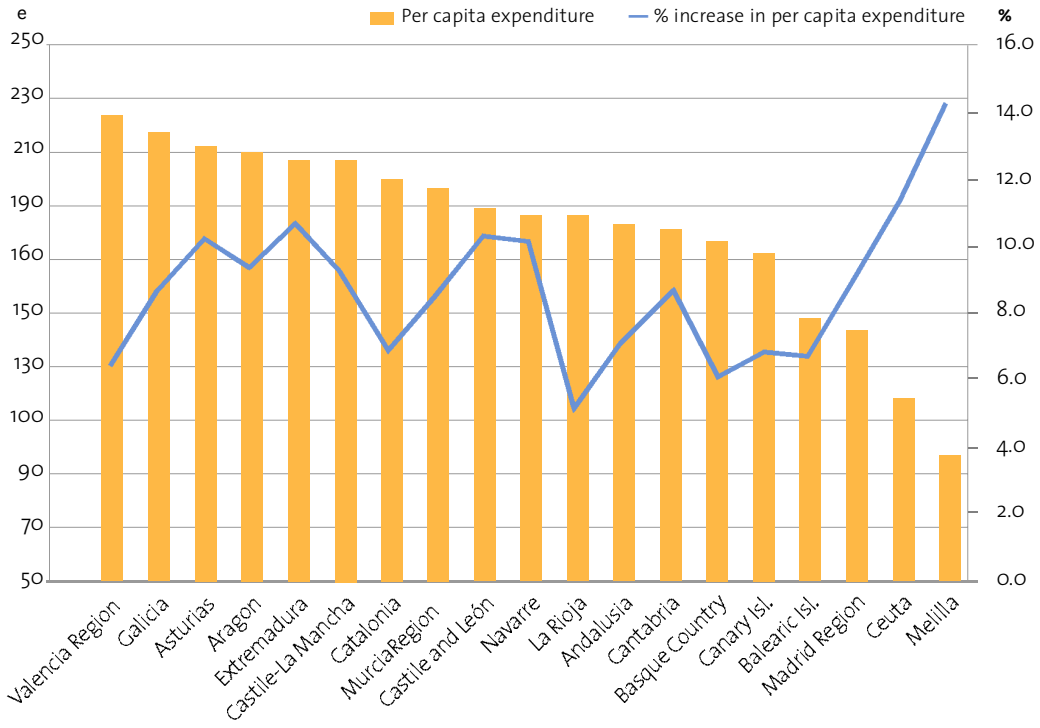
Global figures for the evolution of expenditure in those Regions where healthcare provision was managed by the Insalud until the end of 2001 do not reflect changes related with the devolution process, at least if these regions are taken as a whole. In 2002 their per capita expenditure was in fact lower than the remaining regions while the growth rate was higher. These features are very similar to those observed in prior years.

Breakdown of pharmaceutical expenditure by Regions , 2002

	Share (%)	Per capita expenditure	
		e	Δ % change since 2001
Andalusia	17.3	184.8	7.3
Aragon	3.2	210.4	9.5
Asturias	2.9	213.1	10.2
Balearic Islands	1.7	147.8	7.1
Basque Country	4.8	182.1	6.5
Canary Islands	4.0	172.6	7.2
Cantabria	1.2	183.2	8.8
Castile-La Mancha	4.6	207.6	9.3
Castile and Le n	5.9	188.8	10.3
Catalonia	16.6	203.0	7.1
Ceuta	0.1	117.1	11.2
Extremadura	2.8	208.2	10.6
Galicia	7.5	217.5	8.8
Madrid Region	10.1	145.0	9.0
Melilla	0.1	96.0	13.8
Murcia Region	3.0	195.6	8.6
Navarre	1.3	187.1	10.1
Rioja	0.7	187.1	5.6
Valencia Region	12.2	225.2	6.7
Former INSALUD	36.3	177.7	9.2
Others	63.7	198.7	7.3
Total	**100.0**	**190.6**	**8.0**

Source:Ministry of Health and Consumer Affairs (Summaries of expenditure on prescription medicines) and National Statistical Institute (Population Forecasts, revised August2001).

Per capita expenditure/% increase in per capital expenditure



2.5. Medicine prices

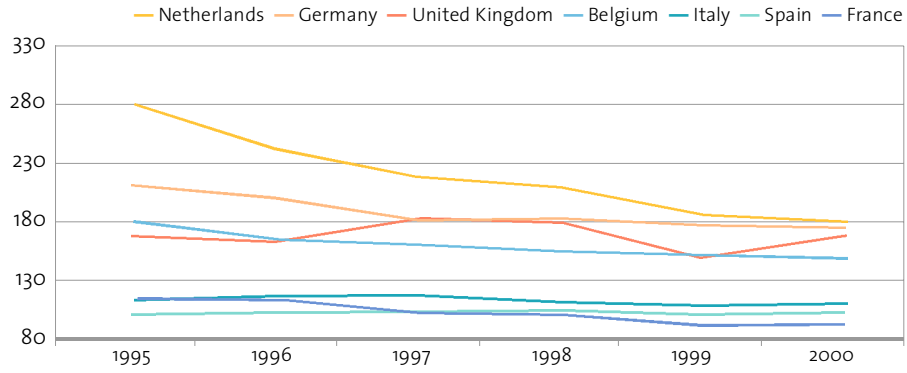
The average laboratory price of medicines in Spain in 2002 was €6.43, although significant differences exist depending on the market segment with average price ranging from €5.14 (ex laboratory) for generics to €12.38 for proprietary medicines aimed at chronic pathologies with low contribution rates on the part of patients.

Spain remains one of the lower priced European countries, though it is evident that the Spanish market is gradually moving closer to those of other neighbouring markets. As in Spain, there are two clearly distinguishable product segments with very different characteristics and evolution. On the one hand, are patented innovations where price differentials between EU member States for have progressively narrowed, while on the other are generics, which the majority of European governments have targeted as a priority to increase their share of domestic markets.

Once harmonisation of registration processes for new medicines have been harmonised in the EU, it appears that the member States are likely to seek convergence in price authorisation for these products. In this regard, international price comparisons have become increasingly prevalent. For example, in countries such as Austria,Belgium, Finland, Sweden and Spain it is now a requirement to report the prices at which a given medicine is sold in other countries. This information has ever more influence over the final pricing decision, and States such as Denmark, Italy and the Netherlands in fact establish their prices on the basis of averages prices in different groups of countries. Even in France, which has a tradi-

tion of low prices, the possibility of referencing the prices of new products to those established in Germany, Italy, Spain and the United Kingdom is now under discussion.
This convergence in the market prices of pharmaceutical products is also apparent from a comparison of weighted average laboratory prices, which strip out distortions caused by differences in distribution margins, in the main European markets over the period between 1995 and 2000. If Spanish prices are indexed at 100, the weighted average prices (WAP) ex laboratory in the Netherlands and Germany, two countries where prices have traditionally been high, were twice the WAP in Spain in 1995. However, in 2000 the WAP in both countries has fallen towards Spanish levels and no longer double them.

Evolution of the Index of Weighted Average Prices (LSP) (Spain = 100)



Source: FARMAINDUSTRIA data (Indicatori Farmaceutici, various years).

This convergence would be even more pronounced if only products launched in recent years were considered.
In the other product segment (generics), one of the main means of favouring penetration is the greater number of marketing authorisations awarded for these products. For example, and as mentioned in the section on the domestic market, over half (55%) of the 185 products marketed in Spain are generic medicines. Furthermore, there has been a practically unanimous move in European markets to foster the generics market through the reference pricing mechanism.
The implementation of reference prices (RP) has accelerated in Europe over the past two years. Thus, since RPs were adopted in the German (1989), Dutch (July 1991), Swedish (January 1993) and Danish (June 1993) systems, the remaining European have waited to see what impact the mechanism would have. Spain was the next country to take the plunge, and reference prices came into force in December 2000. This was the signal for Belgium (June 2001), Italy (September 2001) and Portugal (March 2003) to join in. Even France will join the RP countries in July 2003.
As may be seen from the succession of events referred to above, RPs first appeared in the countries where prices were highest and were either not publicly controlled or only minimally so. In these countries, the two market segments of innovations and existing products (represented by generic medicines) were also more clearly differentiated. The system

then spread to countries where prices had traditionally been low and government intervention significant.
However, this process of harmonisation has not been sufficient to deter parallel trade between the member States, valued at around e3,600 million at laboratory prices in 2001. This represents a significant percentage of total medicine sales in many countries.

Parallel trade and medicine sales in 2001

	% Parallel imports /Domestic sales
United Kingdom	15.0%
Netherlands	9.9%
Denmark	9.7%
Sweden	9.3%
Norway	5.1%
Germany	4.7%

Source:EFPIA.

These practices, which are based on the still considerable price differentials in Europe for certain medicines, have received a boost from the health authorities in some countries where domestic prices are high. This is because the authorities believe that fomenting low-cost imports from other European countries will alleviate public health spending.

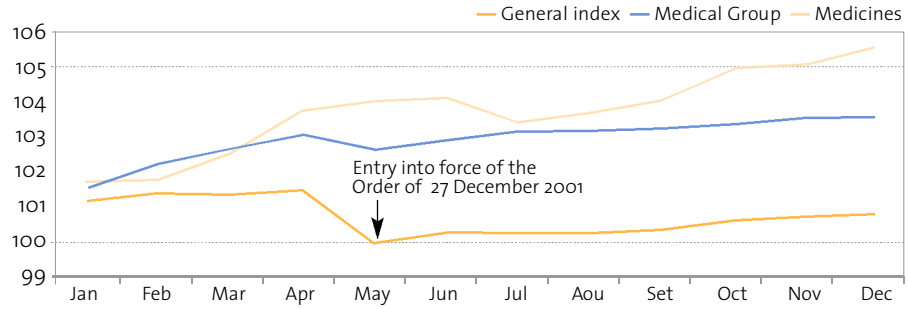
Average price of medicines in the main EU markets (average market price,laboratory sale price) 2001

	Price in	Index Spain=100	
Country	e	e	$ WAP (2001)
Belgium	10.3	176	147
France	5.4	92	75
Germany	12.5	214	175
Italy	6.9	118	115
Netherlands	10.4	178	147
Spain	5.8	100	100
United Kingdom	10.7	183	135

Source: FARMAINDUSTRIA data (Indicatori Farmaceutici, various years) and OECD (Main Economic Indicators).

The latest available data continue to show that Spain has the lowest average prices in the European Union after France and at a very similar level to Italy. This conclusion holds even where differences in purchasing power parity between the various countries are considered, although this narrows differences slightly.

Evolution of Consumer Price Indices (General, Medicines and Medicaments and Other Pharmaceutical Products) in 2002 (2001 = 100)



Source:National Statistical Institute.

Turning our attention now to an analysis of the Spanish domestic market, the behaviour of prices in 2002 clearly reflects the impact of the Reference Pricing Order of December 2001, which approved new standard groups and revised those already in existence, even though the CPI does not accurately reflect the evolution of medicine prices as it fails to take into account the large number of innovations launched on the market.

In a year that has featured high inflation in Spain, pharmaceutical prices reveal negative growth at the year end and have been decisive in the moderate growth of the Medicines Group, which is proportionately the largest component (38.41% for the Medicines Group and 1.08% for the General CPI) following changes in the structure of the consumer price index. Inter alia, the CPI no longer includes family expenditure on medical insurance in the Medical Group, as was the case until 2001. Thus, while general inflation in 2002 was 4.0%, the CPI for Medicines and Other Pharmaceutical Products contracted by 0.3%, as a result of which the increase in prices forming part of the Medical Group was only 2.6%.

Inflation and medicine prices, 2002

Group or caption	% CPI
General (inflation)	4.0
Medical	2.6
• Medicines and others pharmaceutical products	0.3
• Therapeutic products	2.5
• Non-hospital medical and paramedical services	7.3
• Dental services	4.2
• Hospital services	3.8
• Medical insurance (1)	4.4

(1) Though no longer forming part of the Medical Group, this expense has been included for reference purposes.

Source:National Statistical Institute.

2.6. Reference prices

On 4 December 2002 the Ministry of Health and Consumer Affairs approved an Order establishing certain new standard presentations for medicines setting new reference prices.
Some 39 new standard groups are provided for in the Order, affecting 19 active substances and 200 pharmaceutical presentations. As a result, the number of standard groups now included in the reference pricing system is 178, comprising 63 active substances. At 31 December 2002 the market formed by these standard groups represented 14% of the total market in terms of value and 19% in units according to IMS data.
On an annualised basis, the estimated impact of the Order of 4 December 2002 on the Social Security prescription market is estimated to be in the region of €15 million at retail prices plus VAT, and €22 million on the total prescription market.
For the purposes of Social Security sales, the application of these new prices will commence as of 1 May 2003, which will cushion the blow in the current year.
The Ministerial Order of 27 December 2001 came into effect for the purposes of Social

Security sales in May 2002. This Order also established new standard groups and revised the reference prices established previously.
As explained in the FARMAINDUSTRIA Annual Report for 2001, the estimated annual impact of this measure was a reduction of €156 million at retail prices plus VAT, together with a forecast saving of €38 million due to cuts in the prices of 5 active substances. On this basis, it was expected that the market would be constrained by an annual €194 million, which would be €142 million in 2002 since the updated reference prices would not take effect until 1 May.
On the basis of a preliminary analysis of the evolution of the market in 2002, however, it appears that the total market (public and private) linked to the reference pricing system shrank by around €148 million, which is slightly higher than foreseen.

Impact of Reference Prices in 2002 (estimated at RRP+VAT in e million)

	Impact over 12months	Estimated impact 2002	Final data
Review of prices for standard groups per M.O. 13.07.00	90	60	-
Selective 15% price cut (5 active substances)	38	38	-
New standard groups	66	44	-
Total	**194**	**142**	**148**

Nevertheless, a more detailed study of the pharmaceutical market shows that these data do not support the assertion that reference prices are in fact capable of generating the forecast savings in pharmaceutical expenditure.
Though it may be true that the considerable decline in average prices in the reference prices market during 2002 has also shrunk the value of the market in cash terms, it has also reduced the number of units sold, most probably as a consequence of the shift in prescribing towards presentations or molecules that are not affected by the reference pricing system. This may either be because new products providing better therapies have entered the market or the result of doctors' seeking to avoid the substitution of the prescribed product by pharmacies.

Market subject to the reference pricing system in 2002

	Units	Value	Average price
% change	-2.3	-10.8	-8.7

Taking into account that this shift generally results in a more expensive prescription, it is therefore highly likely that the net savings generated by the reference prices were actually lower than calculated.
Since the entry into force of the Ministerial Order of 4 December 2002, the existing standard groups and current reference prices are as shown in the following pages.

Active agents, standard preparations and reference prices following the application of the Ministerial Order dated 4 December 2002

Group code	Standard preparation	Reference RRP+VAT (e)
ACETYLCYSTEINE		
1	100MG 30 sachets	2.39
2	200MG 30 sachets	2.93
3	600MG 20 tablets	5.19
ACYCLOVIR		
4	200MG 25 tablets	27.35
5	200MG 25 soluble tablets	33.22
6	800MG 35 tablets	115.06
7	800MG 35 soluble tablets	126.43
8	5% 2GR cream	2.51
9	5% 15GR cream	16.59
ALLOPURINOL		
10	100MG 25 tablets	1.84
11	100MG 100 tablets	3.43
12	300MG 30 tablets	3.88
ALPRAZOLAM		
13	0.25MG 30 tablets	2.40
14	0.50MG 30 tablets	3.11
15	1MG 30 tablets	5.40
16	2MG 30 tablets	10.61
17	2MG 50 tablets	17.55
AMBROXOL		
18	15MG syrup	3.00
AMOXICILLIN		
19	250MG 120ML	3.73
20	500MG 12 capsules	2.46
21	500MG 24 capsules	3.99
22	500MG 16 sachets	3.26
23	750MG 12 tablets	3.61
24	1G 12 tablets	4.51
25	1G 12 sachets	4.64
115	250 MG 16 sachets	2.84
116	500 MG 24 sachets	4.62
142	750MG 24 tablets	7.73
AMOXICILLIN + CLAVULANICACIO		
118	500/125 12 tablets	6.17
119	125/31.25 60 ML suspension	2.19
120	125/31.25 120 ML suspension	3.78
(*)143	500/125 24 tablets	10.96
(*)144	875/125 12 tablets	8.26

Group code	Standard preparation	Reference RRP+VAT (e)
ATENOLOL		
26	50MG 30 tablets	3.52
27	50MG 60 tablets	6.54
28	100MG 30 tablets	5.08
29	100MG 60 tablets	9.66
BISOPROLOL		
(*)145	10 MG 30 tablets	9.09
(*)146	10 MG 60 tablets	17.99
(*)147	5 MG 30 tablets	4.39
(*)148	5 MG 60 tablets	8.72
CAPTOPRIL		
30	12.5MG 20 tablets	4.94
31	25MG 60 tablets	11.53
32	50MG 30 tablets	11.10
33	100MG 15 tablets	13.24
CAPTOPRIL+HIDROCLOROTHIAZIDE		
128	50/25 30 tablets	15.31
CARBOPLATINUM		
34	50 vial	33.22
35	150 vial	108.62
36	450 vial	249.75
CEFACLOR		
37	125MG suspension	5.70
38	250MG suspension	8.96
(*)149	250 MG 12 capsules	5.54
(*)150	250 MG 24 capsules	9.18
(*)151	500 MG 12 capsules	8.54
CEFONICIDE		
39	500MG vial IM	4.21
40	500MG vial IV	4.21
41	1000MG vial IM	8.54
42	1000MG vial IV	8.72
CEFOTAXIME		
43	250MG injection	2.79
44	500MG injection	3.67
45	1000MG injection I.M	6.29
46	1000MG injection I.V	7.07
CEFTRIAXONE		
47	250MG vial IM	4.15
48	250MG vial IV	4.15

Group code	Standard preparation	Reference RRP+VAT (e)
49	500MG vial IM	7.91
50	500MG vial IV	7.11
51	1G IM vial	15.24
52	1G IV vial	13.34
CEFUROXIME		
53	750MG vial	3.86
117	250MG 2ML vial	1.94
CIPROFLOXACIN		
56	250MG 10 tablets	8.90
57	250MG 20 tablets	17.58
58	500MG 10 tablets	16.72
59	500MG 20 tablets	33.44
60	750MG 10 tablets	25.97
(*)152	250 MG 6 tablets	6.92
CLINDAMYCIN		
121	600 MG 1 vial 4 ML	3.89
(*)153	300 MG ampule 2 ML	2.86
(*)154	900 MG ampule 6 ML	3.67
CLOTRIMAZOLE		
61	1% 30G cream	2.48
62	1% 30ML powder	2.56
63	1% 30ML solution	2.60
64	2% 20G vaginal cream	2.60
65	500MG 1 vaginal tablets	3.09
66	100MG 6 vaginal tablets	2.86
CLOXACILINE		
122	500 MG vial	1.59
DICLOFENAC		
67	50MG 40 tablets	3.55
68	100MG 12 suppositories	2.85
69	100MG 20 tablets	5.24
123	75 MG 6 ampules	2.06
DILTIAZEM		
70	60MG 30 tablets	8.24
71	60MG 60 tablets	16.33
DOXAZOSIN		
124	2MG 28 tablets	13.17
125	4MG 28 tablets	16.88
DOXORUBICIN		
72	10MG vial	10.54
73	50MG vial	44.56
ENALAPRIL		
74	5MG 10 tablets	1.94
75	5MG 60 tablets	8.64
76	20MG 28 tablets	13.76
ESPIRONOLACTONE		
(*)155	100 MG 20 tablets	5.20
(*)156	25 MG 20 tablets	2.65
(*)157	25 MG 50 tablets	4.51
FAMOTIDINE		
77	20MG 20 tablets	12.36
78	40MG 10 tablets	11.50
(*)158	20MG 28 tablets	8.10
(*)159	40MG 14 tablets	8.10
(*)160	40MG 28 tablets	13.33
FLUOROURACILE		
(*)161	250MG 10 vials	8.27
FLUOXETINE		
79	20MG 14 capsules	11.11
80	20MG 70ML solution	11.03
81	20MG 140 solution	20.29
82	20MG 28 capsules	21.93
126	20MG 14 soluble tablets	11.79
127	20MG 28 soluble tablets	23.25
FLUTAMIDE		
83	250MG 50 tablets	56.51
84	250MG 84 tablets	91.47
FLUVOXAMINE		
(*)162	100MG 30 tablets	15.89
(*)163	50MG 30 tablets	9.52
FUROSEMIDE		
85	20MG ampules	2.72
(*)164	40MG 10 tablets	1.62
(*)165	40MG 30 tablets	2.63
GEMFIBROZIL		
86	600MG 60tablets	17.60
87	900MG 30tablets	14.17
IBUPROFEN		
129	600MG 40 tablets	5.07
INDAPAMIDE		
88	2.5MG 30 tablets	3.61
ISOSORBIDE MONONITR.		
(*)166	20MG 40 tablets	4.77
(*)167	20MG 80 tablets	9.84
(*)168	40MG 40 tablets	9.32

Group code	Standard preparation	Reference RRP+VAT (e)
KETOCONAZOL		
(*)169	2% 100ML gel	7.01
LISINOPRIL		
130	5MG 60 tablets	8.87
131	20MG 28 tablets	15.86
LORATADINE		
(*)170	10MG 20 tablets	6.44
(*)171	5MG 120 ML. syrup	3.93
LORMETAZEPAM		
(*)172	1MG 30 tablets	2.92
(*)173	2MG 20 tablets	3.33
LOVASTATIN		
132	20MG 28 tablets	16.00
133	40MG 28 tablets	32.98
METAMIZOL		
(*)174	2G 5 ampules	2.35
(*)175	575MG 10 capsules	2.10
(*)176	575MG 20 capsules	2.54
METFORMINE		
(*)177	850MG 50 tablets	2.52
METHOTREXATE		
89	50MG vial	4.75
METRONIDAZOL		
90	250MG 20 tablets	2.05
NAPROXEN		
91	500MG 40 tablets	6.90
NIFEDIPINE RETARD		
92	20MG 40 tablets	5.08
93	20MG 60 tablets	9.55
NIMODIPINE		
94	30MG 30 tablets	9.72
95	30MG 100 tablets	30.46
NITRENDIPINE		
96	20MG 30 tablets	17.12
NORFLOXACIN		
97	400MG 14 tablets	9.05
OMEPRAZOLE		
98	20MG 14 capsules	15.44
134	20MG 28 capsules	23.64
PENTOXIFYLLINE		
135	400MG 60 tablets	11.62
PIROXICAM		
99	20MG 20 soluble tablets	5.35
136	20MG 20 capsules	4.84
RANITIDINE		
100	150MG 28 tablets	10.94
101	300MG 14 tablets	11.45
102	300MG 28 tablets	19.82
103	50MG 5 ampules	2.09
SELEGILINE		
137	5MG 20 tablets	10.27
138	5MG 50 tablets	25.30
TAMOXIFEN		
104	10MG 30 tablets	6.20
105	10MG 100 tablets	20.56
106	20MG 30 tablets	11.75
107	20MG 60 tablets	22.92
TERAZOSINE		
178	2MG 15 tablets	6.61
179	5MG 30 tablets	20.52
TIMOLOL		
108	0.25% drops	2.47
109	0.5% drops	2.77
TRAMADOL		
110	50MG 20 capsules	5.58
111	50MG 60 capsules	13.74
139	100MG 5 ampules	5.79
140	100MG 30ML drops	16.74
141	100MG 10ML drops	6.55
(*)180	100MG 6 suppositories	3.69
VANCOMYCIN		
112	VANCOMYCIN - 500MG vial	8.77
113	VANCOMYCIN - 1000MG vial	17.38
VINCRISTINE		
114	vial 1ML	8.66
ZOLPIDEM		
(*)181	10MG 30 tablets	5.45

(*) Standard groups included in accordance with the Ministerial Order of 4 December 2002.

New legislation

New legislation approved during 2002 and up to the date of this Annual Report have been as follows:

1 STATE LEGISLATION

PROFARMA ACTION

RESOLUTION of the Secretary of State for Science and Technology Policy dated 24 July 2002 establishing the regulatory bases for PROFARMA II:Promotion of scientific research,development and technological innovation (SDI) in the pharmaceutical and veterinary industry.

SPANISH MEDICINAL PRODUCTS AGENCY

ROYAL DECREE 840/2002 OF 2 AUGUST 2002 AMENDING AND IMPLEMENTING THE BASIC STRUCTURE OF THE MINISTRY OF HEALTH AND CONSUMER AFFAIRS. Spanish Medicinal Products Agency CIRCULAR 12/2002 issued on 17 July 2002 concerning Instructions for requests for scientific advice on the quality, safety and efficacy of medicines for human or veterinary use during the research and development stages with a view to commencing the mutual recognition procedure, and request for other types of advise.

INTERNATIONAL TRADE

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 8/2002 ISSUED ON 12 JUNE 2002 concerning the export of medicinal products.

POLLUTION

INTEGRATED POLLUTION CONTROL AND PREVENTION ACT, 2002 (LAW 16 OF 1 JULY 2002) ROYAL DECREE 117/2003 ISSUED ON 31 JANUARY 2003, concerning limits on emissions of volatile organic compounds due to the use of solvents in certain activities.

SEAL COUPON

ORDER SCO/470/2002 OF 20 FEBRUARY 2002 updating the seal coupon on products and accessories included in National Health System financing.

COMPETITION

Coordination of State and Autonomous Community Powers in matters of Competition Act, 2002 (Law 1 of 21 February 2001).

BASIC LEGISLATION

Tax,Administrative and Social Measures Act, 2002 (LAW 53 of 30 December 2002).

DOPING

SPORTS COUNCIL RESOLUTION OF 10 DECEMBER 2002 approving the list of banned substances and pharmacological groups, as well as illicit doping methods.

TRANSMISSIBLE SPONGIFORM ENCEPHALITIS

ROYAL DECREE 100 24 JANUARY 2003 AMENDING ROYAL DECREE 1911 OF 24 NOVEMBER 2000, which regulates the destruction of specified risk materials related with transmissible spongiform encephalitis.

ORDER APA/718/2002 OF 2 APRIL 2002 amending certain annexes to Royal Decree 3454/2000 of 22 December 2000, by which the integrated coordination programme for animal transmissible spongiform encephalitis vigilance and control was established and regulated.

OTC PRODUCTS

ORDER SCO/1377/2002 OF 5 JUNE 2002 amending the annex to the Order dated 17 September 1982 which implements Royal Decree 2730/1981 governing the registration of over-the-counter drugs.

POST-AUTHORISATION STUDIES

Spanish Medicinal Products Agency CIRCULAR 15/2002 concerning reporting procedures between the pharmaceutical industry and the Spanish Pharmacovigilance System in the area of pharmacovigilance of medicines for human use.

NARCOTICS AND PSYCHOTROPIC SUBSTANCES

ORDER SCO/469/2002 OF 19 FEBRUARY 2002 including certain active substances in Annex I of Royal Decree 2829 dated 6 October 1977 governing psychotropic substances and drugs.

ORDER SCO/1906/2002 OF 15 JULY 2002 including paramethoxymethylamphetamine (PMMA) in list I of Annex I to Royal Decree 2829 dated 6 October 1977 governing psychotropic substances and drugs.

LABELLING AND PROSPECTUSES

Spanish Medicinal Products Agency CIRCULAR 01/2002 of 15 July 2002 concerning amendments to Circular 2/2000, which establishes guidelines for the readability of packaging materials and prospectuses.

Spanish Medicinal Products Agency CIRCULAR 4/2003 of 20 March 2003 concerning the replacement of Annexes to Circular 2/2000 containing the standard terms of the European Pharmacopoeia for the updated

terms of the 2002 version of the Council of Europe document.

SPANISH PHARAMCOPOEIA

ORDER SCO/1905/2002 OF 15 JULY 2002 approving the second edition of the Royal Spanish Pharmacopoeia.

ORDER SCO/575/2003 OF 15 JULY 2002 approving the additions and updates to the Royal Spanish Pharmacopoeia.

EUROPEAN PHARMACOPOEIA

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 3/2002 OF 26 FEBRUARY 2002 regarding updates to monographs and texts and the elimination of the monograph European Pharmacopoeia.

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 4/2002 OF 27 FEBRUARY 2002 regarding updates to monographs and texts of the European Pharmacopoeia.

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 13/2002 OF 23 JULY 2002

Information on Resolutions of the Public Health Committee (Partial Agreement) of the Council of Europe in the matter of the Europe Pharmacopoeia.

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 14/2002 concerning Information on Resolutions of the Public Health Committee (Partial Agreement) of the Council of Europe in the matter of the Europe Pharmacopoeia.

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 16/2002 OF 2 SEPTEMBER 2002 regarding the deletion of monographs and texts from the European Pharmacopoeia.

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 22/2002 OF 2 DECEMBER 2002 concerning Information on Resolutions of the Public Health Committee (Partial Agreement) of the Council of Europe in the matter of the Europe Pharmacopoeia.

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 01/2003 OF 20 JANUARY 2003 concerning Information on Resolutions of the Public Health Committee (Partial Agreement) of the Council of Europe in the matter of the elimination of monographs from the Europe Pharmacopoeia.

PHARMACOVIGILANCE

ROYAL DECREE 711/2002 OF 19 JULY 2002 regulating pharmacovigilance of medicines for human use.

STANDARD TECHNICAL DOCUMENTS

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 10/2002 OF 26 APRIL 2002 on information contained in the Technical Document and Prospectus for medicines containing Hypericum perforatum (HIPERICO).

FINANCING OF MEDICINES

INSTRUCTION ISSUED BY THE OFFICE OF THE SUB-SECRETARY FOR HEALTH AND CONSUMER AFFAIRS ON 13 DECEMBER 2002 to coordinate administrative procedures related with marketing authorisation and public funding of medicines for human use.

BLOOD DERIVATIVES

ROYAL DECREE 710/2002 OF 19 JULY 2002 amending Royal Decree 414 dated 1 March 1996 governing health products containing stable human blood derivatives or plasma.

ORDER SCO/1647/2002 OF 19 JULY 2002 requiring the use of genomic detection tests for the hepatitis C virus (HCV) in blood donations.

ENVIRONMENT

ORDER MAM/304/2002 OF 8 FEBRUARY publishing operations related with the valuation and elimination of waste products and the European waste products list.

PATENTS AND BRANDS

LAW 10 OF 29 APRIL 2002 AMENDING THE PATENTS ACT, 1986 (LAW 11 OF 20 MARCH 1986) in order to incorporate European Parliament and Council Directive 98/44/EC of 6 June 1998 concerning legal protection of biotechnological inventions into Spanish law.

ROYAL DECREE 687/687 OF 12 JULY 2002 approving the Regulations for the implementation of the Brands Act, 2001 (Law 17 of 7 December 2001).

REFERENCE PRICES

ORDER SCO/211/2002 OF 24 JANUARY 2002 correcting certain errata in the Order dated 27 December 2001 which establishes new standard groups of presentations of proprietary medicines and approves the relevant reference prices established in the Order of 13 July 2000.

ORDER SCO/3215/3215 OF 4 DECEMBER 2002 defining new standard groups of medicine presentations and approving the related reference prices.

HEALTH PROVISION

ORDER SCO/585/2002 OF 5 MARCH 2002 updating the annex to the Order of 30 April 1997 regulating complex diet therapy treatments.

HEALTH PRODUCTS

ROYAL DECREE 437/2002 OF 10 MAY 2002 establishing the criteria for the award of operating licences to manufacturers of made-to-measure health devices.

REGISTRATION

SPANISH MEDICINAL PRODUCTS AGENCY CIRCULAR 21/2002 OF 12 DECEMBER 2002 concerning the format of the application for Authorisation of Medicines for Human Use.

2 Regional Governments Legislation

Andalusia

DECREE 232/2002 OF 17 SEPTEMBER issued by the Andalusia Regional Government Health Department regulating Ethics and Health Research bodies and Clinical Trials in Andalusia.

Aragon

ARAGON REGIONAL HEALTH ACT, 2002 (LAW 6 OF 15 APRIL 2002).

DECREE 26/2003 ISSUED ON 14 FEBRUARY 2003 by the Regional Government of Aragon,creating the Ethics and Clinical Research Committee of Aragon.

Cantabria

CANTABRIA REGIONAL HEALTH STRUCTURE ACT, 2002 (LAW 7 OF 10 DECEMBER 2002).

Catalonia

DECREE 152/2002 OF 28 MAY 2002 establishing hygiene and health conditions for the prevention of legionnaires disease.

DECREE 175/2002 OF 25 JUNE 2002 regulating the registration of anticipatory instructions.

ORDER SSS/143/2002 ISSUED BY THE CATALONIA REGIONAL GOVERNMENT HEALTH AND SOCIAL SECURITY DEPARTMENT 30 APRIL creating the Advisory Committee on advertising of health products aimed at the general public.

Valencia

Valencia Regional Patient Rights and Information Act, 2003 **(LAW 1 OF 28 JANUARY 2003).**

Valencia Regional Health Structures Act, 2003 **(LAW 3 OF 6 FEBRUARY 2003).**

Regional Government of Valencia Environment Department **ORDER OF 5 DECEMBER 2002** regulating the Annual Declaration of Packaging and Waste Packaging.

Extremadura

Extremadura Regional Government Health and Consumer Affairs Department **ORDER OF 12 JULY 2002** creating the Register of cases of human transmissible spongiform encephalitis in the Autonomous Community of Extremadura.

Galicia

REGIONAL GOVERNMENT OF GALICIA HEALTH DEPARTMENT DECREE 170/2002 OF 2 MAY 2002 creating the Galician Alert Network for Risks Related with Medicines and Health Products for Human Use.

REGIONAL GOVERNMENT OF GALICIA HEALTH DEPARTMENT DECREE 247/2002 OF 18 JULY 2002 providing for the formation, membership and functions of the Informed Consent Commission.

Balearic Islands

BALEARICS REGIONAL GOVERNMENT HEALTH AND CONSUMER AFFAIRS DEPARTMENT DECREE 116/2002 OF 13 SEPTEMBER 2002 establishing the requirements for distribution warehouses used to store medicines and health products and the procedure for their authorisation, transfer and closure, and regulating safety stocks, as well as the stocks of retail pharmacies.

BALEARICS REGIONAL GOVERNMENT HEALTH AND CONSUMER AFFAIRS DEPARTMENT DECREE 135/2002 OF 8 NOVEMBER 2002 establishing the competent authority to award integrated environmental authorisation,and creating the Integrated Pollution Prevention and Control Committee.

La Rioja

LA RIOJA REGIONAL HEALTH ACT, 2002 (LAW 2 OF 17 APRIL 2002).

Madrid

MADRID REGIONAL ENVIRONMENTAL EVALUATION ACT, 2002 (Law 2 of 19 June 2002 of the Autonomous Community of Madrid Presidency)

MADRID REGIONAL GOVERNMENT HEALTH DEPARTMENT CIRCULAR 1/2002 OF 25 NOVEMBER 2002 concerning visits to doctors and other medicine promotion activities in the Autonomous Community of Madrid Single Public Health Network.

Murcia

MURCIA REGIONAL GOVERNMENT FINANCE DEPARTMENT DECREE 117/2002 OF 27 SEPTEMBER 2002 establishing the basic structure of the Regional Health and Consumer Affairs Department.

Navarre

NAVARRE REGIONAL LAW 5/2002 OF 21 MARCH 2002 amending the Regional health Act, 1990 (Law 10 of 23 November 1990).

NAVARRE REGIONAL LAW 11/2002 OF 6 MAY 2002 concerning patient rights to anticipatory instructions, information and clinical documentation.

Basque Country

BASQUE REGIONAL LAW 7 OF 12 DECEMBER 2002 concerning anticipatory instructions in the area of healthcare.

BASQUE REGIONAL GOVERNMENT HEALTH DEPARTMENT AND TERRITORIAL AND ENVIRONMENTAL DEPARTMENT DECREE 76/2002 OF 26 MARCH 2002 regulating the conditions for the management of health waste products in the Autonomous Community of the Basque Country.

BASQUE REGIONAL GOVERNMENT HEALTH DEPARTMENT DECREE 239/2002 OF 15 OCTOBER 2002 regulating the pharmacovigilance system in the Autonomous Community of the Basque Country.

RESOLUTION ISSUED BY THE DIRECTOR OF HEALTH PLANNING OF THE BASQUE REGIONAL GOVERNMENT HEALTH DEPARTMENT ON 1 OCTOBER 2002 establishing the guidelines for the preparation of the manual for the procurement,preparation, conservation and transport conditions of specimens and samples and the individual registration system of the custody chain, in accordance with the Order regulating authorisations for the creation , modification and operation of clinical laboratories.