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Life Sciences

Spain

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SPAIN

The 'Law & Practice' sections provide easily accessible information on navigating the legal system when conducting business in the jurisdiction. Leading lawyers explain local law and practice at key transactional stages and for crucial aspects of doing business.

Contributed by Faus & Moliner **Authors:** *Jordi Faus, Xavier Moliner, Francisco Aránega, Carmela Losada*

Law & Practice

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CONTENTS

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Faus & Moliner is a modern boutique law firm, specialised in dealing with legal matters typical of the pharmaceutical industry and of other companies which operate in the life sciences sector. The firm decided to pursue this specialisation route because its founding partners were convinced that they would be able to create more value for clients if they not only offered solid legal skills, both theoretical and practical, but also a deep knowledge of the social and economic environment of the sector in which their clients operate. The firm combines legal skills and specialisation with a practical and business-oriented manner of practising law. This allows Faus & Moliner to offer innovative solutions and at the same time to provide adequate responses to the cases which are entrusted to the firm. Since its foundation in 1997, Faus & Moliner has been the market leader in the area of pharmaceutical law in Spain, recognised in several international publications.

Authors

Jordi Faus is a founding partner of Faus & Moliner. He concentrates on regulatory matters, licensing and co-marketing agreements, pricing and reimbursement issues, advertising and antitrust. He has represented various Spanish and foreign companies and associations in a variety of matters and has also substantial expertise in Spanish and international arbitration proceedings, both as counsel and as an arbitrator. Mr Faus is the author of various works on pharmaceutical law, EU law and antitrust, and he lectures on these matters at Spanish and international conferences. He is also a member of the Health Law Section of the Barcelona Bar Association, of the Spanish Association of Regulatory Affairs Professionals and of the Spanish Association of Health Law. Mr Faus is fluent in Spanish, English and French (qualified as an official sworn translator for both English and French).

Xavier Moliner has practised as a lawyer for more than 25 years. He is a founding partner of Faus & Moliner, and concentrates his practice on public procurement and product liability. Mr Moliner has vast experience in product liability litigation, especially in cases involving medicinal products and medical devices, and he regularly advises both Spanish and foreign companies specialising in the life sciences sector. Mr Moliner is fluent in Spanish and English.

Francisco Aránega has been practising law for approximately 20 years. He joined Faus & Moliner in 2015 and has extensive experience providing legal advice in contractual matters and on issues related to compliance, regulatory and advertising of medicinal products and medical devices. He frequently advises on international transactions. For more than ten years, he has been the lecturer responsible for international business law in various Master's programmes and has taught contract and pharmaceutical law in several Spanish universities. Mr Aránega is fluent in Spanish and English and is also able to work in Italian.

Carmela Losada joined the team of Faus & Moliner in 2013 and she specialises in pharmaceutical law and international commercial contracts. Carmela Losada has worked on several articles on pharmaceutical law and she is fluent in Spanish and English.

1. Regulatory Framework

1.1 Key Legislation

Pharmaceutical regulation in Spain currently comprises the following:

- Law 14/1986 on general public health.
- Royal Decree 1/2015, which approves the consolidated version of the Law on guarantees and rational use of medicinal products and medical devices.
- Law 10/2013 on pharmacovigilance and on the prevention of the entry into the legal supply chain of falsified medicinal products.
- Royal Decree 824/2010 on pharmaceutical companies, manufacturers of active ingredients, foreign trade of medicines and investigational medicinal products.
- Royal Decree 1090/2015, which regulates clinical trials, the Ethics Committees for Research and the Spanish registry for clinical trials.
- Royal Decree 1345/2007, which regulates the authorisation, registry and dispensation conditions of medicinal products prepared industrially for human use.

- Royal Decree 782/2013, which regulates distribution of medicinal products.
- Royal Decree 1416/1994, which regulates advertising of medicinal products.
- Royal Decree 870/2013, which regulates online sales to the public of non-prescription-only medicinal products.
- Royal Decree 577/2013, which regulates pharmacovigilance of medicinal products for human use.
- Royal Decree 1015/2009, which regulates access to medicinal products in special situations.
- Royal Decree 271/1990, which regulates prices of medicinal products reimbursed by the National Health System.
- Royal Decree 177/2014, which regulates the reference price system and homogeneous groups of medicinal products in the National Health System and information systems on reimbursement and prices of medicinal products and medical devices.
- Royal Decree 618/2007, which regulates the procedure for establishing particular measures for prescription and dispensation of medicinal products.
- Royal Decree 1718/2010 on medical prescription.
- Royal Decree 1785/2000 on trade of medicinal products within the EU.
- Royal Decree 477/2014, which regulates authorisation of medicinal products for advanced therapies not prepared industrially.

In addition to these rules (i) regional authorities may also adopt some rules which may apply at their level, mainly in the context of organising the dispensation of medicines to patients at healthcare centres and hospitals, and (ii) Spanish trade associations of different sectors of the pharmaceutical industry have adopted, or are in the process of adopting, codes of good practices, which, with binding effects on the members of the respective association, regulate, among other matters, interactions with healthcare professionals.

1.2 Regulatory Bodies

The Ministry of Health

This is the department of the central Spanish government responsible, among other things, for drafting and implementing the rules on pricing and reimbursement of medicinal products that are financed through public funds in Spain.

At the Ministry of Health, a specific pricing committee is competent to review and finally approve applications that companies may file for pricing and reimbursement. The decisions adopted by the Ministry of Health in this regard apply to all of Spain, although pricing and reimbursement may also be affected by the position taken by the regions.

The Spanish Medicines Agency

The Spanish Medicines Agency is also part of the central Spanish government and is responsible, among other things, for granting marketing authorisations for medicinal products in Spain through the national procedure (marketing authorisations for a medicinal product in Spain may also be obtained through the mutual recognition, decentralised and centralised procedures available according to the EU regulations). As regards products which have received a marketing authorisation from the European Commission, the Spanish Medicines Agency only plays a secondary role approving final mock-ups and the contents of the so-called "blue box" in the packaging of the product. The Spanish Medicines Agency is also competent to prepare a Therapeutic Position Report, which is intended to be the only scientific document to consider for the purposes of supporting reimbursement decisions.

The regional authorities

In Spain, the public funds that may be used to finance reimbursement of medicinal products come out of the budget of the 17 regions into which the country is divided. Because of this, the regions have an interest in participating in pricing and reimbursement matters.

At present, this participation takes place through two main routes. One is through some special meetings at the Ministry of Health, where the regions participate in assessing applications for price and reimbursement and where representatives may be appointed as rapporteurs. The second route, which is not actually a formal way provided by the law by which the regions participate in the pricing and reimbursement of medicines, but is of great practical importance, is through the adoption of regional procedures or guidelines influencing how patients may have access to treatments with certain drugs, how physicians may prescribe certain medicines and/or how pharmacies may dispense them.

1.3 Regulations

Decisions taken by regulatory bodies may be challenged through an administrative appeal and through judicial review. In some cases, the administrative appeal is compulsory and has to be filed within a month from the date on which the decision was notified. When the administrative appeal is only optional, the interested party may go directly to court within two months from the date on which the decision was notified. Pending the court case an injunction may be sought. The chances of obtaining an injunction largely depend on whether the applicant shows that it will suffer irreparable harm in the event that the injunction is not granted.

2. Clinical Trials

2.1 Regulation of Clinical Trials

The regulation of clinical trials in Spain changed in 2015 with the adoption of Royal Decree 1090/2015. The most important aspects of the new Royal Decree are the following:

- the procedure for obtaining approvals to carry out a clinical trial in Spain has been simplified, by improving the co-ordination between the Spanish Medicines Agency and the new Ethics Committees for Research into medicinal products;
- it implements a "single ruling" system, which mainly entails that the opinions issued by any of the Ethics Committees for Research into medicinal products have to be accepted by the rest of the committees involved in the trial;
- it contemplates "low risk clinical trials", for which there are less burdensome requirements;
- it introduces the principle of a "single point of contact" between the sponsor and the authorities, and the generalisation of the use of electronic media in the communications between the two, and foresees the approval in the future of a template for clinical trial agreements that will be used by all public hospitals; and
- it provides for more and better information on clinical trials carried out in Spain, which are made available to the public, through the creation of a national registry of clinical trials.

3. Marketing Authorisations

3.1 Process for Obtaining Marketing Authorisation

The main regulation on marketing authorisations for medicinal products in Spain is Royal Decree 1345/2007, which has been in force since December 2007.

The Royal Decree takes as its object all marketing authorisations granted by the Spanish government, whether they are authorisations that result from the national procedure or from the mutual recognition or decentralised procedure.

Nevertheless, some provisions of the Royal Decree also affect the medicines authorised by the European Commission following evaluation by the European Medicines Agency pursuant to the centralised procedure.

Thus, for example, Article 4 of the Royal Decree establishes that said medicines must be registered in the Medicines Registry, although this registration (unlike what happens in the case of the medicines authorised by the Spanish Medicines Agency) is only declaratory. In other words, note will be taken of the Community authorisation, but the authorisation will exist and will be valid from the time of issue by the European Commission.

The Royal Decree also states that medicines authorised by the Commission will be subject to the provisions of Article 21.3 of the Decree (which lays down an obligation to notify the Spanish Medicines Agency of the placing of such products in the market) and of Annexes III and IV relating to the labelling of medicines.

In order to be the holder of a marketing authorisation, it suffices that the applicant, whether an individual or a legal entity, is established in the EU. The applicant only needs to prove that it has a qualified person, as well as the necessary infrastructure for informing about any adverse reactions suspected or arising in Spain or in a third country.

Spanish law does not require the appointment of a local representative of the marketing authorisation holder and there is no legal obstacle to prevent a marketing authorisation holder located in any other EU Member State from supplying its products directly to wholesalers, pharmacy offices or hospitals located in Spain. However, as a matter of practice, appointing such a local representative has become the rule, and it is now very common to appoint a local representative who acts on behalf of the holder of the marketing authorisation in the fulfilment of all or part of its duties, such as in the pricing and reimbursement request for the medicine, the handling of communications with Spanish regulatory authorities, providing a scientific service (including review of marketing materials for compliance with Spanish law) or carrying out local pharmacovigilance reporting.

The designation of the local representative will be stated in the marketing authorisation, and will be registered as such at the Medicines Registry. Such designation does not alter the administrative responsibility of the holder. The agreements between the holder and its local representative may make provision for transferring to the latter the responsibility required by the authorities if legal obligations are not complied with, but the effects of such agreements are limited to the parties and do not extend to the authorities.

3.2 Validity of Marketing Authorisation

Royal Decree 1345/2007 states, in line with EU Directive 2001/83, that a marketing authorisation shall be revoked if the product it refers to is not marketed for three consecutive years.

Also, Article 62 of Royal Decree 1345/2007 imposes an obligation to keep the market supplied and to maintain continuity of service, and each year, during the month of October, the holder of a marketing authorisation will have to declare whether or not it intends to market the product during the following year. If the holder does not make such declaration, it will be deemed to be requesting a suspension of the validity of the marketing authorisation.

Furthermore, the Royal Decree empowers the Spanish Medicines Agency to impose the actual marketing of a medicine and the keeping in force of its marketing authorisation where there are reasons of health or public health interest for so doing, which reasons include that it would otherwise create a pharmaceutical gap either in the market in general or in the pharmaceutical provision of the National Health Sys-

tem. Some companies have argued that this is contrary to EU law provisions, which allow the marketing authorisation holder to cease placing a product in the market by giving two months' prior notice to the authorities.

3.3 Transferring Authorisations from One Party to Another

A change of holder of a marketing authorisation is possible but is subject to authorisation by the Spanish Medicines Agency. Any modifications of the marketing authorisation that result from the change must be processed as variations.

Unlike what happened under the preceding regulations, Royal Decree 1345/2007 does not contemplate the changing of the marketing authorisation holder before the approval procedure has been completed.

3.4 Access to Unauthorised Products

Under Spanish law, early-access programmes allowing a product to be marketed prior to having obtained its marketing authorisation are possible, although they are subject to strict regulatory controls. The use of a product that has not yet obtained a marketing authorisation in Spain but that has obtained a marketing authorisation in another country requires prior administrative approval from the Spanish Medicines Agency. All requests of this nature are studied on a case-by-case basis.

Royal Decree 1345/2007 contains some especially interesting provisions on applications based on informed consent of the applicant or the holder of another marketing authorisation, allowing for these applications to refer to a dossier that is still being assessed by the Spanish Medicines Agency. The medicine for which an approval is sought under this procedure will have to be of identical qualitative-quantitative composition in terms of active substances and of the same pharmaceutical form as the first one, and both parties will have to certify that the pharmaceutical, preclinical and clinical documentation of the two dossiers is identical, except the information related to the medicine-identification data and the design of the labelling.

Off-label use of medicinal products

Under Royal Decree 1015/2009, the use of a licensed medicinal product under conditions different from the ones of the marketing authorisation is subject to the following requirements:

- off-label use is only possible if there is no other medicinal product licensed in Spain which is already authorised to be used in the specific indication according to its summary of product characteristics (SmPC).
- the doctor responsible for the treatment must justify in writing the reasons why the patient should use a specific medicinal product under off-label conditions.
- the patient must consent in writing to the off-label prescription, after having been informed about the benefits and risks of the treatment.
- off-label use must be authorised by the health authority of the region where the healthcare centre is located. As a matter of practice, the system works so that the healthcare centre sends a request to the authority, accompanied by a report by the physician. Once the authorisation has been issued, the healthcare centres of that region no longer need to request another authorisation to use the same medicinal product under these off-label conditions in other patients.
- the Spanish Medicines Agency may approve guidelines on off-label use. The Agency may issue these guidelines when (i) off-label use of a given medicinal product may generate a risk for patients; (ii) the medicinal product may be only prescribed by a hospital specialist; or (iii) when it expects that the impact of the off-label use of the medicinal product may be significant. This last situation would comprise cases where the economic impact may be significant as well as cases where the impact may be of any other nature (ie public health interest concerns).

Compounding of medicinal products at hospital pharmacies

Under Article 7 of Royal Decree-law 16/2012, regional authorities may approve hospital pharmacies for the purposes of carrying out activities involving fractioning, dosage personalisation and also "other operations of manipulation and transformation of medicines". The approval process shall be monitored to ensure that the general quality standards to be set up by the Ministry of Health are respected. Thus, hospital pharmacies may manipulate drugs in the interest of improving the efficiency in their usage and ultimately cutting costs, and this may involve the use of a product under conditions different from those of its marketing authorisation. There are rules on general quality standards for compounding of medicinal products at hospitals approved by the Ministry of Health.

3.5 Ongoing Obligations

Pharmacovigilance rules are mainly contained in Royal Decree 577/2013. In line with the provisions of EU Regulations and Directives, this legislation aims to improve the efficiency of the system and also to allow patients to have a more active role. In this sense, the obligations of the industry regarding information and collaboration with the authorities have been reinforced, and public participation is promoted by allowing patients to notify adverse effects directly. The most important features of this Royal Decree are the following:

- the definition of "adverse reaction" is wide and includes any response to a medicinal product which is harmful and was not investigated beforehand. Therefore, responses produced as a result of abuses, medication errors or off-label

use will be considered as "adverse reactions" for the purposes of these rules;
- the Spanish Medicines Agency must publicise the measures that need to be adopted as a result of adverse reactions;
- patients are able to notify adverse effects directly through the website of the Spanish Medicines Agency;
- apart from having to comply with the guidelines on pharmacovigilance best practices, approved by the European Medicines Agency in co-operation with the EU Member States, some obligations intended to identify potential safety problems are imposed on the industry. In this line, companies may be required to carry out post-authorisation studies. For these purposes, a favourable ruling from an Ethics Committee will still be necessary, but such ruling will be unique and will have to be recognised by all regional authorities; and
- in terms of measures against counterfeiting, there are registries where manufacturers, importers and distributors of active ingredients and intermediaries who participate in the marketing of medicinal products (even those who do not handle physically any product) must be recorded. The obligations regarding traceability of medicinal products are also extended to pharmacies.

3.6 Third Party Access to Pending Application

Whether a third party may access information about pending applications in Spain or challenge the grant of a marketing authorisation, are complex matters under Spanish law.

As a matter of law and practice, the only information which is available in Spain about pending applications for marketing authorisations is the publication of the positive opinion given by the Committee for Human Medicines of the Spanish Medicines Agency (typically, after the positive opinion has been given, not more than four to six weeks elapse until the marketing authorisation is granted, but it is important to mention that the opinion of the Committee is not binding). However, when companies have tried to access other information about applications, the Spanish Medicines Agency has refused to disclose any on the grounds that Article 15 of Royal Decree 1345/2007 states that the documentation of the application and the expert reports are confidential.

After the marketing authorisation has been granted, third parties cannot gain access to documents from the dossier pursuant also to Article 15 of Royal Decree 1345/2007. The only document that a third party can have access to is the assessment report and the SmPC. Access is possible via the website of the Agency. For generic drugs, the Agency does not publish an assessment report.

Things may change in this area as a result of the relatively new general rules on transparency existing in Spain. These rules separate the right to obtain information from the right to locus standi. This is important because so far the Spanish Medicines Agency has always feared that any opening of its position regarding requests for information would imply recognising locus standi to third parties regarding the approval process. Instead, the new rules provide for an appeal mechanism at a Transparency Board, which may then facilitate access.

Changes in this area may also quickly develop in Spain as a result of decisions of EU courts. Thus, although Spanish courts have been known in the past for repeatedly denying locus standi to companies willing to challenge the grant of marketing authorisations to competitors, a recent judgment of the General Court of Justice of the EU, dated 15 September 2015, at no point questions the legitimacy of Novartis to bring judicial actions against the granting of a marketing authorisation to Teva.

4. Pricing and Reimbursement

4.1 Setting and Controlling Prices

As regards price approval for reimbursed medicines, Spain has always been said to follow a cost-plus system under which the maximum ex-factory price should respond to the cost of the product plus a given profit margin. This is what Royal Decree 271/1990 contemplates in accordance with the provisions of Directive EC/89/105.

The cost of the product is to be determined through the analytical application of the "Complete Cost", including R&D and manufacturing costs, and allocations corresponding to commercial and administration costs. As regards the profit component, the rule is that the target profit of each company shall be comprised within a range of 12-18% on capitals allocated to exploitation, including own resources and external resources with financial costs.

As a matter of practice, however, the process entails a negotiation with the authorities. Within this negotiation, the decision on reimbursement and price takes into account the above-mentioned criteria and also the existence of alternative products.

Until recently, the price at which the same or equivalent products were marketed in other EU Member States was also a criterion contemplated under Spanish law to determine the approved price for reimbursed medicines. However, a recent judgment of the Spanish Supreme Court, of 28 October 2015, has declared such criterion not acceptable.

On the other hand, prices for medicines are subject to additional pressure and companies cannot expect to always sell the product at such maximum ex-factory prices. In the hospital environment, for instance, companies are legally obliged to grant a discount at a general rate of 7.5%. A re-

duced rate of 4% applies for orphan drugs, and an increased rate of 15% for products that have been in the market for more than ten years and for which a generic or biosimilar version does not yet exist (unless this is due to product patent issues). Additionally, companies may need to lower their prices at tenders; and in some market segments such as those subject to generic competition, where prices are subject to increasing price competition due to discounts to pharmacies no longer being subject to limitation (until recently discounts to pharmacies were set by law at a maximum of 10%), provided that they are due to early payment or volume of purchases, they are properly reflected in the corresponding invoice and they do not incentivise the purchase of a product over those of competitors.

Rules on prescription, reference pricing and substitution
The rules on how to write prescriptions, reference pricing and substitution are nowadays consolidated in Law 29/2006, as amended.

The system works around the concept of "homogeneous groups." Each of these comprises products having the same characteristics and which are basically interchangeable when dispatched. The Ministry of Health publishes the list of the groups with the actual prices for each product monthly, and companies whose product is priced above the lowest in the group have a period of two to three days to reduce their price and thus match the lowest price in the group.

The general rule is that doctors should write prescriptions by making reference to the International Non-proprietary Name (INN) of the active ingredient. However, they may prescribe using the trade mark of a medicine for follow-on prescriptions in chronic treatments provided that the price of the branded product is not higher than the lowest within the homogeneous group where the product is included, or provided that the product is subject to reference pricing. In all cases, pharmacists must dispense the product which has the lowest price within its homogeneous group (a recent change in the regulation has eliminated the obligation that existed in the past for pharmacists to dispense the generic if the branded product and a generic within the same homogeneous group shared the same lowest price).

The homogeneous groups system mentioned above relies on the idea that products included in each group are substitutable when dispensed. The prices of other products such as biological ones facing competition from biosimilars, could therefore not be tackled through this system. The same could happen with products that have no generic competition. In this situation, the rule is that any product for which a generic or a biosimilar exists, even if it is not substitutable, and products which have no generic competition and have been in the market for more than ten years, may be subject to reference pricing, which basically means that their price will be lowered to the level of the lowest comparable product. Reference prices are revised annually.

4.2 Public Funds
In Spain, the general rule is that prices of medicinal products which are reimbursed by the National Health System are not free and require prior approval. Under Royal Decree-law 16/2012, however, the Ministry of Health is also entitled to control the prices of medicines which are not reimbursed. The aim of this is to ensure that if the government decides to delist a product whose retail price is rather low (in many cases under EUR3), companies cannot raise their prices sharply in an attempt to compensate the situation as regards reimbursed products. The law is not explicit on how the government may exercise the power to control the price of delisted products; it simply states that it may oppose price increases for reasons of public interest.

Under Royal Decree 1/2015, the criteria which must be taken into account in order to decide whether a product is reimbursed or not are the following:

- the seriousness, duration and sequelae of the pathologies for which the product is approved;
- the needs of special groups of persons;
- the therapeutic and social utility of the product;
- the need to limit public pharmaceutical expenditure;
- the existence of already available medicines and the existence of other alternatives for the same illnesses; and
- the degree of innovation of the product.

4.3 Cost-benefit Analysis
Royal Decree 1/2015 states that when deciding on whether a product must be accepted for reimbursement, the Ministry of Health shall also consider, specifically, the impact that financing such a product may have on the public budget and the cost–efficiency ratio of the product based on the Therapeutic Position Report that the Spanish Medicines Agency may prepare. The pricing authorities are also entitled to consider how the product helps sustain the National Health System taking into account its contribution to GDP. Public officials in charge of the system are showing, in day-to-day practice, a clear inclination not to favour companies that do not carry out any industrial operations in Spain or that do not perform R&D activities (including clinical trials). Finally, the law also allows the Ministry of Health to take into account the return mechanisms which may be proposed by the company (discounts, price reviews, etc). This in practice results in the current increase of relevance of the risk-sharing schemes for the reimbursement of medicines.

5. Promotion and Marketing

5.1 Governing Rules

Advertising of medicinal products in Spain is governed by a combination of legislation and industry self-imposed codes of practice. The provisions contained in EU Directives regarding advertising of medicinal products have been implemented through Royal Decree 1416/1994. The Ministry of Health issued an Instruction in 1995 (Circular 6/1995) reflecting the position of the authorities regarding the interpretation of Royal Decree 1416/1994 on certain matters. Some regions which are competent for the implementation of these rules have also issued Guidelines. Some provisions contained in Royal Decree 1/2015 on medicinal products and medical devices may also be relevant, especially with regard to sanctions for breach of the rules on promotion and advertising.

In addition to this set of rules, Farmaindustria, the Spanish Pharmaceutical Industry Association, in 2002, published the Code of Conduct of the pharmaceutical industry, which has been amended and updated several times. The latest version of the Code of Conduct was published in September 2016. The Code updates and consolidates in a single text the rules governing the interaction of the innovative pharmaceutical industry with healthcare organisations and patient organisations.

ANEFP, the industry association which is responsible for over-the-counter (OTC) medicines, has also approved its own Code of Conduct on the promotion of OTC medicinal products. Furthermore, the Ministry of Health published in April 2011 a Guide on the advertising of OTC medicinal products (which includes a Code of Conduct on the promotion of medicinal products to the general public). In addition to medicinal product specific rules, other general legislation may be relevant, such as the 1988 Law on Advertising and the 1991 Law on Unfair Competition (both of them modified by Law 3/2013).

It is important to mention that since 2013 it is no longer necessary to obtain prior administrative approval for the advertising of OTC products. These products may now be promoted without the need for a prior authorisation. This is without prejudice, obviously, to the fact that any advertising is subject to review by the authorities and to sanctions if it does not comply with the rules.

5.2 Breaches of the Promotional Rules

Except for the rules resulting from the industry codes of practice, which are enforced as described below, the responsibility for enforcing the rules on promotion and advertising lies with the regions. The authorities are rather strict in scrutinising materials which companies notify to them and they may suspend an advertisement if it is considered to be in breach of the rules. Furthermore, if the advertisement constitutes a risk to the health or safety of consumers, the authorities may order the publication of the resolution and a corrective statement where the advertisement was published.

Under the Code of Conduct of Farmaindustria, companies have agreed not to file complaints against each other directly before the ordinary courts or the Health Authorities without first raising the issue with the Code of Conduct Commission. The procedure at the Commission may conclude with a fine the amount of which is decided depending on a variety of factors. The damage that a breach of the rules may cause to the image of the industry is one of the criteria to which the Code of Conduct refers. The competent body to impose these sanctions is the Jury of Advertising, a specialised body within the Association for Self-regulation of Advertising. The resolutions of the Jury are made public through its website.

The issues which have been discussed more frequently under these procedures involve the distinction between advertising of and information about products, the conformity of advertising materials to the contents of the SmPCs, and the conditions under which comparative advertising is fair. It is important to stress that comparative advertising is acceptable if the products or characteristics compared are comparable, essential and relevant, and if the comparison is objective, scientifically proven and verifiable through sources immediately accessible to the competitor. The competitor's brand name or trade mark can be used as part of the comparison, provided that such use is proportionate and is not made with the objective of taking an unlawful advantage of the reputation of such trade mark.

5.3 Sanctions for Breaching Promotional Rules

Failing to comply with the rules governing the advertising of medicines may result in administrative sanctions. The general rule is that a breach of the law on this matter may result in a fine being imposed. The amount depends on various factors including negligence, whether the breach was intentional, whether there was fraud or connivance, whether there was a failure to comply with previous requests made by the authorities, the company's turnover, the number of persons affected, the damage caused, and the profits obtained from the infringement.

5.4 Restrictions on the Provision of Gifts/ Sponsorship

An area on which various rulings have been adopted is the limits on hospitality that may be offered to healthcare professionals.

A very important novelty since 2013 concerns transparency obligations. Effective as of 1 January 2014, the Code of Conduct has implemented the rules contained on the EFPIA

Code on disclosure of transfers of value from pharmaceutical companies to healthcare professionals and healthcare organisations and patient organisations. The new obligations are consistently similar to the rules contained in the EFPIA Code. Consequently, since 2015, companies have been obliged to document and publish on their website (first publication actually made in 2016) all transfers of value made during the previous year – meaning any direct or indirect payment or grant, either cash or benefits in kind, and regardless of its purpose – whose recipient is a healthcare professional or healthcare organisation. The only payments excluded from this obligation are those associated with (i) commercial transactions with distributors and pharmacy offices, as well as certain transactions with healthcare organisations; (ii) activities related to products or medicines that are not prescription-only medicines; and (iii) activities not detailed in Appendix I of the Code of Conduct, such as the provision of educational materials or of medical utility, samples, dinners or luncheons. Disclosure must be made on an individual basis or in the aggregate under terms and conditions similar to those set forth in the EFPIA Code.

Market research

Market research studies may be different from advertising and promotion, and the general rule is that involving healthcare professionals in them may be acceptable. However, according to the above-mentioned Code of Conduct of Farmaindustria, market research studies (including social and opinion research) must meet some specific requirements:

- the conduct of the study must not constitute an inducement to recommend, prescribe, purchase, supply, sell or administer a given product;
- studies must be approved by the scientific service or by the compliance officer, and sales personnel cannot play any role in the conduct and implementation of the study;
- written agreements must be signed with the professionals and/or the entities with which the studies will be carried out, specifying the nature of the services to be provided, the professionals' participation and payment conditions;
- the company cannot have access (before, during or after the study) to the identity of health professionals who participate in the study, and cannot participate in their selection, other than by defining the type of healthcare professional who is eligible to participate;
- payments to participating professionals must be based on market criteria and be proportionate to the time devoted, the work done and the responsibilities assumed, and must be adequately documented. Payments cannot be made in kind; and
- the results of the study must not be advertised or used in promotional material.

6. Distribution

6.1 Obtaining an Authorisation to Engage in Wholesale Trade

Distribution of medicines is governed mainly by Royal Decree 782/2013. This regulation provides that the main activity of wholesalers must be distributing medicines to pharmacies located in Spain, and that wholesalers must ensure a timely and continuous distribution service to pharmacies. On the other hand, the regulation does not include any provision forcing pharmaceutical companies to supply products to wholesalers on a general basis. This has been a critical issue in Spain in view of the level of parallel exports that have originated from Spain given its low pricing policy. The Royal Decree, rather, allows the Spanish Medicines Agency to restrict exports in cases of shortage of supply that create therapeutic gaps or that affect products for which no alternatives are available.

The rules on distribution also state that healthcare professionals who may need to acquire medicinal products for treating patients shall buy them from pharmacy offices, but at the same time they contemplate that the Spanish Medicines Agency may approve direct supply of some products by companies or wholesalers.

6.2 Restrictions on Sales of Medicines at a Distance

As regards the internet, Royal Decree 870/2013 deals with the sale to general public, through websites, of medicinal products for human use not subject to prescription. Such internet sales are allowed provided that the products are supplied by a pharmacy, with the intervention of a pharmacist, after such pharmacist has provided personalised advice and in accordance with the rules applicable to the products to be sold. Under this Royal Decree, only approved websites may offer these products, and prior to using the internet as a sales channel the pharmacy must communicate its intention to do so to the regional authority. In order to ensure that the internet channel is properly used, the regulation obliges the pharmacist to make an individual assessment of each order to make sure that the OTC drugs sold through its website are used properly. However, except for legally admitted discounts, no gifts, discounts or similar offers connected with the promotion or sale of medicinal products through websites can be made to the public.

7. Competition Law

7.1 Activities Constituting Infringement

Infringing activities and agreements

Spanish competition law, which incorporates the same principles laid down by European legislation in this area, applies to pharmaceuticals in the same manner that it affects other industries. However, the characteristics of the pharmaceuti-

cal market, in particular the way the demand and the supply for products are structured, has resulted in a special focus on certain areas.

Spanish pricing rules rely on the concept that the maximum ex-factory and retail prices approved by the government only apply to units of products which are financed by the public health system. As a result of this, the system would allow companies to invoice their products at a higher price and then offer chargebacks (in the amount of the difference between the higher price invoiced and the maximum ex-factory price approved by the government) to pharmacies or wholesalers upon them providing evidence that the unit for which they claimed the chargeback was indeed financed by the public health system.

Pricing and other commercial strategies in connection with parallel trade

Over the last years, various companies have implemented systems under the above-mentioned principle, thus supplying products at a list price, and allowing chargebacks for units effectively financed by the public system. Some wholesalers and associations of pharmacies initiated various legal actions against the implementation of such systems before the Spanish competition authorities. In three leading cases, dated 21 May 2009, 14 September 2009 and 17 February 2010, several of these claims were dismissed. The Spanish competition authorities considered that the principle of free pricing (laid down in the Constitution) would be unjustifiably limited if the maximum authorised ex-factory price were applied to products that are not financed by the National Health System. The position of the competition authorities was, however, put into question by the judgment of the Spanish Audiencia Nacional of 5 December 2012, under which these pricing mechanisms were considered to fall under the concept of prohibited agreements which could nevertheless merit an individual exemption. Given that Spanish competition law does not contemplate the granting of individual exemptions since the approval of Law 15/2007, the issue has become moot because companies may keep the system without the need of any individual decision by the competition authorities.

The above-mentioned rulings adopted by the competition authorities also established that the mechanisms laid down by the manufacturers to obtain the data from wholesalers in order to verify which units were eligible for the discount were also legal because the manufacturer only received codified data, not being able to identify of the clients of wholesalers. The position of the competition authorities on this issue has been confirmed by a recent judgment of the Spanish Audiencia Nacional dated 19 March 2014, under which the court has confirmed that the Spanish Data Protection Agency acted correctly when not initiating a case against a company operating under such system.

7.2 Pay-for-Delay Agreements

We are not aware of Spanish cases dealing with pay-for-delay agreements nor of any cases addressing life cycle strategies of originators versus generic drug companies in a thorough manner. However, in a ruling by the Spanish competition authorities, dated 13 February 2014, the behaviour of Pfizer in connection with patent protection for latanoprost was examined in light of the case that had been initiated in Italy. The Spanish competition authorities did not trigger any procedure against Pfizer, as their ruling indicated that Pfizer did not oppose generic competition, even while discussions were taking place at European level regarding the validity of its patent rights.

Additionally, Spanish competition authorities have also investigated commercial practices by various generic companies that were accused of granting illegal discounts to pharmacies thus blocking the entry into the market of smaller companies who were not capable of offering such discounts. The basis for the complaint in this case was Article 3 of Law 29/2006 (currently compiled in Royal Decree 1/1005), under which discounts exceeding 10% were not allowed because they were deemed to be an illegal inducement for the pharmacist to dispense a given product. The prohibition was based on the principle that decisions on dispensation should not be based on economic grounds. The case was dismissed at a ruling adopted on 23 January 2014, where Spanish competition authorities stated that the claimant had not been able to provide evidence of any illegal behaviour by the defendant companies.

8. Product Liability

8.1 Regime for Injury Caused by Pharmaceutical Products

The general regime on liability for defective products or services is established in Royal Decree 1/2007, approving the consolidated text of the General Law on the Protection of Consumers and Users and other complementary regulations. Such regime is found in Articles 128 to 146 of Royal Decree 1/2007.

Article 136 of Royal Decree 1/2007 defines which types of products are subject to the regime on product liability, namely any movable asset, even when this is combined or incorporated into another movable or immovable asset, as well as gas and electricity. The concept of "any movable asset" is very broad and comprises practically all consumer goods.

The regime for product liability established in Royal Decree 1/2007 is of a strict nature and does not provide any scheme of compensation for particular products.

8.2 Prerequisites for Potential Liability

As stated in EU Directive 85/374/EEC, product liability may appear when a product does not provide the safety which a person is entitled to expect, taking all circumstances into account, including its presentation, the use it could reasonably be expected to be given, and the time when the product was put into circulation.

In accordance with Spanish doctrine and case law, there are three large groups of defects that products may suffer from: (i) manufacturing defects; (ii) design defects; and (iii) information defects.

The absence of the necessary warnings or instructions for use, or the inappropriateness of such information, may give rise to an information defect. As a consequence, when the information that accompanies a product is inappropriate or insufficient then such product may be considered to be defective and may give rise to liability in the event that the product causes harm.

In principle, the information and the warnings that shall be taken into account in order to determine whether a product suffers from an information defect shall be the information provided directly to the user of the product.

However, for certain types of products for which the intervention of an intermediary is required, the courts may take the information provided to the intermediary into consideration, in order to determine whether the information provided to the consumer is sufficient and appropriate. Specifically, in the case of medicinal products, Law 41/2002, governing patient autonomy and rights and obligations as regards clinical information and documentation, establishes that it is the doctor's duty to guarantee that the patient has the necessary information to decide freely on the therapeutic strategy prescribed by the doctor. As a consequence, the information provided by the manufacturer to the doctor may be taken into consideration in order to assess the set of information provided to the patient.

8.3 Standard of Proof for Causation

The burden of proving the defect, the harm and the causal link between the harm and the defect (all three being required to be proved for a successful product liability claim) rests on the injured party. In order to establish the causal link, the claimant must provide solid and substantial evidence that supports causation, and the harm must be the result of the defect.

In some cases Spanish courts have accepted that the causal relation be proven by means of presumptions or circumstantial evidence, but the principle of generic causation (ie that in order to prove the causal link it would be sufficient to demonstrate that a product is capable of causing the alleged injury) is not applied. Spanish courts have established that the mere fact that a product is capable of causing harm or damage is not sufficient to establish the defective nature of such product.

In the event that it cannot be established which of several manufacturers is responsible for the defective product, all of the manufacturers will be jointly and severally liable vis-à-vis the injured parties. The manufacturer who compensated the injured party has the right to claim recovery from the other manufacturers, depending on their involvement in causing the damages.

The responsibility for the defect is borne by the manufacturer or by the importer who introduced the product into the EU.

In the event that the manufacturer cannot be identified, then the supplier of the product (the distributor or the "retail" supplier) will be considered as such, unless he informs the injured party of the identity of the manufacturer or of the person who supplied the product to him, within a term of three months. This same rule applies in the case of imported products, in the event that the product does not indicate the name of the importer, even if it indicates the name of the manufacturer.

However, the supplier of the defective product will be liable towards the injured party as if he were the manufacturer in the event that he supplied the product knowing that the defect existed. In such case, the supplier may enforce his right of recovery against the manufacturer.

8.4 Defences for Fault Based or Strict Liability

The only defences that the manufacturer or importer of a medicine may raise in order to avoid liability are the following:

- that he did not put the product into circulation;
- that, given the circumstances of the case, it may be presumed that the defect did not exist when the product was put into circulation;
- that the product had not been manufactured for sale or for any other form of distribution with an economic purpose, nor was it manufactured, imported, supplied or distributed within the context of a professional or entrepreneurial activity; and/or
- that the defect is due to the fact that the product was manufactured in accordance with existing mandatory rules. This does not mean, however, that liability is excluded under a "regulatory compliance defence". Liability cannot be excluded by proving that all regulatory requirements have been complied with.

The so-called "development risks defence" cannot be raised for medicinal products. Therefore, a manufacturer cannot escape liability by arguing that the state of scientific and technical knowledge existing at the time the product was put into circulation did not allow for the discovery of the existence of the defect.

Claims under Royal Decree 1/2007 are barred by limitation if filed later than three years counted from the date the damages were suffered by the injured party, provided that at that time the identity of the party liable for the damages was known to the injured party.

8.5 Recoverable Damages

Under Royal Decree 1/2007, a party having suffered damage caused by a defective product may claim monetary compensation for physical and moral damage. Under Spanish law, the concept of punitive damages does not exist. However, the courts have some discretionary powers in awarding compensatory damages and one may expect the conduct of the defendant to have some impact on the amount of damages awarded.

The overall civil liability of one manufacturer for damages caused by identical products with the same defect is limited to the maximum amount of EUR63,106,270.96.

8.6 Trial

In the case of court proceedings, the case will be resolved by a judge and not by a jury, relying on the materials and evidence presented by the parties, including expert reports. Class actions are possible under the Spanish Code of Civil Procedure but they are not common in Spain.

Cases are heard by civil courts and the process will normally last between 12 and 18 months in first instance, and mediation and arbitration are possible as alternative dispute resolution mechanisms.

Faus & Moliner
Rambla Catalunya 127
Barcelona
Spain
08008

Tel: +34 93 292 21 00
Fax: +34 93 292 21 01
Email: bcn@faus-moliner.com
Web: www.faus-moliner.com

Faus & Moliner Abogados