Commercialisation of healthcare in Spain: overview

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A Q&A guide to the commercialisation of healthcare in Spain.

This Q&A provides an overview of the regulatory framework for the commercialisation of medical products in Spain. It covers the key requirements for manufacturing, marketing and advertising medicines, biological medicines, medical devices, combination products and natural health products.

Medicines

1. What is the definition of medicine (or equivalent) in your jurisdiction?

A medicinal product for human use is defined as any substance or combination of substances presented as having properties for treating or preventing disease in human beings, or which can be used in or administered to human beings with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action (*Royal Legislative Decree 1/2015 of 24 July 2015,*

approving the revised text of the Law on guarantees and rational use of medicines and medical devices (Guarantees Law); *Royal Decree 1345/2007 of 11 October 2007, regulating the procedure for the authorisation, registration and conditions of dispensation of industrially manufactured medicinal products for human use* (RD 1345/2007)).

2. What authorities are responsible for regulating the manufacture, marketing and advertising of medicines?

The Spanish Medicines and Medical Devices Agency (*Agencia Española de Medicamentos y Productos Sanitarios*) (AEMPS), which is part of the Ministry of Health, is the main body responsible for supervising all technical and quality aspects of medical products.

Economic aspects are dealt with by the General Directorate for the Common Portfolio of National Health System and Pharmacy Services (*Dirección General de Cartera Común de Servicios del Sistema Nacional de Salud y Farmacia*) (DGCCS), which is also part of the Ministry of Health. The Ministries of Finance and Economy, Industry and Competition are also represented at the Interministerial Committee on Pricing of Medicines (*Comisión Interministerial de Precios de los Medicamentos*) (CIPM), which is involved in the pricing and reimbursement of medicines.

Spain is divided into 17 autonomous regions (*Comunidades Autónomas*) that have broad powers in relation to health matters and are responsible for, among other matters, providing and funding public healthcare services. To ensure the equal treatment of all citizens throughout Spain, certain basic healthcare must be guaranteed for all Spanish citizens, and the state central authorities are responsible for deciding on its minimum scope. The health authorities of the autonomous regions are also responsible for monitoring compliance with regulations on distribution, dispensation and advertising of medicines and medical devices, among others.

Private associations, through which different market operators have self-regulated their activity, have in some cases established stricter standards than those set out in applicable regulations. Industry associations are very active in Spain, particularly the:

- Pharmaceutical Companies Trade Association (*Asociación Nacional Empresarial de la Industria Farmacéutica*) (Farmaindustria).
- Spanish Generic Medicines Association (*Asociación Española de Medicamentos Genéricos*) (AESEG).
- Spanish Federation of the Healthcare Technology Industry (*Federación Española de Empresas de Tecnología Sanitaria*) (FENIN).

They have played a significant role in approving codes of good practice for the promotion of medicines and medical devices and other interactions with healthcare professionals.

Fedifar (*Federación de Distribuidores Farmacéuticos*) represents the interests of the wholesale sector. Pharmacists have regional professional associations (*Colegios Oficiales de Farmacéuticos*) that are grouped, at a national level, in the Council of Pharmacists' Professional Associations (*Consejo General de Colegios Oficiales de Farmacéuticos*) (CGCOF).

3. What notifications, registrations, approvals and licences are required to manufacture and market medicines and their active pharmaceutical ingredients?

Manufacturing

Natural and legal persons engaged in the manufacture of medicinal products or investigational medicinal products (including exclusively for export), or in any related processes, including fractionation, packaging and presentation for sale, must be authorised by the AEMPS (*Royal Decree 824/2010, of 25 June 2010, regulating pharmaceutical laboratories, manufacturers of active ingredients for pharmaceutical use and foreign trade in medicines and investigational medicines (RD 824/2010)*). Pharmaceutical laboratories importing medicines or investigational medicinal products from third countries must also obtain authorisation. The authorisation requires a prior inspection of the manufacturing facilities by the AEMPS.

The manufacture and the import of active ingredients used as raw materials for medicinal products do not require authorisation, except for activities of manufacturing sterile active ingredients or those of biological origin, for which authorisation as a pharmaceutical manufacturing laboratory must be obtained (*RD 824/2010*). However, companies that manufacture, import or distribute active ingredients must be registered with the relevant AEMPS registry, and must comply in any case with the applicable good manufacturing practices.

Marketing

Marketing authorisation and placing on the market. To be placed on the Spanish market, medicines must:

- Have obtained a prior marketing authorisation from the:
  - AEMPS, under the national, mutual recognition or decentralised procedures; or
  - European Medicines Agency (EMA), under the centralised procedure.
- Be registered with the AEMPS medicines registry.

In addition, before being placed on the market, prescription medicines must be submitted to the national health authorities, which will decide on their inclusion in the reimbursed medicines system.

RD 1345/2007 regulates the national procedure for the granting of marketing authorisations. The authorisation process, which follows the principles established at EU level, requires the submission of a detailed application that covers all aspects of the medicine, the results of pre-clinical, clinical and pharmaceutical investigations, and relevant expert reports. The application is assessed by the AEMPS, which can request additional information. The AEMPS will consider the assessment of the positive therapeutic effects of the medicinal product in relation to any risk related to the quality, safety and efficacy of the medicinal product for patients' health or public health. The AEMPS then issues a reasoned report which, if unfavourable, is sent to the applicant before a decision is taken.

The placing of a medicine on the market for the first time must be notified in advance to the authorities.

Medicines cannot be advertised or sold before completion of these formalities.

Special situations. Unauthorised medicines can be supplied in special situations under Royal Decree 1015/2009 on the availability of medicines in special situations. In particular, the AEMPS can authorise the prescription and use (and import, where necessary) of:

- Investigational medicines, for patients suffering from chronic, severely debilitating or life-threatening conditions that cannot be satisfactorily treated with authorised medicines (compassionate use).
- Medicines authorised in countries other than Spain, if there is no appropriate alternative medicine authorised in Spain, or in cases of shortages.

These authorisations can be granted on a named-patient basis or under a general protocol applicable to a category of patients.

4. What are the differences between the regulation of new innovative medicines and generic or biosimilar versions of those medicines?

Simplified procedures are in place under the Spanish legislation implementing the Code for Human Medicines Directive (*2001/83/EC*) for:

- Generics of medicines that have been authorised in EU member states or by the EMA for at least eight years (even if not authorised in Spain).
- Active principles that are regarded as having had a "well-established use" in the EU for ten years and are known to be effective and safe.

In these cases, applicants for marketing authorisations do not need to provide the results of pre-clinical and clinical trials.

However, generic medicines cannot be commercialised until ten years after the date the initial authorisation of the reference medicinal product is granted, or 11 years if a new indication is approved during the first eight years.

Under Regulation (EC) 726/2004 on the authorisation and supervision of medicinal products and establishing a European Medicines Agency (EMA Regulation), certain biological products, such as advanced therapy medicinal products (ATMPs), can only be authorised by the EMA under the centralised procedure. The authorisation of biosimilars is therefore carried out through the centralised procedure based on clinical, non-clinical and quality studies. The simplified procedure used for the approval of generic drugs can be followed for a biological product that is similar to a previously authorised biological product. However, the results of pre-clinical tests or clinical trials must be provided where a biosimilar does not meet the the definition of generic medicinal product, owing, in particular, to differences relating to raw materials or differences in manufacturing processes of the biosimilar and the reference biological product.

In 2019, the Permanent Pharmacy Commission of the Inter-territorial Council of the National Health System (*Comisión Permanente de Farmacia del Consejo Interterritorial del Sistema Nacional de Salud*) approved a proposal for an action plan to promote the use of biosimilar and generic medicines. This proposal includes a number of initiatives to foster the use of biosimilars and generics, sometimes allowing for positive discrimination in favour of these medicines (such as prioritising the initiation of dossiers for inclusion of generics and biosimilars in the pharmaceutical reimbursement system, adopting prescription by active ingredient, introducing a clawback mechanism for pharmacy discounts, and so on). The implementation of this action plan would require legislative amendments, which have not been proposed to date.

In addition, generics and biosimilars benefit from the "Bolar exemption", which promotes low-cost generic copies of original medicinal products. The Patents Law 24/2015, of 24 July 2015, states that rights granted by a patent or supplementary protection certificate (SPC) do not apply to studies and trials aimed at obtaining authorisation for medicines (in Spain or abroad), including preparing, obtaining and using the active ingredient for this purpose. Therefore, none of these activities can be considered to infringe a patent (or SPC) provided that they are strictly aimed at obtaining the relevant marketing authorisation.

Otherwise, generics and biosimilars in Spain are generally subject to the same requirements on manufacturing, marketing and advertising as other medicines.

5. What are the differences between the regulation of prescription and over-the-counter medicines?

Prescription medicines

Prescription has traditionally been reserved to doctors, dentists or chiropodists. However, Royal Decree 1718/2010 provides that nurses can, under certain conditions, issue "dispensation orders" for certain prescription medicines. To be entitled to indicate, use and authorise the dispensation of prescription medicines, a nurse must:

- Hold the relevant accreditation from the regional authorities.
- Once accredited, indicate, use and authorise the dispensation of medicines exclusively according to the protocol and clinical guidelines specifically developed and approved for these purposes by the Permanent Pharmacy Committee of the Inter-territorial Council of the National Health System.

(*Royal Decree 954/2015 on the indication, use and authorisation to dispense medicines and medical devices for human use.*)

Before marketing a prescription medicine, a pharmaceutical company must have submitted it to the national health authorities for inclusion in the reimbursed medicines system (*see Question 3*). Only prescription medicines can be reimbursed.

Prescription medicines cannot be sold online or advertised to the public.

Certain medicinal products (for example, those that require particular surveillance, supervision and monitoring by a multidisciplinary healthcare team) are classified as "for hospital use", "for hospital diagnosis" or "for special control by a medical practitioner", and their prescription or use is restricted accordingly.

Non-prescription medicines

Non-prescription or over-the-counter (OTCs) medicines cannot be included in the reimbursed medicines system. However, the government can regulate the mechanism for setting the prices of OTC medicines and medical devices. In the event of an exceptional health situation, to protect public health, the CIPM can set the maximum selling price of OTC medicines and medical devices.

The advertising of OTCs does not require prior administrative authorisation, but the competent health authorities must carry out the necessary checks to ensure that the advertising materials:

- Comply with the applicable laws and regulations.
- Faithfully reflect the scientific and technical conditions set out in the marketing authorisation.

In addition, OTCs can be sold online, subject to certain requirements (*Royal Decree 870/2013 on the online sale of non-prescription medicines for human use to the public*).

6. Are there fewer or different requirements for the approval of medicines that have already been licensed or approved in another jurisdiction?

Authorisations granted by the EMA under the centralised procedure are immediately effective in Spain.

Medicines authorised in other EU countries can be recognised in Spain under the mutual recognition procedure set out in the Code for Human Medicines Directive, and further regulated in RD 1345/2007.

There is also a simplified procedure for active principles with a well-established use. The applicant for the marketing authorisation can replace the results of clinical trials and pre-clinical studies with appropriate scientific documentation if it proves that the medicinal product's active ingredients:

- Have been used extensively for at least ten years in the EU.
- Are acknowledged as being effective and safe.

7. Is it possible to sell medicines to or buy medicines from other jurisdictions?

Importing medicines from non-EU jurisdictions requires a specific authorisation from the AEMPS. No authorisation is required for products originating from other EU countries; a distribution licence is sufficient.

In any case, to be placed on the Spanish market, the product must have obtained a valid marketing authorisation in Spain and fulfilled the other formalities referred to in *Question 3*.

These requirements do not apply to products that are to be exported. However, in certain cases, the AEMPS must be informed in advance of the intention to export, and can object to it if there is a risk to public health in Spain (for example, due to product shortages).

In addition, medicinal products can only be purchased by, or sold to, entities in possession of a distribution licence (or by the manufacturers themselves).

8. How is medicine promotion and advertising activity regulated, and what are the general requirements to advertise medicines?

The main regulations governing the promotion of medicines in Spain are set out in the Guarantees Law and Royal Decree 1416/1994 governing the advertising of medicines for human use (Advertising RD). The Ministry of Health and the autonomous regions of Madrid and Catalonia (where most Spanish pharmaceutical companies are based) have approved guidelines on certain provisions of the Advertising RD in relation to promotional activities. The Code of Good Practice for the Pharmaceutical Industry (Farmaindustria Code) further interprets and elaborates on these rules.

The main requirements and restrictions under the current legal framework are as follows:

- Promotion must be compatible with the approved summary of product characteristics (SmPC). In particular, a medicine cannot be promoted before it has obtained a marketing authorisation, and the promotion must strictly refer to the indications and properties contained in the SmPC. The autonomous regions' guidelines and the Farmaindustria Code regulate, for example:
    - the use of certain terminology or phrases;
    - how to reproduce bibliographic references in promotional materials; and
    - how to manage the provision of information that refers to indications or characteristics not contained in the SmPC approved in Spain (off-label information) in international scientific meetings.

- The purpose of visits by medical sales representatives must be to provide objective and technical knowledge. Medical sales representatives must be given adequate training and have sufficient scientific knowledge to

be able to provide information that is as precise and as complete as possible about the medicines they are promoting.

- Promotional materials (including both published advertising and brochures given to healthcare professionals during visits by medical sales representatives) must be scientific, and must be notified to the regional authorities before their distribution, attaching an express declaration that they have been reviewed by the appropriate department of the pharmaceutical company and that they are compatible with the information contained in the SmPC.
- Advertising to the public is not subject to prior administrative authorisation. Only specific categories of medicines can be advertised to the public, in particular those that:
    - are not included in the public reimbursement system;
    - are not subject to medical prescription (*see Question 5*); and
    - do not contain narcotic or psychotropic substances.

    Therefore, pharmaceutical companies must ensure that promotional materials for medicines that can only be advertised to healthcare professionals are not made available to the public in general.

    Advertising to the public cannot:

    - refer to recommendations from scientists, healthcare professionals or other persons that could encourage the consumption of medicines;
    - suggest certainty as to the medicine's effects, lack of side effects, or enhanced efficacy as opposed to other treatments; or
    - suggest that the use of the medicine may improve health or boost sporting performance.
- Advertising materials must not be addressed exclusively or primarily to children.
- Free samples cannot be given to the public.

Advertising over the internet, including social media channels, is subject to the above requirements. The Farmaindustria Code provides that pharmaceutical companies are responsible for content included in digital channels of communication that they control or finance. They must take appropriate control and supervision measures for publications made on those channels by their employees and healthcare professionals with whom they collaborate. Examples of adequate control and supervision measures include rules of conduct, training employees, and including clauses regarding conduct on social media in agreements with professionals with whom they collaborate.

9. Are there additional or alternative regulations for special types of medicines or medicines intended for particular types of patients or diseases?

Orphan medicines

The government can take additional measures relating to the economic and tax treatment of:

- Orphan medicinal products, as defined by the Orphan Medicines Regulation (*141/2000*).
- Medicinal products with no commercial interest (that is, for which there is no or insufficient supply on the national market and that are necessary for the treatment of certain diseases or pathologies.

(*Guarantees Law*.)

In June 2020, the DGCCS adopted a resolution that exempts orphan medicinal products from inclusion in the reference price system under certain conditions.

Advanced therapy medicinal products

Advanced therapy medicinal products (ATMPs) (including somatic cell therapy medicines, tissue-engineered products, and gene therapy medicines) are governed by the:

- Guarantees Law.
- Advanced Therapy Medicinal Products Regulation (*1394/2007*).

ATMPs are generally authorised by the EMA under the centralised procedure, provided that they are manufactured industrially. The manufacturing of non-industrial ATMPs must be authorised by the AEMPS (*Royal Decree 477/2014, of 13 June 201, regulating the authorisation of advanced therapy medicinal products of non-industrial manufacture*). Non-industrial ATMPs are those that are both:

- Prepared on a non-routine basis according to specific quality standards.
- Used in Spain in a hospital under the exclusive professional responsibility of a medical practitioner, to comply with an individual medical prescription for a custom-made product.

10. What controls apply to medicines or components of medicines that derive from humans or animals or incorporate modified genetic material?

Blood and plasma derivatives and other substances of human origin (fluids, glands, excretions, secretions, tissues and any other substances) and their derivatives, when used for therapeutic purposes, are considered medicinal products and subject to the regime generally applicable to medicinal product (*Guarantees Law*). These products must:

- Be obtained from authorised centres meeting certain control, surveillance and traceability requirements.
- Come from donors identified in the relevant donor register.

The importation and authorisation of blood and plasma derivatives as medicinal products can be denied or revoked if they are not derived from altruistic donations made in blood banks or plasmapheresis centres located in EU member states that offer the appropriate guarantees.

The importation and marketing authorisation of blood and plasma derivatives as medicinal products can also be subject to providing evidence that their price does not include an unjustified profit on blood that was donated altruistically.

Biological medicines

11. What is the definition of biological medicines in your jurisdiction and what are the main laws that specifically apply to them (if any)?

Biological products include:

- Immunological medicinal products.
- Medicinal products derived from human blood and human plasma.
- ATMPs.

Under the EMA Regulation, certain biological products, such as ATMPS, can only be authorised by the EMA under the centralised procedure (*see Question 9, Advanced therapy medicinal products*).

When necessary in the interest of public health, the AEMPS can subject:

- Manufacturing each batch of finished biological products to prior authorisation, and condition their marketing to conformity with requirements established in the marketing authorisation and good manufacturing practices.
- Original materials, intermediate products and bulk products to prior authorisation, and condition their use in manufacturing to conformity with requirements established in the marketing authorisation and good manufacturing practices.

These controls are deemed to have been passed when both:

- They were carried out in a country of origin with identical requirements to those of the Guarantees Law.

- The original condition of the product has been maintained.

12. Are there any additional or alternative regulations that apply specifically to biological medicines?

Generally, except for specific rules concerning their marketing authorisation (*see Question 11* and *Question 4* for biosimilars), biological medicines are generally subject to the same manufacturing, marketing and advertising requirements as other medicines. However, biological medicines cannot be substituted by a dispensing pharmacist.

Medical devices

13. What is the definition of medical device (or equivalent) in your jurisdiction? What is the significance of any legal classifications?

Current Spanish regulations on medical devices (Royal Decree 1591/2009 on medical devices (RD on Medical Devices)) will be repealed and replaced by the Medical Devices Regulation (*(EU) 2017/745*) from 26 May 2021.

Under the RD on Medical Devices, a medical device is any instrument, device, equipment, software program, material or other article, whether used alone or in combination (including software programs intended by the manufacturer for specific diagnostic and/or therapeutic purposes and which contribute to its proper functioning), and which:

- Is intended by the manufacturer to be used in humans for the purpose of:
    - diagnosis, prevention, control, treatment or alleviation of a disease;
    - diagnosis, control, treatment, alleviation or compensation of an injury or deficiency;
    - investigation, substitution or modification of the anatomy or a physiological process; or
    - conception control.
- Does not achieve its principal intended function in or on the human body by pharmacological, immunological or metabolic means, but which can be assisted in its function by such means.

There is no formal mechanism in place to obtain a decision from the AEMPS as to whether a product is a medicine or a medical device. However, a specific query can be submitted to the AEMPS at any time.

Medical devices are classified as Class I, IIa, IIb or III, depending on a variety of factors. The procedure for the evaluation of conformity of a device and, therefore, the procedure to place it on the market, depend on its classification.

14. What authorities are responsible for regulating the manufacture, marketing and advertising of medical devices?

The AEMPS is the notified body responsible for assessing conformity of medical devices in Spain, in accordance with the general requirements of national and EU legislation. It is also responsible for monitoring the initial placement of medical devices on the Spanish market.

The regional health authorities are responsible for supervising and monitoring distribution, sale and advertising activities.

15. What notifications, registrations, approvals and licences are required to manufacture and market medicinal devices?

Manufacturing

The manufacture, import (from non-EU countries), grouping and sterilisation of medical devices is subject to administrative authorisation from the AEMPS (*RD on Medical Devices*).

Manufacturing include the following activities (when carried out with a view to place a device on the market under the manufacturer's name):

- Assembling.
- Packaging.
- Processing.
- Fully refurbishing and/or labelling one or more ready-made products and/or assigning them to their intended purpose as a device.

In line with EU regulations, only CE-marked medical devices can be commercialised or put into service in Spain. CE marking can only be placed on products for which there is evidence that they comply with certain essential requirements and which follow the applicable evaluation procedures, which differ depending on the nature of the product. For these purposes, products are classified into four categories:

- Class I.
- Class IIa.
- Class IIb.
- Class III.

The evaluation procedures may involve certification by a "notified body". In Spain, the notified body is the AEMPS.

The following devices are exempted from CE marking requirements:

- Custom-made medical devices.
- Medical devices used in clinical investigation.

In any case, the manufacturer must follow specific evaluation procedures and issue a declaration of conformity.

The AEMPS can authorise medical devices that do not have the CE mark for public health reasons, in situations where there are no other alternatives for the treatment of patients. This is subject to a procedure similar to that of medicines (*see Question 3, Manufacturing*).

Marketing

Any entity that places Class IIa, class IIb or class III devices on the market or puts them into service in Spain for the first time must report this activity to the AEMPS. Any subsequent changes to the information that has been reported to the AEMPS (or the relevant regional authorities) must also be reported.

Any entity established in Spain that is responsible for the initial commercialisation of Class I devices or custom-made devices in the EU must be registered with the AEMPS.

The regional health authorities monitor the distribution of medical devices and can carry out inspections to this end. To assist the authorities in these tasks, distributors of medical devices must file a notification with the relevant regional health authorities before commencing their activities. This notification must include:

- Details of their distribution and retail premises (located in the region).
- The type of products that are sold or distributed.
- The identity of the qualified professional in charge of the premises.

16. Are there fewer or different requirements for medical devices that have already been licensed or approved in another jurisdiction?

Devices that already have CE marks under the rules applicable in other EU countries benefit from a presumption of conformity in Spain.

However, the Spanish health authorities can take measures to withdraw such devices from the market or restrict their commercialisation if they consider that the device, used for its intended purpose, may compromise the health or safety of patients.

17. Is it possible to sell devices to or buy devices from other jurisdictions?

Medical devices imported from other EU countries can freely circulate in Spain. However, they can only be placed on the Spanish market if they meet the requirements described in *Question 15*.

To import devices from non-EU countries, a specific authorisation from the AEMPS is required. The products to be imported must bear the CE mark and have passed the relevant conformity assessment procedures.

Devices can also be manufactured exclusively for export to non-EU countries, in which case they do not need to fulfil the requirements of EU and Spanish law. However, they must be clearly identified as such and differentiated from those to be placed on the EU market.

18. What are the general requirements to advertise medical devices?

As a general rule, written, audiovisual or any other type of promotional materials regarding medical devices must be primarily scientific in terms of content and be distributed to healthcare professionals. However, advertising to the public is permitted under certain conditions. Claims that are to be used in mass media, including the internet, are subject to prior administrative authorisation.

Medical devices reimbursed by the National Health System cannot be advertised to the public. Premiums, gifts or discounts linked to the promotion or sale of these products cannot be offered. Additionally, medical devices intended to be used or applied exclusively by healthcare professionals cannot be advertised to the public.

There are additional restrictions on specific categories of devices. For example, self-diagnosis devices (except for pregnancy, HIV diagnosis and fertility tests) and genetic diagnosis devices cannot be advertised to the public.

19. What product marking is required for authorised medical devices?

Only CE-marked medical devices can be commercialised or put into service in Spain (*see Question 15*).

Combination products

20. Does your jurisdiction recognise combination products? What are the main laws that specifically apply to them (if any)?

Spanish regulations do not specifically recognise the category of combination products (that is, products that have medical device aspects as well as medicinal product aspects). The Spanish authorities generally refer to the guidance issued at EU level, in particular the Guidance document of the European Commission on Borderline products, drug-delivery products and medical devices incorporating, as an integral part, an ancillary medicinal substance or an ancillary human blood derivative (*MEDDEV 2. 1/3 rev 3*).

21. Are there any additional or alternative regulations that apply specifically to combination products?

There are no alternative regulations that apply specifically to combination products. However, the entry into force of the Medical Devices Regulation (in particular Article 117) will introduce specific rules to ensure appropriate interaction in terms of consultations during pre-market assessment, and on the exchange of information in the context of vigilance activities involving combination products.

Natural health products

22. Is there a category for natural health products (or equivalent) (including, for example, traditional medicines, homeopathic medicines, supplements, vitamins and minerals)?

There is no general category of "natural health products" in Spain. Plant-based or herbal medicines and homeopathic medicines are special categories of medicines, while supplements, vitamins and minerals are different regulated products.

The Guarantees Law defines herbal medicines as plants and mixtures of plants, as well as preparations obtained from plants in the form of extracts, lyophilisations, distillates, tinctures, concentrations or any other pharmaceutical preparation presented with therapeutic, diagnostic or preventive properties. Homeopathic medicinal products for human or veterinary use are those obtained from substances called homeopathic strains in accordance with a homeopathic manufacturing procedure described in the European Pharmacopoeia, Royal Spanish Pharmacopoeia, or in a pharmacopoeia used officially in an EU member state.

The basic rules on supplements, vitamins and minerals are set out in Royal Decree 1487/2009 on food supplements (Food Supplements RD), which implements the Food Supplements Directive (*2002/46/EC*). Food supplements are defined as foodstuffs the purpose of which is to supplement a normal diet and which are concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination, marketed in dose form such as:

- Capsules, pastilles, tablets, pills and other similar forms.
- Sachets of powder, ampoules of liquids, drop dispensing bottles or other similar forms of liquids and powders designed to be taken in measured small unit quantities.

To avoid a product being classified as a medicinal product, special attention must be paid to both claims made when marketing the product and to the composition of the product itself.

Under Spanish and EU regulations and case law of the Court of Justice of the European Union (CJEU), a substance or combination of substances can be classified as a medicinal product on the grounds of its presentation or function. A product will not come within the definition of medicinal product by presentation if it is not marketed as being fit to prevent, treat or cure a disease, or include these types of statements in its packaging or advertising. However, depending on the product's composition, it may still come within the definition of medicinal product by function. The assessment must be based on the product's intended use and the actual effects of its specific content on the human body.

According to the case law of the CEU, to determine whether a product falls under the definition of medicinal product by function, the national authorities must decide on a case-by-case basis taking into account all the characteristics of the product, in particular:

- Its composition.
- Its pharmacological, immunological and/or metabolic properties, and the extent to which these can be established in the present state of scientific knowledge.
- The manner in which it is used.
- The extent of its distribution.
- Its familiarity to consumers.
- The risks that its use may entail.

Therefore, the key test is to determine whether the particular contents of each product lead to the conclusion that, used in a normal way, they affect the metabolism or modify bodily functions to an appreciable extent. This must be established by reference to scientific knowledge at any given time and on a product-by-product basis.

23. What authorities are responsible for regulating the manufacture, marketing and advertising of natural health products?

The Spanish Ministry of Health and the AEMPS are responsible for regulating the manufacture, marketing and advertising of homeopathic and herbal medicinal products.

The Spanish Food Safety and Nutrition Agency (*Agencia Española de Seguridad Alimentaria y Nutrición*) (AESAN) is the central government body in charge of promoting food safety generally. The regional health authorities are responsible for monitoring compliance with food safety regulations.

24. What notifications, registrations, approvals and licences are required to manufacture and market natural health products?

Traditional herbal medicines

Under the Guarantees Law, plants traditionally considered as medicinal plants can be freely sold to the public provided that they are offered with no reference to therapeutic, diagnostic or preventive properties; only those authorised as medicines can include such claims. The Ministry of Health can establish a list of plants whose sale to the public will be restricted or prohibited because of their toxicity.

Herbal medicines are subject to essentially the same regulations as other medicines, subject to some particularities set out in RD 1345/2007, including the requirement to be registered in the applicable register at the AEMPS.

Homeopathic medicines

Under RD 1345/2007, homeopathic medicines are classified as:

- **Homeopathic medicines with an approved therapeutic indication.** These are subject to the standard authorisation and registration procedure applicable to medicinal products (*see Question 3*).
- **Homeopathic medicines with no approved therapeutic indications.** These can follow a simplified authorisation and registration process, provided that:
    - they are administered orally or externally;

- they do not refer to any specific indication, in their labelling or any other information material; and
- their degree of dilution is sufficient to guarantee that the medicine is innocuous, and in any case does not exceed a concentration of 1/10,000.

Under the simplified procedure, the scientific evidence can be largely based on bibliographic references. If justified, pre-clinical studies can be omitted.

There are currently about 2,000 homeopathic products that do not hold authorisation as medicines (but were being traditionally commercialised as such) that are still being placed on the market under a transitional regime, pending assessment by the regulatory authority. If this assessment is unfavourable (or the manufacturer does not provide the relevant dossier), the commercialisation of those products will need to be discontinued.

Food supplements

The basic regulations are set out in the Food Supplements RD, which establishes the following rules:

- **Vitamins and minerals.** Only vitamins and minerals listed in the annexes to the Food Supplements RD can be used as ingredients in food supplements. They are also subject to the purity criteria established in EU legislation applicable to foodstuffs generally, or, in the absence of such legislation, to those established in Spanish legislation or by international bodies, whichever are stricter.
- **Other ingredients.** There is no closed list of other ingredients that can (or cannot) be used as ingredients in food supplements. Reports of the Scientific Committee on Food (now the European Food Safety Authority) and other international bodies of recognised scientific expertise are taken into account.

Food supplements must be registered with the General Health Registry for Food Businesses and Foodstuffs.

Manufacturers and distributors of food supplements must register with the General Health Registry for Food Businesses and Foodstuffs. An operator involved in these activities that does not have premises or an establishment in Spain must be registered if its corporate domicile is in Spain.

Registration is achieved by notification and must be done before the start of activities.

In addition, before commercialisation in Spain, the health authorities must be notified that a product is going to be placed on the market by submitting a sample of the product's label. Any amendment to the label and the discontinuation of the marketing of a product must also be notified. This notification must be made by the manufacturer or the person responsible for commercialising the product, to the health authorities of the region where it is domiciled. If this person does not have a domicile in Spain, the notification must be made to the AESAN.

25. Are there fewer or different requirements for natural health products that have already been licensed or approved in another jurisdiction?

Traditional herbal medicines and homeopathic medicines

Traditional herbal medicines and homeopathic medicines are subject to the same rules as apply to medicines generally (*see Question 6*).

Food supplements

A food supplement legally marketed in an EU member state can be marketed in Spain under the mutual recognition principle. To that end, the following must be provided to the AESAN (if the company responsible for commercialisation does not have its registered office in Spain) or to the competent administrative authority of the autonomous region where the company responsible for commercialisation have its registered office:

- A copy of the product label used in the EU country where it was first marketed.
- A copy of the notification sent to that country's authority, together with its subsequent acceptance.

These documents must be provided in Spanish (or translated into Spanish).

26. Is it possible to sell natural health products to or buy natural health products from other jurisdictions and/or electronically?

Traditional herbal medicines and homeopathic medicines

Traditional herbal medicines and homeopathic medicines are subject to the same rules as apply to medicines generally (*see Question 7*).

Food supplements

Food supplements from non-EU countries can be imported into Spain if they comply with the requirements described in *Question 24, Food supplements*.

To be exported, food supplements must comply with Spanish regulations unless:

- Otherwise required by the authorities or legislation of the importing country.
- Compliance is expressly waived by the authorities of the importing country, after having been informed of the reasons for which the food supplement could not be placed on the Spanish market, and provided that it is not harmful to human health.
- An agreement between Spain and the importing country provides for different export requirements.

Food supplements can be sold online like any other consumer product.

27. What are the general requirements to advertise natural health products?

Traditional herbal medicines and homeopathic medicines

Traditional herbal medicines and homeopathic medicines are subject to the same rules as apply to medicines generally (*see Question 8*).

Food supplements

The Nutrition and Health Claims Regulation (*1924/2006*) restricts the use of nutrition and health claims on the labelling, presentation and advertising of foodstuffs. A nutrition claim is any claim that states, suggests or implies that a food has particular beneficial nutritional properties due to the presence, absence, increased or reduced levels of energy or of a particular nutrient or other substance. A health claim is defined as any claim that states, suggests or implies that a relationship exists between a food category, a food or one of its constituents and health. Nutrition labelling is generally required whenever a nutrition or health claim is made (*Nutrition and Health Claims Regulation*). Only nutrition claims listed in the annex to the Nutrition and Health Claims Regulation are admissible. Using a health claim is subject to authorisation under any of the procedures set out in the Regulation.

At a domestic level, the Food Supplements RD provides that the labelling, presentation and advertising of food supplements cannot:

- Include any statement that states or suggests that a balanced, varied diet does not provide adequate quantities of nutrients in general.
- Attribute to food supplements the property of preventing, treating or curing a disease or refer to such properties at all.

In addition, it is generally prohibited to make claims:

- Suggesting specific slimming properties.
- Using endorsements or any kind of authorisations, homologations or tests by Spanish or foreign health authorities.
- Suggesting or affirming an increase in physical, mental, sport or sexual performance.

(*Royal Decree 1907/1996 on advertising and commercial promotion of products, activities or services with alleged health effects*.)

There are also rules relating to the use of recommendations or endorsements in advertising. In particular, the Law on Food Safety and Nutrition prohibits the use of endorsements from associations, corporations, foundations and institutions related to health and nutrition unless they:

- Are non-profit organisations.
- Undertake in writing to devote the financial resources obtained from the endorsement to activities aimed at improving health through research, development and specialised publications on health and nutrition.

Data

28. What data and information laws must be complied with by life sciences businesses that collect, use or otherwise deal in patient data (including through health apps)?

The collection and use of patient data must comply with data regulations, in particular:

- The General Data Protection Regulation (*(EU) 2016/679*) (GDPR).
- Organic Law 3/2018, of 5 December 2018, on the Protection of Personal Data and the Guarantee of Digital Rights.
- Guidance documents issued by the Spanish Data Protection Agency (*Agencia Española de Protección de Datos*) (AEPD).
- Any national or regional special regulations on patient data, including:
    - Law 41/2002, of 14 November 2002;
    - regulations on patient autonomy and rights and obligations regarding clinical information and documentation; and
    - regulations applicable to research and clinical trials (*see Question 29*).

Research

29. What restrictions and regulatory requirements apply to the testing of life sciences products on human and animal subjects?

The current national legislation in force, Royal Decree 1090/2015, of 4 December 2015, regulating clinical trials with medicines, the Ethics Committees for Research with medicines and the Spanish Registry of Clinical Studies, aims to implement the Clinical Trials Regulation (*536/2014*).

Clinical trials of medicinal products require prior authorisation from the AEMPS, following a scientific and ethical evaluation carried out by the AEMPS and the ethics committees.

Regulatory requirements that apply to testing on humans are set out in:

- Law 14/2007, of 3 July 2007, on Biomedical Research.
- Royal Decree-Law 9/2014, of 4 July 2014, establishing quality and safety standards for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells and approving co-ordination and operational standards for their use in humans.

These regulations establish a number of principles and requirements applicable to clinical trials, in particular:

- Requirement to obtain informed consent from participants.
- Protection of personal data.
- Non-profit donation, non-discrimination and traceability of tissues.

Royal Decree 53/2013, of 1 February 2013, contains the basic rules applicable to the protection of animals used in experimentation and for other scientific purposes, including teaching.

Reform

30. Are there any plans to reform the rules on the development, manufacture, marketing and advertising of life sciences products and services?

While several reform proposals have been recently discussed (including amendments to the Advertising RD and a new regulation on the financing of medical devices for outpatients), no reforms are expected to be passed in the near future. However, rules affecting certain areas (such as vaccination and compassionate use) may be amended as a matter of urgency in the coming weeks and months to address the 2019 novel coronavirus disease (COVID-19) pandemic.

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