Commercialisation of healthcare in Portugal: overview

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

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

Medicines

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

Under the Portuguese Human Medicine Act approved by Decree-Law 176/2006 of 30 August 2006 (as amended) (HMA), a medicine is defined as any substance or combination of substances that:

- Is presented as having properties for treating or preventing a disease or its symptoms in human beings.
- Can be used in or administered to human beings with a view to making a medical diagnosis or restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action.

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

INFARMED (*Autoridade Nacional do Medicamento e Produtos de Saúde IP*) is the public authority responsible for regulating the manufacture, marketing and advertising of medicines in Portugal.

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

Both the manufacture and marketing of drugs are subject to authorisation processes that closely follow EU law. Advertising is highly regulated and is subject to various restrictions.

Under exceptional public health grounds, medicines without a marketing authorisation (including medicines for compassionate use in clinical trials) can be used to treat patients in Portugal under a specific, temporary and transitory authorisation granted by INFARMED. INFARMED will grant an authorisation if the medicinal products are either:

- Considered essential for the prevention, diagnosis or treatment of certain pathologies, if there are no alternative medicines with marketing authorisation.
- Necessary to prevent or limit the spread, current or potential, of pathogens, toxins, chemical agents, or nuclear radiation likely to cause harmful effects.

Manufacturing

The national manufacturing authorisation process is set out in Chapter III, Section I of the HMA.

Applications must be submitted to INFARMED by natural or legal persons. An application must contain the following information:

- The specification and pharmaceutical form of the medicine.
- Details of the place of manufacture.
- Evidence of compliance with the applicable technical requirements for:
    - technical director, and their identity and qualifications;
    - premises;
    - equipment; and
    - monitoring.

There are no specific restrictions on foreign applicants. However, the manufacturing facilities must be in Portugal and will be inspected by INFARMED. INFARMED must decide on the application within 90 days of the date the application is submitted. The manufacturing authorisation remains valid until INFARMED cancels it or the holder withdraws it.

Marketing

The HMA sets out the rules for marketing medicinal products (*Chapter IX, HMA*).

A marketing authorisation can be obtained through the:

- National procedure.
- EU member states (including Portugal) procedures, which includes the decentralised procedure and the mutual recognition procedure.
- Centralised procedure of the European Medicines Agency (EMA) (*see Question 9*).

The marketing authorisation application under the national procedure must be submitted to INFARMED, along with the required documents and must include the following:

- Name or corporate designation, permanent address and tax number of the applicant and, where applicable, of the manufacturer.
- Proposed name of the medicinal product.
- Pharmaceutical form, detailed qualitative and quantitative information on all components of the medicine (that is, active substances and excipients) and on its common designation or lack of chemical designation.
- Therapeutic indications and contraindications, and adverse reactions.
- A description of the medicinal product's manufacturing method.
- Posology, method and route of administration, and expected shelf life.

- If applicable, reasons for any precautionary and safety measures to be taken for the storage of the medicinal product, its administration to patients and for the disposal of waste products, together with an indication of any potential risks presented by the medicinal product for the environment.
- A description of the control methods used by the manufacturer and a declaration issued by the manufacturer attesting compliance with good manufacturing practice.
- The results of physico-chemical, biological or microbiological tests, toxicological and pharmacological tests, and clinical trials.
- A summary of the pharmacovigilance system implemented by the applicant and management risk plan.
- A summary of product characteristics.
- One or more specimens or mock-ups of the product's outer packaging, immediate packaging and package leaflet.
- Key stages and timing.
- Copy of the marketing authorisation issued by other EU member states or of its refusal and respective grounds, when applicable.
- Copy of the marketing authorisation issued by non-EU states or of its refusal and respective grounds, when applicable.

INFARMED must issue a final decision on a complete marketing authorisation application within 210 days, subject to potential suspensions due to INFARMED's requests for additional information or to deficiencies in the submitted file.

A marketing authorisation is initially granted and valid for five years and can be renewed by INFARMED on request of the market authorisation holder. After the first renewal, the marketing authorisation becomes indefinitely valid, unless INFARMED decides otherwise due to pharmacovigilance reasons.

After the medicine's marketing authorisation is issued, the market authorisation holder must notify INFARMED of the start date of commercialisation in the national market.

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

The same requirements apply for the manufacture, marketing and sale of innovative medicines and generic or biosimilar versions of those medicines. However, the submission of evidence of certain clinical trials may be waived in certain cases to facilitate market entry for generic and biosimilar versions of innovative medicines.

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

The main differences between the regulation of prescription and over-the counter (OTC) medicines relate to advertising to consumers, which is only allowed for OTC medicines that are not reimbursed by the state. Prescription medicines can only be advertised to health care professionals (*Article 152(2), HMA*). See also *Question 8*.

OTC medicines can be sold outside pharmacies, in para-pharmacies (*parafarmácias*) that cannot sell medicines subject to medical prescription.

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

There are simplified licensing proceedings for medicines already approved in other EU jurisdictions under the mutual recognition procedure.

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

It is possible to sell drugs to, or buy medicines from, other jurisdictions. However, those intending to buy drugs from other jurisdictions and sell them in Portugal must have a distribution authorisation or a parallel importation authorisation.

The HMA sets out the rules for the wholesale distribution of medicinal products (*section IV, Chapter IV, HMA*). Wholesale distribution of medicinal products is subject to prior authorisation from INFARMED.

To obtain a distribution authorisation, the applicant must:

- Have suitable and adequate premises, installations and equipment to ensure proper conservation and distribution of the medicinal products.
- Have a designated qualified person (technical director) to secure the permanent and effective quality of the distribution activity.
- Undertake to fulfil the following obligations:
    - make the premises, installations and equipment accessible at all times to INFARMED for inspection;

- obtain medicinal product supplies only from persons with a distribution authorisation or manufacturing authorisation, or from intermediaries that comply with the applicable law;
- supply medicinal products only to persons who are themselves in possession of a distribution authorisation or who are authorised or entitled to supply medicinal products to the public;
- have an emergency plan that ensures effective implementation of any recall from the market ordered by INFARMED or carried out in co-operation with the manufacturer or marketing authorisation holder for the medicinal product concerned;
- keep records of purchase or sales invoices on computer systems or in any other form, giving for any transaction in medicinal products received or dispatched at least the date, name of the medicinal product, quantity received or supplied, name and address of the supplier or consignee, as appropriate;
- keep e-records of the information available for five years for INFARMED; and
- comply with the principles and guidelines of Good Distribution Practice for medicinal products as set out in INFARMED Decision 47/CD/2015 19 March 2015, which adopted the European Commission Guidelines of 5 November 2013 on Good Distribution Practice of medicinal products for human use (*2013/C 343/01*).

The wholesale supply of medicinal products can only be made to either:

- Persons that have a distribution authorisation (that is, other distributors).
- Persons that are authorised or entitled to supply medicinal products to the public (for example, pharmacies, OTC retailers, and health care centres authorised to acquire medicines directly from distribution wholesalers).

Parallel imports are subject to a prior authorisation procedure (*section II, Chapter IV, HMA*). The authorisation is granted by INFARMED within 45 days of the application, if it does not require further clarification or additional documents.

Parallel imports of medicinal products are allowed within the EU, provided the following conditions are met:

- The medicine in the EU member state of origin has a valid marketing authorisation.
- The medicine is commercialised in compliance with the HMA.
- The medicine has the same:
  - quantitative and qualitative composition in terms of active substances;
  - pharmaceutical form; and
  - therapeutic indications (different excipients can be used or different quantities of the same excipients if they have no therapeutic impact).
- The authorisation does not pose a risk to public health.

The conditions set out in the second and fourth bullet points are presumed to be met if:

- The medicine to be imported is manufactured in another EU member state by a company contractually linked to the marketing authorisation holder in Portugal or by a company that is part of the same corporate group.
- The company that holds the marketing authorisation of the medicine in Portugal manufactures or markets in Portugal the medicine under an agreement with a company contractually linked to the marketing authorisation holder in the member state of origin.

To import medicinal products from non-EU states, an importation authorisation must be obtained from INFARMED (*Article 74, HMA*). Each batch of imported medicines, although manufactured but not controlled or released in a member state, is subject to a complete quality analysis and to a quantitative analysis of the active substance and to other quality analysis in accordance with the respective marketing authorisation procedure. The importer must ensure that imported medicines from non-EU states were manufactured by licensed manufacturers in accordance with the applicable rules of the respective country, which must be equivalent to the EU good manufacture practices.

The manufacture of medicinal products for exportation is subject to a manufacturing authorisation issued by INFARMED (*Article 75, HMA*). Medicinal products exclusively destined to exportation are not subject to HMA rules on conditioning, labelling and presentation. Medicinal products that have been withdrawn from the market for protection of public health cannot be exported. INFARMED can request a scientific opinion on medicinal products destined exclusively to exportation. Additionally, at the request of the manufacturer, exporter or a competent authority of a third state outside the EU, INFARMED can issue a document that certifies the holding of a manufacturing authorisation by a manufacturer of medicinal products in Portugal.

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

Chapter IX of the HMA sets out the rules on the advertising of medicinal products.

Medicines that do not hold a valid marketing authorisation cannot be advertised (*see Question 8*).

The following medicines cannot be advertised to the general public. They can only be advertised to health care professionals in technical publications exclusively accessible to such professionals:

- Medicines subject to a medical prescription.
- Medicines containing substances defined as narcotic and psychotropic under international conventions.
- Medicines reimbursed by the state, including OTC medicines.

Advertisements to health care professionals must include:

- The name of the medicine.
- Essential information compatible with the summary of product characteristics.
- The classification of the medicinal product for dispense purposes (that is, the advertisement must mention that the medicine is subject to medical prescription).
- The state reimbursement regime.

OTC medicines can be advertised to the general public, including through the internet, and must:

- Clearly identify the advertisement as advertising.
- Clearly identify the product as a medicinal product.

Advertisements for OTC medicines cannot contain any material that:

- Gives the impression that a medical consultation or surgical operation is unnecessary, in particular by offering a diagnosis or by suggesting treatment by mail.
- Suggests that the effects of taking the medicine are guaranteed, are unaccompanied by adverse reactions or are better than, or equivalent to, those of another treatment or medicinal product.
- Suggests that the subject's health can be enhanced by taking the medicine.
- Suggests that the subject's health may be affected by not taking the medicine.
- Is directed exclusively or principally at children.
- Refers to a recommendation by scientists, health professionals or persons who, because of their celebrity, may encourage the consumption of medicinal products.
- Suggests that the medicinal product is a foodstuff, cosmetic or other consumer product.
- Suggests that the safety or efficacy of the medicinal product is due to the fact that it is natural.
- May by a description or detailed representation of a case history, lead to erroneous self-diagnosis.
- Refers in improper, alarming or misleading terms to claims of recovery.
- Uses in improper, alarming or misleading terms pictorial representations of changes in the human body caused by disease or injury, or of the action of a medicinal product on the human body or parts of it.

The advertising of any of the above categories of medicinal products must:

- Comply with the particulars listed in the summary of product characteristics.
- Encourage the rational use of the medicinal product by presenting it objectively, without exaggerating its properties.
- Not be misleading.

The Portuguese Association of the Pharmaceutical Industry (*Associação Portuguesa da Indústria Farmacêutica*) (Apifarma) adopted a Code of Conduct for Promotional Practices by the Pharmaceutical Industry with Health care Professionals. The code reflects the rules and principles of the HMA, as well as the European Federation of Pharmaceutical Industries and Associations' Code on the Promotion of Prescription-Only Medicines to, and Interactions with, Healthcare Professionals.

INFARMED is responsible for the supervision and enforcement of the provisions and rulings on the advertising of medicines.

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

The centralised procedure of the EMA is mandatory for orphan medicinal products and medicinal products for human use containing a new active substance for which the therapeutic indication is the treatment of any of the following diseases:

- Acquired immune deficiency syndrome.
- Cancer.
- Neurodegenerative disorder.
- Diabetes.
- Auto-immune diseases and other immune dysfunctions.
- Viral diseases.

(*Regulation (EC) 726/2004 on procedures for the authorisation and supervision of medicinal products for human use*.)

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

In addition to the requirements that are generally applicable to prescription medicines, marketing authorisation application for medicines or components of medicines that derive from humans or animals, or incorporate modified genetic material, are subject to additional requirements. For example, an application must provide a description of the traceability system that the marketing authorisation holder intends to establish and maintain to ensure that the individual product and its starting and raw materials, including all substances coming into contact with the cells

or tissues it may contain, can be traced through the sourcing, manufacturing, packaging, storage, transport and delivery to the hospital, institution or private practice where the product is to be used (*Part IV, HMA*).

Additionally, applicants for marketing authorisation for gene therapy medicinal products must comply with the following specific requirements:

- The application must provide information on all the starting materials used for the manufacture of the active substance, including the products necessary for the genetic modification of human or animal cells and, as applicable, subsequent culture and preservation of the genetically modified cells, taking into consideration the possible absence of purification steps.
- For products containing a microorganism or a virus, the application must provide:
    - data on the genetic modification, sequence analysis, attenuation of virulence, tropism for specific tissues and cell types, cell cycle dependence of the microorganism or virus, and pathogenicity and characteristics of the parental strain; and
    - a description of process-related impurities and product-related impurities, in particular of replication competent virus contaminants if the vector is designed to be replication incompetent.
- For plasmids, quantification of the different plasmid forms must be undertaken throughout the shelf life of the product.
- For genetically modified cells, the characteristics of the cells before and after the genetic modification, as well as before and after any subsequent freezing/storage procedures, must tested.

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)?

A biological medicine is defined as a medicine whose active substance is a biological substance (*Annex I, HMA*). A biological substance means a substance extracted from or produced by a biological source and that needs for its characterisation and the determination of its quality a combination of physical, chemical and biological tests, together with the production process and control.

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

Human medicines derived from biotechnology and other high-tech processes must be evaluated by the EMA through the centralised procedure (*see Question 3, Marketing*). After the granting of the centralised marketing authorisation, the marketing authorisation holder (MAHs) must submit a request to INFARMED for a register number for each presentation of the medicine (*Article 54(2), HMA*).

INFARMED can decide that express authorisation must be granted for clinical trials of:

- Medicines containing biological products of human or animal origin.
- Medicine containing active substance(s) or biological components of human or animal origin.
- Medicines produced using biological components of human or animal origin.

(*Article 27(1), Clinical Investigation Law approved by Law 21/2014 of 16 April, as amended* (CIL).)

Clinical trials that involve the following must always obtain prior authorisation from INFARMED:

- Medicines for genetic therapy.
- Medicines for somatic cell therapy.
- Medicines containing genetically modified organisms.
- Medicines for xenogenic somatic therapy.

For the medicines in bullet points one to three, the 30-day term for granting the authorisation can be extended by an additional 20 days or 50 days if consultation with expert committees is required.

Medicines under clinical trials must be supplied free of charge by the promoter. They can continue to be supplied free of charge after the conclusion of interventional clinical trials until the start of the commercialisation of the medicine, if the investigator considers it necessary to continue using the medicine and no similar effective and safe alternatives are available.

See also answers to *Questions 2 to 10*, which generally apply to biological medicines.

Medical devices

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

A medical device is any instrument, apparel, equipment, software, material or article used in isolation or in combination, including the software destined by its manufacturer to be used specifically for diagnosis or therapeutic purposes and that is necessary for the good functioning of the medical device, whose main effect in the human body is not achieved by pharmacologic, immunologic or metabolic means, although its purpose may be supported by those means, destined by the manufacturer to be used in human beings for:

- Diagnosis, prevention, control, treatment or mitigation of a disease.
- Diagnosis, control, treatment, mitigation or compensation of an injury or deficiency.
- Study, replacement or alteration of the anatomy or of a physiological process.
- Birth control.

(*Article 3, Medical Devices Act approved by Decree-Law 145/2009 of 17 June 2009, as amended* (MDA).)

Medical devices are classified as:

- Active medical devices.
- Custom-made devices.
- Implantable medical devices.
- Implantable active medical devices.
- In vitro diagnostic medical devices.
- Devices intended for clinical investigation.

Medical devices are divided into four different risk classes:

- Class I, low risk.
- Class IIa, medium risk.
- Class IIb, medium risk.
- Class III, high risk.

Each medical device risk class is assessed considering the following factors:

- Length of time in contact with the human body (momentary, short-term and long-term).
- Degree of invasion of human body (invasive, non-invasive).
- Part of the body affected by its use (for example, hands, heart, and lower limbs).
- Potential risks stemming from technical design or manufacture.

Medical devices must have the CE marking, which is a prerequisite for medical devices to be placed on the market and receiving a conformity evaluation.

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

The authority responsible for regulating the manufacture, marketing and advertising of medical devices is INFARMED.

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

The manufacture and distribution of medical devices in Portugal is subject to prior notification to INFARMED.

The MDA sets out specific rules on the manufacture, commercialisation, distribution and advertising of medical devices.

Manufacturing

The manufacturing of medical devices is subject to prior notification to INFARMED, 60 days before the activity's start date. Manufacturing is only allowed if the applicant has:

- A responsible technician that ensures quality of the performed activity.
- Premises and equipment suitable and with capacity to ensure:
    - the manufacture, storage and conservation of medical devices; and
    - compliance with performance and safety requirements.

After considering the notification form, INFARMED can inspect the premises to ascertain whether the premises conform to the operation requirements set out in the MDA. If the inspection does not take place within 60 days after the notification, the manufacture activity can begin, subject to a subsequent inspection and decisions.

A manufacturer of medical devices must:

- Comply with the minimum requirements regarding the manufacturing of medical devices.
- Hold records of every transaction concerning medical devices made under the MDA for five years.

- Allow access to supervision agents to any premises, installations, documents and records to ascertain compliance with the law.

Marketing

Medical devices can only be placed on the national market if they:

- Satisfy the essential requirements set out in the annexes to the MDA.
- Have the CE marking (which is a guarantee that the products conform to the essential requirements to which they are subject).
- Have had a conformity assessment.

(*Chapter II, MDA*.)

The conformity assessment procedure is the sole responsibility of the manufacturer, who must draw up a CE declaration of conformity and notify the competent authority (notified body). INFARMED is the designated notified body in Portugal. It evaluates and verifies if medical devices conform to the requirements of the MDA. INFARMED also approves, issues and maintains the certificates of conformity.

Manufacturers of medical devices placed on the Portuguese market, or their representatives, must notify INFARMED.

A manufacturer that places medical devices in the EU market under its own name and does not have its headquarters in an EU member state must appoint a representative for each medical device. The representative must:

- Be established in an EU member state.
- Act on behalf of, and receive notifications addressed to, the manufacturer by EU authorities and bodies on compliance with legal obligations.

Wholesale distribution is subject to prior notification to INFARMED 60 days before starting distribution. Wholesale distribution of medical devices is only allowed if the interested party has both:

- A responsible technician that ensures the quality of the distribution activity.
- Premises and equipment adequate and with capacity to ensure:
    - good storage, conservation and distribution of medical devices; and
    - compliance with performance and safety requirements.

INFARMED can inspect premises. If an inspection does not take place 60 days after the notification, wholesale distribution can begin.

The distributor, among other duties, must notify INFARMED through an online register platform of the list of medical devices placed in the market to be distributed, identifying the respective brand, group, model, description and purpose.

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

Distributors of medical devices that are CE marked and have already obtained a conformity assessment in another EU country must notify INFARMED (*see Question 15, Marketing*).

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

A wholesale distributor in Portugal can buy medical devices from other jurisdictions if they comply with the rules for placement on the market (*see* Question 15).

For imported medical devices, the Portuguese Tax and Customs Authority (TCA) must verify the:

- CE mark on the device.
- CE conformity declaration issued by the manufacturer of the device.
- Copy of the certificate issued by INFARMED proving notification of manufacture or distribution activity, as applicable.
- CE conformity certificate or manufacturer declaration attesting that the device did not require the intervention of a notified body and is therefore exempt from the requirement to notify a CE conformity certificate.

In the case of serious and reasonable doubts that may prevent the TCA deciding on the safety of the devices or accessories and on the respective conformity documentation, the TCA can suspend the customs clearance procedure until INFARMED decides on the safety of the devices. The importer can also submit to INFARMED an opinion request through a specific form on the conformity of the imported devices.

Entities that intend to export medical devices must notify INFARMED of:

- Start date of the distribution activity.
- Medical devices to be distributed.

Entities that export medical devices to non-EU states can request an exemption from the medical devices notification to INFARMED if the products to be exported, although qualified as medical devices, do not comply with the EU harmonised legislation applicable to medical devices and do not have the CE marking.

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

The advertising of medical devices is governed by Chapter XIII of the MDA.

Medical devices that did not have a conformity assessment or were not notified to the competent authority cannot be advertised. However, there may be exceptions. Certain medical devices cannot be promoted or advertised to the general public and can only be advertised to health care professionals in technical publications (for example, medical devices that require mediation and decision of use to be taken by health professionals).

Advertisements of medical devices to the general public must contain, at a minimum, the following information:

- Name of the medical device or commercial brand.
- Indispensable information regarding the safe use of the medical device, including its purpose and special precautions.
- Advice to the user to carefully read the label and user instructions.

An advertisement for a medical device to the general public must not contain any material that:

- Gives the impression that a medical consultation or surgical operation is unnecessary, in particular by offering a diagnosis or by suggesting treatment by mail.
- Suggests that the effects of the medical device are guaranteed, are unaccompanied by adverse reactions or are better than, or equivalent to, those of another treatment with a medical device or medicine.
- Suggests that the subject's health can be enhanced by using the medical device.
- Suggests that the subject's health may be affected by not using the medical device.
- Is directed exclusively or principally at children.
- Refers to a recommendation by scientists, health professionals or persons who, because of their celebrity, may encourage the use of medical devices.
- Suggests that the medical device is a foodstuff, cosmetic or other consumer product.
- Suggests that the safety or efficacy of the medical device is due to the fact that it is a natural product.
- May by a description or detailed representation of a case history, lead to erroneous self-diagnosis.
- Refers in improper, alarming or misleading terms to claims of recovery.

- Uses in improper, alarming or misleading terms pictorial representations of changes in the human body caused by disease or injury, or of the action of a medical device on the human body or parts of it.

Advertising on the internet is subject to the same rules.

INFARMED is responsible for the supervision and enforcement of the provisions on advertising to health care professionals and the general public.

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

Medical devices can only be placed on the national market if they have the CE marking and comply with other requirements (*see Question 15, Marketing*).

Combination products

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

Portugal recognises combination products in accordance with the Medical Devices Regulation (*(EU) 2017/745*) on medical devices, which includes the following rules on combination products:

- Any device that, when placed on the market or put into service, incorporates, as an integral part, a substance which, if used separately, would be considered to be a medicinal product, including a medicinal product derived from human blood or human plasma, and that has an action ancillary to that of the device, is assessed and authorised as a medical device. However, if the action of that substance is principal and not ancillary to that of the device, the integral product will be considered a medicine and governed by the HMA or Regulation 726/2004, as applicable.
- Any device that is intended to administer a medicinal product as defined in the HMA must be considered a medical device. However, if the device and the medicinal product are placed on the market in such a way that they form a single integral product that is intended exclusively for use in the given combination and is not reusable, that single integral product must be considered a medicine.
- Any device that, when placed on the market or put into service, incorporates, as an integral part, non-viable tissues or cells of human origin or their derivatives that have an action ancillary to that of the device must be assessed and authorised as a medical device.

(*Article 1, Medical Devices Regulation*.)

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

The answers to *Questions 2 to 19* generally apply to the commercialisation of 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)?

Traditional medicines based on plants (herbal medicinal products) and homeopathic medicines are considered medicinal products under the HMA.

Food supplements, which include vitamins and minerals, are not considered medicinal products and are regulated by Decree-Law 136/2003 of 28 June 2003, as amended, which transposed Directive 2002/46/EC on food supplements into national law.

Food supplements are defined as foodstuffs destined to complement or supplement the normal diet regime and constitute concentrated sources of certain nutrients or other substances with a nutritional or physiological effect. Such foodstuffs can be, 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, and other similar forms of liquids and powders designed to be taken in measured small unit quantities (*Decree-Law 136/2003*).

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

INFARMED is the competent authority responsible for regulating the manufacture, marketing and advertising traditional medicines based on plants and homeopathic medicines.

For food supplements, the General Directorate for Food and Animal Health (*Direção Geral de Alimentação e Veterinária*) (DGAV) is the entity responsible for the definition, execution and evaluation of food safety policies. DGAV must be notified before placing food supplements in the market.

The entity responsible for the supervision of compliance with Decree-Law 136/2003 is the Authority for Economic and Food Safety (*Autoridade de Segurança Alimentar e Económica*) (ASAE).

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

Manufacturing

The manufacturing of traditional medicines based on plants and homeopathic medicines is subject to authorisation by INFARMED, in the same way as general medicinal products (*see* Question 3).

Under Decree-Law 136/2003, the manufacturer or those responsible for placing food supplements on the market must give prior notice to DGAV of the commercialisation of food supplements.

Marketing

Traditional medicines based on plants and homeopathic medicines are considered medicinal products under the HMA.

Medicines based on plants are subject to traditional use registration with INFARMED where they:

- Have references exclusively adequate for medicines based on plants and, considering their composition and purpose, are destined and designed to be used without surveillance of a doctor for diagnosis, prescription or monitoring of treatment purposes.
- Are destined to be administered exclusively by one or more of the following means: oral, external or inhaling.
- Have been in longstanding therapeutic use.
- Are not harmful when used in specified conditions, as evidenced by existing and sufficient information.
- May demonstrate, according to existing and sufficient information, pharmacological or plausible efficacy effects, considering their longstanding use.

However, INFARMED can determine that a traditional medicine based on plants requires a marketing authorisation (*see Question 3*).

Homeopathic medicines that comply with the following requirements are subject to a simplified registration procedure:

- Destined to be administered orally or externally.
- Present a degree of dilution that guarantees the harmlessness of the medicine.
- Do not present any special therapeutic indications on the label or in any information regarding the medicine.

If these requirements are not met, a homeopathic medicine requires a marketing authorisation (*see Question 3*).

Food supplements are not considered medicines and their commercialisation is subject to prior notification to the DGAV.

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

As part of the registration procedure, INFARMED must consider if homeopathic medicines have an authorisation or registration in another EU member state allowing their marketing in such state (*Article 136(2), HMA*). For medicines based on plants, INFARMED must consider other registrations granted by other EU member states in assessing traditional use registration requests (*Article 144(2), HMA*).

A manufacturer or importer of food supplements that have already been commercialised in the EU must notify DGAV and specify the name of the authority that received the first commercialisation notification (*Article 9(4), Decree-Law 136/2003*).

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

The provisions on importation and exportation of medicinal products also apply to homeopathic medicines and traditional medicines based on plants, including when sold online (*see Question 7*).

Food supplements can be imported if:

- They comply with the requirements of Decree-Law 136/2003.
- The manufacturer or importer notifies DGAV.

Food supplements can be exported and sold online.

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

The advertising of traditional medicines based on plants is subject to the general rules on medicines advertising (*see Question 8*). All advertisements must include the following wording: "traditional medicine on the basis of plants, for use in the specified conditions, exclusively based on longstanding experience".

The labelling of homeopathic medicines that are subject to simplified registration with INFARMED (*see Question 24, Marketing*) are subject to adapted general rules on medicine advertisement, and must include the following information (no other information can be included):

- Scientific denomination of the homeopathic stocks, as well as of the diluting degree, using symbols of the adopted pharmacopoeia (if there are several stocks, the scientific denomination can be complemented by another given name).
- Name and address of the holder of the simplified registration, and when applicable, of the manufacturer.
- Administration mode.
- Explicit expiry date, including month and year.
- Pharmaceutical form.
- Specific conservation precautions, when applicable.
- Special notices, when the medicine requires it.
- Manufacture lot number.
- Market introduction authorisation registration number.
- The words: "without approved therapeutic indications".

Advertisements of food supplements cannot include references that:

- Attribute to it prophylactic properties or treatment or healing of human diseases, or refer to such properties.
- Expressly or implicitly declare that a balanced and varied food regime does not constitute a sufficient source of nutrients in general.

Advertisements of food supplements must include, sufficiently and adequately highlighted, reference to the terms food supplement that unequivocally identifies the product as such.

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 national data protection legislation (*Law 67/98 of 26 October 1998*), enforced by the Portuguese Data Protection Agency (*Comissão Nacional Nacional de Proteção de Dados*) (CNPD), applies to life sciences businesses that deal with personal health data (for example, in the context of clinical trials, pharmacovigilance, adverse event reporting, and patient data processing). It also applies to health apps that collect personal data. Since 25 May 2018, the General Data Protection Regulation (*(EU) 2016/679*) (GDPR) is also directly applicable in Portugal.

There is a specific legal regime that regulates the processing of personal genetic information and health information, which is set out in Law 12/2005 of 26 January 2005 as executed by Decree Law 131/2014 of 29 August 2014. Under this regime, the collection of human biological samples or related derivatives, with the aim of establishing a database of biological products with personal information, is subject to prior authorisation of the CNPD.

Research

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

Clinical trials on humans are regulated by INFARMED. The Clinical Trials Act (Law 21/2014 of 16 April 2014) implements the Clinical Trials Directive (2001/20/EC), which will be repealed by the Clinical Trials Regulation (*536/2014*) when the European Commission publishes a notice confirming a fully functional EU clinical trials portal and database (which is now expected to occur in 2021).

Any clinical trial on humans is subject to the prior authorisation of INFARMED. Generally, decisions are made within 30 days of the filing of an application. Additional requests for information suspend this deadline until the sponsor provides the requested information.

Clinical trials must also receive a favourable binding opinion from the competent Ethics Committee (*Comissão de Ética competente*) (CEC).

Clinical trial participants must provide written informed consent.

The following conditions must be met before a trial can begin:

- A satisfactory evaluation by INFARMED and the CEC of the anticipated benefits and risks, concluding that the potential benefits overcome the foreseeable risks.
- The existence of a protocol.
- Complete details of the clinical trial sponsor, investigator, principal investigator or investigator-co-ordinator must be provided to the CEC and INFARMED.
- Details of the qualifications of all team members involved in the clinical trial must be provided to the CEC and INFARMED.
- The existence of an investigator's brochure.
- Details of the clinical trial centre(s) and validation of the adequacy of the facilities must be provided to the CEC and INFARMED.
- Provisions for indemnity or compensation in the event of injury or death attributable to the clinical trial.
- The existence of an insurance or indemnity to cover the liability of the investigator and sponsor.
- In the case of multicentre trials involving trial centres of other EU member states, identification of the competent authorities and, if available, the opinions adopted by the respective ethics committees, translated into Portuguese.
- Details of the amounts and, where appropriate, the arrangements for rewarding or compensating investigators and trial subjects, and the relevant aspects of any agreement between the sponsor and the site, must be provided to the CEC and INFARMED.

Certain minimum conditions must be met in respect of trial participants:

- A prior interview with the investigator, in which the participant must be informed of the:
    - clinical trial objectives;
    - risks and inconveniences;
    - associated conditions of performance; and
    - the participant's right to withdraw from the clinical trial at any time.

- Protection of the patient's right to moral and physical integrity.
- Protection of data privacy rights.
- Existence of an insurance or indemnity to cover the liability of the investigator and sponsor.
- Written informed consent, referring to the nature, scope, consequences and risks of the clinical trial.
- Details of the associated medical care must be provided during the clinical trial.
- Designation of a contact person to disclose detailed information to participants.
- Pecuniary benefits or incentives cannot be granted to patients, except for the reimbursement of expenses and the compensation of damages incurred by the participant that arise from participation in the clinical trial.

In addition, a clinical trial must be conducted in accordance with:

- Good clinical practices.
- The approved protocol.
- INFARMED's clinical trial authorisation.
- The decision of the CEC.

Amendments to the protocol can be made provided they:

- Do not affect the safety of participants.
- Do not alter the scientific evidence on which the conduct of the trial is based.

During the course of the trial, the investigator must report any adverse events to the sponsor, except those identified in the investigator's brochure or in the protocol as not requiring immediate (within a 24-hour period) notification. The sponsor must keep detailed records of all adverse events.

Serious unexpected adverse events that have caused or may cause the death of a participant must be registered and notified to:

- INFARMED.
- All the competent public authorities of all the participating EU member states involved in the trial.
- The CEC.

The National Registry for Clinical Studies (RNEC) (*www.rnec.pt*) serves as a tool for the registration and publication of all clinical studies carried out in Portugal and that involve human beings (that is, clinical trials and other studies of a clinical nature involving, among others, investigational products, medicines, or medical devices, and studies that use human biological samples).

The RNEC's objectives are set out in Order 65/2015, 5 March 2015 and include the creation of an information databank of clinical studies to:

- Facilitate the transmission and monitoring of information and notifications submitted to INFARMED and ethics committees.
- Increase access for the research community, health care professionals and the general public to all clinical studies carried out in Portugal.

The use of animals in scientific research is governed by Decree-Law 113/2013 of 7 August 2013, as amended. The regime includes comprehensive rules aimed at the ethical use of animals in medicines testing in Portugal. The applicable rules encourage alternatives to the use of animals in the testing of medicines, and promotes scientific quality and animal welfare where the use of animals cannot be avoided.

Reform

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

One of the objectives of the current National Health Plan is to promote a sustainable policy in the field of medicinal products, and to reconcile budgetary rigour with access by patients to therapeutic innovation in the National Health Service through:

- Reviewing the rules applicable to dispensing and reimbursing medicines for chronic outpatients.
- Increasing the market share of generic medicines (in value) to 30%.
- Encouraging research and national production in the medicines sector.

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- *Medicinal product regulation and product liability in Portugal: overview, Practical Law Life Sciences Global Guide, Thomson Reuters.*
- *Pharmaceutical IP and competition law in Portugal: overview, Practical Law Life Sciences Global Guide, Thomson Reuters.*
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Publications

- *Distribution and marketing of drugs in Portugal: overview, Practical Law Distribution and Marketing of Drugs Global Guide, Thomson Reuters, General Editors: Eric Stupp and Markus Schott, Bar & Karrer AG and Alison Dennis, Field Fisher Waterhouse LLP.*
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