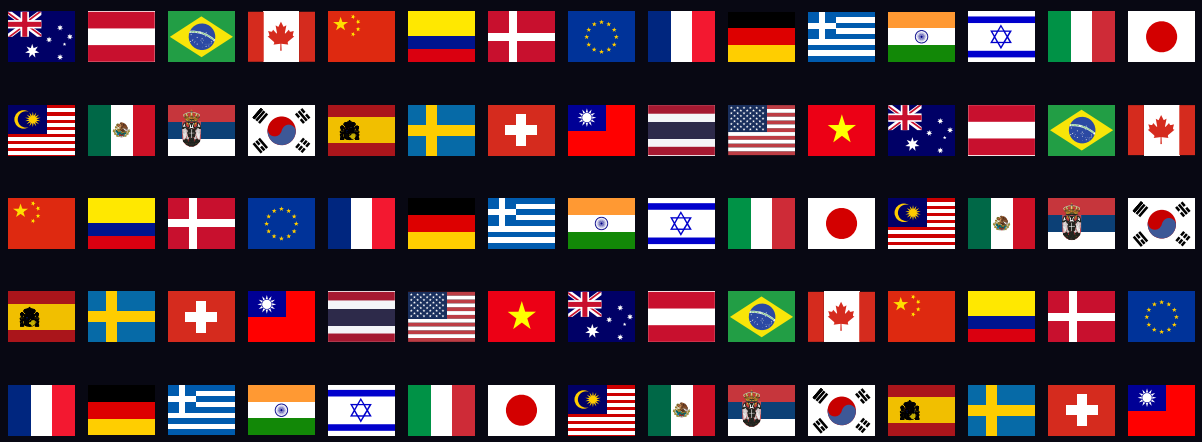
PHARMA & MEDICAL DEVICE REGULATION

Greece



LEXOLOGY
Getting The Deal Through

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Pharma & Medical Device Regulation

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Quick reference guide enabling side-by-side comparison of local insights, including into the regulatory framework; clinical practice; marketing authorisation; amending authorisations; recall; promotion; enforcement of advertising rules; pricing and reimbursement; off-label use and unlicensed products; sale and supply; and recent trends.

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REGULATORY FRAMEWORK

Competent authorities for authorisation

Identify the competent authorities for approval of the marketing of medicinal products and medical devices. What rules apply to deciding whether a product falls into either category or other regulated categories?

The National Organization for Medicines (EOF) is the competent authority for approval of the marketing of medicinal products through the national, mutual recognition and decentralised procedures.

In regard to medical devices, EOF is the supervisory authority by virtue of Ministerial Decision No. Α4γ/Γ.Π.οικ. 88159/2017. For the marketing of medical devices in the Greek market, according to the Medical Devices Regulation (EU) 2017/745 (MD Regulation) a conformity assessment (CE mark) is required, not a marketing authorisation. Currently, the only Notified Body in Greece responsible for the conformity assessment of medical devices is the National Evaluation Center of Quality and Technology in Health (EKAPTY).

According to Greek legislation, medicinal product is (1) any substance or combination of substances presented as having properties for treating or preventing disease in human beings or (2) any substance or combination of substances that may be used in or administered to human beings either with a view of restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to make a medical diagnosis.

On the other hand, medical devices are defined in the MD Regulation, as any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

- diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease;
- diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability;
- investigation, replacement or modification of the anatomy or of a physiological or pathological process or state; or
- providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations, and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.

The issue of product classification has been brought several times before the European Court of Justice. According to Judgment of 29 April 2004 – Case C-150/00, it has been ruled that the national authorities, acting under the control of the Court, must work on a case by-case basis, having regard to all of the product characteristics, in particular their composition, their pharmacological properties to the extent to which they can be established in the present state of scientific knowledge, the manner in which they are used, the extent of their distribution, their familiarity to consumers and the risks that their use may entail. Accordingly, a risk to public health is only one aspect of the product that must be taken into consideration by the competent national authorities. It is obvious that a product that does not pose a real risk to health can nevertheless have an effect on the functioning of the body.

Law stated - 29 June 2023

Approval framework

Describe the general legislative and regulatory framework for approval of marketing of medicinal products and medical devices.

Medicinal products

The approval of marketing of medicinal products is governed by Ministerial Decision 32221/2013 on harmonisation of Greek legislation to the corresponding EU legislation in the field of manufacturing and circulation of medicinal products intended for human use, in compliance with Directive No. 2001/83/EC on the Community code relating to medicinal products for human use, as amended and in force. To obtain a marketing authorisation for a medicinal product, which is not issued in accordance with the procedure of Regulation (EC) 726/2004 (centralised procedure), an application shall be submitted to EOF. The criteria applied for the grant of approval are, in brief, the following.

A marketing authorisation shall be granted only to an applicant established (having its registered place of business) in the European Union and the application for marketing authorisation for a medicinal product shall be accompanied by the following information and documents:

- Name or corporate name and address of the applicant and, where applicable, of the manufacturer.
- Name of the medicinal product.
- Qualitative and quantitative particulars of all the constituents of the medicinal product, including the reference to its international non-proprietary name (INN) recommended by the World Health Organisation (WHO) where there is an INN for the medicinal product, or a reference to the relevant chemical name.
- An evaluation of the potential environmental risks posed by the medicinal product. This impact shall be assessed and, on a case-by-case basis, specific arrangements to limit it shall be envisaged.
- A description of the method of manufacture.
- Therapeutic indications, contra-indications and adverse reactions.
- Posology, pharmaceutical form, method and route of administration and expected shelf life of the medicinal product.
- Justification for any precautionary and safety measures to be taken for the storage of the medicinal product, its administration to patients and the disposal of waste products, together with an indication of the potential risks of the medicinal product to the environment.
- A description of the control methods applied by the manufacturer.
- Written confirmation that the manufacturer of the medicinal product has verified compliance of the manufacturer of the active substance with principles and guidelines of good manufacturing practice by conducting audits in accordance with article 63 of Ministerial Decision 32221/2013.
- The written confirmation shall include a reference to the date of the audit and a statement that the outcome of the audit confirms that the manufacturing complies with the principles and guidelines of good manufacturing practice.
- Results of:
  - Pharmaceutical (physicochemical, biological or microbiological) tests, pre-clinical (toxicological and pharmacological) tests or clinical trials.
- a summary of the applicant's pharmacovigilance system that shall include the following elements:

  - proof that the applicant has at his disposal a qualified person responsible for pharmacovigilance;
  - the member states in which the qualified person resides permanently and carries out his/her tasks;
  - the contact details of the qualified person;
  - a declaration signed by the applicant, stating that the applicant has the necessary means to fulfil the tasks and

responsibilities listed in Ministerial Decision 32221/2013;
- reference to the location where the master file of the pharmacovigilance system for the medicinal product is kept.

- the risk management plan describing the risk management system to be introduced by the applicant for the specific product.
- a declaration to the effect that the clinical trials conducted outside the European Union meet the ethical requirements of clinical trials legislation.
- a summary of the product characteristics, a mock-up of the outer packaging and of the immediate packaging of the medicinal product together with a package leaflet.
- a document from the competent state authority stating that the manufacturer is authorised to manufacture medicinal products in his or her country.
- copies of the following:
  - any marketing authorisation for the medicinal product granted in another member state or in a third country for placing the medicinal product on the market, a summary of the safety data including data contained in periodic safety update reports, where available, and of suspected adverse reactions reports, together with a list of member states in which an application for a marketing authorisation is under examination.
  - a summary of the product characteristics proposed by the applicant or approved by EOF and the package leaflet proposed or approved by EOF.
  - details of any negative decision to grant a marketing authorisation for the product, whether within the Union or in a third country, together with the reasons for that decision.
  - (s) a copy of any designation of the medicinal product as an orphan medicinal product under Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products, accompanied by a copy of the relevant opinion of EOF.

Authorisation of medicinal products through mutual recognition and decentralised procedures are governed by articles 45–56 of Ministerial Decision 32221/2013.

The labelling and packaging of medicinal products, including the leaflet and the summary of product characteristics, are regulated further by the Ministerial Decision 32221/2013.

Medical devices

For the marketing of medical devices in the Greek market a marketing authorisation is not required. The current regulatory framework regarding conformity as well as labelling, packaging and instructions for use of medical devices in Greece includes Regulation (EU) 2017/745 and Regulation (EU) 2017/746 (in vitro medical devices) and Ministerial Decision 1348/2004 on good distribution practices for medical devices. A device may be placed on the market or put into service provided that it complies with Regulation (EU) 2017/745 when duly supplied and properly installed, maintained and used in accordance with its intended purpose.

Further, medical devices lawfully placed on the market under Directives 90/385/EEC and 93/42/EEC before 26 May 2020 (MD Directives) and medical devices placed on the market after 26 May 2020 under a certificate issued by notified bodies in accordance with MD Directives as of 25 May 2017, may continue to be placed on the market or put into service until 27 May 2025.

For the above medical devices, MD Directives shall continue to apply until 27 May 2025. Therefore, Ministerial Decision No. 130648/2009, by virtue of which the national legislation has been harmonised with the provisions of Directive 93/42/EEC, as amended by directives 98/79/EC, 2000/70/EC, 2001/104/EC, 2007/47/EC and Regulation (EC) No.

1882/2003 (MD Ministerial Decision) governing medical devices circulation in Greece, which has not yet been abolished, remains in force for the above categories of medical devices.

According to the MD Ministerial Decision, any manufacturer that places on the market products under his own name, in accordance with the procedures provided for in the MD Ministerial Decision shall inform EOF of the address of its registered place of business and of the description of the products concerned.

For all medical devices of categories I, IIa, IIb and III, the manufacturer or its authorised representative shall submit to EOF all the information necessary for the identification of these products, as well as the labelling and the instructions for use, before the start of use of these products in the Greek territory.

Law stated - 29 June 2023

CLINICAL PRACTICE

Applicable rules

What legislation controls and which rules apply to ethics committee approval and performance of clinical trials in your territory for medicinal products and medical devices?

Medicinal products

Clinical trials in Greece are governed by the provisions of the Clinical Trial Regulation (EU) No. 536/2014 (Clinical Trial Regulation), and the provisions of Ministerial Decision 59676/2016, as amended by the Ministerial Decision 6809/2019 (Government Gazette 2015/03-06-2019), by virtue of which Clinical Trial Regulation has been implemented in Greece.

The conduct of clinical trials in Greece is subject to the National Organization for Medicines (EOF)'s regulatory approval. Prior assessment of the suggested clinical trial by the National Ethics Committee is also required prior to its commencement. The Hellenic Association of Pharmaceutical Companies (SFEE) Code of Conduct, which is considered 'soft law', also applies. See https://www.sfee.gr/wp-content/uploads/2015/04/CODE-BROCHURE_EN-1.pdf .

Medical devices

Clinical investigations of medical devices are in principle governed by the provisions of the Medical Devices Regulation and article 15 of the MD Ministerial Decision, which has not yet been abolished and relevant circulars of EOF (indicatively circular No. 42353/2011). The Code of Conduct of SEIV (Association of Companies of Medical and Biotechnological products), which is considered a 'soft law', also applies.

Law stated - 29 June 2023

Reporting requirements

What requirements exist for reporting the commencement of a trial and its results to the competent authorities or the public?

According to Ministerial Decision No. Γ5α/59676/2016, as amended and in force, to conduct a clinical trial in Greece, prior approval of EOF is required. To obtain approval, the sponsor submits an application file through the portal referred to in article 80 of Regulation 536/2014. The application submission and validation process are carried out in accordance with the procedure referred to in article 5 of EU Regulation 536/2014.

The clinical trial is subject to a scientific and ethical evaluation and is approved in accordance with article 8 of EU Regulation 536/2014. EOF acts in accordance with the above Regulation, depending on whether it has been granted the

status of ‘concerned’ or ‘interested’ member state, while the ethical evaluation is carried out by the National Ethics Committee.

EOF informs the sponsor via the EU portal whether the clinical trial has been approved, whether its approval is subject to conditions or whether it has been rejected. If the National Ethics Committee issues a negative opinion, EOF proceeds to the rejection of the application.

Notification is made by a single decision within five days, as provided for in article 8 of EU Regulation 536/2014. In the case of a negative decision, the sponsor may submit an appeal to the board of EOF within 15 days of the date of notification of the sponsor.

In addition, to start the clinical trial in each approved centre within the Greek territory, a contract must be signed between the sponsor, the principal investigator, the legal representative of the hospital, public or private, and ELKE or ELKEA (Special Account for Research Funds) Management Officer.

Both the Principal Investigator and the sponsor/CRO are required to inform the hospital, EOF and the National Ethics Committee on the progress of the clinical trial and following completion of the trial, to submit a detailed report of the results of the clinical trial.

Medical devices

Pursuant to article 15 of the Medical Devices MD, that has not yet been abolished and relevant circulars of EOF, the manufacturer or the authorised representative that wishes to start a clinical investigation of medical device in Greece notifies EOF, provided that the investigation will take place in Greece. Positive opinion of the National Ethics Committee on the clinical investigation, including a review of the clinical investigation plan, which is submitted to EOF, is also considered as a prerequisite for the commencement of the clinical investigation.

With regard to clinical investigations on implantable medical devices, as well as class III devices and part of class IIa/IIb devices, the manufacturer may start the relevant Clinical Investigations in the Greek territory within 60 days of the submission of the notification to EOF with a complete dossier, unless, within this period, EOF notifies the manufacturer about a negative decision based on public health grounds.

Law stated - 29 June 2023

Consent and insurance

Are there mandatory rules for obtaining trial subjects’ consent to participate? Must sponsors arrange personal injury insurance to a particular limit?

Medicinal products

According to Ministerial Decision No. Γ5α/59676/2016, as amended and in force, informed consent shall be in writing, dated and signed by (1) the principal investigator or a member of the investigating team authorised for this purpose and (2) the subject or his or her legal representative after having been duly informed in accordance with the applicable provisions.

Before informed consent is obtained, the subject shall be informed by means of a prior interview in a language easily understood by him or her. The subject should be able to ask questions at any time and should be given sufficient time to consider his or her decision. The pre-consent interview with the subject should be conducted by a qualified member of the research team designated by the principal investigator. Informed consent shall be documented.

Where the subject is deaf, the information form should be given to him or her in writing along with the opportunity to ask questions in writing. Both the information form and the informed consent form must be certified by the subject and

the member of the investigating team designated for this purpose by the principal investigator that the above procedures have been followed. In such case, at least one impartial witness shall be present throughout the procedure and shall co-sign the above documents.

Where the subject is unable to write or read both the information form and the consent form, they shall be signed by the member of the investigating team designated for this purpose by the principal investigator, and by two impartial witnesses.

Alternatively, in the above cases, consent may be recorded by appropriate alternative means (for example, by audio or video recording, as appropriate) in the presence of at least one impartial. In this case, the consent shall also be signed by the witness.

The sponsor has the obligation to have concluded and maintain in force an insurance contract of at least €300,000, with a reputable insurance company established in an EU member state, to cover both its own liability and that of the principal investigator and the members of the research team per participant.

Medical devices

Participants' informed consent is required to be submitted to EOF prior to the commencement of a clinical investigation concerning a medical device that (1) either does not bear a CE mark or bears a CE mark but the device is going to be tested for uses not covered by the CE mark and, (2) in the case of in vitro diagnostic medical devices, where the product is intended to come into direct or indirect contact with the human body (Circular No. 42353/2011).

Law stated - 29 June 2023

MARKETING AUTHORISATION

Time frame

How long does it take, in general, to obtain an authorisation from application to grant, what fees are payable and what is the normal period of validity of the authorisation?

Greek legislation does not provide for a specific timeline for the National Organization for Medicines (EOF) to respond to a marketing authorisation application. In general, relevant proceedings from application to grant take six months to one year.

The initial period of validity of the marketing authorisation is five years, subject to renewal following reassessment of the risk-benefit balance by the EOF.

Without prejudice to any changes that are not yet available to the public, payable fees may be found in the following link with an option for an unofficial translation to English.

Medical devices are not subject to a marketing authorisation.

Law stated - 29 June 2023

Marketing exclusivity

What protections or exclusivities apply to the marketing period of an approved medicinal product or variation?

Ministerial Decision 32221/2023 provides for a marketing exclusivity period of 10 years from the date of the marketing authorisation of the reference medicinal product being granted. This 10-year period might be extended to a maximum

of 11 years if, during the first eight years of the 10-year period, the marketing authorisation holder obtains authorisation for one or more new therapeutic indications and, during the scientific assessment prior to its authorisation, it is established that these indications will bring a significant clinical benefit compared to existing therapies.

Law stated - 29 June 2023

Protecting research data

What protections or exclusivities apply to the data submitted by originators to gain initial approval and, on variation or new application, to add indications or pharmaceutical forms?

The data submitted by originators are protected by a data protection period of eight years from the date of the marketing authorisation being granted. Regarding substances of well-established medical use, new indications based on significant clinical trials or preclinical studies will bring a non-cumulative period of data exclusivity of one extra year.

Law stated - 29 June 2023

Freedom of information

To what extent and when can third parties make freedom of information applications for copies of research data submitted by applicants for authorisation to market medicinal products or medical devices?

Pursuant to article 33 of the Ministerial Decision 32221/2013, EOF shall without delay make publicly available:

- the marketing authorisation accompanied by the package leaflet, the summary of product characteristics and any conditions laid down in accordance with articles 34, 35 and 36 of Ministerial Decision 32221/2013, together with any time limits laid down for the fulfilment of those conditions, for each medicinal product that EOF has authorised. A summary of the marketing authorisations issued shall be published in the Government Gazette; and
- the assessment report on the medicinal product, with an appropriate justification, after deleting any information of a commercially confidential nature. The justification shall be provided separately for each indication applied for.

Law stated - 29 June 2023

Regulation of specific medicinal products

What are the specific requirements and processes for marketing approval of the major categories of regulated products?

A simplified marketing authorisation procedure is available for certain types of medicinal products, such as the foolowing.

Homeopathic medicines are subject to the following conditions:

- absence of a specific therapeutic indication in the package leaflet or in any information about the medicine;
- oral or external route of administration; and
- the degree of dilution guarantees the innocuousness of the product.

Medicinal products of plant origin that meet all of the following criteria:

- have indications suitable exclusively for traditional herbal medicinal products that, by virtue of their composition and purpose, have been studied and are intended to be used without medical supervision for diagnostic purposes, prescription or therapeutic monitoring;
- are intended exclusively for administration in accordance with a specified content and dosage,
- are preparations to be administered orally, externally and/or by inhalation;
- 15-year period of traditional use has been completed; and
- the data on the traditional use of the medicinal product are sufficient to demonstrate that the product is not harmful under the specified conditions of use and that the pharmacological properties or efficacy of the medicinal product are substantiated by long-term use and experience.

Orphan drugs are authorised under the provisions of Regulation (EC) No. 141/2000 of the European Parliament and of the Council and advanced therapies medicinal products are authorised under the provisions of Regulation (EC) 1394/2007 of the European Parliament and of the Council.

Generics: Without prejudice to the provisions governing the protection of industrial and commercial property, the applicant shall not be required to provide the results of pre-clinical tests and clinical trials if the applicant demonstrates that the medicinal product is a generic of a reference medicinal product that is or has been authorised within the meaning of Ministerial Decision 32221/2013.

Biosimilars: Where a biological medicinal product, similar to a reference biological product, does not meet the conditions of the definition of generic medicinal products, in particular due to differences in the raw materials or manufacturing processes of the biological medicinal product and the reference biological product, the results of appropriate pre-clinical or clinical studies related to these conditions shall be submitted.

With regard to food supplements, the manufacturer or the person placing food supplements on the market in Greece shall immediately notify EOF of such placing on the market (Ministerial Decision 53625/2017).

In respect of medicinal products, Regulations 2017/745 and 2017/746 shall apply.

Law stated - 29 June 2023

Rewards and incentives

What rewards or incentives for approval are applicable to the major product categories, including orphan drugs, drugs for paediatric use, generic drugs and biosimilars?

The authorisation process for the marketing of generic versions of medicinal products is simpler than that for reference medicinal products since, in principle, the applicant is not required to provide the results of preclinical and clinical trials, provided that the applicant can demonstrate that the medicinal product is a generic medicinal product of a reference medicinal product that is or has been authorised for not less than eight years in an EU member state.

Regarding biological medicinal products that are similar to a reference biological medicinal product but do not meet the requirements of the definition of generic medicinal products, the results of appropriate preclinical tests or clinical trials relating to these conditions must be provided.

As regards orphan medicinal products, there is a market exclusivity period conferred by Regulation (EC) 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products. Pursuant to the provisions contained in article 8 of this Regulation, when there is a marketing authorisation granted in Europe for an orphan drug, the authorities in Europe and in all EU member states must refrain during a 10-year period (exceptions are

also provided to this exclusivity period) from accepting another marketing authorisation application or from granting another marketing authorisation when there is an existing marketing authorisation for a similar medicinal product that has the same therapeutic indication.

Paediatric medicinal products are subject to specific incentives as set forth by Regulation (EC) 1901/2006 of the European Parliament and of the Council on medicinal products for paediatric use. This regulation eases the authorisation process for paediatric products, contemplating the possibility of specific investigation plans for such products, waivers regarding the obligation to submit certain studies and information, and deferrals.

Law stated - 29 June 2023

Post-marketing surveillance of safety

What pharmacovigilance or device vigilance obligations apply to the holder of a relevant authorisation once the product is placed on the market?

According to article 136 of Ministerial Decision 32221/2013, the marketing authorisation holder shall implement a pharmacovigilance system equivalent to that of the system of EOF in order to fulfil pharmacovigilance duties.

The marketing authorisation holder shall, through the pharmacovigilance system, scientifically evaluate all information, consider options for minimising and preventing risks and take action where necessary.

The marketing authorisation holder shall conduct regular internal audits of the pharmacovigilance system in place. It shall place a note on the main findings of the internal audit in the master file of the pharmacovigilance system and, based on the findings of the internal audit, ensure that an appropriate corrective action plan is developed and implemented. Once all the corrective actions have been implemented, the note may be withdrawn.

As part of the pharmacovigilance system, the marketing authorisation holder of the medicinal product shall:

- have permanently and continuously at his or her disposal an appropriately qualified person responsible for pharmacovigilance, who resides and operates in the EU;
- keep and have available on request the master file of the pharmacovigilance system;
- implement a risk management system for each medicinal product;
- monitor the outcome of the risk minimisation measures included in the risk management plan or imposed as conditions of the marketing authorisation; and
- updating the risk management system and monitoring pharmacovigilance data to determine whether there are new risks or changed risks or whether there are changes in the risk-benefit balance of medicinal products.

Law stated - 29 June 2023

Other authorisations

What authorisations are required to manufacture, import, export or conduct wholesale distribution and storage of medicinal products and medical devices? What type of information needs to be provided to the authorities with an application, what are the fees, and what is the normal period of validity?

Medicinal products

Manufacture, import and export

For the manufacture of medicines in Greece, a manufacturing authorisation issued by EOF is required, following an

application by the person concerned. A manufacturing authorisation is also required for medicinal products intended exclusively for export, as well as for imports from third countries. For a legal person to be granted with a manufacturing authorisation, the requirements provided for in article 58 of Ministerial Decision 32221/2013 should be met, among which are indicatively the following:

- to determine the drugs and pharmaceutical forms that will be produced or imported, as well as the place of their production and/or control; and
- to have suitable and sufficient premises, technical equipment and control capabilities available for the production or import, in accordance with legislative requirements on manufacturing, control and storage of medicines, in accordance with article 32(c) to have at least one qualified person within the meaning of article 68 of Ministerial Decision 32221/2013.

The applicant provides with his or her application the information that the document complies with the above requirements.

Wholesale distribution and storage

In principle, pursuant to article 103 of Ministerial Decision 32221/2013, wholesale of medicines is permitted only to manufacturers, agents and importers of medicines, including marketing authorisation holders, 3PL companies, etc, holding a licence, which is granted by the National Medicines Authority (EOF). The wholesale distribution authorisation remains in force for a period that cannot exceed five (years and may be renewed for similar periods of time.

For a legal person to be granted with a wholesale licence, the requirements provided for in article 104 of Ministerial Decision 32221/2013 should be met, among which are indicatively the following:

- lease agreement or title of ownership;
- appointment of a pharmacist in charge;
- license to install and operate a warehouse or otherwise a certificate from the relevant municipality regarding the permitted use of land, etc; and
- building permit, etc.

Persons authorised to engage in the wholesale distribution of medicinal products and the premises thereof are subject to EOF's inspections, inter alia, in relation to compliance with good distribution practices (GDP) (articles 104 and 106 paragraph 2 of Ministerial Decision 32221/2013). Moreover, marketing authorisation holders and wholesale distribution authorisation holders that carry out intra-Community distribution of Medicinal Products are required to declare to EOF, in real time, the 12-digit Unique Serial Number of the EOF safety coded stickers of each medicinal product prior to intra-Community distribution or export thereof, along with the country of destination (article 1 of Ministerial Decision No. 18243/2013).

Medical devices

Provisions of Medical Devices Regulation (EU) 2017/745 and 2017/746 shall apply.

Law stated - 29 June 2023

Sanctions

What civil, administrative or criminal sanctions can authorities impose on entities or their directors and officers for breach of the requirements concerning controlled activities?

Breach of the requirements concerning controlled activities may lead to administrative sanctions, criminal liability and/or civil liability.

Administrative sanctions are mainly set out in Law 96/1973 and Ministerial Decision 32221/2013. Breach of the legal requirements for the circulation of medicinal products or medical devices (such as circulation of pharmaceutical and other products, referred to in Law 96/1973 without authorisation or after the expiry or revocation or during the suspension thereof or infringements of the provisions on standardised circulation and compulsory indications on the packaging of medicinal products and other products, etc) are sanctioned with a range of fines up to €100,000. In certain cases (for instance, in the case of repetition of the infringement of circulation of pharmaceutical products without authorisation or after the expiry or revocation or during the suspension thereof), criminal penalties or withdrawal of the marketing authorisation are also provided for.

Law stated - 29 June 2023

Exemptions

What, if any, manufacture and supply of medicinal products is exempt from the requirement to obtain an approval to market?

Medicinal products prepared in pharmacies according to a prescription intended for a specific patient (commonly called non-pharmacy formulation).

Medicinal products prepared in a pharmacy according to a pharmacopoeia's specifications and intended to be administered directly to patients who obtain their medicines from that pharmacy (commonly called the current pharmacopoeia’s galenical formulation).

This is not applicable for medical devices, since no marketing authorisation is required.

Law stated - 29 June 2023

Parallel trade

Are imports allowed into your jurisdiction of finished products already authorised in another jurisdiction, without the importer having to provide the full particulars normally required to obtain an authorisation to market? What are the requirements?

In principle, EOF has the authority to grant a parallel import licence that is valid for five years. The above authorisation ceases to be valid, is revoked or suspended if the marketing authorisation of the parallel imported proprietary medicinal product or the product to which it is sufficiently similar, ceases to be valid or is revoked or suspended, either in Greece (host member state) or in the EU member state from which it is imported (state of origin), for reasons of public health protection and in particular when the marketing of the medicinal product is prohibited and its withdrawal from the market is imposed in cases where it is considered that:

- the medicinal product is harmful;
- lacks therapeutic efficacy;

- the risk-benefit balance is not favourable to the benefit;
- the medicinal product does not have the declared qualitative and quantitative composition; or
- controls on the medicinal product and/or on the ingredients and intermediate stages of manufacture have not been carried out or where another requirement or obligation relating to the granting of the manufacturing authorisation is not fulfilled.

Law stated - 29 June 2023

AMENDING AUTHORISATIONS

Variation

What are the main requirements relating to variation of authorisations for medicinal products and medical devices?

Medicinal products

Any application by the marketing authorisation holder to vary a marketing authorisation granted in accordance with the provisions of Ministerial Decision 32221/2013 shall be submitted to the National Organization for Medicines (EOF), provided that EOF has already authorised the medicinal product concerned, as well as to other member states that have authorised the medicinal product concerned.

Medical devices

Not applicable for medical devices, since no marketing authorisation is required.

Law stated - 29 June 2023

Renewal

What are the main requirements relating to renewal of authorisations for medicinal products and medical devices?

Medicinal products

Marketing authorisation for medicinal products is valid for five years and it may be renewed after five years, following a reassessment of the risk-benefit balance by EOF. In this respect, the marketing authorisation holder shall provide EOF with a consolidated version of the quality, safety and efficacy dossier, including an assessment of the data contained in the reports of suspected adverse reactions and periodic safety update reports submitted in accordance with Ministerial Decision 32221/2013 and all information on variations made since the marketing authorisation was granted, at least nine months before the marketing authorisation expires. If renewed after the first five-year period, the marketing authorisation shall be valid indefinitely, unless EOF decides, for pharmacovigilance reasons, including the exposure of an insufficient number of patients to the medicinal product concerned, to request the submission of a dossier for a further five-year renewal.

Medical devices

Not applicable for medical devices, since no market authorisation is required. For the conformity assessment, Regulations 2017/745 and 2017/746 are applicable.

Law stated - 29 June 2023

Transfer

How easy is it to transfer the existing approvals or rights to market medicines and medical devices? How long does this take in general?

Medicinal products

In general, and without prejudice to any special circumstances, transfer of an existing marketing authorisation of medicinal products before EOF takes around six months to be completed.

Medical devices

Not applicable for medical devices, since no marketing authorisation is required. For the transfer of CE mark of medical devices, Regulations 2017/745 and 2017/746 are applicable.

Law stated - 29 June 2023

RECALL

Defective and unsafe products

What are the normal requirements for handling cases of defective or possibly unsafe products, including approvals required for recall and communication with health professionals?

Medicinal products

In principle, marketing authorisation holders and/or distributors that commercialise a medicinal product have the obligation to have in place an emergency plan to ensure the effective implementation of any measure to withdraw medicinal products from the market ordered by the National Organization for Medicines (EOF) or decided in cooperation with the manufacturer or the marketing authorisation holder of the medicinal product concerned.

Further, the marketing authorisation holder of a medicinal product must immediately inform EOF and the competent authorities of other member states concerned of any action taken by the marketing authorisation holder to suspend the marketing authorisation or withdraw a medicinal product from the market and, where such action relates to the efficacy of the medicinal product or the protection of public health, must state the reasons for it. EOF shall ensure that this information is communicated to the European Medicines Agency.

In addition to the above, EOF has the authority to prohibit the placing on the market of the medicinal product and require its withdrawal from the market when it is considered that:

- the medicinal product is harmful;
- lacks therapeutic efficacy;
- the risk/benefit balance is not favourable to the benefit;
- the medicinal product does not have the declared qualitative and quantitative composition; or
- controls on the medicinal product and/or on the ingredients and intermediate stages of manufacture have not been carried out or where another requirement or obligation relating to the granting of the manufacturing authorisation has not been complied with.

EOF may limit the prohibition of marketing and withdrawal from circulation only to those batches that are disputed.

EOF may in exceptional cases, in respect of a medicinal product whose marketing has been prohibited or suspended or that has been withdrawn from the market for the reasons analysed above, authorise its marketing to patients to whom the medicinal product is already administered during a transitional period to be determined by EOF's decision while the administration of another treatment is pending.

If there are suspicions that a medicinal product poses a serious risk to public health, EOF, if the product has been detected for the first time in Greece, sends without delay a rapid alert notification to all competent authorities of the other member states and to all operators in the supply chain in Greece. In the event that such medicinal products are considered to have been supplied to patients, urgent public notifications are issued within 24 hours to recall such medicinal products from patients. These notifications shall contain sufficient information on the suspected quality defect or falsification and on the risks involved.

Law stated - 29 June 2023

ADVERTISING AND PROMOTION

Regulation

Summarise the rules relating to advertising and promotion of medicinal products and medical devices, explaining when the provision of information will be treated as promotional. Do special rules apply to online advertising?

Medicinal products

According to article 118-132 of Ministerial Decision 32221/2013, it is prohibited to advertise to the public: medicinal products (1) that may be administered only on prescription, (2) containing psychotropic or narcotic substances (within the meaning of international conventions such as the 1961 and 1971 UN Conventions)

Further, the National Organisation of Medicines (EOF) prohibits any advertising of a medicinal product that has not been granted with a marketing authorisation in accordance with Ministerial Decision 32221/2013 or Regulation EC/726/2004.

All elements of the advertising of a medicinal product must correspond to the information contained in the summary of product characteristics.

Further, according to article 123 and 124 of Ministerial Decision 32221/2013, any advertisement of a medicinal product addressed to persons authorised to prescribe or supply the medicinal product shall include:

- the essential information corresponding to the summary of product characteristics.
- the classification of the medicinal product with regard to the conditions of administration, the selling price or indicative price of the various packages;
- an explicit and legible request to report any suspected or likely adverse reaction directly to EOF, in accordance with the national adverse reaction reporting system;
- all information contained in the promotional document shall be accurate, up to date, verifiable and sufficient to enable the recipient to form a personal opinion on the therapeutic value of the medicinal product; and
- references, tables and other illustrations taken from medical journals or scientific literature used in the prospectus shall be faithfully reproduced and their source shall be clearly indicated.

Labelling and patient leaflets, correspondence, accompanied where appropriate by any other non-promotional documents, required to answer specific questions about a particular medicinal product, the specific information and

related documents concerning, for example, changes of packaging, warnings concerning adverse reactions in the context of the general precautions for medicinal products, as well as sales catalogues and price lists, provided that they do not contain any information relating to the medicinal product, as well as information on human health or diseases, where no direct or indirect reference is made to medicinal products are explicitly exempted from the above regulations governing advertisement.

With regard to advertising of non-prescription medicines that is addressed to the public, special rules apply, focusing mainly on the prohibition of any misleading or exaggerating claims.

Further, circular of EOF under No. 37201/2020 governs, along with Ministerial Decision 32221/2013, the sponsoring of scientific events and the participation of HCPs in scientific events by pharmaceutical companies.

The Hellenic Association of Pharmaceutical Companies (SFEE) Code of Conduct is also applicable as 'soft law' with regard to advertising of medicinal products.

In respect of online advertising of medicinal products, in the absence of more specific national regulations or guidelines that might suggest otherwise, this is subject to the same rules applicable to advertising through any other means.

Medical devices

Advertising of medical devices is in principle governed by Regulations 2017/745 and 2017/746.

Further, pursuant to the Ministerial Decision, advertising and promotional material in general must accurately reflect the intended use of the product. Any advertising, presentation or communication that directly or indirectly attributes or implies to the medical device any misleading properties that are not related to the properties of the product is prohibited. All relevant material, whether printed, visual, audio, audio-visual, audiovisual, electronic or in any other way presented and transmitted is subject to the repressive control of EOF.

Moreover, it is prohibited to advertise, distribute, sell and in any way make available to the general public in vitro diagnostic reagents for the detection or confirmation of HIV infection or antibodies to HIV (of all types) in the form of a self-testing kit (ie, for home use by non-experts). These products may be advertised, made available and sold only for professional use in laboratories specifically dedicated to these tests.

In respect of online advertising of medical devices, in the absence of more specific national regulations or guidelines that might suggest otherwise, this is subject to the same rules applicable to advertising through any other means.

Code of Conduct of SEIV is also applicable as soft law with regard to advertising of medical devices.

Law stated - 29 June 2023

Inducement

What regulations exist to discourage the provision of inducements to healthcare professionals to prescribe, sell, supply or recommend use of a particular medicinal product or medical device?

Medicinal products

Pursuant to article 126 of Ministerial Decision 32221/2013 and article 16 of Law 97/1973, it is provided that in the context of promoting the sale of medicinal products to persons authorised to prescribe or supply medicinal products, it is prohibited to give, offer or promise to such persons any gift, pecuniary benefit or benefit in kind, except for items of negligible value related to the profession of doctor or pharmacist.

Further, hospitality, in the context of sales promotion events, shall always be strictly limited to the main objective of the

event and shall not extend to persons other than health professionals. EOF has also issued circular No. 37201/2020 pertinent to scientific events.

SFEE Code of Conduct further provides that offering or promising any gifts, money or benefits in kind relevant to the profession of a physician or pharmacist to persons authorised to prescribe or administer medicines is prohibited, save where the items offered are of immaterial value (ie, not exceeding €15 per piece, VAT included).

With regard to medical devices, in the framework of advertising and direct or indirect promotion thereof, it is prohibited to provide any remuneration or exchange of any kind to physicians, pharmacists or to any other person who, by virtue of his or her position, profession, official or other status, is in a position to favour or generally facilitate the intended promotion or consumption.

Non-compliance with the conditions for advertising and information on medicinal products is subject to EOF's control.

In the case of violation of the provisions of Ministerial Decision 32221/2013 on information and advertising of medicinal products and Law 96/1973 in relation to both medicinal products and medical devices, EOF has the authority to impose sanctions of article 19 of Law 96/1973, as in force, and as specified in article 175 paragraph 2 of Ministerial Decision 32221/2013. In particular:

- administrative fine up to €22,000; and
- recall of Product Marketing Authorisation.

In the case of repetition of the infringement:

- an administrative fine up to € 44,000.

Law stated - 29 June 2023

Reporting transfers of value

What requirements apply to recording and publishing details of transfers of value to healthcare professionals and organisations by companies marketing medicinal products or medical devices?

Pursuant to article 66 paragraph 7a of Law 4316/2014, pharmaceutical companies have a legal obligation to disclose on their website and on the special website of EOF, either individually or in aggregated form, where this is required, every payment and/or transfer of values that they provide to third-party healthcare professionals and scientific healthcare organisations, including but not limited to, donations, sponsorships, registration costs for conferences and scientific events, as defined in particular in the relevant circulars of EOF, travel and accommodation expenses and any other contractual or discretionary benefits relating to the promotion of prescription medicines, where required by the applicable regulatory and legislative provisions.

Law stated - 29 June 2023

Enforcers

Describe the bodies involved in monitoring and ensuring compliance with advertising controls for medicinal products and medical devices, distinguishing between any self-regulatory framework and control by the authorities.

The bodies involved in monitoring and ensuring compliance with advertising controls are for both medicinal products

and medical devices, the EOF and for medicinal products, the SFEE and for medical devices the Association of Companies of Medical and Biotechnological products (SEIV), both of which are bodies that have been formed by pharmaceutical companies or companies of medical and biotechnological products respectively, that are established in Greece to serve self-regulation purposes.

Law stated - 29 June 2023

Sanctions

What are the possible financial or other sanctions for breach of advertising and promotional controls for medicinal products or medical devices?

Control by the authorities

In the case of violation of the provisions of Ministerial Decision 32221/2013 on information and advertising of medicinal products and Law 96/1973 in relation to both medicinal products and medical devices, EOF has the authority to impose the sanctions of article 19 of Law 96/1973, as in force, and as specified in article 175 paragraph 2 of Ministerial Decision 32221/2013. In particular:

- administrative fine up to €22,000; and
- recall of product marketing authorisation.

In the case of repetition of the infringement:

- administrative fine up to €44,000.

Self-regulatory framework: SFEE

Sanctions by the Primary Committee:

- financial penalty of up to €25,000;
- correction of promotional material and obligation of the pharmaceutical company concerned to send the corrected material to its recipients accompanied by a letter indicating the amendments; and
- publication of the text of the decision directly on the SFEE website

In the case of non-compliance – sanctions by a secondary committee:

- re-imposition of the above sanctions imposed by the Primary Committee;
- financial penalty of up to €50,000; and
- publication of the relevant decision on the SFEE website.

In the case of repeated non-compliance by the pharmaceutical company or member of SFEE with the decision of the secondary committee, the latter shall refer the matter to the SFEE Disciplinary Board, which may decide to remove the member from the association. That decision shall be published on the website of the SFEE.

Law stated - 29 June 2023

OFF-LABEL USE AND UNLICENSED PRODUCTS

Off-label use

May health professionals prescribe or use products for 'off-label' indications? May pharmaceutical companies draw health professionals' attention to potential off-label uses?

Article 12 of Law 3816/2010 provides that medicinal products on the reimbursement list may be prescribed and reimbursed by the Hellenic Health Insurance Fund (EOPYY) for indications, combinations and dosages that are not included in their approved indications, as defined in the summary of product characteristics, only if they are included in treatment protocols that are consistent with and based on the relevant international guidelines, have been proposed by the competent scientific companies and have been approved by Central Board of Health of the Ministry of Health (ΚΕΣΥ).

Off-label medicines may be administered and reimbursed by the Hellenic Health Insurance Fund only in exceptional cases and in accordance with the references of international literature and documented on an individual basis, following a substantiated request from healthcare providers through the Electronic Pre-Approval System (ΣΗΠ), which (request) is examined and addressed by EOPYY.

With regard to promotion, in Greece the promotion of off-label use is strictly prohibited.

Under special circumstances, EOF may temporarily use a medicinal product for 'off-label' indications in order to address potential or confirmed dispersal of pathogens, toxins, chemical agents, or nuclear radiation that may cause harm. In this case, marketing authorisation holders, manufacturers and healthcare professionals are not liable for civil or administrative liability for consequences arising from said use, while the provisions of Law No. 2251/1994 on Consumer Protection shall apply.

Law stated - 29 June 2023

Unlicensed products

What rules apply to the manufacture and importation and supply to healthcare providers of unlicensed medicines or medical devices?

In principle, unlicensed medicinal products may not be imported or distributed. The same applies to medical devices that are not in conformity with the applicable requirements.

Under special circumstances, EOF may temporarily authorise the distribution of a non-authorised medicinal product to address potential or confirmed dispersal of pathogens, toxins, chemical agents or nuclear radiation that may cause harm.

Further, to meet special needs, medicinal products may be administered on a bona fide and voluntary order, prepared in accordance with the specifications of an authorised healthcare professional in order to be administered to a specific patient of his or her, under his or her direct personal responsibility.

By virtue of Law 4512/2018, the attending physician may, through Electronic Pre-Approval System (ΣΗΠ), apply electronically for foreign medicines that are not available in Greece in order to cover the needs of a specific patient. The electronic management and examination of such requests regarding the necessity of the use of the reimbursement of medicines that have not been authorised in Greece are conducted through ΣΗΠ.

Law stated - 29 June 2023

Compassionate use

What rules apply to the establishment of compassionate use programmes for unlicensed products?

Pursuant to Ministerial Decision No. 85037/2011, as in force, by way of derogation of article 7 of Ministerial Decision 32221/2013, according to which no medicinal product may be placed in the market without a marketing authorisation, EOF may issue a temporary authorisation for early access to medicinal products (compassionate use) for patients or groups of patients suffering from a disease that causes chronic or severe disability or life-threatening conditions for which no satisfactory treatment with authorised medicinal products has been achieved. The duration of the programme is limited (one year). An extension may be granted only if the conditions for its approval continue to be met and is specifically and adequately justified on public health grounds. Once that medicinal product is authorised, the provisional early access authorisation ceases to be valid.

The management and examination of requests regarding the need for reimbursement of early access medicines that are not provided free of charge by the marketing authorisation holder or the local representative and for which the granting of a temporary individual authorisation is requested by EOF, is performed through the Electronic Pre-approval System (ΣΗΠ).

Law stated - 29 June 2023

SALE AND SUPPLY

Regulation

Are there special rules governing the dispensing or sale of particular types of medicinal products or medical devices?

General rules on the sale and dispensing of medicinal products are set out in Ministerial Decision 32221/2013. The provisions provide specific rules depending on the type of medicinal product. For example, dispensing of narcotic medicinal products requires a specific prescription note, and dispensing of these medicinal products must be notified annually to the National Organization for Medicines (EOF) for control purposes.

Law stated - 29 June 2023

Online supply

What laws and guidelines govern online dispensing, sale and supply of medicinal products and medical devices?

Medicinal products

Online dispensing, sale and supply of prescription medicinal products is not permitted according to the Greek Law. For non-prescription medicines and particularly for medicines that, according to their marketing authorisation, have been classified in the subcategory of pharmaceutical products of general distribution (general distribution medicines or GEDIFA) as defined in Ministerial Decision No. 51194/2016, distance selling to the public via information society services is permitted by the electronic pharmacy shops certified by the legal entity governed by public law Panhellenic Pharmaceutical Association in accordance with the provisions of Ministerial Decision 20293/2016.

Violators are fined from €20,000 to €100,000, and in the case of a repeat violation from €50,000 to €200,000, by decision of the board of the EOF.

The above penalties shall be imposed cumulatively with any other penalty provided for by the applicable legislation.

Medical devices

There is no specific regulation for the online sale of medical devices in Greece, thus provisions of Regulation 2017/745 apply.

Law stated - 29 June 2023

Pricing and reimbursement

What are the controls imposed on pricing of medicines and medical devices and reimbursement by national social security systems that are applicable to manufacturers, distributors and pharmacists?

Medicinal products

The price of reference medicinal products within their data protection period and after the expiry of their data protection period, is defined as the average of the two lowest prices of the member states of the Eurozone, and in any case may not be lower than the daily treatment cost set by decision of the Minister of Health (for the time being it is set at €0.20).

The price of reference medicinal products within their data protection period and after the expiry of their data protection period – if it is higher than the average of the two lowest different prices of the member states of the Eurozone according to the applicable price bulletin – shall be reduced in each repricing by up to 7 per cent of the price of the immediately preceding price bulletin, subject to a threshold of the average of the two lowest different prices of the member states of the Eurozone. Medicines with a Daily Treatment Cost lower (€0.20) are not repriced.

The price formed on the basis of the above (inter alia) pricing rules is the manufacturer price (ex-factory).

Based on the ex-factory price, wholesale, retail and hospital price are determined and included in the Price Bulletin.

The rules for the formulation of the wholesale, retail and hospital prices are specified in Ministerial Decisions (Medicinal Products' Pricing Regulations). The Pricing Regulation currently in force is Ministerial Decision No. 82331/2019.

With regard to generic medicinal products, the price thereof is set at 65 per cent of the price of the corresponding reference product after the expiry of its data protection period. The maximum amount of price reduction for generics during the repricing is set at up to 7 per cent of the price of the immediately preceding Price Bulletin.

The state and the social security funds reimburse medical prescriptions only if they include medicinal products contained in a list of prescription-only medicinal products and only for the approved indications as specified in the summary of product characteristics.

Reimbursable medicinal products are included by virtue of respective ministerial decisions in the 'Reimbursement List' following the successful completion of evaluation and negotiation process with special committees of the Ministry of Health established for this purpose.

For the calculation of the reimbursement price of each medicinal product, a special formula is used, based on the reference price of the medicinal product and the number of daily doses thereof.

Medical devices

In principle, pricing of medical devices is not subject to strict controls as analysed above about medicinal products. The reimbursement price of medical devices is determined on the basis of the average of the three lowest market prices in countries of the European Union, following negotiation of the providers with the negotiation committee (Ministry of Health). Until the completion of the procedure before the Negotiation Committee, the EOF may, by the decision of its board of directors published in the Government Gazette, set maximum prices, inter alia, for medical devices.

Law stated - 29 June 2023

UPDATE AND TRENDS

Forthcoming legislation and regulation

Is there any current or foreseeable draft legislation or other rules that will affect the regulation of pharmaceuticals and medical devices? What is likely to change, and what steps need to be taken in preparation?

In our opinion, the forthcoming revision of EU pharmaceutical law will significantly affect the regulation of pharmaceuticals in Greece.

Law stated - 29 June 2023

Jurisdictions

Australia	Clayton Utz
Austria	Preslmayr Attorneys at Law
Brazil	Kasznar Leonardos
Canada	Stikeman Elliott LLP
China	East & Concord Partners
Colombia	OlarteMoure
Denmark	Accura Advokatpartnerselskab
European Union	DLA Piper
France	Intuity
Germany	Ehlers Ehlers & Partner
Greece	PotamitisVekris
India	ANA Law Group
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Italy	Avvocati Associati Franzosi Dal Negro Setti
Japan	Atsumi & Sakai
Malaysia	Raja, Darryl & Loh
Mexico	OLIVARES
Serbia	BDK Advokati
South Korea	Lee & Ko
Spain	Faus & Moliner
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Switzerland	Wenger Vieli Ltd
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