LEXOLOGY®
Navigator

Life Sciences: Product Regulation and Liability
in Greece

Table of contents

Trends and developments

- Legal developments

Legal framework

- Legislation
- Regulation

Supply

- Manufacture
- Distribution
- Import and export
- Sale and purchase
- Named patient supply

Clinical trials

- Authorisation
- Clinical practices
- Reporting, disclosure and consent
- Insurance
- Data protection

Marketing authorisation

- Authorisation

Pharmacovigilance

- Monitoring
- Data protection

Pricing and reimbursement

- Pricing
- Reimbursement

Advertising and labelling

- Advertising
- Labelling

Relations with healthcare professionals

- Gifts and incentives

Liability

- Defect products
- Remedies
- Exclusion and limitation

Compliance and enforcement

- Enforcement
- Dishonest practices

Law stated date

- Correct as of

Contributors

Greece

KYRIAKIDES GEORGOPOULOS Law Firm
Irene C. Kyriakides
i.kyriakides@kglawfirm.gr

KYRIAKIDES GEORGOPOULOS Law Firm
Nefelie Charalabopoulou
n.charalabopoulou@kglawfirm.gr

Trends and developments

Legal developments

Are there any notable trends or recent legal developments in your jurisdiction's pharmaceutical industry?

Recently, there has been much discussion around changes in the Greek health system. The economic crisis and the Greek submissions in the three programmes of memorandum have provoked serious reconsideration of various healthcare issues, and various parameters of the life sciences sector will undergo amendment in the near future.

The Greek authorities are expected to introduce health technology assessments to the pharmaceutical sector as a way of assessing the interaction between science and technology in healthcare and disease prevention by July 2018. They will gather information from six other countries in order to formulate health policies that are safe, effective, patient focused and cost effective. The health technology assessment should be transparent, unbiased, robust and systematic, while also firmly rooted in research and scientific methodology.

Moreover, as a part of Greece's move towards full compliance with EU law, recent Joint Ministerial Decision G5a/59676/2016 provides for the establishment of a registry of contract research organisations and freelancers to promote safe clinical trials according to the law and good clinical practice.

Legal framework

Legislation

What is the primary legislation governing medicinal products in your jurisdiction?

The Greek pharmaceutical legislation is continuously evolving in an effort to align and comply with EU legislation and standards. The main operative legislative texts are:

- Ministerial Decision DYG3a/32221/2013 on the implementation of Directive 2001/83/EC of the European Parliament and of the Council on the Community Code relating to medicinal products for human use;
- Legislative Decree 96/1973 on the trading of pharmaceutical and cosmetic products;
- Law 1316/1983 on the establishment, organisation and competence of the National Organisation for Medicines, the National Pharmaceutical Industry, the State Pharmaceutical Warehouse and other provisions; and
- Ministerial Decision G5a/59676/2016 on the transposition of Regulation 536/2014 on clinical trials.
- In addition, various circulars are issued by the National Organisation for Medicines (EOF), the monitoring authority for pharmaceutical products, which operate as a means of practical interpretation of the applicable legislation.

The Hellenic Association of Pharmaceutical Companies (SFEE) also plays an important role in the formation of the Greek legislation. Its Code of Ethics (soft law) gives a useful insight into almost every aspect of the pharmaceutical environment, from clinical trials to market access, advertising and promotion.

Are any legislative changes proposed or expected in the near future?

See above.

Regulation

Which bodies regulate medicinal products in your jurisdiction and what is the scope of their powers?

The following bodies regulate medicinal products:

- the Ministry of Health – the ultimate state authority responsible for the regulation and definition of Greek pharmaceutical policy;
- the EOF – the national authority for the regulation and surveillance of the research, manufacturing, marketing and general handling of pharmaceutical and other products (eg, cosmetics, food supplements and veterinary products);
- the National Organisation for Healthcare – the national authority for the regulation and implementation of national insurance policy, including the reimbursement of medicines and collection of clawbacks and rebates;
- the Institute of Pharmaceutical Research and Technology, which imports, produces and distributes to the Greek market pharmaceutical products essential to public health which are not otherwise available locally;
- the SFEE – a self-regulated association which represents the interests of mainly multinational pharmaceutical

companies in Greece; and

• the Pan-Hellenic Pharmaceutical Association – an association that reflects the views and interests of Greek pharmaceutical companies.

Are any other legal regimes applicable to the trade of medicinal products (eg, competition, international trade, data protection, consumer protection)?

When it comes to the trade of medicinal products, most legal fields are applicable including, among others: data protection;

- consumer protection;
- intellectual property;
- competition;
- tax; and
- public law.

Are any medicinal products exempt from regulation (eg, complementary and alternative medicines)?

Any product that is considered to be 'medicinal' as defined under Article 1 of EU Directive 2001/83/EC, is regulated by law.

Supply

Manufacture

What is the authorisation procedure for the manufacture of medicinal products in your jurisdiction?

The manufacture of medicinal products is regulated by EU Directive 2001/83/EC and under the Community Code relating to Medicinal Products for Human Use (November 6 2001), as transferred into Greek law by Ministerial Decision DYG3a/32221/2013. The manufacture of original and generic medicinal products, is subject to holding an authorisation issued at national level by the National Organisation for Medicines (EOF). A manufacturing authorisation is required under the following circumstances:

- even if the medicinal products manufactured are designated for export;
- for total and partial manufacture; and
- for the various processes of dividing up, packaging or presentation.

However, such authorisation is not required for preparation, dividing up or changes in packaging or presentation where these processes are carried out solely for retail supply by pharmacists in dispensing pharmacies or persons legally authorised in Greece.

What is the fee for obtaining authorisation?

In order to apply for an authorisation, a fee of up to €3,000 for sterile medicines and €2,500 for non-sterile medicines must be paid. An additional fee of up to €500 per formulation for sterile medicines and €400 per formulation for non-sterile medicines also applies.

What is the validity period for authorisation?

There is no time limit. However, an authorisation can be suspended or revoked due to any violation of the relative law or a condition or obligation imposed when the authorisation was granted.

How robust are the standard good manufacturing practices followed in your jurisdiction?

Good manufacturing practices are strictly followed by pharmaceutical manufacturers and their adherence is continuously supervised by the EOF through regular inspections and audits of the manufacturing sites.

What are the consequences of failure to obtain manufacturing authorisation and/or follow good manufacturing practices?

According to Article 171 of Ministerial Decision DYG3a/32221/2013, if some of the conditions that must be fulfilled in order to maintain the authorisation are no longer satisfied, the authorisation may be suspended or revoked by the EOF. The manufacturing authorisation holder may also be liable in cases where good manufacturing practices are not followed, and may be held liable for any damages emerging from defective medicinal products.

Distribution

How are the distribution and storage of medicinal products regulated?

The distribution network for medicinal products is complex and usually involves many players. To this end, the relevant legal framework provides appropriate tools to assist the operation of the distribution chain. Specifically, the storage and distribution of medicinal products in Greece is mainly regulated by Ministerial Decision DYG3a/32221/2013, Presidential Decree 88/2004 on the organisation and operational standards of a pharmaceutical warehouse and the Guidelines on Good Distribution Practices of Medicinal Products for Human Use (2013/C 343/01). In addition, the EOF has issued various interpretative circulars, the most important of which are Circulars 96870/2014 and 5664/2014.

Import and export

How are the import and export of medicinal products regulated?

Ministerial Decision DYG3a/32221/2013 regulates the import and export of medicinal products in and outside Europe by making the EOF the responsible monitoring authority. Any import or export from third countries outside the European Union is subject to licensing from the EOF, which also supervises all aspects thereof.

Are parallel imports permitted in your jurisdiction?

Parallel trading of pharmaceuticals is a lawful form of trade between EU member states under the principle of the free movement of goods, and its significance has been emphasised on numerous occasions by EU and local jurisprudence. However, the practice of parallel trading has often caused supply problems for patients in low-price countries such as Greece. Parallel traders buy cheaper Greek stock with a view to repackaging and selling it to countries where prices are higher, thereby drastically reducing supplies for patients in Greece. Hence, parallel trading and, specifically for Greece, parallel exports are often named as the main cause for shortages in medicines without substitutions. Information about pharmaceutical shortages may be found on the EOF website. If the EOF deems shortages to pose a risk to public health, it usually imposes a temporary ban on parallel exports for medicines in short supply or fine the manufacturer for not maintaining a three months' stock for the domestic market as required by Article 29 of Law 1316/1983 and Ministerial Decision 88979/2015.

Sale and purchase

What rules govern the dispensing, sale and purchase of medicinal products?

According to Ministerial Decision DYG3a/32221/2013, a medicinal product may be placed on the local market only after it has obtained a marketing authorisation through the centralised or national procedure. When the EOF issues a marketing authorisation for a medicinal product, it may also classify it as prescription only. It also has discretion to qualify a product's classification further and impose stricter requirements for its administration and supply. In addition, the EOF regularly issues a list of all medicinal products that are being reimbursed by the social security funds and is assisted in that respect by the National Organisation for Healthcare, the national authority for the regulation and implementation of national insurance policy, under the auspices of the Ministry of Health.

Are there any restrictions on the online sale and purchase of medicinal products?

The online sale and purchase by the public of prescription-only medicinal products is strictly prohibited. For all other products (including over-the-counter medicines), online sale is permitted provided that it is carried out by lawfully operating online pharmacies.

Named patient supply

What rules govern named patient supply of pre-launch medicinal products?

Apart from the EU Orphan Medicinal Products Regulation (141/2000), at the national level, Law 1965/1991 states

that the Institute of Pharmaceutical Research and Technology (IFET) is the competent authority regarding the supply of pre-launch medicinal products. If a pharmaceutical product is deemed to be essential to the public but is not available from the local pharmaceutical industry (because it has no commercial benefit, is a new medicinal product without state approval (pre-launch) or its distribution has been discontinued), a specific procedure must be followed, beginning with the patient's doctor applying to the IFET.

Clinical trials

Authorisation

What is the authorisation procedure for conducting clinical trials in your jurisdiction?

The Good Clinical Practice authorisation procedure is governed by Ministerial Decision G5a/59676/2016, which implements the EU Clinical Trials Regulation (2014/536). A strict procedure must be followed, starting with written approval from the National Ethics Committee (NEC), the competent authority for the clinical trials in Greece, along with the National Organisation for Medicines. This approval should be given within 60 days (at most) of the study sponsor submitting the application and completed file. In the meantime, the Scientific Boards and Administrations of the Health Region Administrations of the relevant hospitals must also inform the NEC, within 30 days of the application, of any problems regarding the adequacy of the investigator and the suitability of the hospital facilities. In all cases of interventional clinical trials, the national template agreement must be used.

Clinical practices

How robust are the standard good clinical practices followed in your jurisdiction?

The Guideline on the Good Clinical Practice adopted by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use sets out a set of international ethical and scientific rules aimed to achieve a quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. In Greece, good clinical practices are adopted and, to that end, Greece participates in the Eudract and Eudravigilance databases in order to ensure the safety and transparency of clinical trials.

Reporting, disclosure and consent

What are the reporting and disclosure requirements for the results of clinical trials?

In accordance with Article 37 of EU Regulation 536/2014, the sponsor must notify each member state concerned following the completion of a clinical trial, as well as all third countries in which the clinical trial was conducted through the EU portal. Notification must be made within 15 days from the completion of the clinical trial in the last member state concerned and any third countries where the clinical trial was conducted.

Irrespective of the outcome the sponsor must submit a summary of the study's results to the EU database within one year from the completion of a clinical trial. This should be accompanied by a summary written in a manner that is understandable to laypersons. However, where for any scientific reasons detailed in the study protocol it is not possible to submit a summary of the results within one year, the summary must be submitted as soon as it is available. In this case, the protocol should specify when the results will be submitted, together with a justification. In addition to the summary of the results and the location where the clinical trial is intended to be used to obtain a marketing authorisation for the investigational medicinal product, the applicant must submit the clinical study report within 30 days of the grant of the marketing authorisation or withdrawal of the application to the EU database.

What are the informed consent obligations with respect to clinical trial subjects?

Every clinical trial subject must provide his or her informed consent to participation in writing, following an explicit and elaborate explanation by the physician in charge. Children under the age of 18 and persons incapable of representing themselves can also participate in clinical trials under certain conditions. In all cases, an interview must take place before the trial and a competent, qualified healthcare professional must ensure that the participant has understood the objectives, risks and the possible side effects of the study. Moreover, the subject of the clinical trials must be fully informed as to the duration and conditions of the clinical trial, as well as the cost and amount of insurance coverage. Finally, the subject of the trial is free to withdraw his or her consent at any time.

Insurance

What are the insurance requirements for clinical trials?

In order to conduct a clinical trial, the sponsor should conclude and maintain an insurance contract with a reputable insurer registered in an EU member state to cover the liability of the sponsor, principal investigator and research

members. Thus, the amount of the insurance contract should cover any damage or disability resulting from participation in the clinical trial and, in case of death or permanent disability to work, the reparation should be at least €200,000 per participant.

Data protection

What data protection issues should be considered when conducting clinical trials?

One of the issues commonly addressed in the context of a clinical trial is the use of subjects' personal data. The National Organisation for Medicines has explicitly taken the stance that the codified (anonymised) data of study subjects continues to be considered personal data and authorisation from the Data Protection Authority is necessary. Under the new General Data Protection Regulation (European Regulation 679/2016), which will enter into force in May 2018, compliance with the Data Protection Authority will no longer be required.

Marketing authorisation

Authorisation

What is the marketing authorisation procedure for medicinal products in your jurisdiction?

According to Ministerial Decision DYG3a/32221/2013, the National Organisation for Medicines (EOF) is the competent authority for granting marketing authorisation for medicinal products. The authorisation procedure begins with an application to the EOF, accompanied by the required relevant documents of clinical results, and cannot last more than 210 days.

What criteria are considered in granting marketing authorisation?

A marketing authorisation can be granted only to an applicant established in the European Union and the application should be accompanied by specific documents, proofs, test and clinical trial results and other reports. Less documents are required for a generic product, for which toxicological and pharmaceutical tests and the results of clinical trials need not be submitted, provided that the product under consideration corresponds to a reference product.

What is the fee for obtaining marketing authorisation?

According to Ministerial Decision DYA/171107/2008 on granting marketing authorisation for medicinal products designated for human use, a fee applies depending on the category of the application.

A complete file of scientific documents must be submitted:

- for a new or known active substance (complete file) – €20,000;
- if the licence is based on related literature combined with the applicant's studies – €20,000; and
- if the licence applies to well-established medicinal use – €18,000.

A complete file of scientific documents need not be submitted (simplified application) if:

- the application for marketing authorisation does not fall within the definition of a 'generic', with reference to the so-called product reference – €20,000;
- the application for marketing authorisation for a generic product has the same pharmaceutical form and content to the reference product and only a bio-equal potentiality study is required – €14,000;
- the application for marketing authorisation for a generic product has the same pharmaceutical form and content to the reference product without requiring a bio-equal potentiality study – €9,000; and
- the request for authorisation is submitted after a concession for data use of an already approved drug – €5,000.

The fee for a marketing authorisation if the application is based on a combination of known active substances is €20,000.

What is the validity period for marketing authorisation?

A marketing authorisation is valid for five years and can be renewed for consecutive five-year periods on application by the holder at least three months before the expiry date.

What are the consequences of failure to obtain marketing authorisation?

In case of a failure to obtain or maintain a marketing authorisation, the applicant or holder of the authorisation may not circulate the relevant medical products in the market, and depending on the grounds of the failure, more penalties could be imposed.

Pharmacovigilance

Monitoring

What post-market monitoring mechanisms are in place to ensure the ongoing safety and efficacy of medicinal products after marketing authorisation has been granted?

After obtaining marketing authorisation, there are both European and national mechanisms for supervising the safety and efficacy of pharmaceutical products. The pharmacovigilance system in the European Union operates between member states' regulatory authorities, the European Commission and the European Medicines Agency. In some member states, regional centres operate under the coordination of the national competent authority. The agency's role is to coordinate the EU pharmacovigilance system and to operate specific systems, services and processes as laid down in the EU legislation. The National Organisation for Medicines is the responsible authority for the pharmacovigilance in Greece.

Data protection

What data protection issues should be considered when conducting pharmacovigilance activities?

Every marketing authorisation holder has particular pharmacovigilance obligations to observe any adverse effects and report them to the competent Greek and European authorities. However, the data detailing adverse effects in patients should be handled carefully and according to the relevant Personal Data Law (2472/1997), which will be amended following the implementation of European Regulation 679/2016 (the General Data Protection Regulation).

Pricing and reimbursement

Pricing

Are there rules governing the pricing of medicinal products in your jurisdiction?

On the basis of Laws 4336/2015 and 4337/2015, and their implementing ministerial decisions, during the data protection period for reference products, the maximum producer's price is defined as the average of the three lowest prices in Europe for the same product. As a result, the expiry of the data protection period in combination with the marketing authorisation of the first respective generic medicine leads to a major price drop for the reference product. The price of generic products is easily defined at 65% of the price of the respective reference product after expiry of the data exclusivity period.

Reimbursement

What is the structure for state reimbursement of medicinal product costs?

In Greece, all medicinal products that require a prescription (apart from over-the-counter products) are reimbursed by social insurance. Reimbursement status is awarded on the basis of three categories according to disease severity and socioeconomic conditions of the beneficiary, as follows:

- the standard reimbursement rate is 75% (ie, patients participate by 25% in their pharmaceutical expenditure);
- treatments for chronic conditions (eg, osteoporosis, Parkinson's disease and coronary heart disease) attract a 90% reimbursement; and
- treatments for severe, debilitating or life-threatening disease (eg, cancer, multiple sclerosis and hormone deficiency) attract a 100% reimbursement.

The average co-payment rate is estimated at 15%.

Advertising and labelling

Advertising

How is the advertising of medicinal products to healthcare professionals and the general public regulated in your jurisdiction?

Legal provisions pertaining to the advertising and promotion of medicinal products may be found in various legislative acts and regulations, the most important of which are the following:

- Legislative Decree 96/1973 on the trading of pharmaceutical and cosmetic products;
- Law 1316/1983 on the establishment, organisation and competence of the National Organisation of Medicines, the National Pharmaceutical Industry, the State Pharmaceutical Warehouse and other provisions;
- Ministerial Decision Y6a/22261/2002 on the advertising of medicinal products that may be administered without prescription; and
- Ministerial Decision DYC3a/32221/29.4.2013 on the implementation of Directive 2001/83/EC of the European Parliament and of the Council on the Community Code relating to medicinal products for human use (Article 121 and following).

It is also worth noting that various circulars of the National Organisation for Medicines (EOF) also operate as a means of practical interpretation of the above referenced applicable legislation.

Finally, the Hellenic Association of Pharmaceutical Companies (SFEE) Code of Ethics, which regulates the promotion of pharmaceutical products by its members (ie, multinational pharma companies), can be considered a useful tool, rather than a legally binding instrument, since it adheres to the relevant legislation and incorporates concise and updated provisions in alignment to the relevant regulatory framework. In practice, the Code of Ethics is respected by the majority of pharmaceutical companies in Greece, irrespective of their actual SFEE membership.

Do any special rules apply to online advertising of medicinal products?

Pharmaceutical companies, when advertising their products online, must follow the same strict rules of advertising by other means, respecting the operating provisions regarding advertising to the general public on the one hand and to healthcare providers on the other.

Labelling

What are the packaging and labelling requirements for medicinal products?

Ministerial Decision DYG3a/32221/2013 sets out the rules in relation to the packaging and labelling of pharmaceuticals. Article 77 and following provide the information that must be included on the package of a medicinal product.

How is the promotion of off-label use regulated?

The law prohibits the advertisement of pharmaceutical products or indications that have not been approved or authorised by the National Organisation for Medicines. Information on off-label use of products may be given only by independent scientists to healthcare professionals to update them on new scientific developments, and not to the public in general.

Relations with healthcare professionals

Gifts and incentives

What rules apply to the provision of gifts, discounts and other incentives to healthcare professionals?

Articles 126 and 128 of Ministerial Decision DYG3a/32221/2013 prohibit pharmaceutical companies from offering gifts, benefits or promises of any kind to healthcare professionals as incentives to prescribe a medicinal product, except items of insignificant value (€10-€15) which are strictly related to their profession. This provision is also incorporated in Article 66 of Law 4316/2014 and the Hellenic Association of Pharmaceutical Companies Code of Ethics.

Liability

Defect products

How can a liability claim for a defective medicinal product be brought?

The holder of the marketing authorisation of a medicinal product is considered to be the manufacturer for the purposes of EU Directive 85/374/EEC, which means that it is held strictly liable for any damages emerging from defective medicinal products. On this basis, a liability claim can be raised in both the civil and criminal courts.

Which parties can be held liable for a defective medicinal product?

A marketing authorisation holder is liable for the pharmaceutical product at all stages of its circulation on the Greek market, and this liability cannot be restricted or excluded. The designation of a local representative does not exonerate a marketing authorisation holder from its liability, while the former is held independently liable in parallel.

Remedies

What remedies are available to successful claimants?

Depending on the claim and the harm suffered, successful claimants could be awarded all kinds of damage (including loss of profit and moral damages).

Exclusion and limitation

On what grounds can liability be excluded?

In accordance with local laws, in principle, liability cannot be excluded in any way.

What preventive steps can be taken to limit liability?

In principle, liability may not be excluded. However, actions such as an increased internal control system and an emergency plan can lead to positive results regarding the limitation of defective product incidents.

Compliance and enforcement

Enforcement

What measures are in place to enforce the laws governing medicinal products?

In general, the National Organisation for Medicines (EOF), as the supervising authority, enjoys extensive powers, both preventive and suppressive, for the purpose of enforcing the pertinent legislation. Indicatively, it can perform inspections, revoke licences, ban exports and order corrective actions and recalls. Articles 162 to 178 of Ministerial Decision YA DYG3a/GP 32221 also provide for serious penalties where the applicable law is violated, from recalls to fines.

Dishonest practices

What mechanisms are in place to combat bribery, fraud, collusion, counterfeiting and other dishonest practices in the pharmaceutical sector?

Apart from internal corporate responsibility and control systems that almost every pharmaceutical company employs, the EOF, in cooperation with the European Medicines Agency, also plays a significant role in combating bribery, fraud, collusion, counterfeiting and other dishonest practices, by ensuring the adherence to the relevant rules by all parties involved in the pharmaceutical industry. In that respect, the EOF has the discretion to cooperate with all relevant national authorities such as tax authorities, the public prosecutor and other competent state departments.

Law stated date

Correct as of

Please state the date as of which the law stated here is accurate.

April 2018