Medicinal product regulation and product liability in Turkey: overview

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A Q&A guide to medicinal product regulation and product liability law in Turkey.

The Q&A gives a high level overview of key issues including pricing and state funding, manufacturing, marketing, clinical trials, advertising, labelling, and product recall and liability.

For information on pharmaceutical patents, trade marks, competition law, patent licensing, generic entry, abuse of dominance and parallel imports, visit *Pharmaceutical IP and Competition Law in Turkey: overview*.

To compare answers across multiple jurisdictions, visit the Medicinal product regulation and product liability *Country Q&A tool*.

The Q&A is part of the global guide to life sciences law. For a full list of jurisdictional Q&As visit *global.practicallaw.com/lifesciences-guide*.

Regulatory overview

1. What are the main legislation and regulatory authorities for pharmaceuticals in your jurisdiction?

Legislation

The primary legislation is the Code on Pharmaceuticals and Pharmaceutical Preparations (*İspençiyari ve Tıbbi Müstahzarlar Kanunu*) No. 1262 (Pharmaceutical Code), which was published in the Official Gazette dated 26 May 1928. The Pharmaceutical Code is implemented through secondary legislation (such as regulations, communiqués, and guidelines) that further regulates all aspects of the pharmaceutical market.

Additionally, sector-specific legislation may have an impact on pharmaceuticals, although such legislation applies to various other fields that intersect with pharmaceuticals and are not regulated under the Pharmaceutical Code.

Regulatory authorities

The Turkish state is the main buyer in the pharmaceutical sector due to the broad coverage of public health insurance (with the entry into force of the General Health Insurance legislation, it is expected that everyone residing in Turkey will be included in state health insurance coverage).

The main regulatory authority is the Ministry of Health. It oversees the pharmaceutical sector through its independent institution, the Pharmaceutical Product and Medical Device Institution (Institution). The Institution regulates all aspects of pharmaceuticals, including marketing authorisation, production, pricing, import/export, and clinical trials.

2. Briefly outline how biologicals and combination products are regulated in your jurisdiction.

The definition of human medicinal products adopted by the Ministry of Health and the Pharmaceutical Product and Medical Device Institution (Institution) covers combination products and has been extended to regulate biological products. The secondary legislation and regulations covering human medicinal products also regulate biological and combination products to the extent applicable.

Under the Regulation on the Licensing of Medicinal Products for Human Use (Licensing Regulation), medicinal products for human use are defined as any natural and/or synthetic origin active substance or "combination" of substances administered to human beings with a view to treating and/or preventing a disease, making a diagnosis, or correcting or modifying a physiological function. Although the Licensing Regulation does not directly define biological products, they are referenced throughout the text.

There are additional guidelines issued by the Institution, which along with the Guideline on Biosimilar Medicinal Products provide details on which biologicals are medicinal products, such as those that both:

- Are produced or extracted from a biological source.

- Require some production process and control, along with a combination of physiochemical biological tests to determine the quality of their active substance.

3. Briefly outline how medical devices and diagnostics are regulated in your jurisdiction. Is there any specific regulation of health IT issues and mobile medical applications?

Medical devices and diagnostics are mainly regulated by the:

- Regulation on Medical Devices (*Tıbbi Cihaz Yönetmeliği*).
- Regulation on Active Implantable Medical Devices (*Vücuda Yerleştirilebilir Aktif Tıbbi Cihazlar Yönetmeliği*).
- Regulation on In Vitro Diagnostic Medical Devices (*Vücut Dışında Kullanılan (In Vitro) Tıbbi Tanı Cihazları Yönetmeliği*).
- Regulation on Sales, Marketing and Promotion of Medical Devices (*Tıbbi Cihaz Satış, Reklam ve Tanıtım Yönetmeliği*).
- Regulation on Clinical Trials of Medical Devices (*Tıbbi Cihaz Klinik Araştırmaları Yönetmeliği*).
- Regulation on Test, Control and Calibration of Medical Devices (*Tıbbi Cihazların Test, Kontrol ve Kalibrasyonu Hakkında Yönetmelik*).

The Ministry of Health and the Pharmaceutical Product and Medical Device Institution are planning an offset-like regime specifically for healthcare-related public private partnership (PPP) projects, by requiring participants to use or buy Turkish medical devices for certain portions of such tendered projects.

There is no specific regulation of health IT issues and mobile medical applications. However, promotional activities relating to those, which are generally the main point of concern, are subject to the regulations applicable to promotional activities for pharmaceuticals and medical devices.

Pricing, state funding and reimbursement

4. What is the structure of the national healthcare system, and how is it funded?

The Code on Fundamental Health Services No. 3359 authorises the Ministry of Health to issue healthcare regulations and establish an equal healthcare system, allowing every person living in Turkey to access it.

The Ministry of Health is in charge of establishing hospitals and public health institutions to provide medical services to the public. These services are funded by the state budget allocated to health services. Reimbursement of health services provided by health institutions such as physical examinations, operations, and medical tests, are generally covered under the general health insurance supported by the personal contributions of patients. Pharmaceuticals prescribed to patients are reimbursed through the reimbursement plan by the Ministry of Health, supported by direct personal contributions of individuals or deductions from the wages of public officials.

The Higher Education Code No. 2547 grants universities with medical faculties the authority to establish hospitals. Various university hospitals throughout Turkey have been established through this method.

Private hospitals are also common, especially in cities with a high population. Private health insurance coverage is very low in Turkey compared to state coverage.

5. How are the prices of medicinal products regulated?

With the new administrative regime introduced in Turkey in July 2018, the President has the authority to set principles for determining pharmaceutical prices through pricing decisions, on a proposal of the Ministry of Health.

The most recent Decree on the Pricing of Pharmaceuticals for Human Use (New Pricing Decree) was published in the Official Gazette on 24 February 2017 and entered into force on the same date. The New Pricing Decree abolished the previous decree, which was dated 15 June 2015 (Old Pricing Decree). Additionally, the Communiqué on the Pricing of Pharmaceuticals for Human Use (Communiqué on Pricing) was published in the Official Gazette and entered into force on 24 February 2017 to set out pricing principles and methods of calculation.

Similar to the Old Pricing Decree, the Ministry of Health has set up a reference price system. The New Pricing Decree replaced the terminology "reference country" and "reference price" by "origin country" and "real source price" (that is, the wholesale price of products licensed in the country of origin and put into the market of origin as announced in euros in the price list) respectively. Under the reference price system, the real source price, the calculation of which is explained in detail in secondary legislation, is taken into account to determine the prices. Accordingly, the prices of pharmaceuticals are set by determining the lowest real source price among the reference EU countries (France, Spain, Italy, Portugal and Greece). Prices can also be set by taking into account the lowest price in the country of import (other than the countries indicated above) or the country of batch release. The real source price is determined by taking the active substance and its form/dosage into account.

The Communiqué on Pricing also replaces the terms "20-year-old product" by "price-protected product". 20-year-old products were defined in the previous legislation as those which active substance(s) entered the market before 1 August 1987. The Communiqué on Pricing defines price-protected products as those that entered the market in their pharmaceutical form before 1 August 1987.

The source price of a non-price-protected reference product is 100% of the real source price until its generic enters the market. In the event of generic entry, the source price of the non-price-protected reference product is reduced to

60% of the real source price. Non-price-protected generic products can be priced up to 60% of the real source price. Price-protected generic products can be priced up to 80% of the real source price.

Products that are not subject to real source price regulations are (*New Pricing Decree*):

- Price-protected products with an ex-factory price under TRY8.09.
- Non-price-protected products with an ex-factory price under TRY4.24.

Certain exceptions apply for specific types of pharmaceuticals, such as orphan drugs.

Certain warehouse and pharmacy profit margins are also added above the price determined through the reference pricing system (along with VAT) to calculate the retail price of a product.

The Ministry of Health bases pricing on the euro exchange rate, which affects the prices of pharmaceuticals significantly. The New Pricing Decree introduced a new exchange rate ratio, which states that the real source price (known as reference price under the Old Pricing Decree) must now be calculated by taking into account 60% of the previous year's average EUR/TRY exchange rate as announced by the Turkish Central Bank. The exchange rate has been pegged to TRY3.40 for 2019.

6. When is the cost of a medicinal product funded by the state or reimbursed? How is the pharmacist compensated for his dispensing services?

The Social Security Institution (SSI) is in charge of the reimbursement of pharmaceuticals. The general scope of public health insurance is quite broad in Turkey, and therefore the SSI buys most pharmaceutical products sold in Turkey through the reimbursement system.

Pharmaceutical products to be reimbursed by the public health system must be registered with the reimbursement list of the SSI. This means that additional discounts up to 41% are applied to prices of products, depending on the determined price of the product under the Health Implementation Communiqué dated March 2013 (as amended periodically). In addition, the SSI introduced an alternative reimbursement regime that may also result in extra discounts to be applied to product prices, depending on case specific agreements negotiated and signed between pharmaceutical companies and the SSI.

As with the previous legislation, the Communiqué on Pricing sets the profit ratios of pharmaceutical warehouses and pharmacies to be applied over the ex-factory prices. Over-the-counter transactions for prescription drugs are still common, despite legislative efforts to combat this practice. Therefore, direct payment by patients to pharmacies is another source of income.

Clinical trials

7. Outline the regulation of clinical trials.

Legislation and regulatory authorities

Supplemental Article 10 of the Code on Fundamental Health Services No. 3359 introduced in 2011 is the basis for the regulation of clinical trials. Previously, clinical trials were governed by a clinical trials regulation issued by the Ministry of Health. However, the regulation was abrogated by the courts on the ground that such a crucial matter directly linked with human health cannot be legislated through a regulation but must be legislated on a statutory basis.

The Regulation on Clinical Trials of Medicinal Products for Human Use and Biological Products, and the Regulation on Clinical Trials of Medical Devices (Regulation on Clinical Trials) provide in-depth regulatory requirements. This legislation also takes into account the relevant EU directives on good clinical practices and the Ministry of Health's Good Clinical Practice Guideline.

The Pharmaceutical Product and Medical Device Institution's (Institution) Clinical Trials Department has the authority to rule on clinical trial-related issues, including applications.

Authorisations

Turkish clinical trials comply with internationally recognised standards through the Good Clinical Practices Guideline of the Ministry of Health, which is based on the World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects 1964.

Clinical trial sponsors must apply for authorisation from the Institution. The application file must include an ethics committee approval, although it is possible to simultaneously apply for authorisation from the Institution and approval from the ethics committee. Local ethics committees are established at university hospitals, training and research hospitals, and public hospital associations (*kamu hastane birlikleri*). There are around 100 ethics committees in different regions of Turkey. Details of them are in the Regulation on Clinical Trials.

The approval of one local ethics committee (of the co-ordinating clinical centre) is sufficient in multi-centre trials. The local ethics committee must give its opinion on:

- Procedure and documents used to inform trial subjects.
- Consent of trial subjects.
- Issues regarding rights, security and well-being of trial subjects.

Under the Regulation on Clinical Trials, sponsors have the right to apply and conduct trials through contract research organisations (CRO) domiciled in Turkey, but are required to do so if the sponsor does not have a representative in Turkey.

Consent

Clinical trial subjects or their legal representatives must be informed about the trial under the Regulation on Clinical Trials through an informed consent form, which must include the following information:

- Objective of the trial.
- Methodology of the trial.
- Expected benefits of the trial.
- Foreseeable risks, difficulties, and properties of the trial that may be unfavourable to the subject's health or personal traits.
- Conditions to conduct the trial.
- Subject's right to withdraw from the trial.

The informed consent form must be drafted in an easily understandable manner and give sufficient information. Informed consent form drafts must be submitted to the local ethics committees for their review and approval before initiation of a trial, along with the ethics committee approval application.

Trial pre-conditions

Under the Regulation on Clinical Trials, a sponsor entity must be present at every clinical trial. The sponsor is responsible for initiating, conducting and financing the clinical trial. The sponsor must have a presence in Turkey or work with a CRO in Turkey.

Under the Regulation on Clinical Trials, it is an obligation by law to protect trial subjects against risks that may arise, by taking out insurance policies on trial subjects. This obligation covers all clinical trials except for Phase IV clinical trials and observational studies.

For medical device clinical trials, insurance covering the medical devices and subjects of the trial must be provided, unless the:

- Medical device bears the CE mark.
- Medical device is used for the purpose designated by its producer.
- Relevant ethics committee determines that the benefit-risk ratio of the trial is appropriate.

Procedural requirements

Under the Regulation on Clinical Trials, the clinical trial must be conducted by a team appropriate to the nature of the trial. A principal researcher must lead the trial team.

In addition, if a new circumstance that could affect the safety of the trial subjects emerges, the sponsor or the researcher must take the necessary safety precautions to ensure the safety of the subjects and notify this to the relevant ethics committee and the Institution. Otherwise, the Institution can suspend the trial. Issues requiring

notification are set out in the Good Clinical Practices Guideline issued by the Ministry of Health. When a notification is filed, the ethics committee resolves on such applications in 15 days. The Institution then issues its decision within 30 days following receipt of the ethics committee decision.

Under the Regulation on Clinical Trials, the sponsor and the researcher must report serious adverse effects occurring during the clinical trial to the ethics committee and the Institution.

Manufacturing

8. What is the authorisation process for manufacturing medicinal products?

Application

Applications for manufacturing medicinal products in Turkey must be made to the Pharmaceutical Product and Medical Device Institution (Institution).

Conditions

On 21 October 2017, the Regulation on the Manufacturing of Medicinal Products (*Beşeri Tıbbi Ürünlerin İmalathaneleri Hakkında Yönetmelik*) (Regulation on Manufacturing) was published in the Official Gazette and entered into force and abolished the previous regulation on the same matter. The Regulation on Manufacturing sets out the conditions that must be met to obtain authorisation for manufacturing medicinal products, which are:

- Employing a production manager, quality assurance manager, quality control manager and sufficient personnel who have the necessary knowledge and experience of medicinal products, who are deemed responsible for the manufacturing process by the manufacturer and the Institution.
- Establishing a quality control group.
- Ensuring that the manufacturing facility complies with the guidelines of good manufacturing practices for medicinal products (global standards in relation to good manufacturing practices are followed in Turkey).
- Presenting workplace opening and operation permit and production flow schemes.
- Presenting an environmental impact assessment report if necessary.

Restrictions on foreign applicants

There are no specific restrictions on foreign applicants.

Key stages and timing

Article 5 of the Regulation on Manufacturing states that manufacturing site permits must be granted within 90 days of the application date. If the Institution requests the applicant to provide additional documentation, the applicant will have an additional 30 days to respond to such request. The 30-day period will stop once the applicant provides such documentation, and the remainder of the 90-day period will resume.

Fee

Fees for obtaining a manufacturing site permit differ depending on the application. The Institution publishes an annual list in Turkish on its website stating the fees for each type of application.

Period of authorisation and renewals

Manufacturing site permits are granted indefinitely, and remain in effect as long as authorisation holders remain in compliance with the application requirements.

Monitoring compliance and imposing penalties

The Institution is entitled to inspect the manufacturing site before or after granting the authorisation. The Institution is not obliged to give any prior notice regarding an inspection. At the end of an inspection, the Institution will prepare a report on the manufacturing site's compliance with legal requirements.

The manufacturing permit and/or the responsible manager's authorisation can be partly or fully cancelled or suspended if the manufacturing site does not comply with the Regulation on Manufacturing.

Under Article 18 of the Pharmaceutical Code, administrative fines from TRY17,094 to TRY854,804 (these amounts apply for 2019 and are adjusted annually) can be imposed for manufacturing, selling, and/or supplying medicinal products that do not comply with the legislation. Penalties are doubled for repeated violations.

Marketing

Authorisation and abridged procedure

9. What is the authorisation process for marketing medicinal products?

Application

An application to obtain a marketing authorisation for pharmaceutical products must be made to the Pharmaceutical Product and Medical Device Institution (Institution).

Authorisation conditions

Under Article 16 of the Licensing Regulation, the following criteria must be taken into account by the Institution when deciding whether to grant a marketing authorisation for a human medicinal product:

- Whether it is effective in its designated usage conditions.
- Whether the pharmaceutical product's safety has been proved.
- Whether the pharmaceutical product features the appropriate technical and pharmaceutical properties.

Article 7 of the Licensing Regulation requires legal entities applying for marketing authorisation to employ at least one person with an undergraduate diploma in pharmacy, medicine, or chemistry, who is also eligible to practise one of these professions in Turkey.

Detailed requirements and a list of documents to be provided alongside the marketing authorisation application are set out in Article 8 of the Licensing Regulation. The applicant must prepare a common technical document file (CTD) (OTD, in Turkish) and apply to the Institution. Details about the CTD file are stipulated in the guidelines issued by the Institution.

If a medicinal product is to be imported into Turkey, Article 8 of the Licensing Regulation requires that the applicant provide a certificate, along with its Turkish translation, indicating that the applicant is a representative authorised to import, authorise, and sell the medicinal product in Turkey.

Key stages and timing

The preliminary evaluation period for a marketing authorisation application is 30 days (if there is a lack of documentation, the Institution notifies the applicant of the missing documents and the applicant must submit the missing documents to the Institution within 30 days. The Institution will conclude the preliminary evaluation within 30 days of the applicant’s submission of the missing documents to the Institution). Except in extraordinary circumstances, once the preliminary evaluation period has ended, the Institution must issue a decision on the application within 210 days.

The Institution must decide on applications within 180 days for pharmaceutical products that meet any of the following criteria:

- Are original.
- Are innovative.
- Would reduce public healthcare expenditure.

However, in practice, obtaining a marketing authorisation for a new product in Turkey may take around two years. The procedure is often extended due to the Good Manufacturing Practices (GMP) certificate required by the Institution. Article 8 of the Licensing Regulation requires a GMP certificate for manufacturing facilities to be submitted with the application. If the manufacturing facility is in Turkey, the Institution issues the GMP certificate. If the pharmaceutical product is manufactured abroad, the GMP certificate can either be issued by the Institution or recognised by the Institution if it is granted by an authorised foreign institution.

The Institution does not recognise GMP certificates issued by a range of countries due to its mutual recognition policy. In this case, the Institution generally audits the relevant facilities itself and issues the GMP certificate for marketing authorisation applications in Turkey. The workload of the Institution, an insufficient number of

personnel, and delays due to audits performed abroad often forces marketing authorisation periods to last longer in practice than anticipated by the legislation.

Fee

Fees for marketing authorisation applications differ depending on the application. A detailed list of these fees is listed on the Institution's website (in Turkish).

Period of authorisation and renewals

A marketing authorisation for a human medicinal product is granted for five years.

To renew the marketing authorisation, information on the medical product's quality, safety, and effectiveness, along with pharmacovigilance data, must be submitted three months before the marketing authorisation's expiration date. Failure to renew the marketing authorisation within the five-year period does not automatically result in expiration of the marketing authorisation. In practice, the renewal procedure for pharmaceutical products is not always followed, and certain products are currently marketed without renewing their authorisations.

Monitoring compliance and imposing penalties

The Regulation on the Safety of Pharmaceuticals (*İlaçların Güvenliliği Hakkında Yönetmelik*) regulates the responsibilities of marketing authorisation holders, healthcare providers, health institutions, and the Institution to ensure the safety of pharmaceutical products with a marketing authorisation or with a pending marketing authorisation application.

The Institution is entitled to establish a pharmacovigilance system to collect data regarding the risks of pharmaceuticals. The Turkish Pharmacovigilance Centre (TUFAM) is the entity that collects this data on behalf of the Institution. TUFAM is a member of the World Health Organization's (WHO) Programme for International Drug Monitoring and sends data to the WHO on a regular basis.

Marketing authorisation holders must also establish their own pharmacovigilance system, appoint a pharmacovigilance officer from within the company, and set up a risk management system.

The Institution can require the marketing authorisation holder to submit its risk management system if a new issue arises that could alter the benefit-risk ratio of a pharmaceutical. The Institution can also require the marketing authorisation holder to submit data to demonstrate that the pharmaceutical has retained its benefit-risk ratio.

Under Article 32 of the Regulation on the Safety of Pharmaceuticals, the Institution is entitled to inspect the marketing authorisation holder or applicant. If the marketing authorisation holder is in breach of the Regulation on the Safety of Pharmaceuticals, the Institution will allow the authorisation holder anywhere from 15 days to three months to correct their breach and comply with the Regulation. The marketing authorisation will be suspended if the breach is not rectified within this period. Suspension of a marketing authorisation results in the cessation of the manufacturing and import of the pharmaceutical. If the product continues to be manufactured and marketed following the suspension or cancellation of a marketing authorisation, administrative fines and imprisonment sanctions may apply under the Pharmaceutical Code.

10. What commitments and pharmacovigilance obligations apply after a company has obtained marketing authorisation? Are there further conditions concerning how the drug is distributed and accessible to patients?

The Regulation on the Safety of Pharmaceuticals requires healthcare professionals and marketing authorisation holders to notify any observed adverse effects to the Turkish Pharmacovigilance Centre (TUFAM) within 15 days.

Article 24 of the Licensing Regulation imposes the following responsibilities for marketing authorisation holders:

- The medicinal product must be manufactured in compliance with the specifications of the Pharmaceutical Product and Medical Device Institution (Institution).
- Any amendment with regard to production and control of the medicinal product must be reported to the Institution.
- Any variations to the medicinal product must be notified to the Institution.
- Necessary precautions must be taken to prevent contamination or infection regarding biological medicinal products.
- Measures taken to reverse the suspension of a marketing authorisation or withdrawal of a medicinal product from the market must be reported to the Institution.

Under Articles 5 and 22 of the Regulation on the Safety of Pharmaceuticals, marketing authorisation holders must do all of the following:

- Notify the Institution of any changes that may modify the benefit-risk ratio of the pharmaceutical by tracking any recalls or limitations issued in other countries in which the pharmaceutical was granted authorisation and submitting periodic risk-benefit ratio reports.
- Establish a pharmacovigilance system and take any necessary precautions after receiving data from the system.
- Employ a full-time pharmacovigilance officer and inform the Institution of this appointment (this is not required if the duties of the pharmacovigilance officer are conducted by a contracted pharmacovigilance company).
- Maintain a main pharmacovigilance folder and submit it to the Institution when required.
- Form and maintain a risk management system.
- Report any adverse effects observed in Turkey within 15 days to TUFAM.
- Archive any possible adverse effects reported from any country where the pharmaceutical is marketed, and note any possible adverse effects that occurred during the post-authorisation safety studies.
- Continuously evaluate the safety of pharmaceuticals by preparing periodical reports regarding the benefit-risk ratio of pharmaceuticals.

11. Which medicinal products can benefit from the abridged procedure for marketing authorisation and what conditions and procedure apply? What information can the applicant rely on?

Under Article 9 of the Licensing Regulation, applying through the abridged procedure exempts the applicant from providing toxicological and pharmacological tests and results from clinical trials. This procedure is used for generic products entering into the market. At least one of the following criteria must be met to be eligible to benefit from the abridged procedure:

- The product is fundamentally similar to a medicinal product that has already been granted a marketing authorisation. Additionally, the holder of the marketing authorisation has allowed the applicant to use the data in the original application file.
- The components of the medicinal product have reasonable activity and admissible reliability settled in medical use.
- The applicant's generic medicinal product is fundamentally similar to an original medical product in which the data exclusivity period has expired. The data exclusivity period lasts for six years, starting from the date the product received marketing authorisation for the first time in the Turkish-EU Customs Union area. This period is only applied to products that received authorisation after 1 January 2005 (and for products that were authorised for the first time after 1 January 2001 and for which no generic application was filed until 1 January 2005).

12. Are foreign marketing authorisations recognised in your jurisdiction?

Foreign marketing authorisations are not recognised in Turkey.

Parallel imports

13. Are parallel imports of medicinal products into your jurisdiction allowed?

Parallel imports of medicinal products are not allowed in Turkey. A pharmaceutical product must be manufactured or imported under either a local marketing authorisation or an authorisation of a similar nature from the Pharmaceutical Product and Medical Device Institution (Institution).

However, free circulation of CE marked medical devices cannot be prevented if the registration obligation for certain devices is met through registration in the National Database of the Institution (TITUBB).

Restrictions on dealings with healthcare professionals

14. What are the restrictions on marketing practices such as gifts, sponsoring, consultancy agreements or incentive schemes for healthcare establishments or individual medical practitioners?

The Regulation on Promotional Activities of Medicinal Products for Human Use and the Regulation on Sales, Marketing, and Promotion of Medical Devices imposes certain restrictions and rules regarding the marketing of human medicinal products and medical devices. These are:

- Human medicinal products and medical devices that are only intended to be used by healthcare professionals or placed in the Social Security Institution's reimbursement list cannot be advertised to the public.
- The promotion of human medicinal products and medical devices (for which public marketing is prohibited) is only allowed if it is done through brochures, symposiums, meetings, or personal visits to healthcare professionals.
- The value of promotional materials/gifts cannot be more than 2.5% of the monthly gross minimum wage determined in Turkey (currently around TRY64).
- It is prohibited to encourage the prescription, use, and recommendation of medicinal products and medical devices by offering any benefits or incentives to healthcare professionals.

Symposiums or conferences sponsored by marketing authorisation or sales (for medical devices) permit holders that are attended by healthcare professionals are also restricted and closely monitored by the Pharmaceutical Product and Medical Device Institution in terms of the amount of sponsorship, place of the symposium or meeting, type of costs covered, and so on. Restrictions on donations also apply.

In addition, Article 29 of the Public Officials Code (*Devlet Memurları Kanunu*) and Article 15 of the Regulation on the Principles of Ethical Conduct of Public Officials (*Kamu Görevlileri Etik Davranış İlkeleri ile Başvuru Usul ve Esasları Hakkında Yönetmelik*) prohibit public officials from receiving or requesting gifts or any kind of benefits.

Receiving or providing a bribe is a criminal offence under Article 252 of the Criminal Code (*Türk Ceza Kanunu*). In line with the Criminal Code, apart from the sanctions imposed on both the briber and recipient of the bribe, special measures may be imposed on a legal entity that benefits from a bribe. These include:

- Cancellation of official permits, such as a marketing authorisation.
- Seizures of financial value, such as property and earnings.

Sales and marketing

15. What are the restrictions on selling medicinal products? Are there specific regulations for the sale of medicinal products on the internet, by e-mail and by mail order?

Article 28 of the Code on Pharmacists and Pharmacies (*Eczacılar ve Eczaneler Hakkında Kanun*) requires certain medicinal products to be sold exclusively at pharmacies. These include human medicinal products, traditional herbal products, dietary food, and infant formulas.

Article 24 of the Code on Pharmacists and Pharmacies prohibits the sale of medicinal products through the internet or any other kind of electronic platform. Therefore, the sale of medicinal products through the internet, e-mail, or mail order is not allowed in Turkey.

Advertising

16. What are the restrictions on advertising medicinal products?

Legislation and regulatory authority

The Pharmaceutical Code and the Regulation of Promotional Activities of Medicinal Products for Human Use and its related legislation regulate the advertising of medicinal products. The Pharmaceutical Product and Medical Device Institution (Institution) is the regulatory body.

Restrictions

Advertising to the public of human medicinal products is strictly prohibited in Turkey.

In relation to advertising directed at healthcare professionals, the Pharmaceutical Code prohibits advertisements that overstate and exaggerate the curative properties of medicinal products. Additionally, advertisements of prescription medicinal products can only be published in medical magazines and newspapers addressed to healthcare professionals. The Institution's prior approval must be obtained before publishing such advertisements.

Healthcare professionals and health institutions cannot take part in pharmaceutical product advertising without the prior approval of the Institution. Heavy administrative fines (up to five times the preceding year's total sales value of the product) are imposed on authorisation holders breaching the advertising restrictions.

Internet advertising

The advertising of medicinal products over the internet is strictly prohibited in Turkey.

Data protection

17. Do data protection laws impact on pharmaceutical regulation in your jurisdiction?

Turkey ratified the Strasbourg Convention for the Protection of Individuals with Regard to Automatic Processing of Personal Data 1981 (Strasbourg Data Processing Convention) on 18 February 2016, which ultimately led to the adoption of the Data Protection Law (DP Law) on 24 March 2016. The DP law was published in the Official Gazette on 7 April 2016 and entered into force on 7 October 2016, following a six-month grace period covering certain provisions. The DP Law is largely based on Directive 95/46/EC on data protection. The secondary legislation of the DP Law is slowly evolving.

The DP Law provides key definitions, such as personal data, processing of personal data, data controller, data processor, explicit consent, and anonymisation, and also sets out the principles for the processing, collection, transfer and protection of personal data, as well as the obligations of data controllers.

Data protection laws in Turkey have an impact on pharmaceutical companies dealing with health data. Sensitive personal data cannot be processed without the explicit consent of the data subject. However, sensitive personal data other than data relating to health and sexuality can be processed without explicit consent in cases required by law. Sensitive data relating to health and sexual life can only be processed without explicit consent for the purposes of protection of public health, preventive medicine, medical diagnoses, and financing of health services, and only by authorised legal entities or persons who are under an obligation of confidentiality. The status of pharmaceutical companies under this provision remains ambiguous. It is still to be clarified whether pharmaceutical companies that have a legal obligation to collect health data for adverse event reporting purposes will be given the same status as health institutions as described in this provision.

The Regulation on Personal Health Data (Health Data Regulation) was published in the Official Gazette dated 21 June 2019 and numbered 30808, and came into force on the same date. The Health Data Regulation addresses the personal health data processed by organisations affiliated with the Ministry of Health, as well as private and public legal entities processing personal health data. The Health Data Regulation complies with the DP Law and generally mirrors its provisions on the processing and protection of personal health data. The Health Data Regulation defines personal health data as "any information regarding the physical and spiritual health of identified or identifiable natural persons and information regarding health services provided to these persons". This covers patient data within the scope of adverse event notifications or clinical trials sponsored by pharmaceutical companies.

Data exclusivity provisions also apply (*see Question 11*).

Packaging and labelling

18. Outline the regulation of the packaging and labelling of medicinal products.

Legislation and regulatory authority

The Regulation on Packaging Information, Inserts, and Tracking of Medicinal Products for Human Use (Regulation on Packaging) was published in the Official Gazette on 25 April 2017 and entered into force the same day. The Regulation on Packaging abolished the previous regulation, namely the Regulation on Packaging and Labelling of Medicinal Products for Human Use, and is the main regulation for the packaging and labelling of medicinal products. The Pharmaceutical Product and Medical Device Institution (Institution) remains the competent regulatory authority.

Information requirements

The packaging of products must contain certain information, which can be summarised as follows (*Regulation on Packaging*):

- Name, strength, and pharmaceutical form of the medicinal product. If necessary, the name on the licence or permit approved by the Institution should be written, indicating if it is intended for babies, children, or adults.
- Unit amount, mode of administration, and weight or volume of the active substances.
- Number of units (tablets, ampoules, or bottles) in the package, and volume and weight or dosage number of active substances in pharmaceutical form.
- Names of excipients such as colourants, preservatives, antioxidants, flavouring substances, and alcohol.
- List of excipients known to have certain effects.
- Application method and instructions (if necessary).
- A special warning stating that the medicinal product must be stored away from children and in its package, as well as other special warnings (as necessary).
- Storage conditions of the medicinal product.
- A special warning regarding the disposal of unused products or waste products and the appropriate collection system if necessary.
- Recyclable symbol, number, and abbreviation of the package type.

- Manufacturer's and authorisation/permit holder's name and address.
- Medicinal product's authorisation or permit number.
- Medicinal product's batch number and expiration date.
- Medicinal product's expiration date.
- Instruction for users, if necessary.
- Applicable warnings.
- Whether the medicinal product is subject to a prescription,
- A barcode.
- Information on pricing (optional).

Other conditions

The product information on the packaging must be in Turkish, and product information in any official language of EU member countries can also be added (*Article 13/2, Regulation on Packaging*).

Product liability

19. Outline the key regulators and their powers in relation to medicinal product liability.

The Code on Preparation and Implementation of Technical Legislation in Relation to Products No. 4703 (Products Code) sets out the general framework for market monitoring and audits to be performed on any product put on the market in Turkey and can be regarded as the main legislation regarding product safety.

A draft Code on Product Safety and Technical Regulation has been prepared to replace the Product Code but has not yet been put into effect.

The general provisions of the Code of Obligations and the Consumer Protection Law also apply to issues regarding medicinal product safety and liability.

Under the Recall Regulation (*Geri Çekme Yönetmeliği*), the Pharmaceutical Product and Medical Device Institution (Institution) is the key regulator in the recall of medicinal products. Article 5 of the Recall Regulation provides the Institution with the power to do the following after it detects a defective medicinal product on the market:

- Demand information or an explanation from the responsible company.

- Evaluate the explanations of the responsible company and decide on the class and level of the recall.
- Follow up on the status of the recall.
- Halt production or import of the defective medicinal product if necessary.
- Finalise the recall process carried out by the responsible company and handle the procedures for closing the recall file.
- Take necessary precautions if the responsible company is deemed incompetent in the recall process.
- Authorise the medicinal product's release into the market if it finds that the defect has been corrected.
- Issue a second recall if necessary.

The Institution can impose penalties for non-compliance (*see Question 20*).

20. Are there any mandatory requirements relating to medicinal product safety?

The Regulation on the Safety of Pharmaceuticals regulates the mandatory provisions and responsibilities of marketing authorisation holders, healthcare providers, health institutions, and the Pharmaceutical Product and Medical Device Institution (Institution) to ensure the safety of pharmaceutical products (*see Question 9 and Question 10*).

For mandatory requirements regarding pharmacovigilance, see *Question 10*.

Under the recall regime, the responsible company must (*Article 6, Recall Regulation*):

- Implement a recall procedure.
- Notify the Pharmaceutical Product and Medical Device Institution (Institution) regarding any medicinal product that is or could be defective.
- Conduct the recall process.
- Provide explanations to the Institution regarding a possible recall.

The manufacturer of the defective medicinal product must indemnify the relevant parties for damage incurred due to the defective product and recall (*Article 16, Recall Regulation*).

The Institution can impose penalties specified under the Product Code in the case of breaches of the product safety and recall regulations. The Criminal Code and Code on Misdemeanours may also apply. The marketing authorisation of a pharmaceutical product that was not recalled despite a recall decision of the Institution or that does not have its recall file closed for three years will be suspended. If the recall file still remains open after a year, the suspension of the marketing authorisation will result in cancellation of the marketing authorisation.

21. Outline the key areas of law applicable to medicinal product liability, including key legislation and recent case law.

Contract

The following contractual relationships are formed in a typical supply chain of a pharmaceutical product:

- Manufacturer and pharmaceutical warehouse.
- Pharmaceutical warehouse and pharmacy.
- Pharmacy and consumer.

These relationships may weaken or prevent a consumer's direct contractual claims against the manufacturer of the pharmaceutical product under this route.

Tort

Under Article 49 of the Code of Obligations, a person who has caused damage to another person through a fault-based or unlawful act must pay compensation for this damage. To claim damages through a tort suit, the following elements must be established:

- An unlawful act.
- Fault of the perpetrator.
- Damage.
- A causal link between the unlawful act and the damage.

It is possible for a consumer to file a tort claim against the manufacturer of the pharmaceutical product. However:

- The prescription period for tort claims is just two years, which may be an obstacle to bringing a claim.
- It is common for a civil court to rule on its lack of jurisdiction, based on the consumer court jurisdiction, in product liability claims.

Pharmaceutical product liability claims are complex for consumer courts since they generally deal with basic claims.

Product liability (statute)

Under the Regulation on the Liability of Damages Raised from Defective Products (*Ayıplı Malın Neden Olduğu Zararlardan Sorumluluk Hakkında Yönetmelik*), a manufacturer/importer of a defective product is liable for any death, injury, or property damage caused by a defective product. This is a strict liability regime.

However, Article 7 of the Draft Code on Product Safety and Technical Regulation, which is not in force, would enable the manufacturer/importer to be liable only if the product does not comply with product safety measures (unlike the stricter condition for a product to be defective required by the current regulation).

22. Who is potentially liable for defective medicinal products?

A manufacturer and market authorisation holder that produces or imports a defective pharmaceutical product is liable in tort and under product liability legislation. However, in practice, physicians are pursued for complications caused by defective medicinal products through malpractice lawsuits. This is mainly because physicians are the first point of contact for patients, and patients are not usually able to distinguish malpractice claims from product liability claims.

23. What defences are available to product liability claims? Is it possible to limit liability for defective medicinal products?

Use and warning information contained in medicinal product package inserts provide specific defences to medicinal product liability claims, including defences such as abnormal use/misuse, assumption of risk, and intended user. There are also standard defences that can be invoked against any type of claim. For example, the defendant may request that the court dismiss a tort or product liability claim alleging that the elements required for bringing such a claim are not present. The defendant may also claim that the statute of limitations has expired, which would also result in dismissal of the case (*see Question 24*).

The most common legal actions in Turkey for what may otherwise have been product liability claims are malpractice claims (*see Question 22*), for which the normal procedural processes provide both a defence for medical practitioners and an obstacle to claimants. It is common for courts hearing malpractice lawsuits to appoint the Forensic Medicine Institution (*Adli Tıp Kurumu*) as an expert witness. Due to its workload, it takes around two years for the Forensic Medicine Institution to submit its expert opinion report to the court. It is also common for the Board of the Forensic Medicine Institution, which is composed of physicians, to conclude its expert opinion report in favour of the defendant physician. These issues are heavily criticised in practice.

24. How can a product liability claim be brought?

Limitation periods

For claims arising from contractual liability, the limitation period is two years from the transfer of the product from the seller to the buyer. The seller and buyer can agree on a longer period. The two-year limitation is inapplicable if the seller sells the product under gross fault.

For liability claims in tort, the limitation period is two years from the date when the claimant becomes aware of the damage and identity of the person liable for the damage. Claims become time barred after ten years.

Under Article 12 of the Consumer Protection Code, a two-year limitation period applies starting from the date the consumer receives the defective product. However, a longer term can be determined by legislation or by the parties. No limitation applies if the defect is hidden due to gross fault or fraud.

Class actions

Class actions are not allowed under Turkish law. However, under Article 113 of the Civil Procedure Code, associations and other legal entities can bring lawsuits to protect their members' interests. Therefore, it is possible for consumer associations to file class actions on behalf of their members for product liability claims.

25. What remedies are available to the claimant? Are punitive damages allowed for product liability claims?

For contractual liability, the consumer can claim the following remedies from the seller (*Article 227, Code of Obligations*):

- Cancel the contract by returning the product.
- Claim a discount on the purchase price.
- Claim repair of the product free of charge if the repair does not involve an excessive cost.
- Request replacement of the product with a non-defective product, if possible.

In tort law, the consumer can claim reimbursement for both material and immaterial damages. The court will determine the damages incurred by the consumer and rule on the amount sufficient to reimburse the damages.

Punitive damages are not allowed in Turkey.

Reform

26. Are there proposals for reform and when are they likely to come into force?

Several regulations were issued from 2017 concerning various aspects of the pharmaceutical sector, such as pricing, packaging, and manufacturing. These abolish the previous regulations, clarify uncertainties, and address complexity in the legislation:

- On 30 May 2017, the Pharmaceutical Product and Medical Device Institution (Institution) released a Draft Guideline on Biosimilar Medical Products (Draft Guideline). The Draft Guideline defines biological products as a human medicinal product for which the active substance or substances are produced from a biological source or purified from a biological source through a production process and control, along with a combination of physiochemical biological tests to determine the quality of their active substance. However, this Draft Guideline has not yet been issued by the Institution.
- On 8 November 2018, the Institution released a Draft Regulation on Licensing Medical Products for Human Use. The Draft Regulation further eliminates difficulties that may be faced in the licensing application process. This regulation is still a draft and has yet to be issued.
- The Institution prepared several draft secondary pieces of legislation on a variety of topics, such as homeopathic pharmaceuticals licensing, advanced treatment medical products, pharmacovigilance audits, Phase 1 clinical trial centres and sales, and the advertising and promotion of medical devices. However, they are still in draft form and have yet to be issued.

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