Recent Developments in Healthcare Legislation

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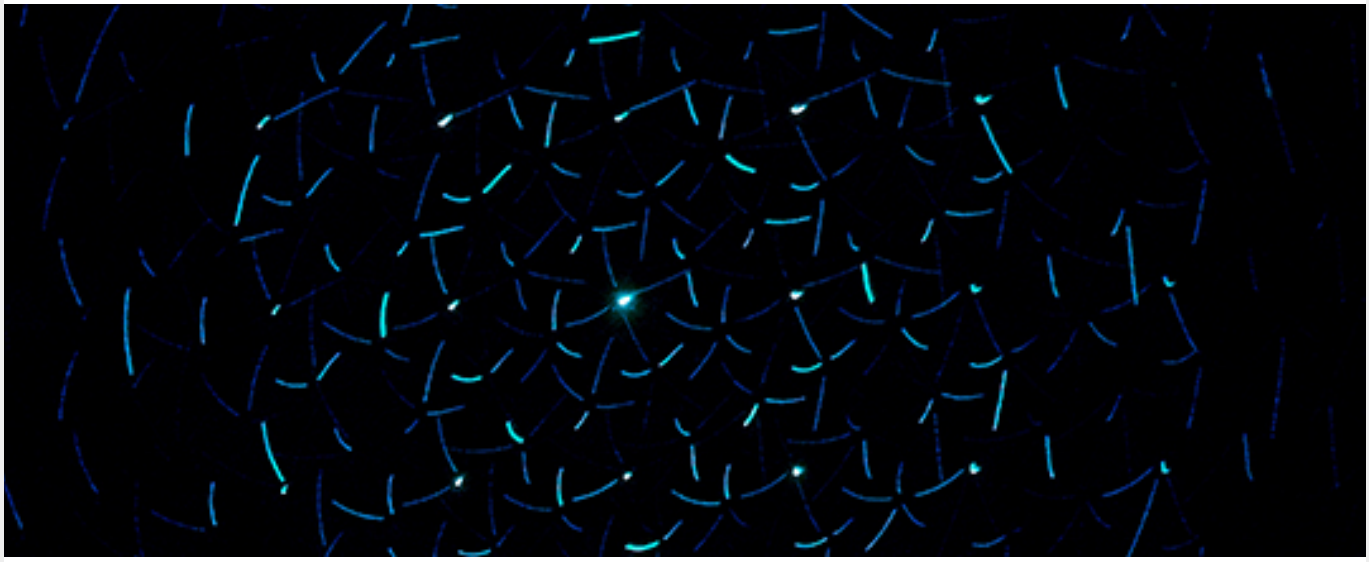

Dear Clients, Colleagues and Friends,

We would like to share with you a summary of the recent changes and developments in the healthcare legislation:

Guideline on Applications for Venues Within the Scope of Good Distribution Practices (GDP). Published and entered into force on 24 September 2022, this guideline provides guidance on activity permit applications within the scope of Good Distribution Practices to be filed by pharmaceutical establishments and transfer centres. The guideline includes explanations on the form and content of GDP activity permit applications and provides detailed information regarding the procedures in relation to the application process.

Amendments to the Regulation on the Licensing of Medicinal Products for Human Use. As per the amendment published in the Official Gazette dated 24 September 2022, a number of regulations on licensing of medicinal products for human use have been introduced for purposes of complying with the World Health Organisation ("**WHO**") and European Union legislation. In this context, among others, in case a licensing application is submitted to the Turkish Medicines and Medical Devices Agency ("**Agency**") for a product, which is identical to a product that has been approved by a foreign reference pharmaceutical agency, a licensing assessment period of 90 days -instead of the actual licensing assessment period of 210 days- will apply for the applications within the scope of reliance practices, where assessments of reference pharmaceutical agencies are taken into consideration. On the other hand, inconsistency in data regarding the formulation and quality of the product submitted in the licensing application has been included among the reasons for rejection of the application on merits.

In addition, on 14 December 2022, a number of further amendments have been made to the Regulation on the Licensing of Medicinal Products for Human Use. In this context, among others, it has been provided that if a nonconformity is detected in a medicinal product for human use, an assessment including product safety should be carried out by the Agency and the license of the medicinal product for human use may be suspended as per the outcome of this assessment. Further, it has been provided that the licensing processes of medicinal

products for human use such as blood products, immunological human products and industrially prepared radiopharmaceuticals must be completed by 31 December 2023.

Guideline on Reliance Practices Regarding the Licensing Process of Medicinal Products for Human Use. The Agency has published this guideline regarding reliance practices which came into spotlight with the amendment of the Regulation on the Licensing of Medicinal Products for Human Use dated 24 September 2022. The guideline sets out the criteria for acceptance of the assessments made by the WHO, the International Council for Harmonisation (*ICH*) and the Medicines and Healthcare products Regulatory Agency (*MHRA*), which have comparable standards with the Agency. Accordingly, in order for a medicinal product for human use to be accepted within the scope of reliance practices, it is required to be identical in terms of features such as composition, pharmaceutical form, intended use, storage conditions, production process, and place of production.

Circular on Medical Device Regulations. With this circular published on 30 September 2022, the Agency has introduced regulations on (i) employment of a compliance officer, (ii) obligation to make a registration notification to the European Database (*EUDAMED*), (iii) obligations of importers and distributors regarding labelling and repackaging of medical devices, and (iv) requirements on the Product Tracking System (*Ürün Takip Sistemi – ÜTS, in Turkish*).

Regulation on Serial Release of Vaccines and Immune Serums. The national serial release and launch to the market permit processes, which were previously regulated under the "Serial Release Guideline" published on 11 February 2022 are now regulated under the Regulation on Serial Release of Vaccines and Immune Serums dated 30 September 2022. The regulation provides a regulatory framework on the requirements for the vaccines and immune serums that are filled and/or manufactured in Turkey and vaccines and immune serums that are serially released abroad to be placed on the market.

Guideline on Pharmacovigilance System. The organisational structure and duties of the Agency's pharmacovigilance system as well as the duties of the Turkish Pharmacovigilance Centre (*Türkiye Farmakovijilans Merkezi – TÜFAM, in Turkish*) are covered in detail and the stakeholders of the pharmacovigilance system are listed under the guideline, which has been published on 30 November 2022. The guideline also provides on which topics the Agency and pharmaceutical companies, universities and healthcare professionals (which are among the stakeholders of the Agency) may contact Turkish Pharmacovigilance Centre within the scope of pharmacovigilance systems.

Announcement Regarding Implementing Regulations (EU) 2022/2346 and (EU) 2022/2347. On 16 December 2022, the Agency published an announcement on the regulations published by the European Commission ("**Commission**") regarding the product groups listed in Annex XVI of the Medical Devices Regulation. The Commission Implementing Regulation (EU) No. 2022/2346 published by the Commission regulates the common specifications to be applied to each and all Annex XVI devices. Within the scope of these specifications, risks to be considered in the phases of design, manufacturing, distribution and use and product-related information regarding contact lenses are included. For example, it is provided in light of product safety data that lenses should not be disinfected with tap water and liposuction product manufacturers should analyse and eliminate or minimize the risks such as inflammation in connection with the medical device. On the other hand, Commission Implementing Regulation (EU) No. 2022/2347 explains the risks of Annex XVI devices observed in light of scientific data and accordingly provides explanations for their reclassification.

Amendment to the Guideline on Applications for Good Manufacturing Practices (GMP) Inspections of Overseas Production Facilities. The fifth revision on the Guideline on Applications for GMP Inspections of Overseas Production Facilities entered into force on 27 December 2022. The guideline includes the procedures and principles regarding the applications for GMP inspections of medicinal products for human use to be

manufactured abroad and imported to Turkey, and provides details on the application processes. This version which is published within the scope of the Agency's efforts to be among the regulatory authorities listed by the WHO defines remote and/or hybrid inspection methods.

Amendment to the Guideline on Early Access to Medicines for Humanitarian Purposes Programme. With the Guideline on Early Access to Medicines for Humanitarian Purposes Programme "*Compassionate Use*", which entered into force on 19 January 2023, the guideline of the same name dated 1 January 2009 has been repealed. The guideline sets out the details of the objectives and conditions of the programme for the provision of medicinal products that are not licensed in Turkey to patients, free of charge, on humanitarian grounds in cases where no results can be obtained with medicinal products licensed or authorised in Turkey or standard medical methods, or in cases of life-threatening diseases and similar conditions.

Good Pharmacovigilance Practices (GPP) Guideline - Module XI. Among the GPP guidelines published in modules by the Agency, the Good Pharmacovigilance Practices (GPP) Guideline Module XI - Post-Marketing Benefit/Risk Assessment entered into force on 20 January 2023. The guideline stipulates the criteria to determine that the benefits of medicinal products for human use outweigh the risks, and in this version, the details on actions to be taken following the benefit/risk assessment, if deemed necessary by the Agency, are regulated. These actions include prohibition of supply of the product and suspension, cancellation or refusal to extend the validity period of the license.

Regulation on Licensing of Foods for Special Medical Purposes. Published in the Official Gazette dated 28 January 2023, the regulation will enter into force on 1 July 2023. The regulation introduces a licensing requirement for foods with special medicinal purposes, for which no license was previously required. As of 1 July 2023, foods with special medicinal purposes, which are not licensed will not be placed on the market. Further, a sales permit will need to be issued by the Agency for launching to the market the products for which licensing application is approved.

Regulation on Procurement of Pharmaceuticals from Abroad. The regulation which entered into force on 3 February 2023 provides for the procedures and principles (i) regarding procurement from abroad for personal use and with prescription of medicinal products for human use, which are not licensed in Turkey, or which are licensed but not available on the market, and (ii) of bulk procurement from abroad of medicinal products by hospitals. In this context, the Guideline on the Supply and Use of Pharmaceuticals from Abroad dated 23 October 2021 and its annexes were repealed.

In addition, in order to elaborate on the implementations regarding the Regulation on the Procurement of Pharmaceuticals from Abroad, the Guideline on the Procurement of Pharmaceuticals from Abroad was published on 20 April 2023 by revising the previous guideline, and thereafter a further revised version of the guideline was published on 25 April 2023. The guideline, *inter alia*, sets out the procedures regarding the application for supply of medicinal products from abroad in line with the provisions of the regulation, and provides for the requirements for conformity application of medicinal products for human use.

Guideline on License Renewal for Medicinal Products for Human Use. The guideline entered into force on 24 January 2023 and its revised version was published on 7 February 2023. The guideline provides for the information and documents to be submitted to the Agency for the license renewal application as well as points to consider and application assessment processes. The revised guideline facilitates adding the annotation "*the license remains valid*" for products the license of which bears the annotation "*extended for 5 years*". It is also stipulated that no approval letter regarding the up-to-datedness of the short product information and instructions for use, quality summary, quality approval letter or periodic benefit/risk assessment report approval letter will be required within the scope of applications for these products.

Guideline on Co-Marketed Medicinal Products for Human Use. The rules on co-marketing of medicinal products for human use, which are regulated under the Regulation on the Licensing of Medicinal Products for Human Use are regulated in detail by the Agency under this new guideline. Published and entered into force on 17 February 2023, this guideline includes the rules regarding license applications to be made for co-marketed products, points to consider in these applications and the rules regarding the assessment of products marketed under a license. Among others, the guideline provides for the requirement of having a licensed main product in order to apply for a co-marketing license, information and documents to be submitted, and suspension and cancellation of the main product license.

Guideline on Withdrawal and Recall of Medical Devices and In Vitro Diagnostic Medical Devices from the Market. This guideline, which entered into force on 24 February 2023, sets out (i) risk assessments that the Agency and economic operators (manufacturers, authorised representatives, importers, distributors or real or legal persons that are responsible for placing the devices on the market or putting them into service) are obliged to carry out, (ii) classification of non-conformity of devices and (iii) procedures for withdrawal and recall of medical devices from the market with the decision of the Agency. The guideline further regulates in detail the responsibilities of economic operators who are engaged in storage, distribution, sale, use and putting into service of devices. Accordingly, in addition to their other obligations, economic operators should effectively and promptly carry out the withdrawal or recall of medical devices from the market, inform the competent authorities and perform the planned activities regarding the devices with the coordination of the Agency.

Decision Amending the Decision on the Pricing of Medicinal Products for Human Use. The decision which was published in the Official Gazette dated 14 March 2023 includes amendments that are indeed important to sector players. These include, among others, (i) how the actual source price will be calculated for pricing of imported products, which have retail sales or which will demand retail sales price, in circumstances where the source product to be taken as basis for pricing cannot be determined and (ii) pharmacist profit rates.

Amendment to the Guideline on Application and Assessment of Conditional License (Emergency Use Approval). The guideline regarding the conditional licensing of medicinal products for human use in emergency situations initially entered into force on 13 January 2021, was significantly amended on 24 January 2023 and a revised version of the same was published on 31 March 2023. This revision includes, *inter alia*, the timeline for the assessment of conditional licensing applications.

Amendments to the Medical Devices Regulation and Medical Devices for In Vitro Diagnostic Medical Device Regulation. The Regulation Amending the Medical Device Regulation and the Regulation Amending the In Vitro Diagnostic Medical Device Regulation entered into force upon being published in the Official Gazette dated 2 April 2023. These regulations, which include cosmetic amendments in general terms, also aim harmonisation with the European Union legislation. Moreover, additional transitional provisions have been incorporated into the Medical Devices Regulation. For example, it is stipulated that class III devices that have been certified under the repealed regulations can be placed on the market or put into service until 31 December 2027 under certain conditions.

Communiqué on Electronic Instructions for Use of Medical Devices. This communiqué, which entered into force after being published in the Official Gazette dated 6 April 2023 regulates the cases where medical device's instructions for use can be provided by manufacturers in electronic form, their content and website requirements. Accordingly, instructions for use for (i) implantable and active implantable medical devices and their accessories, (ii) fixed installation medical devices and their accessories, (iii) medical devices and their accessories equipped with an internal system that visually displays instructions for use, and (iv) software within the scope of the Medical Devices Regulation may be provided in electronic form instead of paper form. Also, with this communiqué, the Communiqué on Electronic Instructions for Use of Medical Devices dated 2 April 2015 has been repealed.

Regulation on the Use of Health Declaration in Respect of Foods and Food Supplements. This regulation, which provides for the rules on the use of health declaration in respect of foods and food supplements entered into force upon being published in the Official Gazette dated 20 April 2023. Health declaration, which is a statement that mentions, asserts or implies the relation of any food group, food or elements in the composition of food with human health has importance in terms of consumer protection. The regulation generally outlines the rules on the use of health declarations and stipulates that the Law No. 1262 on Pharmaceuticals and Medicinal Preparations and the Law No. 5996 on Veterinary Services, Plant Health, Food and Feed will be applicable in terms of possible administrative sanctions.

In addition, the Guideline on the Use of Health Declarations in Respect of Foods and Food Supplements prepared in accordance with the above-mentioned regulation was published on 26 April 2023. The rules for the use of health declarations determined under the regulation are detailed in this guideline. The guideline also includes examples of appropriate and inappropriate health declarations, thus aims to embody the health declarations that will be deemed appropriate by the Agency.

Amendment to the Guideline on Import Applications and Market Authorization. The guideline, which initially entered into force on 29 August 2022 was revised due to the necessities in practice and with a view to complying with the current legislation, and the revised version was published on 5 May 2023. The guideline sets forth the requirements for market authorization for a number of products, including traditional herbal medicinal products, human medicinal products which are not subject to oversight, blood products or human medicinal products containing them. With the revisions of 5 May 2023, detailed explanations as regards to the information and documentation to be submitted in the application have been provided. The revised guideline will apply to the applications to be filed as of 5 June 2023.

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