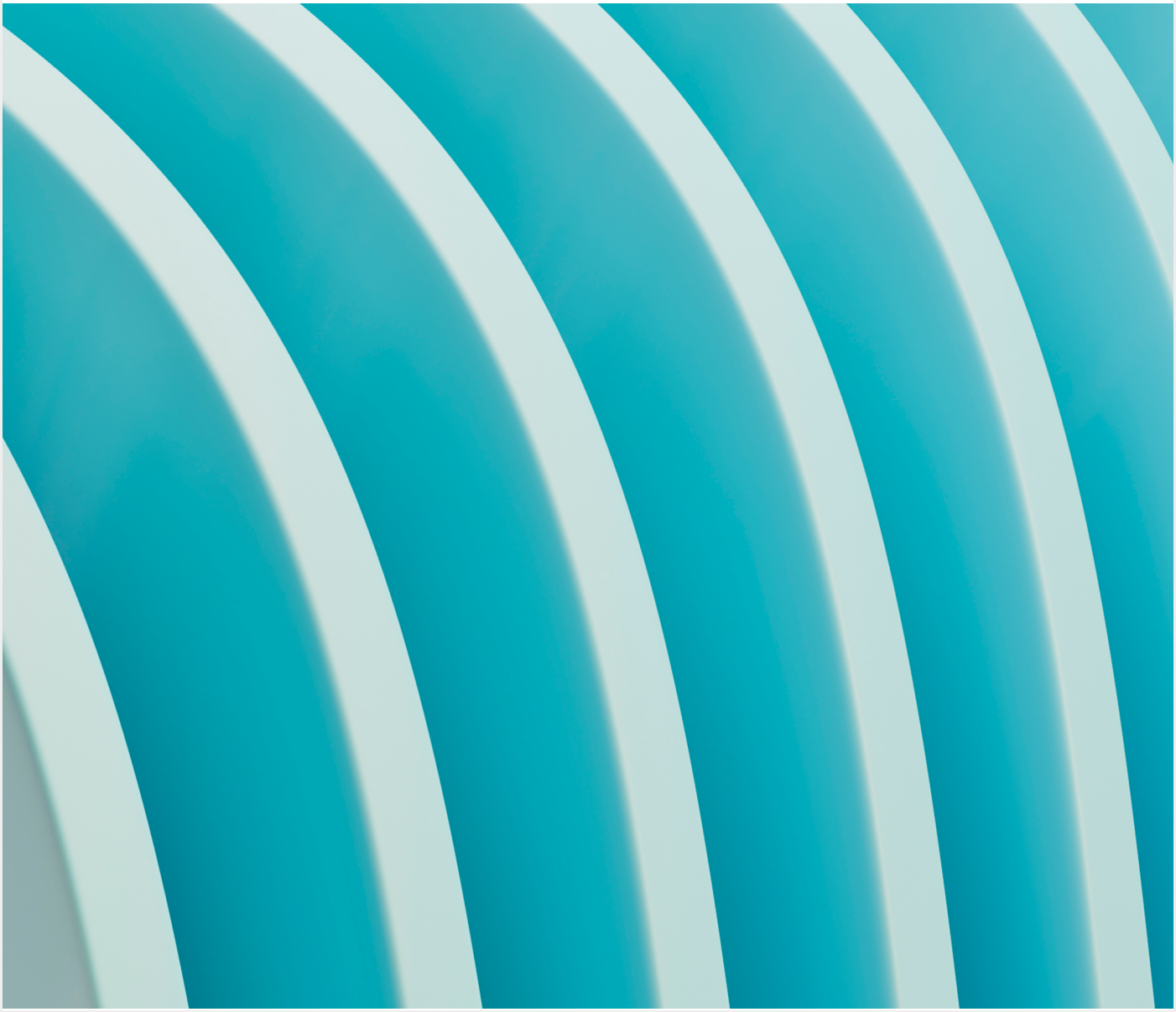
Paksoy | 25+

Recent Developments in **Healthcare Legislation**

2024 Spring Edition

A summary of the recent changes and developments in the healthcare legislation



Contents

MEDICINAL PRODUCTS FOR HUMAN USE

- Amendment to the Guideline on the Clinical Trial Applications to the Clinical Trial Department of the Turkish Medicines and Medical Devices Agency
- Amendment to the Guideline on Non-Clinical Evaluation of Animal Immunoglobulins/ Immune Serums for Human Use Against Viral and Bacterial Agents
- Guideline on the Labelling of Investigational Products and Ancillary Medicinal Products
- Amendment to the Guideline on Clinical Trial Applications to Ethics Committees
- Amendment to the GMP Guideline on Manufacturing Facilities for Medicinal Products for Human Use
- Türkiye Pharmaceutical Market Observation Report
- Amendment to the Guideline on the Procurement of Medicinal Products from Abroad
- Guideline on Ancillary Medicinal Products
- Amendment to the Guideline on Import Applications and Authorisation for Market Release Authorization
- Draft Regulation on the Promotional Activities of Medicinal Products for Human Use and Foods for Special Medical Purposes

Medical Devices

- Communiqué on the Determination of Common Specifications for Product Groups Without an Intended Medical Purpose Listed in Annex XVI of the Medical Device Regulation
- Announcement dated 20 March 2024 on the Market Entry and Circulation of Medical Devices Not Be Certified by the Manufacturer in Accordance With the New Medical Device Regulation ("MDR")
- Announcement dated 24 April 2024 on the Product Tracking System Processes for Products Ineligible for Time Extension by the Manufacturer
- Medical Devices Sector Review
- Draft Communiqué on Determination of Common Specifications for Certain Class D In Vitro Diagnostic Medical Devices

Cosmetics

- Guideline on Cosmetic Product Safety Assessor Training and Certification
- Announcement on the Initiation of the Revision of the Cosmetic Products Regulation within the Scope of the EU Legislation

MEDICINAL PRODUCTS FOR HUMAN USE

Amendment to the Guideline on the Clinical Trial Applications to the Clinical Trial Department of the Turkish Medicines and Medical Devices Agency

With the guideline amendment dated 18 March 2024, the investigational products application file, which was previously required to be submitted only if deemed necessary, is now included as a mandatory document for the initial application. Additionally, the benefit-risk assessment plan or report, containing scientific explanations on why the expected benefits of the clinical trial outweigh the risks, as well as the measures to mitigate such risks, has also been included as a mandatory document for the initial application. It is also stated that the applications submitted to the Turkish Medicines and Medical Devices Agency ("**Agency**") must be made electronically, meaning that no physical documents are required unless the Agency specifically requests the original documents. Moreover, the guideline's previous requirement to initiate the trial within a "*reasonable period*" has been clarified to align with the Regulation on Clinical Trials of Medicinal Products for Human Use by specifying the period as two years from the delivery of the authorization.

Amendment to the Guideline on Non-Clinical Evaluation of Animal Immunoglobulins/ Immune Serums for Human Use Against Viral and Bacterial Agents

According to the guideline amendment dated 18 March 2024, the "*abnormal toxicity test*" has been removed from the analyses to be performed on finished products, in accordance with the current European Pharmacopoeia. The abnormal toxicity involved injecting finished products into test animals such as lab mice, and the product was considered to pass the test if no signs of illness appeared, no changes in body weight occurred and the test animal survived for seven days. This test was previously removed from the list of analyses by the European Federation of Pharmaceutical Industries and Associations (EFPIA) as of 1 January 2019, due to being considered an outdated method and providing insufficient benefit in terms of determining product safety.

Guideline on the Labelling of Investigational Products and Ancillary Medicinal Products

The guideline published on 22 March 2024 outlines the rules for the information to be included on the outer and inner packaging, as well as labels of the investigational products1 and ancillary medicinal products2 used in clinical trials conducted in Türkiye. This is aimed at ensuring the traceability of investigational and ancillary medicinal products for human use through an effective quality system.

---

1 The investigational product is defined as a human medicinal product that is tested or used as a reference in a clinical trial, including placebos.

2 Ancillary medicinal product is defined as a human medicinal product licensed in Türkiye that is not a clinical trial product, but is used in accordance with the requirements or needs of the clinical trial protocol.

Amendment to the Guideline on Clinical Trial Applications to Ethics Committees

With the amendment dated 22 March 2024, the notification period for the completion of the clinical trial, which needs to be submitted to both the Ethics Committee and the Agency, following the completion of the clinical trial and the closure of all centers in Türkiye has been reduced from 90 days to 15 days. If the clinical trial is completed in all countries where it is conducted, the notification period is set at 30 days. Additionally, it has been stipulated that the benefit-risk assessment report should also be included in the application file submitted to the Ethics Committee.

Amendment to the GMP Guideline on Manufacturing Facilities for Medicinal Products for Human Use

As per the amendment dated 27 March 2024, the Guideline on Good Manufacturing Practices for Manufacturing Facilities of Medicinal Products for Human Use has been updated to align with the latest edition of the GMP guideline published by the Pharmaceutical Inspection Cooperation Scheme. Accordingly, the regulations in Annex-1 (*Manufacture of Sterile Medicinal Products*), Annex-13 (*Manufacture of Investigational Medicinal Products*) and Annex-16 (*Certification by the Responsible Manager and Batch Release*) of the guideline have been elaborated upon and brought into conformity with the international convention.

Türkiye Pharmaceutical Market Observation Report

On 5 April 2024, a report was published by the Health Technologies Assessment Unit of the Department of Economic Assessments and Pharmaceutical Supply Management to examine the pharmaceutical market in Türkiye, based on sales volume and value data for the year 2022. The report illustrates that the Turkish pharmaceutical market, which had a size of TRY 21.10 billion in 2016, increased approximately 5.5 times and reached a sales value of TRY 116.47 billion in 2022. Additionally, the report notes that in 2022, 57.5% of the licensed biotechnological pharmaceutical products among the top 20 in terms of sales volume within boxed medicines were classified under the ATC classification as "A10 - Drugs used in the treatment of diabetes."

Amendment to the Guideline on the Procurement of Medicinal Products from Abroad

As known, first medicinal product applications for procuring medicinal products from abroad can be made by the attending practitioners for patients who currently use or are unable to use all available licensed medicinal products and treatment options, in cases where the diagnosis and/or treatment of their condition necessitates the use of medicinal products. With the amendment dated 17 April 2024, it has been stipulated that the examinations to be conducted within the scope of such applications will assess the medicinal product's licensing authority, its accessibility in the market, and compliance with regulatory requirements. Additionally, the Foreign Drug Evaluation Board may request any supplementary documents and information for evaluation purposes. In cases deemed necessary, opinions may be sought from commissions established within the Agency or relevant public institutions. Furthermore, for the first medicinal product applications made by attending practitioners for medicines that are licenced in Türkiye but not available in the market for various reasons, it is provided that following the approval of the Foreign Drug Evaluation Board, medicines containing the relevant active substance and form can be procured in accordance with the conditions determined by the Agency. Furthermore, it is noted that reference medicinal products used in research and studies for the development of medicinal products for human use in Türkiye can be procured from foreign medication suppliers following approval from the Agency.

Guideline on Ancillary Medicinal Products

The guideline published on 20 May 2024 introduces regulations regarding the definition and use of ancillary medicinal products in accordance with international standards within the framework of harmonising with European Union ("**EU**") legislation. The guideline provides detailed information on topics such as the quality requirements that must be adhered to for ancillary medicinal products within the principle of good clinical practice, labelling requirements, the documents that need to be submitted in clinical trial applications related to ancillary medicinal products, and the safety notifications that must be made regarding suspected adverse events associated with ancillary medicinal products.

Amendment to the Guideline on Import Applications and Authorisation for Market Release Authorization

With the revision dated 27 May 2024, several amendments have been made regarding the import application requirements for products within the scope of the guideline, such as medicinal products for human use that are not subject to control, blood products, immunological medicinal products for human use, traditional herbal medicinal products, and allergenic products. These amendments also address the requirements for the market release authorizations of blood products or medicinal products for human use containing blood components, immunological medicinal products for human use, and allergenic products. The updated guideline provisions will be valid for applications made from 27 May 2024, onwards, based on their respective effective dates. The changes introduced primarily concern the documents to be submitted during the applications for (i) control document approvals, (ii) control document and market release authorizations, (iii) import of promotional samples, and (iv) customs exemption certificate, as well as the scope of product groups requiring invoice annotation approvals.

Draft Regulation on the Promotional Activities of Medicinal Products for Human Use and Foods for Special Medical Purposes

To establish the necessary rules for the promotional activities of medicinal products for human use and special medical purpose foods, the draft regulation titled "Regulation on the Promotional Activities of Medicinal Products for Human Use and Foods for Special Medical Purpose," which envisages amendments to the "Regulation on the Promotional Activities of Medicinal Products for Human Use" published in the Official Gazette no. 29405 dated 3 July 2015, was shared with the public on 28 May 2024, and opened for stakeholder feedback until 10 June 2024. The draft regulation includes the principles to be followed in the promotional activities of the relevant products, incorporating special medical purpose foods. These foods are defined as "products developed and specially formulated for use under medical supervision, obtained through industrial methods, and nutritionally complete or incomplete, intended for the dietary management of patients whose capacity to ingest, digest, absorb, metabolize, or excrete nutrients or metabolites is limited, reduced, or impaired, and whose dietary management cannot be achieved by modification of the normal diet alone.

Medical Devices

Communiqué on the Determination of Common Specifications for Product Groups Without an Intended Medical Purpose Listed in Annex XVI of the Medical Device Regulation

The Communiqué on the Determination of Common Specifications for Product Groups Without an Intended Medical Purpose Listed in Annex XVI of the Medical Device Regulation which has been published in the Official Gazette dated 14 March 2023 and numbered 32489 abolished the Guideline on the Determination of Common Specifications for Product Groups Without an Intended Medical Purpose Listed in Annex XVI of the Medical Device Regulation. In this regard, this topic has been comprehensively addressed in the communiqué in a broader manner to bring conformity with the EU legislation. For further details on the amendment, please review the Paksoy publication at https://ww2.paksoy.av.tr/Files/Publications/Paksoy%20Briefing%20%20Developments%20in%20Medical%20Device%20Legislation.pdf.

Announcement dated 20 March 2024 on the Market Entry and Circulation of Medical Devices Not Be Certified by the Manufacturer in Accordance With the New Medical Device Regulation ("MDR")

As known, with the MDR, manufacturers of medical devices placed on the market under the repealed EU Medical Devices Directive ("**MDD**") may only benefit from the transitional provisions until the specified dates, provided that they intend to place the devices on the market within the scope of the MDR as well. Pursuant to the announcement dated 20 March 2024, medical devices manufactured under the MDD that cannot benefit from the transitional provisions and will not be placed on the market under the MDR, will not be allowed to be placed on the market after 26 May 2024. However, medical devices already placed on the market before this date may remain on the market for the duration of their product shelf life, if applicable.

Announcement dated 24 April 2024 on the Product Tracking System Processes for Products Ineligible for Time Extension by the Manufacturer

Following the aforementioned announcement dated 20 March 2024, the Agency published an additional complementary announcement on 24 April 2024. In this context, it is required that forward single product movement notifications (*e.g., production notification, import notification, delivery notification, consumer delivery notification*) should not be made for devices unable to benefit from the transitional provisions and whose individual product stocks are present in the Product Tracking System (namely "*Ürün Takip Sistemi*" or "**ÜTS**") as of 26 May 2024. For devices placed on the market in accordance with the legislation before this date, single product movement notifications can be made for the duration of their shelf life. As for products not placed on the market as of 26 May 2024, existing individual product stocks in ÜTS should be removed by submitting (i) production cancellation notification, (ii) import cancellation notification, or (iii) HEK/loss notification (*Announcement of Exchange of Scrap Materials and Expired Materials*) as appropriate under the "*stock adjustment*" option. The Agency also emphasised in this announcement that the market entry of products not benefiting from the transitional provisions is prohibited according to the legislation, and non-compliance may lead to necessary measures being taken in accordance with the Law No. 7223 on Product Safety and Technical Regulations and relevant secondary regulations.

Medical Devices Sector Review

On 4 April 2024, the Agency conducted a comprehensive review comparing Türkiye's medical device sector activities with global standards. The evaluation underscored the positive impact of the free circulation of medical devices carrying the CE certificate on Türkiye's medical device sector, facilitating import and export without additional requirements. Analysis of healthcare expenditures in Türkiye from 2012 to 2022, based on data from the Turkish Statistical Institute, reveals a progressive increase in per capita healthcare expenditures, reaching TRY 7,171 per capita in 2022. It is noted that the majority of medical device purchases in Türkiye are made by the public sector, particularly the General Directorate of Public Hospitals of Türkiye. Market projections from the Q4 2022 Türkiye Medical Devices report by Fitch Solutions indicate that disposable materials (e.g., syringes, needles, catheters, first aid kits, surgical gloves) are anticipated to hold the highest market value in 2026, while patient-assistive devices (including hearing aids, respiratory devices, pacemakers, etc.) and other equipment are expected to have lower market values. In general, the review highlights that the medical device sector in Türkiye is predominantly import-oriented, with domestic production largely focusing on products with low to moderate technological complexity. Additionally, the Sector Review summarizes the investment incentives aimed at enhancing Türkiye's competitiveness in the medical device sector. Particularly, the investment incentive system established under "Decision on State Aids in Investments" numbered 2012/3305 was explained, aiming to boost R&D investments. According to the January 2024 data from the Ministry of Industry and Technology, investment incentives amounting to TRY 4.2 million were provided in 2023, creating employment opportunities to 2,170 individuals in the sector. However, it has been emphasized that Türkiye's R&D expenditures remain low compared to OECD countries, necessitating the development of various policies to increase this amount.

The Agency's activities have also been evaluated within the Industry Certificate. In this context, the efforts of the Agency towards harmonising the medical device regulations with the EU legislation - particularly the transition process of In Vitro Diagnostic Devices Regulation - were addressed. Since the introduction of the ÜTS system on 12 June 2017, a total of 3,263 manufacturer/importer companies and 2,145,692 medical devices subject to import and manufacture have been registered in the ÜTS system, based on data obtained from ÜTS for the year 2023. In addition, in terms of clinical trials, the number of clinical trial applications increased from 167 in 2017 to 240 in 2023, according to data available on Public Disclosure Platform.

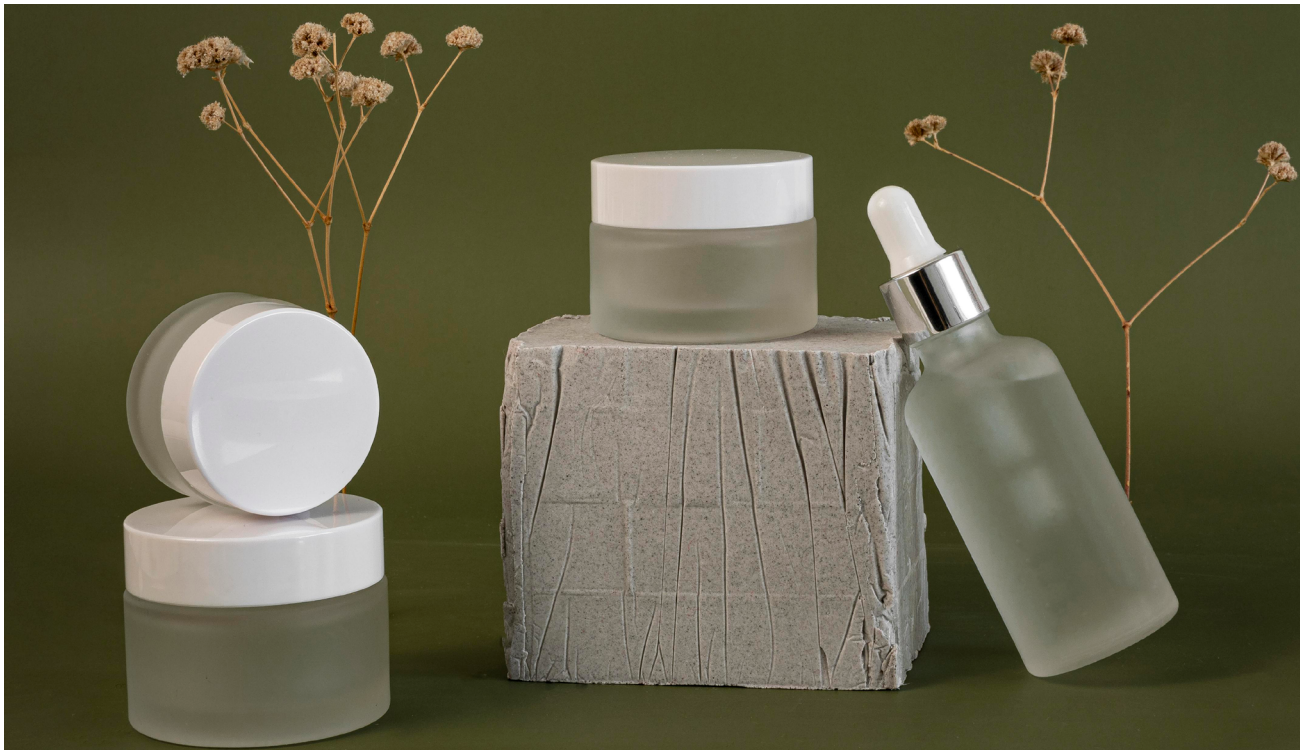
Draft Communiqué on Determination of Common Specifications for Certain Class D In Vitro Diagnostic Medical Devices

As part of EU harmonization efforts, preparations have commenced to regulate details related to medical devices aimed at detecting various infection markers such as specific blood group antigens, HIV infection, Hepatitis B, C, and D viruses through a communiqué. Upon the entry into force of this communiqué, it is planned to repeal the Regulation on Common Technical Specifications for Medical Diagnostic Devices Used Outside the Body. The draft communiqué, along with appendices detailing common specifications for diagnostic medical devices, has been submitted for stakeholders' feedback on 15 April 2024.

Cosmetics

Guideline on Cosmetic Product Safety Assessor Training and Certification

Details regarding the training programs and certification process for cosmetic product safety assessors have been outlined with a new guideline published on 21 March 2024. This guideline specifies the profession requirements for obtaining a cosmetic product safety assessor certificate, stating that, in addition to pharmacists and physicians, other professions listed in the guideline, such as chemical engineers, dentists, and biologists, may also be recognized as cosmetic product safety assessors by the Agency. Candidates seeking certification must complete the specified trainings and pass theoretical and practical exams. Additionally, the guideline regulates that certificates obtained after the publication date will be valid for five years, while those



issued before this date will be valid for three years from the effective date of the guideline. Furthermore, certain amendments were made to this guideline on 6 May 2024, incorporating details on training periods, instructor profiles, as well as examination and certification processes.

Announcement on the Initiation of the Revision of the Cosmetic Products Regulation within the Scope of the EU Legislation

With an announcement published on the Agency's website on 5 April 2024, it has been announced that the updating of Cosmetic Products Regulation, which was prepared in parallel with the Cosmetic Regulation 1223/2009 (EC), has begun in line with the European Commission Regulations 2024/858 and 2024/996. The amendment in the EU states that certain substances such as Vitamin A, Alpha-Arbutin, Arbutin, and some substances with potential endocrine-disrupting properties may pose a risk to human health when used in cosmetic products above certain concentrations. Therefore, new restrictions on the use of these substances have been introduced. It is expected that these restrictions will be added to our legislation in the upcoming days.

Nihan Bacanak
Partner
nbacanak@paksoy.av.tr

Meriç Saçak Albaş
Associate
msacak@paksoy.av.tr

İrem Deyneli
Associate
ideyneli@paksoy.av.tr