

REGULATION ON LICENSING OF MEDICINAL PRODUCTS FOR HUMAN USE

FIRST SECTION Purpose, Scope, Legal Basis and Definitions Purpose

ARTICLE 1 – (1) The purpose of this Regulation is to set out the procedures and principles to be applied in licensing operations, and the practices concerning licensed medicinal products for human use, in order to ensure that medicinal products for human use possess the required efficacy and safety and the requisite quality. Scope

ARTICLE 2 – (1) This Regulation covers medicinal products for human use that are industrially prepared or manufactured by a method involving an industrial process, as well as natural persons and commercial companies that have applied for or been granted a licence for such products (Amended phrase: OG-3/12/2024-32741). (2) This Regulation does not cover: a) Any medicinal product, prepared in a pharmacy in accordance with a prescription for a single patient, referred to as a magistral product, b) Any medicinal product referred to as an officinal product, prepared by a pharmacy in accordance with the formulas of a pharmacopoeia with the aim of being supplied directly to the patient, c) (Amended phrase: OG-3/12/2024-32741) medicinal products intended for use in research and development studies, without prejudice to the provisions of the Regulation on Clinical Trials of Medicinal Products for Human Use published in the Official Gazette No. 32203 dated 27/5/2023, ç) Semi-finished products intended by the manufacturer holding the authorisation for use in further processing, d) Any radionuclides prepared in a sealed source form, e) Whole blood, plasma or blood fractions of human origin, with the exception of plasma and plasma-derived products prepared by a method involving an industrial process, f) Traditional herbal medicinal products, g) Homeopathic medicinal products, ğ) Foods for special medical purposes, h) Advanced therapy medicinal products, ı) (Additional: OG-24/9/2022-31963) Medicinal teas, i) (Additional: OG-24/9/2022-31963) Medicinal products used in aromatherapy. (3) Where, taking into account all of its characteristics, there is doubt as to whether a product falls within the definition of a medicinal product for human use or within the definition of a product covered by other relevant legislation, the provisions of this Regulation shall apply. Legal Basis

ARTICLE 3 – (1) This Regulation has been prepared based on the provisions of the Pharmaceutical and Medical Preparations Law No. 1262 dated 14/5/1928, subparagraph (k) of the first paragraph of Article 3 of the Fundamental Law on Health Services No. 3359 dated 7/5/1987, Article 6 of the Blood and Blood Products Law No. 5624 dated 11/4/2007 (Additional phrase: OG-3/12/2024-32741), the Product Safety and Technical Regulations Law No. 7223 dated 5/3/2020, and Articles 508 and 796 of the Presidential Decree No. 4 dated 15/07/2018 on the Organisation of Ministries, Related and Affiliated Institutions and Organisations and Other Institutions and Organisations. Definitions

ARTICLE 4 – (1) The following terms used in this Regulation shall mean: a) Package information: The information on the inner or outer packaging, b) (Amended phrase: OG-24/9/2022-31963) Medicinal product for human use (drug): 1) Any substance or combination of substances presented as having properties for treating or preventing disease in humans, or 2) Any substance or combination of substances that may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or for the purpose of making a medical diagnosis, c) Name of the medicinal product for human use: The invented trade name, which is liable to confusion with the common name of the medicinal product for human use, or the common or scientific name accompanied by a trade mark or the name of the marketing authorisation or permit holder of the medicinal product for human use, ç) Risks related to the use of the medicinal product for human use: 1) Risks related to the quality, safety and efficacy of the medicinal product for human use with regard to patient health or public health, or 2) Risks that may cause undesirable effects on the environment, d) Strength of the medicinal product for human use: The quantitative content of the active substance(s) contained in each dosage unit, unit

volume or unit weight of the medicinal product for human use, depending on the pharmaceutical form, e) Herbal substance: Mainly dried, sometimes fresh, whole, fragmented or cut plants, parts of plants, algae, fungi, lichens and certain exudates that have not been subjected to a specific treatment, to be given together with the botanical name according to the binomial system of the medicinal plants used, genus, species, subspecies, variety, author, and the scientific name of the plant part used, f) Herbal preparation: Preparations in the form of comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates, obtained by subjecting herbal substances to processes such as extraction, distillation, expression, fractionation, purification, concentration or fermentation, g) Herbal medicinal product: Any medicinal product containing, as active substance(s), one or more herbal substances or one or more herbal preparations, or mixtures in which one or more of such herbal preparations are present, ğ) Finished product: A medicinal product for human use that has undergone all stages of manufacture and is ready for use in its final packaging, h) Biosimilar medicinal product: A medicinal product for human use that demonstrates a high degree of similarity to a licensed reference biological medicinal product in terms of quality, efficacy and safety, ı) Substance: Any substance of natural origin used as a pharmaceutical raw material, i) Essential similar medicinal product: A medicinal product that has the same qualitative and quantitative composition in active substance(s) as the reference medicinal product, has the same pharmaceutical form, and whose bioequivalence has been demonstrated by appropriate bioavailability studies (Different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety or efficacy. In such cases, additional information shall be submitted by the applicant in order to demonstrate the safety or efficacy of the different salts, esters or derivatives of the licensed active substance(s). Various immediate-release oral pharmaceutical forms shall be considered to be one and the same pharmaceutical form. Where the applicant fulfils the relevant criteria described in detail in the guidelines on the essential similar medicinal product, there shall be no need to submit bioavailability studies.), j) Active substance: Any substance or combination of substances intended to be used in the manufacture of a medicinal product for human use, which, when so used, constitutes the active component of the product with a view to restoring, correcting or modifying physiological functions or exerting a pharmacological, immunological or metabolic action for the purpose of making a medical diagnosis, k) Pharmacopoeia: The Turkish Pharmacopoeia (European Pharmacopoeia Adaptation), the European Pharmacopoeia, the United States Pharmacopoeia, the British Pharmacopoeia and the Japanese Pharmacopoeia; and, in cases where these pharmacopoeias are not applicable, the pharmacopoeia deemed appropriate by the Agency, l) Pharmaceutical form: The presentation form in which the medicinal product for human use is manufactured in accordance with its intended use, m) Customs Union Area: The Customs Union Customs Area defined in the third paragraph of Article 3 of Decision No 1/95 of the Association Council establishing the Customs Union between Türkiye and the European Union, n) Hybrid application: A marketing authorisation application supported in part by the data of the reference product and in part by data obtained from studies on the new product, o) Immunological medicinal product for human use: 1) Vaccines, toxins and serums containing agents used to induce active immunity, such as cholera vaccine, BCG, polio vaccines and smallpox vaccine; in particular, agents used to diagnose the state of immunity, including tuberculin and tuberculin PPD, toxins for the Schick and Dick Tests, and agents used to induce passive immunity, such as diphtheria antitoxin, anti-smallpox globulin and antilymphocytic globulin, or 2) "Allergen products" within the meaning of any medicinal product intended to identify or induce the specific acquired change in the immunological response resulting from contact with an allergising agent, or 3) Products with an immunoglobulin structure derived from the blood of animals (rabbits, horses and the like) and exerting an effect on the human immune system, including any medicinal product for human use, ö) Law: The Pharmaceutical and Medical Preparations Law No. 1262 dated 14/5/1928, p) Blood product: Medicinal products for human use obtained from human blood or plasma by industrial

methods, containing, in particular, products such as albumin, immunoglobulin and coagulation factors, whose active substance(s) are blood components, r) Summary of product characteristics: The written information prepared for healthcare professionals regarding the medicinal product for human use, s) Kit: Any preparation to be combined with or reconstituted with radionuclides, generally prior to administration, in order to obtain the finished radiopharmaceutical, ş) Patient information leaflet: The written information prepared for the user, supplied together with the medicinal product for human use, t) Agency: The Turkish Medicines and Medical Devices Agency (TİTCK), u) Licensing company: 1) The company that authorises a natural person or a trading company with respect to the licensing and sale in Türkiye of the imported medicinal product for human use (Amended phrase: OG-3/12/2024-32741), or 2) The company that authorises a natural person or a trading company with respect to the manufacture, licensing and sale in Türkiye of the medicinal product for human use manufactured under licence (Amended phrase: OG-3/12/2024-32741), ü) Substance: Any substance which may be of human origin (human blood and products derived from human blood), animal origin (microorganisms, organs and organ parts, animal secretions, toxins, extracts, blood products), plant origin (microorganisms, plants, parts of plants, plant secretions, plant extracts) or chemical origin (elements, naturally occurring chemical materials, chemical products obtained by chemical change or by synthesis), v) (Amended: OG-24/9/2022-31963) Co-marketed product: A medicinal product for human use that has the same qualitative and quantitative composition, the same pharmaceutical form, the same manufacturing site(s) as a licensed medicinal product for human use, and that is entirely identical in all respects except for its trade name, y) Priority Assessment Board: The Board established for the purpose of granting priority to applications for medicinal products for human use that are first in treatment or diagnosis, that bring innovation, or that are needed from a public health perspective in order to ensure the sustainability of access to medicines or the rapid delivery of the medicine to society and that are of strategic importance, in the procedures and operations of the Agency, whose working procedures and principles are determined in accordance with the relevant guideline, z) Radiopharmaceutical: A medicinal product for human use which, when ready for use, contains one or more radionuclides in its structure, prepared for medicinal use, aa) Radionuclide: A nuclide whose nucleus undergoes spontaneous decay, resulting in one or more

bb) Radionuclide generator: Any system containing a fixed parent radionuclide from which a daughter radionuclide that can be obtained by elution or by another method is produced, and which is used in radiopharmaceutical products, cc) Radionuclide precursor: Any other radionuclide produced for the radioactive labelling of another substance prior to administration, çç) (Amended: OG-24/9/2022-31963) Reference medicinal product: A medicinal product for human use which has been proven to possess scientifically acceptable efficacy, quality and safety, which has been licensed or authorised, with a complete dossier together with administrative, quality, (Amended phrase: OG-27/5/2023-32203) non-clinical and clinical data, by the Agency, by the competent authorities of ICH (International Council for Harmonisation) founding or permanent member countries, (Amended phrase: OG-27/5/2023-32203) by the Australian National Medicines Authority (TGA) or by the United Kingdom National Medicines Authority (MHRA) with respect to its active substance(s), dd) Licence: The document issued by the Agency indicating that a medicinal product for human use may be manufactured in a particular pharmaceutical form and strength with a particular formulation, and placed on the market in accordance with the approved product information, ee) Licence holder: The natural person or trading company holding the licence of the medicinal product for human use, (Amended phrase: OG-3/12/2024-32741) ff) Licensing: The review and approval procedures carried out by the Agency for a medicinal product for human use to be placed on the market, gg) Licensed medicinal product for human use: A medicinal product for human use licensed by the Agency, ready for use, to be placed on the market in a particular packaging and under a particular name, ğğ) Batch (Lot): The quantity of a medicinal product for human use obtained in a single manufacturing cycle during production, in which homogeneity is ensured, hh) International Nonproprietary Name (INN): The international name of an active

substance, which cannot be subject to proprietary ownership, adopted or recommended by the World Health Organization, and which should not be used in trademark registration in accordance with the rules of the World Health Organization, ii) Manufacturing site: The place where the pharmaceutical form of the medicinal product for human use (bulk product) is manufactured prior to inner packaging, except in cases where medicinal products for human use manufactured with technologies that are not available or scarcely available in our country are evaluated by the Agency on an application basis, ii) Benefit/risk balance: The evaluation of a medicinal product together with all quality, safety and efficacy risks it poses to the health of patients or to public health, in relation to its therapeutic effects, jj) Excipient: The substances, other than the active substance(s) contained in the composition of the medicinal product for human use and the packaging material, included in the composition of the medicinal product for human use, kk) Common name: The INN recommended by the World Health Organization, or, where an INN does not exist, the name of the active substance as it appears in classical sources scientifically accepted as reference, ll) (Added: OG-3/12/2024-32741) Mandatory situation application: An application containing a change that necessitates a modification to the product dossier during the licensing process of a medicinal product for human use, and which is considered mandatory upon evaluation by the Agency at the request of the applicant, shall mean.

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ARTICLE 5 – (1) No medicinal product for human use may be placed on the market without being authorised by the Agency in accordance with the provisions of this Regulation. (2) The authorisation requirement also applies to radionuclide generators, kits, radionuclide precursor radiopharmaceuticals and industrially prepared radiopharmaceuticals. (3) For radiopharmaceuticals prepared, at the time of their use, in a healthcare institution authorised to use radiopharmaceutical medicinal products, by that institution or an authorised person in accordance with the manufacturing instructions, from specially authorised radionuclide generators, kits or radionuclide precursors, as well as for positron-emitting radionuclides and radiopharmaceuticals obtained therefrom, no authorisation is required. (4) For magistral radiopharmaceuticals, no authorisation is required, provided that their use remains limited to the relevant healthcare institution, where literature demonstrating that their efficacy and safety have been proven worldwide or in Türkiye and that they have entered routine use is submitted to the Agency and deemed appropriate by the Agency. (5) Where, for magistral radiopharmaceuticals previously authorised, an application for authorisation is made for the industrial manufacture of these products by persons other than the existing authorisation holders, the authorisations granted prior to the date of issue of the authorisation shall remain valid, provided that they comply with the relevant guidelines. However, where a supply problem is experienced in the market despite the placing on the market of the authorised radiopharmaceutical product, permission may be granted, upon request and subject to approval by the Agency, for a period of up to twelve months for magistral radiopharmaceuticals (Additional phrase: OG-23/5/2025-32908) and for the ingredients used in the preparation of magistral radiopharmaceuticals, without requiring an authorisation and provided that their use remains limited to the relevant healthcare institution.

(6) The permission granted by the Agency for magistral radiopharmaceutical medicinal products under this Article shall be valid for as long as the existing staff qualifications and infrastructure declared as of the application date are maintained. Authorisation application and application procedure

ARTICLE 6 – (1) (Amended phrase: OG-3/12/2024-32741) Natural persons or trading companies established in Türkiye shall submit an authorisation application to the Agency in accordance with Annex-1 in order to obtain an authorisation for the purpose of placing a medicinal product for human use on the market. (2) In the event of an application, the Agency may provide scientific advice to the applicant prior to the authorisation application or during the authorisation

procedure, subject to a fee specified in the tariff of fees. (3) (Repealed: OG-24/9/2022-31963) (4) Except in cases deemed necessary by the Agency, force majeure or compulsory situations; authorisation applications shall be accepted only electronically, and all correspondence during the authorisation procedure shall be carried out exclusively in the electronic environment. Persons eligible to submit an authorisation application

ARTICLE 7 – (1) Pursuant to Article 5 of the Law, those wishing to obtain an authorisation in order to place a medicinal product for human use on the market shall: a) for natural persons: have graduated from a higher education institution providing education in the fields of pharmacy, medicine or chemistry, and be entitled to practise their profession in Türkiye; b) (Amended phrase: OG-3/12/2024-32741) for trading companies: employ a person possessing the qualifications specified in subparagraph (a) of the first paragraph as the "qualified person". (2) Natural persons belonging to the dental profession and entitled to practise their profession in Türkiye shall also have the right to submit authorisation applications for medicinal products for human use used in dentistry. Information and documents to be submitted in the authorisation application

ARTICLE 8 – (1) Natural persons (Amended phrase: OG-3/12/2024-32741) or trading companies wishing to obtain a licence for a medicinal product for human use shall apply to the Agency with documents prepared in accordance with Annex-1 and containing the following: a) The diploma of the applicant showing membership in one of the professions specified in Article 7, or a notarised copy thereof, or a graduation certificate obtained from the Council of Higher Education. b) A certified document showing that the applicant is authorised to make the application. c) (Amended: OG-3/12/2024-32741) Where the applicant is a trading company, the Turkish Trade Registry Gazette indicating the duties and titles of the responsible persons. ç) The name or trade name of the applicant, permanent address, registered electronic mail (KEP) address, (Amended phrase: OG-3/12/2024-32741) telephone number, e-mail address and fax number. d) The name, permanent address, (Amended phrase: OG-3/12/2024-32741) telephone number, e-mail address and fax number of the manufacturing site(s) for all stages of manufacture. e) The name of the medicinal product for human use. f) A qualitative and quantitative statement of all active substance(s) and excipients contained in the medicinal product for human use, expressed using the common names of the active substance(s). g) A description of the manufacturing method. ğ) Therapeutic indications, contraindications and adverse reactions. h) Posology, pharmaceutical form, method and route of administration, shelf life, pack size. ı) Measures and safety precautions to be taken regarding the storage of the medicinal product for human use, its administration to patients, and the disposal of waste products in accordance with the provisions of the Waste Management Regulation published in the Official Gazette No. 29314 dated 2/4/2015, taking into account the potential risks that the medicinal product for human use may pose to the environment. i) A description of the control methods used by the manufacturer and, where applicable, presented in accordance with the pharmacopoeia (Where deemed appropriate by the Agency, some of the analyses, tests and controls listed on a product basis may be waived, provided that quality, efficacy and safety are not affected).

j) The results of pharmaceutical tests consisting of physicochemical, biological or microbiological tests. k) The results of pre-clinical (Amended phrase: OG-24/9/2022-31963) tests consisting of toxicological and pharmacological tests. l) The results of clinical studies. m) (Amended: OG-24/9/2022-31963) Where the clinical (Amended phrase: OG-3/12/2024-32741) trials are conducted in Türkiye; information or documentation indicating that the Agency granted a trial authorisation for the clinical (Amended phrase: OG-3/12/2024-32741) trials in question, and where they are conducted outside Türkiye; 1) (Amended phrase: OG-3/12/2024-32741) An applicant declaration containing a statement that the clinical trials comply with the scientific and ethical requirements set out in the Regulation on Clinical Trials of Medicinal Products for Human Use. 2) For clinical (Amended phrase: OG-3/12/2024-32741) trials authorised by the Agency, the Therapeutic Goods Administration (TGA) of Australia, the Medicines and Healthcare products Regulatory Agency (MHRA) of the United Kingdom, or competent authorities that are founders or

permanent members of the International Council for Harmonisation (ICH); information or documentation indicating that the Agency, the Therapeutic Goods Administration (TGA) of Australia, the Medicines and Healthcare products Regulatory Agency (MHRA) of the United Kingdom, or competent authorities that are founders or permanent members of the International Council for Harmonisation (ICH) granted a trial authorisation for the clinical (Amended phrase: OG-3/12/2024-32741) trials in question. 3) (Amended: OG-3/12/2024-32741) For clinical trials authorised by health authorities other than the Agency, the Therapeutic Goods Administration (TGA) of Australia, the Medicines and Healthcare products Regulatory Agency (MHRA) of the United Kingdom, or competent authorities that are founders or permanent members of the International Council for Harmonisation (ICH); an inspection report issued by the Agency, the Therapeutic Goods Administration (TGA) of Australia, the Medicines and Healthcare products Regulatory Agency (MHRA) of the United Kingdom, or competent authorities that are founders or permanent members of the International Council for Harmonisation (ICH), pertaining to the trial sites selected from among the centres where the clinical trials in question were conducted, in accordance with the guideline published by the Agency, preferably relating to the relevant study or, where this is not possible, relating to a different study conducted within the two years preceding the completion date of the relevant study, in line with the requirements of the relevant guideline and demonstrating that the relevant study was conducted in accordance with Good Clinical Practice (GCP). n) In the case of importation of the medicinal product for human use, a document issued by the licensor company showing that the natural person (Amended phrase: OG-3/12/2024-32741) or trading company performing the importation is the sole authorised representative for the importation into Türkiye, licensing and sale of the product in question, and, in the case of co-marketing, that co-marketing authorisation has been granted to a natural person (Amended phrase: OG-3/12/2024-32741) or trading company other than the sole authorised representative in Türkiye. o) In the case of manufacture of the medicinal product for human use under licence, a document issued by the licensor company showing that the natural person (Amended phrase: OG-3/12/2024-32741) or trading company performing the manufacture is the sole authorised representative for the licensing, manufacture and sale of the product in question in Türkiye, and, in the case of co-marketing, that co-marketing authorisation has been granted to a natural person (Amended phrase: OG-3/12/2024-32741) or trading company other than the sole authorised representative in Türkiye. ö) (Amended: OG-26/12/2023-32411) Where a medicinal product for human use manufactured or to be manufactured in Türkiye is made subject to co-marketing, the co-marketing agreement containing the written approvals of the natural persons (Amended phrase: OG-3/12/2024-32741) or trading companies that will carry out the co-marketing, and the trade registry certificates of the parties. p) (Amended: OG-24/9/2022-31963) In applications for co-marketed medicinal products for human use, a commitment stating that the medicinal products for human use subject to co-marketing are entirely identical, that all variation applications will be made in accordance with the relevant guideline, and that manufacture will take place at the same manufacturing site(s). r) Applicable to applicants that do not hold a licence from the Nuclear Regulatory Authority; where it is desired to authorise a company licensed by the Nuclear Regulatory Authority for the distribution and sale of radiopharmaceutical products manufactured domestically, and for the importation, distribution and sale of imported radiopharmaceutical products; the agreement concluded between the two companies stating that the company licensed by the Nuclear Regulatory Authority is the sole authorised party for the operations in question, and the (Amended phrase: OG-26/12/2023-32411) trade registry certificates of the parties.

s) Regarding the active substance manufacturing sites of medicinal products for human use, in addition to the written declaration submitted in accordance with the second paragraph of Article 14 of the Regulation on Manufacturing Sites of Medicinal Products for Human Use published in the Official Gazette No. 30217 dated 21/10/2017; for active substance(s) subject to inspection by the Agency, a document issued by the Agency for the active substance

manufacturing site(s) demonstrating that manufacture is carried out in accordance with good manufacturing practice guidelines, except for products for which the assessment made by the Priority Assessment Board deems it appropriate to submit the documentation after the licensing application; or a document accepted by the Agency, issued by an authorised health authority for manufacturing stages for which the Agency does not issue a document, demonstrating that manufacture is carried out in accordance with internationally accepted good manufacturing practice guidelines; or, for active substance manufacturing sites operating in Türkiye, a Manufacturing Site Authorisation Certificate; and for active substances not subject to inspection by the Agency and, where applicable, for the manufacturing sites of intermediates used in the manufacturing process of the active substance, respectively: 1) (Amended: OG-27/5/2023-32203) A document issued by an authorised health authority for these sites, demonstrating that the active substance(s) and, where applicable, the intermediate product(s) used in the manufacturing process of the active substance are manufactured in accordance with internationally accepted good manufacturing practices.

Where this document is not physically issued, information or documentation accepted by the Agency demonstrating that the active substance(s) has been manufactured in accordance with internationally accepted good manufacturing practices. 2) In cases where it is demonstrated that the documents specified in the first sub-item cannot be submitted, an audit report drawn up as a result of an audit conducted in accordance with the second paragraph of Article 14 of the Regulation on Manufacturing Sites of Human Medicinal Products by the responsible manager of the finished product manufacturing site, for the active substance(s), and a declaration accepted by the Agency. 3) (Added: OG-27/5/2023-32203) In cases where the documents specified in the first sub-item cannot be submitted for the intermediate product manufacturing site(s) used in the manufacturing process of the active substance, a declaration stating that manufacturing has been carried out in accordance with good manufacturing practices, drawn up on the basis of an audit conducted by the active substance manufacturer, and, if requested by the Agency, the audit report. 5) For human medicinal products other than those deemed appropriate by the Priority Assessment Board to be submitted after the licensing application, for all manufacturing steps of the finished product, a document pertaining to the manufacturing site issued by the Agency; or, for manufacturing steps for which no document is issued by the Agency, a document accepted by the Agency showing that manufacturing has been carried out in accordance with internationally accepted good manufacturing practice guidelines, issued by a competent health authority; or, where such document is not physically issued, information or documentation accepted by the Agency showing that manufacturing has been carried out in accordance with internationally accepted good manufacturing practice guidelines; or a document issued by the official authorities of countries having a mutual recognition agreement with our country, showing that manufacturing may be carried out within the framework of good manufacturing practices; or a manufacturing site authorisation certificate for human medicinal products to be manufactured in Türkiye. t) For human medicinal products to be manufactured in Türkiye, where the applicant is not the manufacturer, a contract manufacturing agreement concluded with a manufacturer satisfying the conditions specified in the Regulation on Manufacturing Sites of Human Medicinal Products, and the (Amended phrase: OG-26/12/2023-32411) trade registry certificates of the parties. u) (Amended: OG-3/12/2024-32741) Products for which application has been deemed appropriate by the Priority Assessment Board, being products the use of which is foreseen in serious public health problems that adversely affect the normal life and activities of the whole or certain segments of society — in particular situations arising against public health threats recognised by the World Health Organization or the European Union, or accepted by the Ministry of Health (pandemics, biological threats and the like) and possessing strategic importance for the sustainability of healthcare services as determined by the Ministry — being excepted; for the applied imported or locally licensed product, the list of other country/countries where licensing applications have been filed, together with a certified copy of the licence approved by the health authority of one of the

countries on the list prior to the licence being issued in Türkiye, or a Certificate of Pharmaceutical Product, or, where such documents are not issued, information or documentation accepted by the Agency showing that the licensing of the product by the relevant authority has been approved. ü) Where the licensing application for the human medicinal product concerned has been rejected by the competent authority of other countries, or has been withdrawn by the applicant, or where the licensed product has been withdrawn or its licence has been suspended, a list of these countries must be provided, together with the name of the human medicinal product in the country concerned, the date and the rationale of the procedures carried out. v) In the licensing application for a radionuclide generator, in addition to the documents required under this Article, a detailed description of the system and of the components constituting the system, which may affect the quality and composition of the daughter nuclide preparation, and qualitative and quantitative details of the eluate or sublimate. y) The summary of product characteristics prepared in accordance with Article 10, the patient information leaflet prepared in accordance with the Regulation on Packaging Information, Patient Information Leaflet and Tracking of Human Medicinal Products published in the Official Gazette No. 30048 dated 25/4/2017, and samples of the packaging in the dimensions and design in which the human medicinal product is to be placed on the market; and, in the case of importation or licensed production of the human medicinal product, in addition thereto, the summary of product characteristics, patient information leaflet and packaging samples of the current reference medicinal product for the product, approved by the competent authorities of the other country or countries, where applicable, where the product has been placed on the market, indicating the date of approval, where available. z) The pharmacovigilance-related documents that must be submitted at the time of the licensing application, in accordance with the Regulation on the Safety of Medicines published in the Official Gazette No. 28973 dated 15/4/2014. aa) Under the Regulation on Promotional Activities for Human Medicinal Products published in the Official Gazette No. 29405 dated 3/7/2015, a document describing the scientific service and the address of this service, its KEP (registered electronic mail) address, (Amended phrase: OG-3/12/2024-32741) telephone number, e-mail address and fax number. bb) Where applicable, documents demonstrating that the human medicinal product for which the licensing application is filed meets the requirements set out in Articles 33 or 36. cc) An assessment of the potential environmental risks posed by the human medicinal product. çç) (Added: OG-3/12/2024-32741) Where the active substance is procured domestically, the supply agreement concluded between the active substance supplier and the licensing applicant together with the invoice; where it is procured from abroad, a letter of conformity prepared in accordance with the relevant guideline published by the Agency. (2) All official documents procured from abroad must bear an apostille or consular certification. It is essential that all documents be submitted in Turkish. Sections deemed appropriate by the Agency may be submitted in English. However, documents prepared in languages other than English must be submitted together with a sworn Turkish translation. Where a sworn translation cannot be made in our country, a sworn translation document translated into Turkish or English in another country may be accepted. (3) Detailed summaries of the documents relating to the results of the physicochemical, biological or microbiological tests specified in sub-items (j), (k) and (l) of the first paragraph, of the (Amended phrase: OG-24/9/2022-31963) non-clinical tests and of the clinical trials, prepared in accordance with Article 11, must be submitted. (4) It is mandatory to notify the Agency of any of the information set out in this Article that is updated. (5) The authorisation referred to in sub-item (r) of the first paragraph does not remove the legal obligations of the applicant or licence holder. Informed consent application, established medical use application, allergen product application, equivalent medicinal product application, hybrid application, biosimilar medicinal product application, fixed

t combination application

ARTICLE 9 – (1) Without prejudice to the provisions of the Industrial Property Law No. 6769 dated 22/12/2016;

a) The applicant shall not be required to submit the results of toxicological and pharmacological tests and clinical trials, provided that the applicant proves one of the following:

1) In applications made with informed consent, where the human medicinal product for which a marketing authorisation application is filed is essentially identical, in terms of qualitative and quantitative composition of active substance(s) and in the same pharmaceutical form, to a medicinal product previously authorised in Turkey, and where the marketing authorisation holder of the reference medicinal product consents to the use of the pharmaceutical, (Amended phrase: OG-24/9/2022-31963) preclinical and clinical documentation contained in the reference medicinal product dossier for the purpose of examining the said application;

2) In well-established medicinal use applications, where the active substance(s) of the human medicinal product for which a marketing authorisation application is filed has a well-established medicinal use, with recognised efficacy and an acceptable level of safety, and has been used for at least ten years in any country, as determined in the product-based assessment carried out by the Agency prior to the marketing authorisation application through detailed scientific literature, appropriate scientific literature shall be submitted instead of the preclinical tests and clinical trial results in Annex-1; (Amended phrase: OG-24/9/2022-31963)

3) In applications where the efficacy and safety of the allergen product for which a marketing authorisation application is filed is demonstrated by reference to published literature or to a reference medicinal product for its indication and route of administration;

4) In equivalent medicinal product applications to be made where the human medicinal product for which a marketing authorisation application is filed is essentially similar to a reference medicinal product authorised in accordance with the legislation in force and whose data exclusivity period has expired;

In the application of subparagraph (4), data exclusivity shall apply to reference medicinal products to be authorised for the first time in one of the countries within the Customs Union Area after 1/1/2005; the period thereof is six years, commencing from the date of first authorisation within the Customs Union Area. For products benefiting from patent protection in Turkey, the six-year data exclusivity shall be limited to the duration of that patent.

b) A hybrid application shall be made where the definition of an equivalent medicinal product is not fully met for the human medicinal product, or where bioequivalence cannot be demonstrated by bioavailability studies, or where there are differences from the reference medicinal product in the active substance(s), therapeutic indication, strength, pharmaceutical form or route of administration. In such applications, it is mandatory to submit the results of appropriate preclinical tests or clinical trials. (Amended phrase: OG-24/9/2022-31963)

c) For biosimilar medicinal products that cannot meet the conditions in the definition of an equivalent medicinal product, in particular due to differences in starting materials or differences in manufacturing processes from the reference biological medicinal product, the results of the relevant appropriate preclinical tests or clinical trials shall be submitted. (Amended phrase: OG-24/9/2022-31963) The additional data to be submitted must comply with the criteria set out in Annex-1 and in the relevant guideline published by the Agency. The test and clinical trial results contained in the dossier of the reference medicinal product may not be submitted.

ç) In fixed combination applications made for medicinal products containing active substance(s) used in the composition of human medicinal products authorised in our country and used in combination for therapeutic purposes, in addition to appropriate bioavailability or bioequivalence data, it is mandatory to submit literature information demonstrating that the said active substance(s) are effective and safe when used in combination, as well as retrospective studies conducted with data collected from hospitals in Turkey, where available. If the studies submitted are deemed insufficient by the Agency, it shall be mandatory to submit the results of

clinical trials conducted with the new combination, the scope of which shall be determined by the Agency.

d) In fixed combination applications made for medicinal products containing active substances that are used in the composition of human medicinal products authorised worldwide but not used in combination for therapeutic purposes, it shall be mandatory to submit the results of clinical trials related to this combination and, where necessary, the results of preclinical tests. (Amended phrase: OG-24/9/2022-31963) However, providing scientific references for each active substance shall not be required unless requested by the Agency.

Summary of Product Characteristics

ARTICLE 10 – (1) The summary of product characteristics shall be submitted containing the following information:

- a) The name of the human medicinal product, its strength and its pharmaceutical form.
- b) The qualitative and quantitative expression of the active substance(s) contained in the human medicinal product, using common names, and, where excipients that should be included in this section are present, the qualitative and quantitative information on those substances. Where materials of animal origin are used in the active substances and excipients of the human medicinal product, the origin thereof.
- c) The pharmaceutical form.
- ç) Clinical particulars:
 - 1) Therapeutic indications,
 - 2) Posology and method of administration,
 - 3) Contraindications,
 - 4) Special warnings and precautions for use and, for immunological human medicinal products, special precautions for persons who come into contact with and administer such products to patients, and precautions to be taken by patients,
 - 5) Interaction with other medicinal products and other forms of interaction,
 - 6) Use during pregnancy and lactation,
 - 7) Effects on ability to drive and use machines,
 - 8) Undesirable effects,
 - 9) Overdose and its treatment.
- d) Pharmacological properties:
 - 1) Pharmacodynamic properties,
 - 2) Pharmacokinetic properties,
 - 3) Preclinical safety data. (Amended phrase: OG-24/9/2022-31963)
- e) Pharmaceutical particulars:
 - 1) List of excipients,
 - 2) Incompatibilities,
 - 3) The shelf life of the human medicinal product and, where necessary, the shelf life after reconstitution or after first opening of the immediate packaging,
 - 4) Special precautions for storage,
 - 5) Nature and contents of the packaging,
 - 6) Disposal of unused medicinal products or waste materials derived from such products and other special precautions.
- f) The marketing authorisation holder.
- g) The marketing authorisation number.
- ğ) The date of the marketing authorisation.
- h) The date of the latest revision of the summary of product characteristics.
- ı) For radiopharmaceuticals, full details of radiation dosimetry.
- i) For radiopharmaceuticals, detailed instructions for use, additional detailed instructions for preparation and quality control, and, where necessary, the maximum storage period in compliance

with the specifications of the eluate or ready-for-use product.

j) The requirements set out in the Regulation on the Safety of Medicines.

Expert reports

ARTICLE 11 – (1) When applying to the Agency, the applicant shall submit expert reports signed by the relevant experts for each of the chemical, pharmacological, biological, toxicological and clinical parts of the licensing file. (2) In accordance with their qualifications, the duties of the experts who are to prepare the reports shall be as follows: a) To perform the duties within their own disciplines, such as analysis, pharmacology and similar experimental sciences, or clinical trials, and to objectively describe the qualitative and quantitative results obtained. b) To describe their observations in accordance with Annex-1, in particular: 1) For analytical experts, stating that it has been determined, using the control methods employed by the manufacturer, whether the product conforms to the declared composition of the medicinal product for human use, 2) Stating that the toxicity and pharmacological properties of the medicinal product for human use have been observed, 3) In the case of clinicians, stating whether assurance has been obtained, in accordance with the provisions of this Regulation, that the documents submitted by the applicant to the Agency demonstrate the effect of the product in question on the patients treated therewith, whether the patients tolerate the product well, and the clinician's recommendation regarding posology, contraindications and adverse reactions. (3) The expert's curriculum vitae, a declaration of his/her professional relationship with the applicant and, where necessary, the justification for the documents used for the application shall be provided. (4) The experts' detailed reports shall form part of the documents appended to the application submitted by the applicant to the Agency.

SECTION THREE Evaluation of the Licensing Application and Licensing Preliminary evaluation of the application

ARTICLE 12 – (1) Licensing applications may be submitted by applicants throughout the year. However, taking into account the licensing capacity of the Agency, the licensing process may only be initiated in February, May, August and November (Additional phrase: OG-3/12/2024-32741) in line with the relevant guideline. (2) Whether the application file submitted to the Agency to obtain a license for a medicinal product for human use constitutes a complete application, with regard to the documents required to be submitted depending on the nature of the application and the electronic licensing application requirements, shall be examined by the Agency through a preliminary evaluation. This evaluation shall be carried out in the order of the application date. However, the preliminary evaluation procedures of applications deemed appropriate by the Agency's Priority Evaluation Board to be evaluated with priority or high priority in licensing procedures shall be carried out with priority. (3) The necessary evaluation shall be carried out within thirty days of the application file reaching the Agency, and the outcome shall be notified to the applicant. Where the application is found to be incomplete, the applicant shall complete the deficiencies within thirty days. Following the submission of the completed deficiencies to the Agency, the second preliminary evaluation to be carried out shall also be concluded within thirty days. Rejection of the application on procedural grounds

ARTICLE 13 – (1) In the following cases, the application shall be rejected on procedural grounds and (Replaced phrase: OG-3/12/2024-32741) cancelled: a) Failure to submit a second application within the due time by completing the deficiencies identified in the first preliminary evaluation carried out by the Agency under Article 12, or failure to complete the deficiencies related to the first preliminary evaluation in the second preliminary evaluation application, b) Failure to pay the licensing fee within sixty days following the date on which the applicant is officially notified that the licensing process has been completed, c) Failure to submit to the Agency, at the latest within thirty days, the information and documents requested by the Agency outside the preliminary evaluation process, or the necessary explanation stating that such information and documents cannot be submitted, together with the information on the date on which they will be

submitted. ç) (Addition: OG-27/5/2023-32203) Failure to submit the necessary information and documents to the Agency by the end of the period specified in the second paragraph. (2) (Addition: OG-27/5/2023-32203) (Amendment: OG-3/12/2024-32741) The information and documents to be submitted to the Agency must be found appropriate by the Agency in terms of current scientific requirements, and the date information submitted for the said information and documents pursuant to subparagraph (c) of the first paragraph must not exceed three years. The Agency may apply an exception to this matter for conditional licensing applications made under Article 33. (3) (Addition: OG-27/5/2023-32203) (Amendment: OG-3/12/2024-32741) In the case of a new licensing application for medicinal products for human use whose application has been rejected on procedural grounds under subparagraph (c) of the first paragraph, where priority decisions granted by the Priority Evaluation Board exist for the products in question in licensing or inspection processes, such decisions shall be deemed valid, and the licensing processes of the relevant products shall be initiated directly. (4) (Addition: OG-27/5/2023-32203) (Amendment: OG-3/12/2024-32741) In the case of a new licensing application for medicinal products for human use whose application has been rejected on procedural grounds under subparagraph (c) of the first paragraph, the up-to-date file reflecting the amendments approved or requested by the Agency and a commitment letter indicating that the amendments have been reflected shall be submitted with the file. If, despite this commitment, it is determined that the amendments approved and requested by the Agency have not been reflected in the up-to-date file, the file shall be rejected again, and the priority decisions granted by the Priority Evaluation Board for the product in question in licensing or inspection processes shall be cancelled. (5) (Addition: OG-3/12/2024-32741) In licensing applications made for jointly marketed products, where the licensing renewal procedure of the referenced medicinal product for human use under Article 21 has not been completed, the application shall be rejected. Licensing period

ARTICLE 14 – (1) (Amendment: OG-3/12/2024-32741) During the preliminary evaluation, the Agency examines the licensing application in accordance with the licensing criteria and officially notifies the applicant whether the application has been accepted or rejected. The notification that the application has been accepted shall not be regarded as the commencement of the licensing period. For complete licensing applications whose evaluation has been completed and which have been accepted, the Agency shall additionally notify the license holder of the date on which the licensing period commences. The date of this notification shall be regarded as the commencement date of the licensing period. The licensing process shall be concluded within the following two hundred and ten days. Furthermore, the time elapsed for evaluations by organisations outside the Agency, the time elapsed for public holidays, excluding weekend holidays, and the time elapsed for extraordinary circumstances shall not be included in the licensing period. (2) In licensing applications made for jointly marketed products, the Agency shall examine only the Module 1 part of the licensing application file, prepared in accordance with Annex-1, out of the licensing application file submitted with a complete and full dossier, and the two hundred and ten-day licensing period shall be ninety days for these applications. A licensing application may also be made solely with Module 1 prepared in accordance with Annex-1. For licensing applications for jointly marketed products made in this manner, the other modules may not be submitted during the licensing process or after licensing. (3) (Amendment: OG-24/9/2022-31963) For medicinal products for human use for which a licensing application is made under Article 37/A, the licensing period, which is two hundred and ten days, shall be ninety days. (4) (Addition: OG-24/9/2022-31963) In cases where additional information and documents are requested from the applicant by the Agency during the licensing process under Articles 8, 9, 10, 33, 36 and 37/A, where necessary, the licensing period shall be suspended until the relevant information and documents are obtained. Prioritisation in licensing processes

ARTICLE 15 – (1) (Amended: OG-27/5/2023-32203) Licensing procedures are carried out through electronic systems according to the starting date of the licensing process. However, applications for products filed pursuant to Articles 8, 9, 33, 36 or 37/A that are deemed

appropriate by the Agency's Priority Assessment Board are given priority in the licensing procedures. (2) (Amended: OG-27/5/2023-32203) The licensing procedures for products in this situation are completed within the periods specified in the relevant guidelines published by the Agency. (3) (Amended: OG-24/9/2022-31963) The provisions set forth in the first and fourth paragraphs of Article 14 concerning the suspension of the period are also applicable to the medicinal products for human use determined within the scope of this Article. Licensing criteria

ARTICLE 16 – (1) When granting a licence for a medicinal product for human use, the criteria to be taken into account by the Agency with respect to the product are the following: a) The quality being demonstrated by appropriate technological and pharmaceutical characteristics. b) The efficacy being proven under the proposed conditions of use. c) The safety being proven. Assessment of applications

ARTICLE 17 – (1) When assessing applications, at minimum the following aspects shall be taken into consideration: a) Scientific and technological examination of the documents proving the efficacy and safety of a product and demonstrating its quality. b) (Repealed: OG-3/12/2024-32741) c) The control tests carried out to determine whether blood products are free of viral contamination proving the safety of the product, and the declaration of the source from which the plasma used in the preparation of these products was obtained. Rejection of the application on the merits

ARTICLE 18 – (1) (Repealed: OG-3/12/2024-32741) (2) In the process of assessing the application made to the Agency for the licensing of a medicinal product for human use, after the applicant has been granted, for each of the circumstances set out below, at most (Amended phrase: OG-3/12/2024-32741) five response rights (two response rights may be used orally), as a result of the assessment of the documents and information submitted, the product being found to: a) Have a potential risk exceeding the beneficial effect of the treatment under normal conditions of use, or b) Have insufficient therapeutic effect, or its therapeutic effect not being sufficiently proven, or c) (Amended: OG-3/12/2024-32741) Where applicable, its bioavailability being insufficient or inappropriate, or ç) In applications for biosimilar medicinal products, the similarity to the reference biological product (Amended phrase: OG-24/9/2022-31963) not being proven, or d) (Added: OG-24/9/2022-31963) (Amended: OG-3/12/2024-32741) Its qualitative and quantitative formula, or the data relating to its quality being insufficient or inappropriate, in such cases as determined, the licensing application shall be rejected on the merits. (3) (Added: OG-24/9/2022-31963) Information relating to the assessment of licensing applications rejected within the scope of this Article shall not be published. (4) (Added: OG-26/12/2023-32411) Where the information and documents requested by the Agency, outside the preliminary assessment process, or the necessary explanation that such information and documents cannot be submitted, together with the date on which they are to be submitted, are not provided to the Agency within thirty days at the latest, the licensing application shall be rejected on the merits. Notification of and objection to the rejection of the application on the merits

ARTICLE 19 – (1) (Amended: OG-24/9/2022-31963) In the event that the licensing application is rejected on the merits, the decision is notified to the applicant with its justification, or where notification cannot be made, it may be announced on the Agency's website. The applicant has the right to object to the Agency within forty-five days from the date of notification or announcement. If no objection is made within forty-five days, the application documents are returned to their holder. Where the applicant fails to collect the documents, the provisions of the Regulation on State Archive Services published in the Official Gazette No. 30922 dated 18/10/2019 shall apply. (2) The objection shall be assessed by the Agency within ninety days and the result shall be notified to the applicant. During the assessment of the objection, if deemed necessary, the applicant shall be granted the right to provide oral explanations and defence. (3) The decision resulting from the assessment of the objection is final, and no objection may be made to the Agency regarding the said decision. (4) The rejection of the application on the merits does not prevent the applicant from making a new licensing application. Granting of the licence

ARTICLE 20 – (1) As a result of the examination and assessment of the documents submitted to the Agency by the applicant, a licence is issued for the medicinal product for human use found to comply with the provisions laid down in this Regulation, and the applicant is informed thereof. (2) (Amended: OG-24/9/2022-31963) With the exception of medicinal products for human use where there is only a difference in flavour among lozenges, oral sprays, chewing tablets, fish oil preparations, nicotine gums and paediatric vitamin syrups, and medicinal products for human use where there is only a difference between single-dose and multi-dose use, and the primary packaging forms of large-volume parenterals in vial and bag form, as well as variation applications falling within the scope of the Regulation on Variations to Licensed Medicinal Products for Human Use published in the Official Gazette No. 31693 dated 18/12/2021; a second licence shall not be granted for a product having the same qualitative and quantitative composition per unit dose in terms of the active substance(s), the same indication and the same pharmaceutical form as a medicinal product for human use licensed by the Agency, to the same (Amended phrase: OG-3/12/2024-32741) natural person or trading company, even under a different trade name. However, applications for medicinal products for human use which are scientifically and technologically demonstrated to provide superiority over a licensed medicinal product for human use, or which have a justification deemed appropriate by the Agency, shall be assessed separately. In the assessment concerning the acceptance of the active substance(s) as being the same within the scope of this paragraph, subparagraph (i) of the first paragraph of Article 4 shall be taken as the basis. (3) The same (Amended phrase: OG-3/12/2024-32741) natural person or trading company may not use a different trade name for medicinal products for human use containing the same active substance(s) and indication, with different strengths or routes of administration or pharmaceutical forms. (4) (Amended: OG-24/9/2022-31963) A licence may not be granted for a medicinal product for human use bearing the same name as a traditional herbal medicinal product, medical device or homeopathic medicinal product. (5) Licences, certificates and other documents of international validity may also be prepared by the Agency as physical documents. (6) (Amended: OG-24/9/2022-31963) The list of medicinal products for human use licensed by the Agency is announced, at least once a month, on the Agency's official website under the name List of Licensed Medicinal Products for Human Use, and once a year in the Official Gazette. (7) (Added: OG-24/9/2022-31963) The Agency may prepare a public assessment report that does not contain commercially confidential information relating to the pharmaceutical and pre-clinical tests, clinical trials, risk management system and pharmacovigilance system of the medicinal product for human use concerned. This assessment report is updated when new information that is important for the assessment of the quality, safety or efficacy of the medicinal product for human use concerned is obtained. The public assessment report includes, in particular, a summary containing a section on the conditions of use of the medicinal product for human use. Validity period of the licence

ARTICLE 21 – (1) The assessment regarding the renewal of the marketing authorisation shall be carried out by the Agency five years after the date of granting, taking into account the benefit/risk balance. In accordance with the provisions of the Regulation on the Safety of Medicines, the marketing authorisation holder shall submit to the Agency, nine months before the expiry of the five-year period, a file containing all current information on efficacy, safety and quality, including the assessment of suspected adverse reaction reports and periodic benefit/risk evaluation reports, as well as information on all variations made since the authorisation of the product.

(2) Once the marketing authorisation has been renewed, it shall remain valid indefinitely, unless the Agency decides to conduct an additional five-year renewal assessment for the relevant medicinal product for human use for pharmacovigilance-related reasons, including insufficient exposure of patients to the product.

(3) In cases where five-year pharmacovigilance data for the product cannot be submitted due to the fact that it has not been placed on the market, the assessment regarding the validity of the marketing authorisation shall be carried out after the available pharmacovigilance data have

been prepared and submitted in accordance with the relevant legislative provisions.

Suspension of the marketing authorisation

ARTICLE 22 – (1) In relation to an authorised product; a) the occurrence of harmful effects under normal conditions of use, b) the determination that the product has no therapeutic effect or that its therapeutic effect is insufficient, c) its manufacture with a formula different from the formula on which the authorisation was based, ç) the making of changes, without the knowledge or approval of the Agency, to the formula underlying the authorisation, qualitative and quantitative composition, pharmaceutical form, packaging and summary of product characteristics, d) the failure of the marketing authorisation holder to take into account scientific and technical progress with regard to manufacturing and control methods and the failure to make the necessary changes in order to ensure that the medicinal product for human use is manufactured and controlled in accordance with generally accepted scientific methods, or the failure to submit such changes to the Agency for approval where they have been made, e) the failure to take into account the warning issued for products found to be defective as a result of market surveillance activities conducted, and the continuation of defective manufacture, f) the determination that the manufacturing method and the control methods used by the manufacturer referred to in subparagraphs (g) and (i) of the first paragraph of Article 8 are not applied as specified, g) non-compliance with the legislative provisions concerning packaging information and package leaflet, ğ) the failure to make or notify the necessary updates in the summary of product characteristics and the package leaflet, h) the failure of the marketing authorisation holder to respond to the instructions of the Agency within the period determined by the Agency in relation to the medicinal product for human use, ı) the determination that the documents submitted in an application made for a medicinal product for human use pursuant to the provisions of this Regulation contain inaccuracies that would affect the quality, efficacy or safety of the product, or the loss of validity of the submitted documents, i) provided that it is deemed appropriate by the Agency, and without prejudice to cases where the product is not manufactured for the market of a single country or cannot be placed on the market of our country due to the size of the commercial batch; the failure to place on the market at least one commercial batch of a medicinal product for human use within the first thirty months following the date of its authorisation, j) the determination that, for a medicinal product for human use authorised within the scope of the QR code system, which is manufactured in our country and has previously been placed on the market, no commercial batch has been placed on domestic or foreign markets for thirty consecutive months; or, for products imported into our country, that no commercial batch has been placed on the domestic market; or, for medicinal products for human use outside the scope of the QR code system, the failure to submit to the Agency official documents demonstrating that they have been placed on the market, k) the decision to suspend the marketing authorisation as a result of the benefit/risk assessment conducted by the Agency for the notifications received within the framework of pharmacovigilance activities, l) the determination of circumstances requiring the suspension of the marketing authorisation in accordance with the provisions of the Regulation on the Safety of Medicines, m) (Amended: OG-24/9/2022-31963) the failure to fulfil the obligations set out in the first and second paragraphs of Article 25, n) the failure to fulfil the commitments referred to in subparagraph (c) of the first paragraph of Article 26, o) (Amended: OG-24/9/2022-31963) the failure of the marketing authorisation holder to place on the market, within six months of the date of the request, a medicinal product for human use of importance for public health and the sustainability of access to medicines, despite the request of the Agency, ö) (Added: OG-27/5/2023-32203) the failure of the marketing authorisation holder to submit, in applications for the transfer of the marketing authorisation made under Article 26, the document demonstrating that manufacturing is carried out in accordance with the guidelines on good manufacturing practices at the manufacturing site/sites underlying the authorisation, and the Manufacturing Site Licence for active substance manufacturing site/sites operating in Türkiye, p) (Added: OG-26/12/2023-32411) the failure to fulfil the obligation set out in subparagraph (ı) of the second paragraph of Article 25, (Amended phrase: OG-14/12/2022-32043) (2) in the event that a

non-compliance relating to at least one of the above situations is determined and proven, the marketing authorisation of the medicinal product for human use shall be suspended by the Agency in accordance with the outcome of the assessment to be conducted by the Agency, including safety aspects, in relation to the non-compliance concerned, or upon the request of the marketing authorisation holder for the cancellation of the authorisation of the product.

(2) The production for market supply or importation of the medicinal product for human use whose authorisation has been suspended shall be halted. Medicinal products for human use that have already been imported or produced may not be placed on the market unless otherwise decided by the Agency. The decision concerning the medicinal products for human use present on the market shall be given by the Agency, taking into account the grounds for the suspension of the authorisation.

(3) The Agency may grant exceptions to the application of subparagraphs (i) and (j) of the first paragraph for medicinal products for human use that are exported and may lead to serious public health problems in the event of their unavailability when needed, or for which there is no need at all in the market of our country.

(4) The list of medicinal products for human use whose authorisation has been suspended shall be published on the official website of the Agency.

(5) (Amended: OG-3/12/2024-32741) Where it is intended to place back on the market products whose authorisation has been suspended for the reasons specified in subparagraphs (i) or (j) of the first paragraph, an application shall be made to the Agency, in accordance with the procedures determined by the Agency, together with an undertaking that the product will be placed on the market within eighteen months at the latest. If the relevant application is deemed appropriate by the Agency, the marketing authorisation of the product shall be released from suspension. For products not placed on the market within the undertaken period, action shall be taken pursuant to Article 23.

Cancellation of the marketing authorisation

ARTICLE 23 – (Amended: OG-24/9/2022-31963) (1) In the event that one of the following conditions exists, the marketing authorization granted for a medicinal product for human use shall be revoked: a) (Amended: OG-27/5/2023-32203) Failure to submit, within six months at the latest from the date of suspension, documents proving the contrary of the grounds for suspension, or the documents explaining the situation not being deemed appropriate by the Agency, for products whose authorization has been suspended due to one or more of the reasons listed in the first paragraph of Article 22. b) Upon the request of the marketing authorization holder and the approval of the Agency, provided that there is no seizure or injunction decision notified to the Agency on the authorization. c) Failure to place the products on the market within the period committed pursuant to the fifth paragraph of Article 22.

(2) In the event that the authorization of a co-marketed product for which the application was made with a complete dossier is revoked, the authorizations of the co-marketed products whose authorization applications were accepted only with Module 1 prepared in accordance with Annex-1 shall also be revoked. However, the authorization status of the product(s) for which a co-marketing authorization was issued with a complete dossier shall be updated upon application to the Agency in accordance with the relevant guideline. (3) In variation applications made within the scope of the Regulation on Variations to Marketing Authorizations of Medicinal Products for Human Use, where the applicants request the revocation of existing authorizations, the existing authorizations shall be revoked simultaneously, without suspension, upon issuance of the authorization for the products subject to the variation application. (4) The manufacture or importation of a medicinal product for human use whose authorization has been revoked shall be terminated. The decision regarding medicinal products for human use already on the market shall be given by the Agency, taking into consideration the grounds for the revocation of the authorization. (5) Authorizations suspended upon approval of the revocation procedure pursuant

to paragraph (b) of the first paragraph shall be announced on the official website of the Agency for six months. Authorizations whose suspension is announced on the official website of the Agency under this paragraph shall, upon request, be transferred — provided that the conditions for an authorization transfer application are met — to (Amended phrase: OG-3/12/2024-32741) natural persons or trading companies that have undertaken to place the product on the market and that fulfill the conditions for making an authorization application as laid down in this Regulation, provided that such persons so request and the consent of the marketing authorization holder is obtained. The revocation procedures of the authorizations subject to a transfer application shall not be continued. (6) Where products for which revocation of the authorization is requested pursuant to paragraph (b) of the first paragraph are co-marketed medicinal products for human use whose authorization application was made with a complete dossier, it shall be mandatory for the marketing authorization holder to submit to the Agency the list of the other medicinal product(s) for human use that are subject to co-marketing. (7) (Amended: OG-27/5/2023-32203) The authorization suspension period of products suspended pursuant to paragraphs (i), (j), (o) and (ö) of the first paragraph of Article 22 may be extended up to (Amended phrase: OG-26/12/2023-32411) thirty months upon approval by the Agency. (8) (Amended: OG-27/5/2023-32203) For medicinal products for human use that are included in the list of medicines abroad or that cannot be supplied and would therefore pose a risk to public health, the Agency may extend the authorization suspension period with respect to the matters covered by the fifth and seventh paragraphs. (9) The list of medicinal products for human use whose authorizations have been revoked by the Agency shall be announced on the official website of the Agency. (10) (Added: OG-27/5/2023-32203) Where, as a result of the annual assessment for a medicinal product for human use conditionally authorized under Article 34, the Agency decides to revoke the conditional authorization, the authorization revocation procedures for the products concerned shall be carried out without a suspension procedure pursuant to Article 22.

Loss of the Authorization or the Product Dossiers

ARTICLE 24 – (1) In the event of loss of the authorization granted by the Agency, an application for a lost authorization shall be made to the Agency by the marketing authorization holder with a newspaper announcement evidencing the loss of the authorization. In this case, a new authorization certificate shall be issued. (2) In the event of loss of the dossier of a medicinal product for human use for which an authorization application has been made, an application for the lost authorization dossier shall be made to the Agency by the applicant or the marketing authorization holder. For applications whose justification is deemed appropriate by the Agency, a copy of the dossier shall be provided to the applicant.

Responsibilities of the Marketing Authorization Holder

ARTICLE 25 – (1) The marketing authorization holder is obliged to notify the Agency at least thirty days in advance if, for any reason, it will be unable to supply to the market a product that is on the market. (2) The marketing authorization holder is responsible to the Agency for the following matters with respect to the medicinal product for human use for which it holds the authorization: a) Manufacture of the medicinal product for human use in accordance with the specifications provided in the annex to the application and accepted by the Agency.

b) Submission to the approval of the Agency of any and all modifications necessary in order to take into account scientific and technical progress with respect to manufacturing and control methods and to ensure that the medicinal product for human use is manufactured and controlled by generally accepted scientific methods. c) Updating, where necessary, the summary of product characteristics and the patient information leaflet to ensure the correct and safe use of the medicinal product for human use. ç) Notification of the relevant modification to the Agency, in the event of any modification relating to the medicinal product for human use, within the framework of the provisions of the relevant guideline. d) Timely response to the matters requested by the

Agency regarding the medicinal product for human use. e) Fulfilment of the obligations specified in the Regulation on the Safety of Medicines within the framework of pharmacovigilance activities. f) Taking the necessary measures to prevent possible infections in cases where the medicinal product for human use is a biological medicinal product. g) Ensuring the availability on the market of the medicinal product for human use for which it holds the authorization. ğ) Immediate notification to the the Agency, with all details, of any and all measures taken in the event that the authorization is suspended or the product is withdrawn from the market on grounds of the efficacy of the medicinal product for human use or the protection of public health. h) (Amended: OG-27/5/2023-32203) Notification to the Agency of the following with respect to medicinal products for human use that are imported, exported or manufactured in our country under license, on grounds of quality, efficacy or safety: the suspension or revocation of the authorization, or the withdrawal or recall from the market, in other countries where they are authorized; the rejection of the authorization application, or the withdrawal of the application by the applicant, in other countries where an authorization application has been made. ı) Payment of the determined fees and charges related to medicinal products for human use. (3) (Amended: OG-14/12/2022-32043) (2) The authorization or application holder is obliged to make applications in accordance with the principles set forth in this Regulation, to fulfil the commitments submitted to the Agency and to confirm the accuracy of the information and documents submitted to the Agency, and accepts any and all liability arising from the consequences of such information and documents. (4) The authorization or application holder is responsible for retaining the originals of all documents submitted to the Agency regarding its product and for submitting them to the Agency upon request. (5) The authorization of a medicinal product for human use shall not affect the legal and criminal liability of the marketing authorization holder. (6) (Added: OG-24/9/2022-31963) The Agency may also request additional information and documents for products for which an authorization has been issued in accordance with current scientific requirements. The marketing authorization holder is obliged to submit the information and documents requested by the Agency to the Agency within the specified period. (7) (Added: OG-24/9/2022-31963) Marketing authorization holders are obliged to enter the records of the products into the Agency's information management system in accordance with the requirements determined by the Agency and to ensure that these data are kept up to date.

Transfer of the Authorization

ARTICLE 26 – (1) The marketing authorisation of a human medicinal product licensed by the Agency may be transferred. The following documents shall be submitted to the Agency for authorisation transfer procedures: a) (Amended: OG-24/9/2022-31963) A court judgment certifying that the authorisation has been transferred by court order, a decision of the enforcement office indicating that the authorisation has been sold through compulsory enforcement, or, regarding the parties to the transfer agreement, their (Amended phrase: OG-26/12/2023-32411) trade registry certificate together with an agreement executed before a notary public and containing the following particulars: 1) The name, authorisation date and number of the human medicinal product subject to the authorisation transfer procedure, 2) The names and addresses of the natural persons (Amended phrase: OG-3/12/2024-32741) or commercial companies that will transfer and that will acquire the authorisation, 3) A minutes certifying that the current human medicinal product file, approved by the Agency, complete and up to date, has been delivered in full to the acquiring person. b) Demonstrating that the person acquiring the authorisation is able to fulfil all the responsibilities expected of the authorisation holder: 1) The original or notarised copy of a diploma demonstrating membership in one of the professions specified in Article 7 for persons eligible to apply for an authorisation, or a graduation certificate obtained from the Council of Higher Education, 2) (Amended: OG-3/12/2024-32741) In the case of a commercial company, the Turkish Trade Registry Gazette indicating the duties and titles of the responsible persons, 3) Documents concerning the pharmacovigilance contact person within the scope of the Regulation on the Safety of Medicines, 4) Within the scope of the Regulation on Promotional Activities for Human Medicinal Products, the document describing the scientific service and the address, telephone number and registered electronic mail (KEP) address of that service. c) (Amended: OG-27/5/2023-32203) The name, surname, address, telephone number and registered electronic mail (KEP) address of the person acquiring the authorisation, together with the updated Summary of Product Characteristics of the human medicinal product, patient information leaflet, one sample each of the inner and outer packaging and, in the case of transfers executed through a notary, the original of the previously issued authorisation for the product in question; in cases where the updated Summary of Product Characteristics and patient information leaflet cannot be submitted, a commitment letter, fully prepared by the acquiring party, to the effect that all necessary amendments and updates concerning the Summary of Product Characteristics and patient information leaflet of the human medicinal product will be made, in accordance with the relevant guidelines, after the completion of the authorisation transfer procedures of the human medicinal product, and that no application for a sales permit will be made without obtaining approval; a document demonstrating that manufacturing at the manufacturing site(s) on which the authorisation is based is carried out in compliance with the good manufacturing practice guidelines, and, for active substance manufacturing site(s) operating in Turkey, a Manufacturing Site Licence Certificate, ç) (Amended: OG-3/12/2024-32741) In the case of importation of the human medicinal product, a document issued by the licensor company demonstrating that the natural person (Amended phrase: OG-3/12/2024-32741) or commercial company engaged in importation is the sole authorised representative for the importation into Turkey, authorisation in Turkey and sale of the product in question, and, in the case of co-marketing, that co-marketing authorisation has been granted to a natural person or commercial company other than the sole authorised representative in Turkey; together with the co-marketing agreement containing the written approvals of the natural persons or commercial companies that will engage in co-marketing regarding co-marketing, and the trade registry certificates of the parties, d) (Amended: OG-3/12/2024-32741) In the case where the human medicinal product is manufactured under licence, a document issued by the licensor company demonstrating that the natural person (Amended phrase: OG-3/12/2024-32741) or commercial company engaged in manufacturing is the sole authorised representative for the authorisation in Turkey, manufacture and sale of the product in question, and, in the case of co-marketing, that co-marketing

authorisation has been granted to a natural person or commercial company other than the sole authorised representative in Turkey; together with the co-marketing agreement containing the written approvals of the natural persons or commercial companies that will engage in co-marketing regarding co-marketing, and the trade registry certificates of the parties, e) (Amended: OG-24/9/2022-31963) For human medicinal products manufactured in Turkey, in cases where the applicant is not the manufacturer, a contract manufacturing agreement concluded with a manufacturer meeting the conditions specified in the Regulation on Human Medicinal Product Manufacturing Facilities and the (Amended phrase: OG-26/12/2023-32411) trade registry certificates of the parties. f) (Added: OG-3/12/2024-32741) In cases where a human medicinal product manufactured in Turkey is made subject to co-marketing, the co-marketing agreement containing the written approvals of the natural persons (Amended phrase: OG-3/12/2024-32741) or commercial companies that will engage in co-marketing regarding co-marketing, and the trade registry certificates of the parties. (2) In transfers executed through a notary public, in addition to the documents listed in the first paragraph, the following provisions shall apply: a) A commitment letter prepared by the acquiring company, stating that no changes have been made to the human medicinal product at the time of the transfer application, shall be submitted. b) (Amended: OG-27/5/2023-32203) Provided that the cases deemed necessary by the Agency are exceptions, in accordance with the relevant guideline published by the Agency, where a commitment letter, prepared by the acquiring company, to the effect that all necessary amendments and updates concerning the human medicinal product will be made following the completion of the transfer procedure, is submitted in full, the updates required for the existing product file and the procedures for remedying any deficiencies, where applicable, shall be carried out, in accordance with the relevant guidelines, after the authorisation transfer procedures of the human medicinal product have been completed, and no application for a sales permit may be made without obtaining approval. However, in cases deemed necessary by the Agency, an application may be requested for the updates to the existing product file and the procedures for remedying any deficiencies, where applicable. c) Upon request; subject to the written and notarised mutual agreement of the companies transferring and acquiring the authorisation, the manufacture of products bearing the old barcode and their placement on the market solely by the acquiring company shall be permitted for a period of one year after the date on which the new authorisation is issued (Amended phrase: OG-3/12/2024-32741). The control procedures concerning the manufacturing notifications of products in this situation shall be carried out through the Pharmaceutical Track and Trace System. Such products may remain on the market until their expiry dates. The placement on the market of products transferred at the time of importation shall be discontinued by the transferring company. Products bearing the old barcode may be imported for a period of one year after the date on which the new authorisation is issued (Amended phrase: OG-3/12/2024-32741), subject to the written and notarised mutual agreement of the companies transferring and acquiring the authorisation. However, such products may be placed on the market by the transferring company, provided that a manufacturing notification is submitted to the Pharmaceutical Track and Trace System by the transferring company and the products are transferred to the acquiring company through the Pharmaceutical Track and Trace System. (3) Where the licensor company changes the natural person (Amended phrase: OG-3/12/2024-32741) or commercial company it has authorised with respect to the authorisation/sale/manufacture of the product in question in Turkey, in addition to the documents listed in the first paragraph of this Article, the submission of a letter from the existing authorisation holder notifying that it has returned the original of the authorisation shall be required; where a court decision demonstrating that the authorisation of the existing authorisation holder has ceased is submitted, the fulfilment of all requirements set out in this Article, together with the Module 1 file of the human medicinal product prepared in accordance with Annex-1, shall be mandatory, except for paragraph (a) of the first paragraph. However, where the product in this situation is the sole diagnostic or sole treatment option for a disease in our country, the Agency may accept and conclude the transfer

application regarding the authorisation/licence or registration certificate without awaiting the court decision. (4) The Agency shall evaluate the authorisation transfer application within thirty days. (5) (Added: OG-24/9/2022-31963) The information and documents requested by the Agency, or the necessary explanation, together with the date information indicating that such information and documents could not be submitted, at the latest within thirty days

If not submitted to the Agency (Amended phrase: OG-26/12/2023-32411), the transfer application shall be cancelled and the file shall be returned. (6) (Added: OG-3/12/2024-32741) A transfer shall not be effected for medicinal products for human use whose license renewal procedure has not been carried out. Transfer of the License Application

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ARTICLE 27 – (1) A (Amended phrase: OG-3/12/2024-32741) natural person or commercial company applying for a marketing authorisation may transfer the rights arising from the application to another (Amended phrase: OG-3/12/2024-32741) natural person or commercial company, provided that the relevant conditions specified in Article 26 are fulfilled.

Obtaining a sales permit

ARTICLE 28 – (1) It is mandatory to obtain a sales permit for a medicinal product for human use that will be placed on the market for the first time following authorisation by the Agency in accordance with the provisions of this Regulation. (2) (Amended: OG-24/9/2022-31963) For medicinal products for human use that will be placed on the market for the first time following authorisation by the Agency, the marketing authorisation holder shall, for medicinal products for human use whose sales price application to the warehouse has been approved by the Agency, submit to the Agency, together with the sales permit application: the document issued by the Agency if the storage activities are carried out (Amended phrase: OG-3/12/2024-32741) in facilities belonging to the holder itself, the document issued by the Agency pertaining to the warehouse in other cases, the document signed between the parties for the storage of the product, and the (Amended: OG-26/12/2023-32411) trade registry certificate of the parties. (3) (Amended: OG-24/9/2022-31963) The Agency examines the sample packaging and patient information leaflet of the medicinal product for human use for which a sales permit application has been made and whose price has been approved by the Agency, with respect to the required information. (4) (Amended: OG-24/9/2022-31963) It is not necessary to obtain a new sales permit for procedures that lead to changes in the packaging information or characteristics on which the authorisation is based, or in the patient information leaflet, of the medicinal product for human use. However, before being placed on the market for the transfer of the manufacturing site from abroad to our country or from our country to abroad, the replacement of the strain(s) in a seasonal, pre-pandemic or pandemic influenza vaccine with a new one, a change in the pack size, following marketing authorisation transfer procedures, or for products whose suspended authorisation has been reinstated pursuant to the fifth paragraph of Article 22, a sales permit shall be obtained by applying to the Agency without submitting the documents specified in the second paragraph. (5) (Added: OG-24/9/2022-31963) For medicinal products for human use that are recognised by the World Health Organization or the European Union, that will be used in emergencies against public health threats accepted by the Ministry of Health, and the supply of which will be carried out solely by the public, the Agency may define restrictions in the sales permit concerning the public healthcare institutions and organisations to which the products in question may be supplied. The restrictions in question shall be specified in the sales permit.

Placing on the market permit for blood products

ARTICLE 29 – (1) (Amended: OG-24/9/2022-31963) For blood products holding a sales permit, which are licensed and for which a marketing authorisation application has been made, or which hold a marketing authorisation, the authorisation/licence holder shall, before placing the product on the market, apply to the Agency in addition to the matters set out in Article 28, in accordance with the guideline published by the Agency, in order to obtain a placing on the market permit for each batch of the product. (2) (Amended: OG-27/5/2023-32203) Prior to the placing on the market permit, in the case of blood products or medicinal products for human use containing blood products, or where the blood product is present in the composition of the medicinal product for human use as an active or excipient substance; the analyses determined according to the product shall have been carried out for each batch of the products at the Agency laboratory or at a laboratory accepted by the Agency for this purpose. (3) (Amended: OG-24/9/2022-31963) In order to obtain a placing on the market permit for blood products or medicinal products for human use containing blood products, if the quantity requested to be put up for sale, together with the documents and information specified below, is submitted to the Agency and the aforementioned documents are deemed appropriate by the Agency together with the analyses carried out in accordance with the second paragraph, a placing on the market permit shall be granted for the medicinal products for human use in question: a) The name and composition of the medicinal product for human use, b) For each batch of bulk blood product or each batch of finished blood product, or in cases where the blood product is not present as an active substance in the composition of the medicinal product for human use, for each batch of the excipient that is a blood product, a batch release certificate certified by a Health Authority and approved by the Agency (if the document is obtained from abroad, with apostille/consular legalisation), or, if the batch release certificate cannot be submitted, the documents specified in the guideline published by the Agency, c) A certified certificate of analysis for each batch of bulk or finished product, ç) A document issued by the marketing authorisation holder and, where applicable, the licensor or the manufacturer, indicating with quantities in which country/countries each batch has been sold, and, for cases where it has not yet been sold, a document declaring the status of the unsold products; in cases where only importation into our country is in question for the batch, a document indicating with quantities in which country/countries the other products in which each batch of the plasma pools used in the batch in question has been used have been sold, d) (Amended: OG-27/5/2023-32203) The rules on which plasma donation is based, the collection date of the plasma and the donor type (voluntary, paid), prepared by the licensor or the manufacturer, and a commitment that a list of the donors or donor centres will be submitted where the Agency deems it necessary, e) Documents, prepared in accordance with the guideline published by the Agency, indicating that HBsAg, HIV 1/2 and HCV RNA tests have been performed on the samples belonging to each plasma pool and their results, f) (Amended: OG-27/5/2023-32203) For each batch of the final bulk or finished product and, in cases where the blood product is not present as an active substance in the composition of the medicinal product for human use, for each batch of the excipient(s) that is a blood product; a document issued by the manufacturer or licensor certifying that the donors are safe with respect to diseases determined by the Agency or suspected diseases (for example, Creutzfeld-Jakob (CJ) disease) and that there are no donors with these diseases among the donors, g) A current variation commitment for the product with the specified batch number, prepared by the marketing authorisation holder and, where applicable, the licensor or the manufacturer. (4) (Amended: OG-27/5/2023-32203) For medicinal products for human use for which it is envisaged that blood products will be imported as bulk products and placed on the market through the manufacture of the finished product in our country, for each batch of the bulk product to be imported, in addition to the matters set out in subparagraphs (a), (b), (c), (d), (e) and (f) of the third paragraph, the original document issued by the marketing authorisation holder and, where applicable, the licensor, indicating the country/countries where the other products in which the plasma pools used in the bulk product

have been used are authorised/manufactured and in which country/countries they have been sold, must be submitted to the Agency. For blood products imported as bulk, manufactured in our country, and accordingly authorised and granted a sales permit, provided that all documents within the scope of this paragraph are submitted and the analyses carried out in accordance with the second paragraph and the relevant information and documents are deemed appropriate, a placing on the market permit shall be granted in accordance with the guideline published by the Agency upon submission of only the commitment expressed in subparagraph (g) of the third paragraph. (5) (Added: OG-24/9/2022-31963) In cases where the blood product is present in the composition of the medicinal product for human use as an excipient in addition to the active substance, in addition to the currently requested documents, for each batch of the excipient(s) that is a blood product, the information and documents set out in subparagraphs (b), (c), (e) and (f) of the third paragraph must also be submitted to the Agency.

Placing on the market permit for immunological medicinal products for human use

ARTICLE 30 – (1) For immunological medicinal products for human use that are licensed or authorized with a sales permit, excluding allergen products, and for which a licensing application has been filed; the marketing authorization holder shall apply to the Agency, before placing the product on the market, in order to obtain a market release permit for each batch of the product. (2) For immunological medicinal products for human use that are authorized and for which a licensing application has been filed, the analyses determined according to the product must have been performed at the Agency laboratory or at a laboratory accepted by the Agency for this purpose, prior to the market release permit. (3) (Amended: OG-24/9/2022-31963) In order to obtain a market release permit for immunological medicinal products for human use that are authorized and for which a licensing application has been filed or that are licensed, the following documents and information shall be submitted to the Agency, together with the declaration of the quantity requested to be placed on the market: a) For each batch, for the bulk or finished product, a Health Authority-certified batch release certificate deemed appropriate by the Agency (if the document is obtained from abroad, with an apostille annotation/consular approval); in cases where the batch release certificate cannot be submitted, the documents specified in the guideline published by the Agency, b) For each batch of bulk or finished product, a certified certificate of analysis, c) A current variation commitment for the product to be imported, with the batch number specified, issued by the marketing authorization holder company and, where applicable, by the licensor or the manufacturer, (4) (Amended: OG-24/9/2022-31963) In cases it deems necessary, the Agency may request that all or part of the analyses contained in the batch release certificate specified in subparagraph (a) of the third paragraph be performed by the Agency laboratory. (5) (Added: OG-24/9/2022-31963) For immunological medicinal products for human use that are authorized and for which a licensing application has been filed or that are licensed, a market release permit shall be granted for the relevant batch if the documents submitted within the scope of the application, and the analysis results of the products that are authorized and for which a licensing application has been filed, are found to be satisfactory. (6) (Amended: OG-27/5/2023-32203) For licensed allergen products with a sales permit, excluding the allergen products specified in the relevant guideline; the marketing authorization holder shall apply to the Agency, before placing the product on the market, with the information and documents specified in the guideline published by the Agency in order to obtain a market release permit for each batch of the product. For licensed allergen products, a market release permit shall be granted for the relevant batch if the documents submitted within the scope of the application are found to be satisfactory. (7) (Added: OG-24/9/2022-31963) For blood-component-based medicinal products for human use whose active substance(s) is/are not derived from human blood or plasma but whose manufacturing process involves blood components derived from human blood or plasma, the analyses determined by the Agency according to the product must have been performed for each batch at the Agency laboratory or at a laboratory accepted by the Agency for this purpose. For the said products, an application shall be made with the information and documents specified

in the guideline published by the Agency. (8) (Added: OG-24/9/2022-31963) For vaccines and immune sera that are licensed or conditionally licensed (Emergency Use Authorization) and are to be filled (Amended phrase: OG-27/5/2023-32203) or manufactured in our country, an application shall be made for the market release permit of each batch of the finished product with the information and documents specified in the guideline published by the Agency.

Variations after licensing

ARTICLE 31 – (1) Except for Article 26, after a medicinal product for human use has been licensed, the marketing authorization holder shall apply to the Agency for all changes relating to that product in accordance with the provisions of the relevant regulation and guideline. (2) In the event of an application, and subject to a fee included in the price tariff, the Agency may provide scientific advice to the applicant after the medicinal product for human use has been licensed.

SECTION FOUR Licensing under Conditional and Exceptional Circumstances, Compulsory Licensing, Trust (1)

Determination of the special situation

ARTICLE 32 – (1) The determination of the special situation regarding the need for conditional and exceptional licensing of medicinal products for human use shall be carried out by the Priority Assessment Board. For medicinal products for human use that, as a result of the assessment carried out by the Priority Assessment Board, are found appropriate for a conditional or exceptional licensing application, an application shall be made to the Agency in accordance with Article 33 or 36.

Application for conditional licensing (emergency use authorization)

ARTICLE 33 – (1) For medicinal products for human use falling under at least one of the following, excluding changes involving the modification or addition of new therapeutic indications of a licensed medicinal product for human use, an application for conditional licensing may be made to the Agency: a) Medicinal products for human use intended for the treatment, prevention or medical diagnosis of diseases that are life-threatening or cause serious disability, b) Medicinal products for human use to be used in emergency situations against public health threats recognized by the World Health Organization or the European Union or accepted by the Ministry of Health. (2) Notwithstanding the fact that comprehensive clinical data on efficacy and safety have not yet been obtained, a conditional license may be granted if all of the following requirements are met: a) The benefit/risk balance of the medicinal product for human use being positive, b) The applicant's ability to provide comprehensive clinical data, c) Fulfilment of an unmet medical need, ç) The public health benefit provided by the availability on the market of the relevant medicinal product for human use, despite its need for additional data, being greater than the risk that would arise from its unavailability. (3) The unmet medical need referred to in subparagraph (c) of the second paragraph means that there is no medical diagnostic, disease prevention or treatment method in our country that sufficiently meets this need, or that, even if a method meeting the need exists, this method would provide a substantial therapeutic advantage for patients. (4) Applications to be made under this Article shall be made in accordance with the guideline published by the Agency.

Assessment of applications for conditional licensing (emergency use authorization), the duration and renewal of the conditional license

ARTICLE 34 – (1) For a medicinal product for human use for which an application for conditional licensing has been made pursuant to Article 33, licensing shall be carried out or licenses shall be renewed under the following conditions: a) It shall be stated in the summary of product characteristics and the patient information leaflet that the product is still inadequate in certain respects, that the validity period of the license is one year, and that the license will be re-assessed annually. b) The marketing authorization holder must apply for renewal of the license,

at the latest ninety days before the end of the validity period of the license, together with an interim report on the status of the specific obligations to which it is subject. c) If the license renewal application has been made within the period specified in subparagraph (b), the product may remain on the market until the Agency notifies its decision. ç) The marketing authorization holder must submit a periodic benefit/risk assessment report to the Agency, immediately upon request by the Agency or at least every six months. (2) The Agency shall conclude the license renewal application referred to in subparagraph (b) of the first paragraph within ninety days.

Specific obligations relating to the conditional license (emergency use authorization)

ARTICLE 35 – (1) The specific obligations applicable to a human medicinal product for which a conditional marketing authorization application has been made shall be determined by the Agency.

(2) Following the determination of specific obligations, for products granted conditional marketing authorization, the marketing authorization holder shall be required to complete ongoing studies or to conduct new studies in order to ensure that the requirements set forth in the second paragraph of Article 33 are fulfilled and that a positive benefit/risk balance is confirmed. Specific obligations may additionally be imposed for the collection of pharmacovigilance data. (3) The Agency shall publish the specific obligations for conditionally authorized products and the timeline required for the completion of these obligations on the official website of the Agency. (4) Upon fulfillment of all specific obligations, a marketing authorization not subject to specific obligations shall be issued by the Agency. Application for exceptional marketing authorization, evaluation of the application, and validity of the authorization

ARTICLE 36 – (1) In the exceptional circumstances listed below, an application for exceptional marketing authorization may be made, provided that certain conditions, particularly relating to the safety of the human medicinal product, are fulfilled by the applicant: a) The therapeutic indications of the human medicinal product in question are so rare that comprehensive evidence cannot reasonably be expected to be provided by the applicant, or b) In the light of current scientific knowledge, detailed information cannot be provided, or c) The collection of such information would be contrary to generally accepted principles of medical ethics. (2) An exceptional marketing authorization may be granted only where the applicant demonstrates, with objective and verifiable reasons, that comprehensive data on efficacy and safety under normal conditions of use of the medicinal product cannot be provided, and it fulfills the requirements set out in Annex-1. (3) The validity of the authorization shall be subject to the annual reassessment of these conditions. Compulsory license

ARTICLE 37 – (1) For products deemed appropriate by the President of the Republic to be manufactured under a compulsory license within the scope of Article 132 of the Industrial Property Code, a marketing authorization application may be made to the Agency in accordance with the requirements, the detailed matters of which shall be determined by the Agency. Reliance

ARTICLE 37/A- (Added: OG-24/9/2022-31963) (1) Previous assessments carried out by other medicinal authorities with comparable standards or by regional or international organizations may be taken into consideration in accordance with the guideline published by the Agency. Fees

ARTICLE 38 – (1) The Agency may apply fees for the activities covered by this Regulation. SECTION FIVE Miscellaneous and Final Provisions Guidelines

ARTICLE 39 – (1) The Agency shall, where it deems necessary, publish guidelines or communiqués for the implementation of this Regulation. Confidentiality

ARTICLE 40 – (1) Information submitted to the Agency by the applicant in order to obtain a marketing authorization for a human medicinal product shall be confidential. Such confidentiality shall be protected by the Agency. Recall

ARTICLE 41 – (1) For products falling within the scope of this Regulation, in cases where recall is at issue, the provisions of the Recall Regulation published in the Official Gazette No. 29537 dated 19/11/2015 shall apply to the collection and recall procedures. Repealed regulations

ARTICLE 42 – (1) The Regulation on the Licensing of Human Medicinal Products published in the Official Gazette No. 25705 dated 19/1/2005 and the Regulation on the Evaluation of Bioavailability and Bioequivalence of Pharmaceutical Preparations published in the Official Gazette No. 21942 dated 27/5/1994 have been repealed. References

ARTICLE 43 – (1) References made to the Regulation on the Licensing of Human Medicinal Products, repealed by Article 42, shall be deemed to be made to this Regulation. Alignment with European Union legislation

ARTICLE 44 – (1) This Regulation has been prepared within the framework of alignment with the European Union legislation, taking into consideration Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on medicinal products for human use and Commission Regulation (EC) No 507/2006 of 29 March 2006 on the conditional marketing authorisation for medicinal products for human use.

Exceptional circumstances

ADDITIONAL ARTICLE 1- (Added: OG-3/12/2024-32741)

(1) In the event of serious supply problems that would adversely affect the normal life and activities of the whole or certain segments of society, the Agency may permit the placing on the market of a licensed medicinal product for human use in limited quantities and for a limited period, upon the request of the marketing authorisation holder, provided that it is limited to individual cases, that the relevant situation does not compromise product safety, and that it is deemed appropriate by the Priority Assessment Board, for the purpose of ensuring the sustainability of healthcare services by the Ministry.

Variation applications for medicinal products for human use containing an integral medical device

ADDITIONAL ARTICLE 2- (Added: OG-3/12/2024-32741)

(1) In cases where a medicinal product for human use, for which a variation application has been filed under the Regulation on Variations to Licensed Medicinal Products for Human Use, contains an integral medical device, if it is declared by the applicant that there is no modification/addition/removal to the integral medical device of the already licensed medicinal product for human use, nor any modification affecting the performance of the device, a CE certificate or notified body opinion regarding the integral medical device of the medicinal product for human use subject to the variation application shall not be required.

Products with permits and registration certificates

PROVISIONAL ARTICLE 1 – (Amended: OG-26/12/2023-32411) (3)

(1) For products that hold an interim product permit pursuant to Provisional Articles 1 and 2 of the Regulation on Traditional Herbal Medicinal Products published in the Official Gazette dated 6/10/2010 and numbered 27721, or for which an application for a marketing authorisation has been filed while procedures for an interim product permit were ongoing, and which have been decided to be evaluated within the scope of medicinal products for human use and whose licensing process is ongoing, it is mandatory to complete the licensing process within two years from the entry into force of this Regulation. Within this period, the permits of those products holding an interim product permit that have failed to obtain a marketing authorisation shall be revoked. The manufacture, import and placing on the market of these products whose interim product permits have been revoked shall not be permitted. Products present on the market may remain on the market until the end of their shelf life.

(2) For blood products and immunological medicinal products for human use that are placed on the market under an import permit and for which a marketing authorisation application has been filed, it is mandatory to complete the licensing process by 31/12/2023. Within this period, the import permits of products that have failed to obtain a marketing authorisation shall become invalid.

(3) For radionuclide generators, kits, radionuclide precursor radiopharmaceuticals and industrially prepared radiopharmaceuticals that are placed on the market under a registration certificate and for which a marketing authorisation application has been filed, it is mandatory to complete the licensing process by 31/12/2025. Within this period, the registration certificates of products that have failed to obtain a marketing authorisation shall become invalid.

Transition to certified marketing authorisation

PROVISIONAL ARTICLE 2 – (1) For medicinal products for human use without a certified marketing authorisation, an application for transition to a certified marketing authorisation shall be filed with the Agency within sixty months from the entry into force of this Regulation, in line with the transition schedule announced by the Agency. For medicinal products for human use for which the original marketing authorisation cannot be submitted for making an application within this scope, a lost marketing authorisation application shall be filed.

(2) Variation applications filed with the Agency for medicinal products for human use for which no transition application to a certified marketing authorisation has been made within the periods specified in the schedule set forth in the first paragraph shall not be processed.

(3) It is not mandatory to file a transition application to a certified marketing authorisation for medicinal products for human use whose marketing authorisation has been suspended. For a medicinal product for human use whose marketing authorisation has been suspended and which has no certified marketing authorisation, it is necessary to obtain a certified marketing authorisation for the product in question before it is placed on the market.

Marketing authorisation transition application for immunological medicinal products for human use or blood products

PROVISIONAL ARTICLE 3- (Amended together with the Heading: OG-24/9/2022-31963) (1) For blood-component-based medicinal products for human use whose active substance(s) are not obtained from human blood or plasma but whose manufacturing process includes blood components obtained from human blood or plasma, currently licensed as blood products, an application shall be filed with the Agency within two years from the entry into force of this Regulation for an immunological medicinal product for human use marketing authorisation. For these applications, it is mandatory to complete the marketing authorisation variation process within one year from the date of application. For medicinal products for human use whose marketing authorisation variation process has not been completed within this period, the suspension of the marketing authorisation shall be applied in accordance with paragraph (h) of the first subparagraph of Article 22.

(2) For blood-component-based medicinal products for human use containing blood components obtained from human blood or plasma as their active substance(s), currently licensed as immunological products, an application shall be filed with the Agency for a blood product medicinal product for human use marketing authorisation by 1/1/2024.

Marketing presentation permit analysis for blood products

PROVISIONAL ARTICLE 4 – (Repealed: OG-24/9/2022-31963)

Co-marketed medicinal products for human use

PROVISIONAL ARTICLE 5 – (1) For medicinal products for human use for which a co-marketing marketing authorisation application was filed prior to the publication date of this Regulation by submitting only Module 1 prepared in accordance with Annex-1, and whose authorisation process is ongoing, if the marketing authorisation holders wish to convert their application dossiers into complete dossiers, they shall submit all required modules to the Agency within thirty days of the publication of the Regulation.

(2) For medicinal products for human use subject to co-marketing that were licensed prior to the publication date of this Regulation by submitting only Module 1 prepared in accordance with

Annex-1, if the marketing authorisation holders wish to convert their marketing authorisation dossiers into complete dossiers, they shall submit all required modules to the Agency in updated form within six months after the publication of the Regulation.

Provisional permits for allergen products

PROVISIONAL ARTICLE 6- (Added: OG-24/9/2022-31963) (1) Allergen products manufactured in any of the countries within the European Union and currently present on the market in European Union member states may be placed on the market until 1/1/2026 (Amended phrase: OG-3/12/2024-32741), provided that the following requirements are met: a) A provisional permit application is filed with Module 1 prepared in accordance with Annex-1. b) Annex 6.15 of the application form contained in Module 1 includes only the current Certificate of a Pharmaceutical Product demonstrating that the product in question is present on the market of the relevant country. c) During the preliminary assessment, the Agency examines the allergen product provisional permit application made with Module 1 and officially notifies the applicant whether the application has been accepted or rejected. The notification of acceptance of the application is deemed to be the starting date of the provisional permit assessment process. The provisional permit assessment process is concluded within thirty days at the latest. The time elapsed for assessments by external organisations to the Agency; the time elapsed for official holidays, excluding weekend holidays, and the time elapsed for extraordinary circumstances are not included in the provisional permit period. ç) The provisional permit date, provisional permit number and provisional permit holder information shall be included in the SmPC, PL and packaging information of the product until the licensing process is completed. d) In order for products granted a provisional permit to be placed on the market, an application is made to the Agency in accordance with the requirements set forth in Article 28 and the relevant guideline. e) Marketing authorisation applications for products granted a provisional permit, filed with the submission of all modules in accordance with Articles 6 and 8, shall be evaluated in accordance with Article 12, and if found suitable, the scientific and administrative assessment process shall be initiated. If the said process is also found suitable, the product is licensed. For marketing authorisation applications made with Module 1, upon submission of all modules, the application

and the scientific and administrative assessment thereof is deemed appropriate by the Agency, the product shall be licensed. For licensed products, an application for a sales permit shall be made to the Agency, together with the information forming the basis of the licence and in accordance with the requirements set out in Article 28, in order for the products to be placed on the market. f) (Amended phrase: OG-3/12/2024-32741) It is required that the application be completed with all modules and that the products in question be licensed by 1/1/2026. Within this period, the provisional authorisation of products whose licensing procedure is not completed or whose licence application is rejected on procedural or substantive grounds shall be revoked and their placing on the market shall be suspended. Provisional authorisation applications to be made anew for products whose applications have been rejected under this paragraph shall not be taken into evaluation by the Agency. g) Where, in the course of the scientific evaluation of products granted provisional authorisation and whose licensing procedure is ongoing, the application is rejected on substantive grounds in accordance with the provisions of Article 18, the provisional authorisation shall be revoked, the placing on the product on the market shall be suspended, and the products on the market shall be withdrawn from the market in accordance with the relevant provisions of the Withdrawal Regulation.

Equivalent medicinal products and hybrid applications **PROVISIONAL ARTICLE 7-** (Added: OG-24/9/2022-31963) (1) In licence applications for equivalent medicinal products and hybrid products to be made by 31/12/2022, equivalent medicinal products licensed in our country may be used as reference medicinal products.

Medical devices for which a notified body opinion or CE certificate is required **PROVISIONAL ARTICLE 8-** (Added: OG-24/9/2022-31963) (1) For medicinal products for human use incorporating

an integrated medical device, for which a licence application is made or which are licensed in accordance with this Regulation, (Amended phrase: OG-3/12/2024-32741) it is mandatory to submit a notified body opinion or CE certificate in the manner specified in Annex-1, in accordance with the dates specified in sub-paragraphs (1) and (2) of paragraph (b) of the fifth paragraph of Provisional Article 1 of the Medical Devices Regulation published in the Official Gazette No. 31499 duplicate, dated 2/6/2021, and licence applications made until the said date shall be made in accordance with the provisions of the relevant guideline.

Procedural rejection of the application PROVISIONAL ARTICLE 9- (Added: OG-24/9/2022-31963) (1) Paragraph (c) of the first paragraph of Article 13 shall not apply until 1/1/2023.

Acceptance of clinical trials PROVISIONAL ARTICLE 10- (Added: OG-24/9/2022-31963) (1) Sub-paragraphs (2) and (3) of paragraph (m) of the first paragraph of Article 8 shall not apply until (Amended phrase: OG-3/12/2024-32741) 1/1/2026 (Amended phrase: OG-27/5/2023-32203).

Definition of reference medicinal product PROVISIONAL ARTICLE 11- (Added: OG-24/9/2022-31963) (1) With the exception of biosimilar and bioavailability studies, paragraph (çç) of the first paragraph of Article 4 shall not apply until 1/1/2024. Until the said date, a medicinal product for human use which has been licensed or authorised to be placed on the market for the first time anywhere in the world in terms of the active substance(s), and which has been proven to possess scientifically acceptable efficacy, quality and safety, shall be accepted as the reference medicinal product.

Medicinal products for human use not included in the list of licensed medicinal products for human use PROVISIONAL ARTICLE 12- (Added: OG-24/9/2022-31963) (1) For products not included in the list of licensed medicinal products for human use announced by the Agency on its official website pursuant to this Regulation, the licence holders shall apply to the Agency by 31/12/2022, together with the documents determined by the Agency. Products whose applications are found appropriate shall be added to the list. The licences of products whose inclusion in the list is not deemed appropriate, or for which no application is made in accordance with the requirements determined by the Agency by 31/12/2022, shall be deemed invalid.

Products with an ongoing licensing procedure PROVISIONAL ARTICLE 13- (Added: OG-3/12/2024-32741) (1) The licensing procedures of medicinal products for human use whose licensing procedure is ongoing as of 1/3/2024 and for which an analysis result forming the basis of the licence has not yet been found appropriate shall not be completed without an analysis conformity. For medicinal products for human use in the licence application process whose first analysis result forming the basis of the licence is found inappropriate, the analysis shall be repeated by requesting a remedied sample from the company. If nonconformity is also found in the second analysis, an evaluation meeting shall be held with the company representatives regarding the analysis method; the analysis method of the new sample shall be determined and the analysis shall be carried out. If nonconformity is also found in the third analysis, a final evaluation meeting shall be held with the company representatives, the analysis nonconformity shall be described, a new analysis method shall be determined and the analysis shall be performed for the last time. Notwithstanding the completion of the analysis steps specified, where it is determined that the qualitative or quantitative formula of the medicinal product for human use is nonconforming or that the declared specifications of the medicinal product for human use are outside the acceptable limits, the licence application shall be rejected. (2) For medicinal products for human use whose analysis procedures forming the basis of the licence are still ongoing as of 1/3/2024, the parameters under analysis must be concluded as appropriate in order for the licensing procedures to be completed. If the analysis result in question is not found appropriate, the procedures shall be carried out in accordance with the first paragraph.

Products transitioning from the class of traditional herbal medicinal products to the class of medicinal products for human use PROVISIONAL ARTICLE 14- (Added: OG-3/12/2024-32741) (1) For products transitioning from the class of traditional herbal medicinal products to the class of

medicinal products for human use, it is mandatory to make the licence application within one year from the date on which the transition decision is officially notified to the applicant, and to complete the licence application within five years. Within this period, the traditional herbal medicinal product licences of products for which no licence application is made and which cannot obtain a licence shall become invalid.

Acceptance of transfer applications for medicinal products for human use for which licence renewal has not been carried out PROVISIONAL ARTICLE 15- (Added: OG-3/12/2024-32741) (1) The sixth paragraph of Article 26 shall not apply until 1/7/2025.

z. Entry into Force

ARTICLE 45 – (1) Of this Regulation; a) subparagraphs (i) and (j) of the first paragraph of Article 22 shall enter into force one year after the date of its publication, b) (Repealed: OG-24/9/2022-31963) c) the other provisions shall enter into force on the date of its publication. Execution

ARTICLE 46 – (1) The President of the Turkish Medicines and Medical Devices Agency shall execute the provisions of this Regulation. _____ (1) By the amendment published in the Official Gazette No. 31963 dated 24/9/2022, the heading of the fourth part of the Regulation, which was "Licensing in Conditional and Exceptional Circumstances", has been amended as incorporated into the Regulation. (2) This amendment shall enter into force on the date of its publication, with effect from 11/12/2022. (3) This amendment shall enter into force on the date of its publication, with effect from 11/12/2023.

[Click here for the Annex.](#)

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