**Dear colleagues,**

In this digest you will find the most important news on registration, safety and quality management of **medicinal products** in Azerbaijan, Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Mongolia, Tajikistan, Turkmenistan, Ukraine and Uzbekistan, which entered into force at the end of 2018 and in the first half of 2019.

**The most significant news in brief:**

In **Armenia** On March 30, 2019 the Decree of the Government of the Republic of Armenia No. 162-N dated February 28, 2019 "On Establishing the Procedures for State Registration, Renewal, and Variations of the Term of the Certificate of Medicinal Product in the Republic of Armenia" entered into force, which made significant changes to the registration procedures.

In **Kyrgyzstan** in December 2018 a new Order for the organization of a pharmacovigilance system developed in accordance with the EAEU GVP **entered** into force.

In March 2019 significant changes to the procedure for registering **medicinal products** came into force, including: issuance of an unlimited marketing authorization after renewal; the introduction of an accelerated and simplified procedure for the registration of medicinal products registered in the USA, UK, Switzerland, the European Union and Japan, as well as prequalified by WHO; simplified and accelerated registration of orphan products etc.

Also a single information system for all regulatory processes is being introduced in Kyrgyzstan, which transfers the relationship between the regulator and the medical and pharmaceutical market operators in an electronic format (online medicinal product registration system, online certification of medicinal products and medical devices, a single window for customs clearance of medicinal products and medical devices when imported).

In early April **Kazakhstan** introduced changes to the inspection procedure: the register of pharmaceutical inspectors of the Republic of Kazakhstan, supplemented list of documents that are attached to the Application for Inspection and specified cases of inspections.

In mid-April significant changes were made to the Rules for Medicinal Products Expert Evaluation: many paragraphs of the order were set out in a new edition. The deadline for submission of an Application for renewal was changed and amounted to 180 days before the expiration of the marketing authorization, instead of 6 months after the marketing authorization expired. At the end of May this Order was canceled.

At the end of April changes were made to the requirements for labeling and instruction for medical use: additional information was added and the requirements for documents were detailed.

In **Uzbekistan** at the end of October 2018 a Regulation on the procedure for recognizing the results of registration of medicinal products and substances of countries with high regulatory requirements was adopted. In mid-February 2019 the first Presidium on the recognition procedure was held and the first registrations were granted under the simplified procedure, which became evidence of the successful implementation of the recognition procedure.

In **Ukraine** in early April 2019 amendments to the Procedure for State Registration of Medicinal Products and a number of related legislative acts entered into force. Among the most significant changes are:

- the deadline for submitting an Application for Renewal has been changed from 90 to 180 days before the expiration of the marketing authorization (we recommend to apply for renewal in 10-12 months before the registration end date).

- the period of validity of marketing authorizations issued under the special procedure (Order No. 721 of the Ministry of Health) for the registration of medicinal products purchased by specialized international organizations has been extended by 1 year (until March 31, 2020).

In mid-July the Law "On Ensuring the Functioning of the Ukrainian Language as a State Language" entered into force, for many of which provisions transitional periods of 6 months or more have been established.

In **Eurasian Economic Union** till the end of May 2019 only 2 medicinal products were registered according to the unified EAEU rules, for both Kazakhstan was chosen as the reference country. In total, 68 applications for medicinal products registration are pending in the EU Unified Information System.

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**You can find more information about these and other changes below.**

If you have any questions - we will be glad to answer them by e-mail info@cratia.ua, by telephone +38 044 332-42-94, or at a meeting at our office.

## Armenia:

On March 30, 2019 the Resolution of the Government of the Republic of Armenia No. 162-N dated February 28, 2019 "On Establishing the Procedures for State Registration, Renewal, and Variations of the Term of the Certificate of Medicinal Product in the Republic of Armenia" entered into force. The Resolution approved:

1) The procedure for state registration, Renewal, Variations of the term of the certificate of medicinal product in the Republic of Armenia, as well as the refusal of state registration, renewal, renewal of the certificate, suspension of registration and recognition as invalid;
2) The procedure for the purpose of state registration, Renewal, Variations of the certificate of medicinal products for expert evaluation, as well as submission after registration changes and expert evaluation;
3) A list of necessary documents for state registration, Renewal, renewal of the certificate of medicinal products for expert evaluation, as well as for submission after registration changes and expert evaluation;
4) A list of changes not requiring a new registration of the registered medicinal product;
5) The procedure for recognition of professional review and review reports by the competent authority of other countries.

Please note that medicinal products are registered according to a simplified and general procedure in the Republic of Armenia. The simplified registration procedure applies to products registered in ICH member countries, as well as to WHO prequalified medicinal products. The maximum duration of the simplified procedure is 31 calendar days, not taking into account the 10 calendar days that are given to respond to deficiencies.

## Kazakhstan:

On April 10, 2019 the Ministry of Health Order No. 742 of November 19, 2009 was amended with the changes "On Approval of the Rules for Inspecting the Circulation of Medicinal Products, Medical Devices and Medical Equipment". The most significant changes are:

1) definitions of good laboratory practice (GLP), good clinical practice (GCP), good manufacturing practice (GMP), good distribution practice (GDP), good pharmacy practice (GPP), good pharmacovigilance practice (GVP), and other good pharmaceutical practices have been added;
2) the list of documents that are attached to the Application for inspection has been supplemented: among the previously required documents, a copy of the license for activities and a list of medicinal products produced (planned for production) at the production site (for manufacturers); copies of documented standard operating procedures are also required.
3) detailed information indicating all cases of production inspection:
   - obtaining a certificate (conclusion) or extending its validity, as well as in accordance with good pharmacovigilance practice (GVP);
   - for the purposes of licensing pharmaceutical activities, registration, expert evaluation of medicinal products or conducting investigations related to the safety, quality and efficacy of medicinal products, medical devices, in accordance with the pharmaceutical inspection program;
   - based on the results of a previous pharmaceutical inspection in order to confirm the elimination of identified non-conformities;
   - for confirmation by entities that have received a certificate confirming compliance of the facility with the requirements of good pharmaceutical practices in the field of medicinal products circulation at least once every two years in accordance with the inspection schedule approved by the head of the state body or territorial unit.

4) amendments were made to the actions of the inspection team during the inspection, for example, during the inspection, audio and/or video recording, photo shooting is carried out.
5) terms of the inspection procedure have been changed.

On April 24, 2019 amendments were approved by Order of the Ministry of Health of the Republic of Kazakhstan No. KR DSM-48 to the "Rules for the compilation and execution of instructions for medical use and the general characteristics of medicinal products and medical devices" (Order No. 414 of May 29, 2015).
In the updated version of the Order, additional information was introduced and each item in the Procedure for compiling instructions for medical use (patient leaflet) was detailed. The Procedure also contains instructions on compiling instructions for medical use.

On May 15, 2019 the Order of the Minister of Health of the Republic of Kazakhstan "On Approval of the Rules for Medicinal Products and Medical Devices Expert Evaluation" No. 736 (dated April 19, 2019) came into force. The most painful and debated issue was the updated paragraph, in which the deadlines for submitting an application for expert evaluation for Renewal were changed from *"until the end and no later than 6 months after the end of MA"* (in the old version of the Order) to "not less than 180 days before the expiration of validity of the marketing authorization", which deprived many applicants of the opportunity to submit medicinal products for the Renewal procedure and receive unlimited marketing authorizations. At the end of May, these changes **were canceled**; at the moment, Renewal dossiers can be submitted before the expiration date of the marketing authorization.

## Kyrgyzstan:

On December 26, 2018 Decree No. 564 dated December 6, 2018 "On Approval of the Procedure for Organizing a Pharmacovigilance System" came into force, which approved the new Procedure for Organizing a Pharmacovigilance System developed in accordance with the EAEU Good Pharmacovigilance Practice (GVP). This Procedure establishes the Applicant's obligation to **create and maintain a local pharmacovigilance system**, appoint an authorized person responsible for pharmacovigilance, monitor and report adverse events, etc. The Risk Management Plan (RMP) must be included in the package of documents for new registration and Renewal. The 3-year deadline for the provision of PSUR after the initial registration of the medicinal product has been updated.

On March 4, 2019 amendments to Resolution No. 405 dated August 28, 2018 "On Certain Issues Relating to Registration in the Field of Medicinal Products Circulation" came into force and significantly changed the procedure, deadlines, requirements for registration materials and other regulatory aspects, entered into force, including:

1) the new Procedure for state registration of medicinal products has been approved;
2) new validity periods of the marketing authorization have been introduced: 5 years at initial registration and unlimited after the registration confirmation;
3) **an accelerated registration procedure** has been introduced for medicinal products approved by the US FDA, PMDA, Swissmedic and MHRA, or registered according to the central procedure with the EMA, and if they are on the list of prequalified medicinal products of the World Health Organization. The duration of the expert evaluation is 45 calendar days, and laboratory tests are not carried out.
4) the registration of **orphan products** has been simplified and accelerated, including:
   - government payments related to the registration (new registration, confirmation of registration, and amendments) of orphan products and humanitarian aid products have been abolished upon receipt of appropriate confirmation from the authorized body that the product belongs to one or another group of medicinal products;
   - when submitting a dossier for orphan products to replace the data of Module 4 and 5, a summary of non-clinical and clinical data with justification of the benefit-risk ratio may be submitted.

5) the requirements of national legislation are gradually harmonized with the EAEU Unified Rules: national rules for expert evaluation refer to Resolutions of the Eurasian Economic Commission Council, including:
   - the registration dossier of a foreign manufacturer is drafted in CTD format in accordance with the Rules for Registration and Expert Evaluation of Medicinal Products for Medical Use, approved by Resolution No. 78 of the EEC Council dated November 3, 2016, with the exception of the regulatory document for the finished product and instructions for medical use, the requirements for which are specified in the Appendices 2 and 3 to the above Order;
   - labeling of medicinal products is carried out in accordance with the Requirements for the Labeling of Medicinal Products for Medical Use and Veterinary Medicines, approved by Resolution No. 76 of the EEC Council dated November 3, 2016;
   - non-clinical studies of medicinal products are carried out in accordance with the Rules of Good Laboratory Practice of the EAEU in the field of medicinal products circulation, approved by the Resolution No. 81 of the EEC Council of November 3, 2016;
   - clinical studies of medicinal products are carried out in accordance with the Rules of Good Clinical Practice of the EAEU, approved by Resolution No. 79 of the EEC Council dated November 3, 2016;
   - recognition of the Pharmacopoeia of other states has been aligned with the Pharmacopoeia Harmonization Concept of the EAEU Member States approved by Resolution No. 119 of the EEC Board of September 22, 2015. In the absence of relevant articles (monographs) recognized by the Pharmacopoeia, articles (monographs) of universally recognized foreign pharmacopoeias, pharmacopeias of countries participating in intergovernmental agreements in the field of standardization, metrology and certification are used;
6) the deadlines for registration, renewal and variations procedures have been approved:
   - a new medicinal product registration is carried out within 180 days, plus 90 days to respond to the comments of primary and specialized expert evaluations;
   - Renewal (confirmation of registration) is carried out within 90 days, plus 90 days for responses to the comments of primary and specialized expert evaluations;
   - post-registration changes – the expert evaluation is carried out within 30-60 days, 30-90 days to respond to the comments of the primary and specialized expert evaluations (depending on the type of changes);
7) criteria for laboratory testing of samples have been approved:
   - if there is a GMP certificate for a production site issued by regulatory authorities of countries in the ICH region;
   - if there is a certificate/protocol of analysis/testing for the last 6 months conducted by a laboratory accredited under ISO 17025 located in the territory of the EAEU;
   - the possibility of conducting laboratory control in the manufacturer's laboratory in the presence of representatives of an expert organization in case of inaccessibility, high cost of samples, including orphan products, narcotic drugs, psychotropic drugs, etc.
8) criteria for determining the confidentiality of registration materials have been introduced;
9) updated requirements for variations in the registration dossiers have been introduced.
10) new requirements for the suspension of the marketing authorization and its revocation have been introduced.

The Ministry of Health of the Kyrgyz Republic announced the introduction of a unified information system for all regulatory processes, which transfers the relationship of the regulator and operators of the medical and pharmaceutical markets into an electronic format (online registration system of medicinal products, online certification of medicinal products and medical devices, a single window for customs clearance of medicinal products and medical devices when imported). The electronic medicinal product database

system is being developed in accordance with the Program of the Government of the Kyrgyz Republic No. 743 dated October 27, 2015 and is planned to be implemented after 2020.

## Uzbekistan:

On October 25, 2018 the **procedure for recognition of registration** came into force, approved by the Decree of the Cabinet of Ministers of the Republic of Uzbekistan No. 862 dated October 24, 2018 "On Approval of the Regulation on the Procedure for Recognition of Results of Medicinal Products Registration Outside the Republic of Uzbekistan".

The list of countries and international organizations, which registration procedures results are recognized in the Republic of Uzbekistan, has been approved by Decree No. PP-3948 of September 24, 2018 "On additional measures to improve the procedure for state registration and circulation of medicinal products." Thus, the recognition procedure is provided for medicinal products registered by the EMA and US FDA by the regulatory authorities of Japan, Canada, Switzerland, Australia, Belgium, UK, Germany, Denmark, Ireland, Spain, Italy, the Netherlands, Norway, Slovenia, Finland, France, Sweden, Israel and Korea.

The most significant aspects of the recognition procedure:

1) The official registration recognition period is not more than 15 working days. This period does not include the time for payment of the fee for consideration of the procedure (no more than 30 calendar days from the date of issue of the invoice for payment).
2) An abbreviated set of documents is required for the recognition procedure. It is required to submit samples of the medicinal product in the amount necessary for a 3-fold analysis and reference standards.
3) The validity of the results of the first recognition is 5 years. After the procedure for extending the results of recognition (Renewal), an unlimited confirmation of recognition is issued.
4) During the validity of the recognition results, the applicant may submit changes and additions to the registration materials in accordance with the established procedure.

In mid-February 2019 the first Presidium on the recognition procedure took place and the first registrations were received under the simplified procedure, which evidenced the successful implementation of the recognition procedure.

Please note that since November 1, 2018 the requirement to issue a marketing authorization for a medicinal product registered under the recognition procedure has been canceled in Uzbekistan. The registration results are entered into the State Register of Medicinal Products, Medical Devices and Medical Equipment instead, and an excerpt from the Register may be generated and provided to the applicant (upon request).

## Ukraine:

On April 9, 2019 the Resolution of the Cabinet of Ministers No. 296 dated March 27, 2019 entered into force, which amended the Resolution of the Cabinet of Ministers of Ukraine No. 376 dated May 26, 2005 "On Approval of the Procedure for State Registration (Renewal) of Medicinal Products and Amounts of Fees for Their State Registration (Renewal)" and Order of the Ministry of Health of Ukraine No. 358 dated August 29, 2003 "On Approval of the Form and Description of the Medicinal Product Marketing Authorization".

These changes establish that the Application for **renewal** of a medicinal product must be submitted no earlier than one year, but **not later than 180 calendar days** before the expiration of the marketing authorization. If the Application is submitted after the specified deadline, renewal is carried out according to the procedure provided for the state registration of a medicinal product. Please note that earlier a deadline of 90 calendar days was established before the expiration of the marketing authorization.

The above changes also **extended the validity period** of marketing authorizations for medicinal products registered in accordance with the Ministry of Health of Ukraine Order No. 721 dated November 3, 2015 "On Approval of the Order for the Authenticity Examination of the Registration Materials Related to Medicinal Products Submitted for State Registration with the Purpose of their Purchase by a Specialized Organization."

On May 16, 2019 the Law of Ukraine "On Ensuring the Functioning of the Ukrainian Language as a State Language" (hereinafter referred to as the Law) was published, which entered into force on July 16, 2019. The Law significantly affects user information (product labeling, instructions, interface), advertising and promotional materials, websites, public events (seminars, conferences) etc. For a significant part of the provisions, transition periods of 6 months and more have been established.

## Eurasian Economic Union:

At the end of May 2019, **68 applications for the registration** of medicinal products and four applications for the registration of medical devices are already pending in the Unified Information System of the Union. The first marketing authorization for a medicinal product registered under the unified rules of the Union was issued by Kazakhstan in November last year. Currently, according to the requirements of the EAEU, **2 products have been registered** for which Kazakhstan has been chosen as the reference country.

On March 29, 2019, the Agreement on Labeling of Goods in the Eurasian Economic Union (EAEU) entered into force, signed by the heads of government of the Union countries more than a year ago, on February 2, 2018. The Agreement defines the general rules for the functioning of the product labeling system within the EAEU (medicinal products, in particular) and establishes basic approaches. The main objective of the Agreement is to ensure the legal circulation of goods within the Eurasian Economic Union, to protect consumer rights and to prevent actions that mislead consumers.
Prior to approval of the labeling in the territory of the reference state, within three months the commission will consider the proposed labeling and decide on the introduction of labeling in the countries of recognition. The Agreement will not go against the operation of existing national labeling systems.

In almost every country a large number of events take place over 6 months, but in this digest we tried to reflect only the most significant regulatory changes. If you have any questions or clarifications, please contact us and we will be happy to share our knowledge and experience with you.

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