Dear colleagues,

In this digest you will find the most important news on registration, safety and quality management of **medicinal products** in the CIS region: Azerbaijan, Armenia, Belarus, Kazakhstan, Kyrgyzstan, Moldova, Tajikistan, Turkmenistan, Uzbekistan and such countries as Georgia, Ukraine, Mongolia, as well as the countries of the Eurasian Economic Union.

Summary of the most important news:

In **Azerbaijan,** changes to the registration procedure for medicinal products have come into force since July 1, and the accelerated registration procedure has been introduced. Also, the rules for conducting pharmacovigilance have come into force, obliging the marketing authorization holders to establish and maintain a pharmacovigilance system in Azerbaijan, appoint a local contact person and perform other activities.

In **Armenia**, the requirements for package labeling and instructions for use have been brought in line with the requirements of the EAEU. The guide on the monitoring of adverse reactions, the rules for the implementation and maintenance of the pharmacovigilance system has been published.

In **Belarus**, the procedure for accelerated and simplified registration of medicinal products has been introduced, and significant changes have been made to the system of the state quality control. The possibility of using a sticker in Russian or Belarusian for labeling of product packaging has been determined.

In **Kazakhstan**, the rules of expert evaluation have been set out in the updated version, the requirements for the registration dossier have been changed, and the accelerated expert evaluation has been introduced.

In **Kyrgyzstan**, mandatory regulation of prices for medicinal products has been introduced.

In **Moldova**, the new website has been created for the competent authority.

In **Ukraine**, the list of countries, for which the simplified procedure for recognizing a GMP certificate is allowed, has been reduced, and the possibility of remote inspection has been introduced. The legislation on simplified registration of medicinal products purchased by specialized organizations has been updated, and changes have been made to the procedure for simplified and accelerated registration of medicinal products by recognition procedure.

In **Uzbekistan**, the system of reference pricing has been gradually introduced since July 1.

The **EAEU** extended the mutual recognition of GMP certificates issued by EAEU member states; the EAEU Pharmacopoeia has been approved.

You will find out more details on these and other changes below.

Azerbaijan:

On July 1, 2020, the Resolution of the Cabinet of Ministers of the Republic of Azerbaijan No. 502 "Procedure for the expert evaluation of medicines" came into force. The most significant innovations are:

1) **An application for re-registration** of the medicinal product **must be submitted no later than 210 calendar days** before the expiration of the marketing authorization.

When re-registering a medicinal product, an expert assessment of the benefit-risk ratio is carried out. Additionally, a periodic safety update report, risk management plan, pharmacovigilance system master file and other documents may be requested.

2) The **accelerated procedure for the expert evaluation** of medicinal products approved by the European Medicines Agency (EMA) under the centralized procedure and/or prequalified by WHO has been introduced. The period for specialized expert evaluation of registration materials for such medicinal products is 45 days, and laboratory analysis of samples is not carried out.

The period of specialized expert evaluation of registration materials for other medicines is 210 days.

The period for providing replies to comments should not exceed 90 days.

3) The registration dossier is submitted in the CTD format in electronic form, except for Module 1. The composition of the administrative part of the dossier has not changed, but the requirements for the legalization of some documentation, including the document on registration (authorization) of a medicinal product from the country of origin, have been tightened. The absence of such a document may result to withdrawal of registration of the product.

4) The classification of changes has been introduced: IA, IB, II, changes due to a technical mistake in the dossier and changes subject to new registration.

An Applicant (MAH) is obliged to declare any changes that affect the quality, safety and efficacy of the medicinal product, as well as urgent safety changes (changes in the instructions for use with immediate notification) within a period not exceeding 60 days after their introduction.

A transitional period has been introduced for the changes to come into force, which can be up to 6 months after the approval of such changes, except for type IA changes, for which the transition period is 12 months.

When submitting changes related to different types, each type of change is evaluated separately.

5) The quality control system for medicinal products during import has been introduced. The importer submits a package of documents to the competent authority, including importer's license, batch quality certificate, certificate of origin and other documents. The competent authority takes samples and analyzes the quality within a maximum of 20 days.

From July 1, 2020, the Resolution of the Cabinet of Ministers of the Republic of Azerbaijan No. 503 dated December 25, 2019 “Rules for Pharmacovigilance of Medicines” came into force.

These rules introduce the obligations of the marketing authorization holders to **establish and maintain the pharmacovigilance system in the Republic of Azerbaijan**, including the appointment of an authorized (local) person for pharmacovigilance (LCP), who meets the qualification requirements, and is recruited in accordance with the Labor Code of the Republic of Azerbaijan.

Other most significant innovations:

1) Information (name, surname, patronymic, education and work experience) about the authorized person and his/her deputy, including contact information (address, phone number, fax, e-mail), are submitted to the competent authority of Azerbaijan no later than 7 days after appointment to the position, and in case of replacement of the LCP and his/her deputy, the marketing authorization holder appoints new employees to their places and informs the competent authority no later than 3 months.

The marketing authorization holder must ensure that the LCP and his/her deputy participate in the basic pharmacovigilance training program organized by the competent authority.

2) The competent authority, within the framework of pharmacovigilance, conducts an expert evaluation of the documents on pharmacovigilance:

- Risk Management Plan (RMP);
- Periodic Safety Update Report (PSUR);
- Pharmacovigilance System Master File (PSMF).

The expert evaluation is carried out on the basis of the "Agreement on the provision of expert evaluation of documents (RMP, PSUR, PSMF)" concluded between the competent authority and the marketing authorization holder. This Agreement also regulates the term and cost of the expert evaluation carried out by the competent authority.

Terms and frequency of PSUR submission are determined based on the List of EURDs and Frequency of Submission of PSURs available on the official website of the EMA. For drugs not included in this list, the frequency of the PSUR is as follows:

- within the first 2 years after the state registration of the medicinal product in the Republic of Azerbaijan or every 6 months from the date of the International Birth Date (IBD);
- once a year for the next 2 years;
- subsequently – every 3 years.

3) The marketing authorization holder monitors the safety data and informs the competent authority in case of changes in risks or any changes in the benefit-risk ratio of the medicinal product.

Deadlines for submitting reports:

- about all side effects arising from the use of the medicinal product in the Republic of Azerbaijan and/or found in the scientific and medical literature: within 15 calendar days upon receipt thereof;
- about all side effects received from other countries that change the benefit-risk ratio: immediately upon receipt thereof;
- about the discovered sources of all side effects from the use of the medicinal product in the Republic of Azerbaijan (including in the scientific and medical literature) within 15 calendar days;
- about all cases of suspected infection of a patient with a disease as a result of the use of the medicinal product: immediately upon receipt.

4) The competent authority has the right to audit the pharmacovigilance system of the marketing authorization holder.

5) The national guidance on Good Pharmacovigilance Practice (GVP) is being introduced, which was not yet adopted (pending approval) when compiling this news digest.

Armenia:

On January 21, 2020, the Ministry of Health of the Republic of Armenia approved Order N02-N "On Approval of Requirements for the Labeling of Medicinal Products, Pharmaceutical Substances, Medicinal Plant Materials, an Investigational Medicinal Product, as well as Instructions for Medical Use, General Characteristics and Trade Names of Medicinal Products for Human Use, and about Excipients Mandatorily Indicated on the Secondary Packaging."

This Order brings the requirements of national legislation to the labeling of medicinal products, instructions for use (leaflet) and trade names of medicinal products in line with the requirements of the EAEU:

- information on the packaging of medicinal products is compiled in accordance with the requirements of the Decision of the Council of the Eurasian Economic Commission No. 76 dated November 3, 2016;
- instructions for medical use (leaflet) and general characteristics of medicinal products are compiled in accordance with the requirements of the Decision of the Council of the Eurasian Economic Commission No. 88 dated November 3, 2016;
- trade names of medicinal products must comply with the Recommendation of the Board of the Eurasian Economic Commission No. 2 dated January 29, 2019 "On the Guidelines for the Selection of Trade Names of Medicinal Products" and the Recommendation of the Board of the Eurasian Economic Commission No. 13 dated April 23, 2019 "On the Rules for the Preparation of Group Names of Medicinal Products."

At the end of 2019, guidelines to monitoring adverse reactions in the Republic of Armenia were published. These Guidelines regulate the local requirements for the marketing authorization holder to provide information on side effects, the deadlines for submission, and also describes practical recommendations regarding the process of supporting the pharmacovigilance system at the national level, in particular, the requirements for the correct execution of the necessary documents on pharmacovigilance and their submission to the national competent authority on pharmacovigilance.

Please note that according to the Order of the Ministry of Health of the Republic of Armenia N23-N dated May 17, 2017, all marketing authorization holders are required to:

- have a documented system of pharmacovigilance in the territory of the Republic of Armenia and a documented system of quality assurance of pharmacovigilance;
- store and submit the Pharmacovigilance System Master File (PSMF);
- assign QPPV/LPPV;
- create a risk management system;

- manage and report adverse drug reactions;
- create and submit Periodic Safety Update Reports (PSUR);
- conduct post-marketing safety studies;
- control all available data and information on signals, enter them into the database of the national competent authority;
- take measures to minimize risks;
- notify the competent authority of urgent safety concerns.

Please note that from January 1, 2021, Applications for registration of medicinal products in Armenia will be accepted only in accordance with the Unified Rules for Registration of the EAEU.

Belarus:

On June 5, 2020, **a simplified procedure for state registration of medicinal products** came into force, approved by Decree of the President of the Republic of Belarus No. 499 dated December 31, 2019 "On the circulation of medicines", Resolution of the Council of Ministers of the Republic of Belarus No. 191 dated April 1, 2020 "On measures to implementation of the Decree of the President of the Republic of Belarus of December 31, 2019 No. 499" and Resolution of the Ministry of Health No. 51 ""On establishing the list of documents for carrying out a complex of preliminary technical work related to the expert evaluation of documents preceding the state registration of medicines under the simplified procedure."

This simplified registration is applicable for:

1. Medicinal products registered by the authorized bodies of Australia, Austria, USA, Canada, Switzerland, Japan, Great Britain, Germany, Denmark, the Netherlands, Sweden, Spain and Portugal.
2. Medicinal products registered by the EMA under a centralized procedure.
3. Medicinal products for the treatment of tuberculosis, hepatitis C, HIV infection, as well as vaccines that underwent the WHO prequalification program.

The term for expert work should not exceed 30 days. The marketing authorization is issued for a period of 5 years.

Presidential Order No. 499 and Resolution of the Council of Ministers No. 191 have implemented significant changes in the **state drug quality control system**:

- the state institution "State Pharmaceutical Supervision in the Sphere of Drug Circulation Gosfarmnadzor" has been created;
- the procedure for inspection and issuance of an opinion on the conformity of places for storing medicines has been introduced in accordance with the Rules of Good Distribution Practice, approved by Decision of the Council of the Eurasian Economic Commission No. 80 dated November 3, 2016;
- the procedure to control the quality of a foreign-made medicinal product and issue a test report before its implementation has been introduced.

The State Institution “State Pharmaceutical Supervision in the Sphere of Drug Circulation Gosfarmnadzor” was established to control the quality of medicinal products at all stages of their circulation in Belarus. In particular, the institution conducts inspections for compliance with the Rules of Good Distribution Practice, selects samples of medicinal products and conducts their analysis, provides the Ministry of Health with draft decisions on the suspension of circulation and withdrawal from circulation of low-quality, falsified or expired medicinal products.

Amendments to Resolution of the Council of Ministers of the Republic of Belarus No. 156 dated February 17, 2012 simplified the requirements for labeling of pharmaceutical packaging. Foreign medicinal products with labeling in a foreign language and **a sticker in Belarusian or Russian** may be allowed for state registration (re-registration) and medical use.

On November 5, 2019, amendments were made to Decree of the Ministry of Health of the Republic of Belarus No. 52, namely, the requirements for the Quality Section of the registration dossier were added. Among the most significant changes: it is necessary to include analytical methods for excipients in the regulatory documentation, it is necessary to provide primary documentation (chromatograms, photographs, etc.) for non-pharmacopoeial methods, it is necessary to indicate pharmacopoeial methods in the quality certificate, it is necessary to provide specifications for intermediate control.

Please note that from January 1, 2021, Applications for registration of medicinal products in Belarus will be accepted only in accordance with the Unified Rules for Registration of the EAEU.

Kazakhstan:

On March 21, 2020, changes were made to Order of the Minister of Health of the Republic of Kazakhstan No. 736 "On Approval of the Rules for the Expert Evaluation of Medicinal Products and Medical Devices." The rules are set out in the updated version: the classification of changes in the marketing authorization, the registration dossier submission system and language requirements have been changed, the Application form has been updated, the structure of the first module has been modified.

The changes introduced **an accelerated expert evaluation**, the terms of which for medicinal products are 120 calendar days. Accelerated expert evaluation of medicinal products is used for the following:

- medicines for the prevention, treatment, diagnosis of orphan diseases;
- prevention of emergency situations, occurrence and elimination of the consequences of epidemics, pandemic of infectious diseases;
- medicines prequalified by WHO.

Order of the Minister of Health of the Republic of Kazakhstan No. KR DSM-72/2020 dated June 23, 2020 clarified the procedure for the import and sale of medicinal products with the previous version of the instructions for use (leaflet) within 6 months from the date of approval of the changes.

Please note that from January 1, 2021, Applications for registration of medicinal products in Kazakhstan will be accepted only in accordance with the Unified Rules for Registration of the EAEU.

Kyrgyzstan:

By Resolution of the Government of the Kyrgyz Republic No. 579 dated October 29, 2019 "On Approval of the Interim Rules for the Regulation of Prices for Medicinal Products in the Kyrgyz Republic", within the framework of Government's Action Plan for 2019-2023, the procedure for **regulating prices for medicinal products** in circulation in territory of the Republic has been developed.

According to the Decree, the sale of medicinal products, the price of which is not properly registered, is prohibited. Thus, it is necessary to submit an application and a set of documents to the authorized body, according to which experts will be able to analyze the cost of this product or its analogue in the reference countries. The established price will be included in the Price Catalog of the Kyrgyz Republic in accordance with the developed Rules.

At the moment, a draft Resolution “On Amendments and Additions to Resolution of the Government of the Kyrgyz Republic No. 579 dated October 29, 2019 “On Approval of the Interim Rules for the Regulation of Prices for Medicinal Products in the Kyrgyz Republic,” which is under consideration, has been published on the official website of the Department www.pharm.kg in the Regulation of Prices for Medicinal Products Section.

Moldova:

The Agency for Medicinal Products and Medical Devices of Moldova has changed its official website to amdm.gov.md. This change is related to Agency's plans to fill the site with the necessary information regarding legislation, develop a register available to users and duplicate the site in three languages: Romanian, Russian and English.

Ukraine:

On July 21, 2020, amendments to Order of the Ministry of Health of Ukraine No. 1130 "On Approval of the Procedure for Confirmation of Compliance of the Manufacturing Conditions of Medicines with the Requirements of Good Manufacturing Practice" came into force. The most significant changes include as follows:

- **the list of countries for which the recognition procedure of the GMP certificate of conformity is conducted has been reduced** to EU27 + MRA + UK;
- during the recognition procedure, submission of registration (authorization) in EU27 + MRA + UK is provided for in the event that at least one stage of drug manufacturing is carried out outside the countries to which the recognition procedure applies;
- remote assessment of manufacture is provided for during pandemic and emergency situations.

Certificates of conformity of the manufacturing conditions of medicinal products with GMP requirements issued by regulatory authorities of other countries are not subject to the recognition procedure – it will be necessary to apply the manufacture inspection procedure.

At the beginning of July 2020, the State Service of Ukraine on Medicines and Drugs Control announced that to optimize the expert evaluation process of applications and documents that are submitted for the purpose of issuing a certificate or conclusion on conformity of the manufacturing conditions with GMP requirements, state-owned enterprises may be involved:

- Ukrainian Pharmaceutical Quality Institute, SE
- Central Laboratory for Quality Analysis of Medicines and Medical Products, SE.

Applicants or their representatives who submit documents for the recognition of a GMP certificate must conclude an Agreement with an expert government agency and pay the cost of the work.

On June 15, 2020, to replace Order of the Ministry of Health No. 721, Order No. 1391 was adopted, which approved the Procedure for verifying medicinal product materials for their authenticity. The new Procedure is used for **accelerated registration of medicinal products** that are purchased by (1) international specialized procurement organizations and (2) a person authorized to carry out procurement in the healthcare sector (Medical Procurement of Ukraine, SE).

On July 17, 2020, amendments to Order of the Ministry of Health No. 1245 came into force, which approved the registration procedure under the **simplified fast-track procedure** for medicinal products registered by the competent authorities of the United States, Switzerland, Japan, Australia, Canada or the European Union under the centralized procedure.

Please note that on January 1, 2021, **the transition period ends**, after which the units of measurement on the product label are put into circulation and must be reflected using the International System of Units, SI.

Uzbekistan:

From July 1, 2020, Resolution No. PP-4554 dated December 31, 2019 "On additional measures to deepen reforms in the pharmaceutical industry of the Republic of Uzbekistan" came into force to gradually introduce a reference pricing system for medicinal products and launch a mandatory procedure for issuing prescriptions for the international nonproprietary name of medicinal products.

Eurasian Economic Union:

Registration of medicinal products according to the uniform rules of the Union should become mandatory in all member countries (Armenia, Belarus, Kazakhstan, Kyrgyzstan, and Russia) from January 1, 2021. At the same time, all medicinal products registered according to national procedures must be brought into line with the EAEU norms by the end of 2025. At the time of preparing the news digest, 78 products are contained in the Unified Register of Registered Medicines of the Eurasian Economic Union.

On September 4, 2020, the EEC Council approved changes to **the procedure for the recognition of inspection results**: when conducting national registration procedures until December 31, 2025, mutual recognition of GMP certificates issued by the EAEU member states was established. These changes will help to avoid manufacture re-inspection by each of the EAEU countries.

On August 11, 2020, by Decision of the EEC Board No. 100, **the EAEU Pharmacopoeia was approved**, with the date of entry into force from March 1, 2021. Manufacturers of medicinal products previously registered in the common market of the Union will need to bring regulatory documents on quality in accordance with the requirements of the Pharmacopoeia of the Eurasian Economic Union by January 1, 2026.

On July 7, 2020, Decision of the EEC Board No. 86 came into force on amending clause 5 of the Requirements for the study of stability of medicinal products and pharmaceutical substances in terms of defining the concept of "batch manufacturing date". The definition corresponds to the wording adopted by the International Council on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and the World Health Organization (WHO).

On November 26, 2019, the Decision "On approval of the Guidelines for preclinical safety studies for the purpose of conducting clinical trials and registration of medicinal products" was adopted, which entered into force 6 months later.