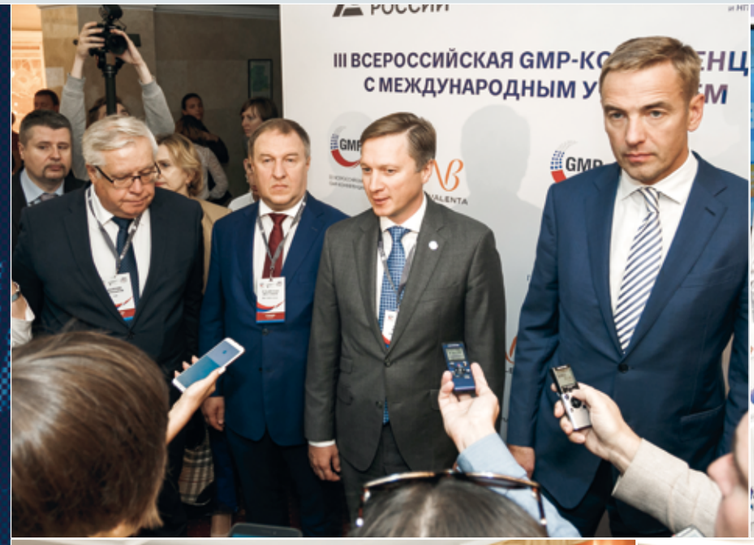
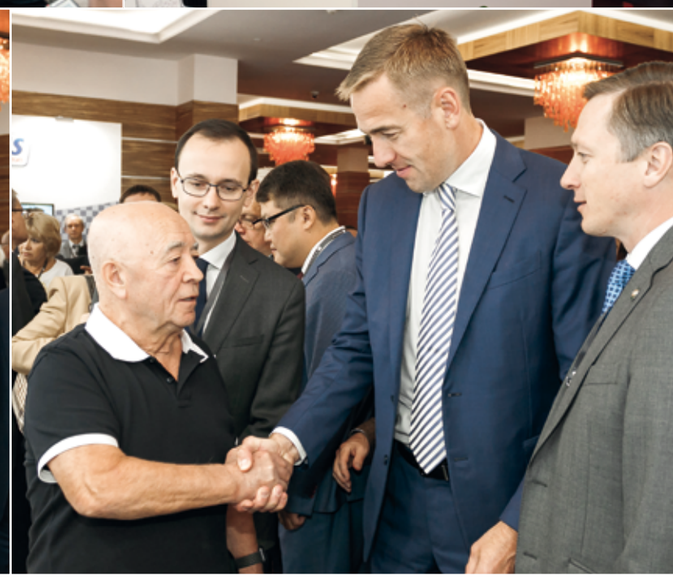
III All-Russia GMP Conference

with International Participation in Kazan

GMP III All-RUSSIA GMP-CONFERENCE

15 September 2018





This year, the conference was held in the hospitable Kazan – the capital city of Tatarstan. More than 1000 participants took part in the event, which became a record number of all previous years.

On August 27, during the opening ceremony, welcoming remarks addressed to the participants came from the office of the President of the Republic of Tatarstan, the Ministry of Health of the Russian Federation, the Federal Service for Surveillance in Healthcare, the National Center for Standardization and Health of the Russian Ministry of Health, and the Eurasian Economic Commission.

Viktor Yevtukhov, State Secretary – Deputy Minister of Industry and Trade of the Russian Federation addressed the participants and guests of the conference, *"Today, more than a thousand participants gathered for the event. We see that interest in the area grows heavily with every year, and this underlines its importance. It is important that the All-Russia GMP conference this year has significantly expanded its agenda, providing more opportunities for discussions, negotiations and obtaining expertise on the market. I am confident that the conference will add to the development and further strengthening of Russian pharmaceutical manufacturers."*

DRIVERS OF THE RUSSIAN PHARMACEUTICAL MARKET

A plenary session dedicated to the 'Drivers of pharmaceutical market growth. Global View' came up first on the business agenda of the III All-Russia GMP conference with international participation **Russia and the World. Management of the pharmaceutical market growth potential**.

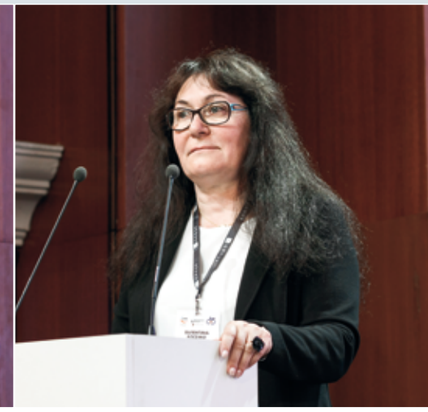
The moderator of the discussion, **Vladimir Shipkov**, Executive Director of the Association of International Pharmaceutical Manufacturers (AIPM), referred to measures offered by the Chinese government in support of their pharmaceutical industry. They include – among others – attractive market environment and a shorter wait time for registration of innovative pharmaceutical products most wanted in the healthcare system and already registered in the ICH region, i.e. no more than three months for orphan drugs, and six months – for non-orphan ones.

Valentina Kosenko, Deputy Head of the Federal Service for Surveillance in Healthcare talked about legislative measures in Russia used for active development of pharmaceuticals. For example, the risk-based approach in drug circulation lifts the burden off bonafide participants on the pharmaceutical market, and helps identify those who are reluctant to follow government regulations.

Aleksey Alekhin, Head of the Department of Pharmaceutical and Medical Industry Development of the Russian Ministry of Industry and Trade took part in the session. He identified a number of drivers that have impact on the pharmaceutical market, i.e. interaction between key players of the pharmaceutical market, protection of intellectual property, and growing exports. Regulatory standards remain the main driver, *"One of the regulatory reforms to be implemented by the Russian Health Ministry is the introduction of a conditional registration system. This will allow carrying out extended clinical trials immediately at the time of introducing medicines to patients or their commercial sales. The Russian Ministry of Industry and Trade has actively supported pharmaceutical manufacture within the frameworks of the government program."*





Business representatives from NovaMedika, Novartis, and the General Director of GeroPharm Group, **Petr Rodionov**, shared their views on what exactly can make a difference for the growing pharmaceutical market. ***"Looking at the basic drivers and influencing factors in the industry, we are certain that regulatory norms provide the foundation on which the industry develops. Without the standards, supporting measures would be less effective".***

Examples of support at the regional level were sounded in the reports of the Minister of Industry and Trade of the Republic of Tatarstan, **Albert Karimov**, and Deputy Head of the Moscow Department for Science, Industrial Policy, and Entrepreneurship, **Kristina Volkonitskaya**.

BUSINESS MEETS GOVERNMENT

On Day One – during the panel discussion devoted to **the Pharmaceutical industry of the Future. Government and business perspectives.** – the participants touched on the most urgent issues including interaction of key players in the pharmaceutical market. The panel was honored by officials from the Russian Ministry of Industry and Trade, the Russian Health Ministry, the State Institute of Drugs and Good Practices; and business circles from BIOCAD, Nanolek, Teva, GEROFARM, MSD, Merck Biopharma Russia & CIS, as well as a representative of Pharmaceutical Innovations (Association of Pharmaceutical Companies). The audience shared their understanding of what the industry should be like in ten years. The Ministry of Industry and Trade is actively working on Pharma-2030 Strategy, and the conference has become another tool to fine-tune this document of utmost importance for Russian pharmaceutical industry.

"On behalf of the Russian Ministry of Industry and Trade, I would like to thank all those who took part in drafting the strategy. We held a series of meetings and developed a unanimous position of all stakeholders, highlighted the milestones that should be followed in the Development Strategy for pharmaceutical industry. I would like to draw your attention to the fact that since we are in charge of evolving production competencies through 2030, the whole document is about industry. And there no doubt that as an industry we need to rely on market laws," said **Alexey Alekhin**, Head of the Department of Pharmaceutical and Medical Industry Development of the Ministry of Industry and Trade of the Russian Federation.

Education and human resources simply could not be left out of the discussed issues. Leaders of the prominent academic institutions, i.e. the St. Petersburg State Chemical and Pharmaceutical University, the Kazan Federal University, the Scientific Centre for Expert Evaluation of Medicinal Products shared their professional expertise in that respect. Personnel training now requires additional investments that universities and colleges cannot always accommodate. Challenges of globalization and digitalization of economy, growing appeal of IT technologies make education in the industry impossible without modeling systems.

The delegates called on Strategy authors to pay attention to success stories of foreign product localization. Representatives of foreign companies – Merck Biopharma Russia & CIS and Teva – shared their insights on making Russian market a priority for investments.

"The Strategy should be aimed at finding solutions to secure an innovative breakthrough for Russian pharmaceutical industry. Russia should become a country where innovations from all over the world are striving – it concerns molecules that are already being developed in the Russian Federation and those that are designed abroad; sooner or later they will find the way to the Russian market most probably through the localization mechanism," said **Andrey Kolesnikov,** TEVA CEO for GR and Market Access in Russia and Eurasia.

Effective interaction between all market participants is the key to the development not only of the pharmaceutical industry, but also of the country's economy as a whole. Defining clear goals and objectives for the next ten years will now set priorities in the training of export and production specialists. As the session moderator – **Dmitry Chagin**, Chairman of the Board of the EAEU Pharmaceutical Manufacturing Association – expressed hope and confidence to hear Russian businesses at the largest international conferences sharing success stories of localizing their products in foreign countries.

NEW GMP TRENDS IN THE EAEU REGULATORY SYSTEM

On Day Two of the III All-Russia GMP conference, **Elena Denisova**, Deputy Head of the Department of Pharmaceutical and Medical Industry Development of the Russian Ministry of









Industry and Trade, moderated a panel discussion dedicated to New GMP trends in the EAEU regulatory system .

In meetings with their international peers, the delegates reviewed a number of issues including new trends in the technical regulation of the EAEU good manufacturing practices, common pharmaceutical market, rules and procedures of GMP inspections in line with the EAEU guidelines, and current inspection standards.

Valery Koreshkov, Member of the EEC Board (Minister) for Technical Regulation, spoke about legal foundations of GMP regulation in the Eurasian Economic Union. The commission is currently developing a large block of the 3rd level documents covering all key aspects of GMP inspections.

"A GMP compliance certificate is an essential part of the registration dossier. The GMP rules have been developed based on international experience, and European guidelines, in particular."

Dmitriy Rozhdestvenskiy, Head of the Coordination Department for drugs and medical devices circulation of the EEC Department of Technical Regulation and Accreditation, drew the audience's attention to different types of inspections that must be considered and correctly interpreted to shape up proper marketing tactics, *"The first thing that comes to mind, in addition to the existing routine and random inspections, they can be divided by team composition into single-auditor and team inspections."*

Professor **Natalya Pyatigorskaya**, Head of the Industrial Pharmacy Department of the Sechenov First Moscow State Medical University, Member of the Council for Pharmaceutical Competence, Ph.D., expanded on EAEU regulatory requirements for certification of qualified persons in pharmaceutical manufacture. According to Professor Pyatigorskaya, the certification procedure includes verification of required education, relevant training and work experience of qualified persons in line with the EAEU procedure and GMP rules of the Union, regulating QP job portfolio. Based on the findings, a respective EAEU regulating authority certifies the QP indicating pharmaceutical manufacturing activities for which the QP was certified.

GDP inspections results for the past years came from **Yelena Stepkina**, Head of the Administration for Implementation and Development of Good Pharmaceutical Practices and International Standards of the National Center for Expertise of drugs, medical devices and medical equipment of the Kazakhstan Ministry of Health and Social Development. The denial rate of GDP inspection results is going down compared to last year's figures. Yelena mentioned some defects leading to deviations: improper storage, lack of evidence of equipment qualification, inadequate documentation, and others.

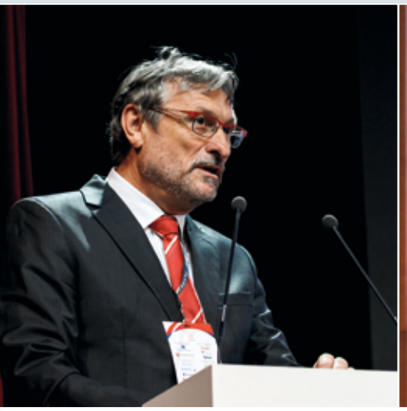
Nurylbek Asylbekov, Deputy Chair of the Pharmaceutical Committee of the Kazakhstan Health Ministry shared GMP-inspections experience. Among major defects, he noted lack of validation of critical processes, lack of qualification of technological equipment, insufficient information provided in the registration dossier, and contamination in cleanrooms.

Chinara Mambetalieva, Head of the Quality Assessment of Drugs and Medical Products, Department of Medicines and Medical Devices, Kyrgyzstan Health Ministry, told the audience about legal framework governing the establishment of Pharmaceutical Inspectorate in the Kyrgyz Republic. As provided for in the General Quality Requirements of EAEU Pharmaceutical Inspectorates (Decision No. 82 of the EEC Council dated November 03, 2016) the Statute of the Department of Good Practices and Quality System of the Pharmaceutical Inspectorate are currently in the works. It will include policies, quality manual, SOPs, records and reports, training for the pharmaceutical inspectors. Among upcoming trends, Chinara mentioned effective interaction with inspectors of the EAEU regulatory authorities in the area of pharmaceutical circulation and eventual integration into the Pharmaceutical Inspection Cooperation Scheme (PIC/S).

That did not exhausted the discussion. Participants and speakers reviewed the regulatory system in detail during master classes scheduled for the following day, the Day of Best Practices. Practical master classes of leading industry experts on current issues of pharmaceutical manufacture: GMP inspection, data integrity, qualified persons, and production regulation (radiopharmaceuticals case study).

"Last year, we noted genuine interest that QC/QA experts demonstrated in our practical sessions. Most participants preferred to attend the GMP inspection class: delegates with great interest and involvement took part in our event where we navigated the audience through the most difficult situations that our inspectors encountered. This year we plan to increase the site to accommodate all comers; also we will have no simultaneauos sessions so that our guests are able to visit all scheduled master classes," – said **Natalia Chadova**, Head of the Administration for Pharmaceutical Products Inspection and Evaluation of the State Institute of Drugs and Good Practices.


supported by State Institute of Drugs and Good Practices






INTERNATIONAL IMPACT OF THE III ALL-RUSSIA GMP CONFERENCE

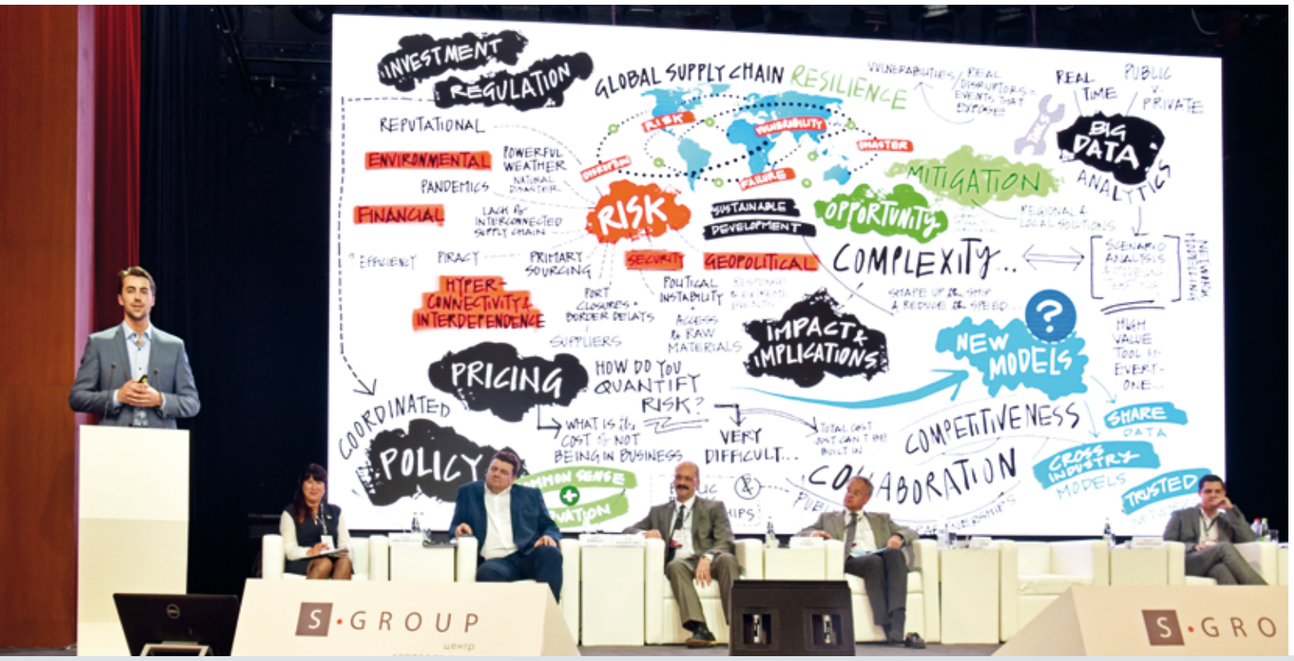
The program book described Day Two as the day of international activities. Russia is part of the global pharmaceutical market. Interaction between countries, common market, international experience in GMP, GDP, GEP, labeling of pharmaceuticals made their way into the conference agenda.

Vladislav Shestakov, Director of the State Institute of Drugs and Good Practices started the day with highlighting main discussion topics such as: distinctions of pharmaceutical legislation and GMP regulation in different countries, regulatory convergence of GMP inspections and procedures, impact of global regulatory approaches on development of drugs, and opportunities for country-to-country interaction.

An important goal of the event was to harmonize the GMP rules and make efforts towards mutual recognition in the international community. This year more than ten foreign regulators took part in the conference, including Japan, the U.S., Cuba, Mexico, Bulgaria, Croatia, Kazakhstan, Kyrgyzstan, and others.

"GMP harmonization and mutual recognition – as we know – are quite a job to do. In this regard, today the ability to integrate effectively into crosscountry associations is at the forefront. Day Two of the conference mostly covered the said issues," said **Vladislav Shestakov**.

Pharmaceutical company Akrikhin organized an expert discussion of the issues of smart use of resources and country-to-country cooperation in GMP area as well as mutual recognition. **Elena Popova**, Director for Regulatory Policy in Healthcare Sector, Association of International Pharmaceutical Manufacturers (AIPM) moderated the session.



Within the framework of the session, the participants discussed the role of the European Medical Agency in GMP inspection and quality assurance; current issues of drug quality evaluation throughout its life cycle; reviewed Russian and international requirements; specifics of pharmaceutical legislation and GMP regulation in different countries; approaches to GMP inspections in different regulatory jurisdictions (the EU vs the U.S.), etc.

For example, **Isabela Majich** – Head of the Croatian Inspectorate (HALMED) – talked about practical outcomes of the MRA of GMP inspections signed between the United States and the European Union. She noted that 'capability' of the Inspectorate does not mean adhering to the inspection order and production control identical to those of the US FDA. She cited some assessment criteria of inspectorate's preparedness: legal and regulatory power to conduct inspections in accordance with the GMP rules, experience of ethical resolution of conflicts of interest, experience of evaluation and mitigation of risks, employment of inspectors with relevant qualifications, work experience, skills and knowledge necessary to identify manufacturing malfunctions that pose potential risks to patients, and tools available for protection of public from harm of low-quality pharmaceuticals.

Stephan Rönninger – Amgen's Director for Quality and External Relations – drew attention to the existing state of affairs in GMP inspections. There have been a lot of changes and improvements: innovation and best practices have drowned out of the traditional industries, the volume of foreign inspections increased significantly compared to 2010, new laws and regulations came into force. There is almost no interruption in pharmaceutical supplies.

Bogdan Kirilov – Executive Director of the Bulgarian Drug Agency – noted that successes of the Russian GMP Inspectorate and the Russian pharmaceutical industry would have been impossible without their cooperation based on two principles – professionalism and enthusiasm.

At the end of the session, **Anna Arutyunova** – Quality Director of Valenta Pharm – presented on the company's tactics for compliance with quality standards, *"Quality policy exists in our company since its foundation. Because it is aimed at the company's strategic goals, we have been carrying out production activities for many years in accordance with GMP standards. One of the fundamentals of our company's quality policy is ongoing improvement, therefore, we extended the standards of good practices to cover not only the manufacture, but also many other aspects: i.e. preclinical and clinical GLP/GCP trials, pharmaceutical QbD developments, QPPV pharmacovigilance, etc. One of the tactical moves in the process of improvement was the launch of a high-tech research and production complex, where all processes are implemented in accordance with the best world quality standards. This means to demonstrate efforts Valenta Pharm takes to follow international standards and apply the best world's practices throughout the life cycle of innovative and other drugs – from their development, research and registration to production and subsequent monitoring. We readily embrace advanced technologies, digitalization of technological processes, and the newest standards in personnel development, procedures, and infrastructure. I can say with confidence that quality assurance should be a strategic goal of all responsible manufacturers who value their reputation, aim at development, and seek to improve life quality of their fellow citizens."*

Tatarstan's pharmaceutical industry attracts investments into the region – that was the motto for presentation of the Republic's investment, scientific, and educational capacity for pharmaceutical and biopharmaceutical companies that plan to localize in Russia, organize contract manufacturing or joint development of innovative drugs.

"Significance of the conference for each of us and for pharmaceutical industry in general is obvious. It is necessary for knowledge transfer, sharing information on main GMP trends in the pharmaceutical market. Compliance with GMP standards is an important development strategy for Russian pharmaceutical industry. New markets and increased exports of domestic products will remain out of reach without strict compliance with international quality standards. The conference this year substantially expanded its business agenda, there has been more opportunities for discussions and negotiations between experts and pharmaceutical market professionals. The conference revealed Tatarstan's potential. The Republic has created a unique investment climate. Scientific and technical capacity for the successful development of the pharmaceutical industry, universities, high tech laboratories – all are concentrated here", – commented **Timur Khanannov**, CEO of TatKhimPharmPreparaty JSC.

International experience in implementation of labelling of medicines for human use was also part of the internation-

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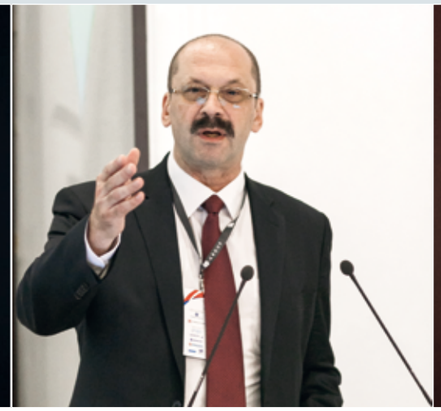

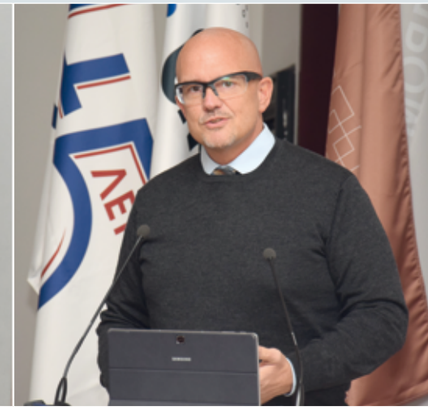

al day discussions. Experts exchanged opinions on mandatory labeling in Russia, reviewed international regulators' take on introduction of pharmaceuticals traceability systems, and the current state of affairs in Russia.

Joseph Traple – Head of the Global Technologies Division of Takeda Pharmaceuticals International – spoke about international experience in implementing labeling and came to the following conclusion, 'It is necessary to demand that suppliers stick to standardized solutions using software that complies with the GAMP5 standard, as well as GMP regulatory requirements.'

Andrey Akhantyev – Head of Economic Security, GEROPHARM – noted that his company supports pharmaceutical labeling in all seriousness, *"We fully support the project introducing labeling and monitoring of drugs circulation, because we believe that this will completely clear the pharmaceutical market of adulterated and falsified products. We have equipped our production lines with the necessary equipment and software, and we have repeatedly tested the entire supply chain. At the present time – however – it is extremely important to agree on clear, transparent, and consistent rules – especially for those participants who are yet to join the project.*

A majority of pharmaceutical manufacturers fear that uncalled for and unjustified cryptographic protection (with codes generated and sold by a monopolistic private company) as well as absence of clear regulations will slow down the project and fail Federal law 61 introducing mandatory labeling. It may also increase risks associated with rejected products, exports of drugs, dependence on an outsourced crypto codes, transfer of a hefty array of commercial data to a private company with vague obligations, and grave liabilities to stakeholders in pharmaceutical industry and the government."

Overview of GEP trends. EAEU ISPE discussion rounded up the international agenda. The discussed issues included technical regulation and standardization of manufacturing guidelines and rules, interaction between professionals in the pharmaceutical industry, high tech API production, and Pharma 4.0.

BEST PRACTICES DAY

August 29 was the final day of the III All-Russia GMP conference with international participation. The venue was zoned into master classes. Leading experts covered current issues of pharmaceutical manufacture. The organizers took a serious approach to preparation and had collected requests from industry professionals for discussion topics beforehand.

Liliya Titova, Executive Director of the Union of Professional Pharmaceutical Organizations noted that the entire conference was very practical, which distinguished it from other similar events, and allowed participants to get specific skills that are hard to find in professional literature. According to her, the third day – the day of the master classes – is the best day of the conference.

Sanofi Russia supported the master class on GMP-inspection that marked the beginning of the busy schedule day. **Natalia Chadova** – Head of the Administration for Pharmaceutical Products Inspection and Evaluation of the State Institute of Drugs and Good Practices of the Russian Ministry of Industry and Trade moderated the event.

The participants discussed inspection of drug manufacture, management of GMP inspections, as well as differences between GMP inspectorates in different countries. **Elena Denisova**, Deputy Head of Department of Pharmaceutical and Medical Industry Development of the Russian Ministry of Industry and Trade noted: *"Our inspectorate needs assistance in its first steps, the Russian pharmacopoeia – however – does not need to be adjusted to others. The first Russian pharmacopoeia appeared at the age of Catherine the Great, that is, in the mid-18th century, so the history of our pharmacopoeia is very rich; we have experience no less than other countries. We say yes to harmonization, but no to mimicking."*

Olga Maklakova, Quality Director Akrihin Staraya Kupavna raised the issue of GMP inspections from the manufacturer's point of view. In her speech, she touched upon the GMP inspection of Russian manufacturers by the EAEU procedures, *"I think it is in the applicants' best interests to submit registration dossiers according to the EAEU rules, and we are all pressed for time prior to the inspection. Therefore, QA should be proactive in registration, supportive of the company's intent to receive EAEU certificates, and take concerted and timely actions."*

At the end of the master class, the results of the survey conducted by the organizers prior to the conference were summed up to identify areas of the industry and, in particular, GMP inspections, which should be improved according to manufacturers and experts.

Manufacturing regulation of certain pharmaceuticals groups (radiopharmaceuticals, blood products, etc) were at the center of discussion among pharmaceutical industry professionals at a master class supported by Pharmimex.

Experts, including foreign inspectors, raised the following questions: licensing of nuclear medicine facilities, production of API's for RPh's, and requirements for new RPh's development.

Natalia Aladysheva, Deputy Head of the Division for Pharmaceutical Licensing and Inspections of the Russian Ministry of Industry and Trade, moderated the class. She established a successful dialogue between representatives of the state inspectorates and drug manufacturers.

Igor Falkovsky, Head of the Department of Good Engineering Practices of the State Institute of Drugs and Good Practices moderated the third day's master class on data integrity. It brought together representatives of international companies responsible for compliance. At the master class, **Gilda D'Incerti,** PQE General Director presented a Data Integrity Guide for the industry, which was developed in cooperation with the The State Institute of Drugs and Good Practices.

SUMMARY

Sixty companies supported the III All-Russia GMP conference with international participation in 2018. Valenta Pharm was the general partner, while Gedeon Richter and TatKhimPharmPreparaty were strategic partners. Many pharmaceutical manufacturers supported both the conference, and specific sessions. For example, Amgen partnered in the session dedicated to Modern regulatory system. New trends and interaction modes, as well as the closing ceremony.

The event aroused great interest in the media: about 40 accredited outlets, more than 15 information partners, including industrial and federal ones. The conference was also supported by professional organizations such as the Russian Association of Pharmacy Networks, the Association of Russian Pharmaceutical Manufacturers, the Moscow Pharmaceutical Society and the Union of Professional Pharmaceutical Organizations.

Full halls at each session and each master class have proven the relevance and significance of the conference, which means that in one year from now experts of pharmaceutical industry will convene again at the GMP conference. ■