



State Agency
of Medicines
Republic of Latvia

A black and white photograph of various laboratory glassware, including several small vials, a large graduated cylinder, and a beaker, arranged on a dark surface.

ANNUAL REPORT

STATE AGENCY OF MEDICINES
2019

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Foreword



In 2019, we continued to pursue the client-oriented direction, as a result of which the State Agency of Medicines (hereinafter – Agency) was **recognised as the leader of the “Consult First” initiative and was also the winner in the nomination “Merchant’s Choice”**.

Agency’s leadership in this assessment was driven mostly by client reviews – **our employees were characterised as competent and forthcoming during interviews, proactively helping to find solutions for individual and specific issues**, thus, creating productive dialogue between the institution and its clients.



Last year, the National Health Service delegated new functions to the Agency: from 1 July we carried out approval and evaluation of medical technologies utilised in healthcare and assessment of cost-effectiveness of medicinal products, medical devices and medical technologies utilised in healthcare. This function was successfully integrated in Agency’s processes, and we created a structure and content for the new opinion format and facilitated traceability of the application.

Implementation of the LEAN approach in the work organisation and process management of the Agency has also improved client service. Throughout the year, employees took part in LEAN training and implemented the acquired skills in their daily duties and work tasks. Last year, Agency's experts had the opportunity to participate in training cycles for raising qualification and exchange programs as part of the international collaboration program supported by the government of the Netherlands.

Last year we launched another **important pilot project – assembly and processing of information regarding remaining stock of medicinal products available to wholesalers**. As part of this pilot project, wholesalers voluntarily submitted weekly electronic reports regarding their remaining stock of medicinal products and vaccines included in the list of reimbursable medicines. This pilot project is proof that it is possible to achieve results by starting with small steps, and this is also a financially smart decision as the solution for monitoring of remaining stock was developed using minimal resources. This business analytical tool may be used for decision making at pharmacies and healthcare institutions, as well as state institutions, including decisions regarding planning of medicinal product supplies. For example, how to locate a medicinal product required for a patient faster by identifying the wholesaler where the medicinal product is in stock. Business intelligence tools are useful in state administration and nowadays they are necessary in order to process large volumes of data quickly and efficiently, find solutions to such significant necessities as availability of medicinal products to residents in Latvia as it becomes an increasingly bigger issue in healthcare posing a substantial risk to patient health. This initiative – business analytics tools for assembly and maintenance of medicinal product wholesaler data to facilitate availability of medicines – **was recognised as one of the top three innovations in state administration in Latvia in 2019**.

A significant step towards the era of modern technology was the **transfer of information regarding marketing authorisation and renewal of medicinal products, as well as annulment of marketing authorisation to the Agency's website**. Now this information is easily available online. By using different selection criteria, clients can find out when the marketing authorisation of a medicinal product was issued, renewed or annulled. In addition, since last year marketing authorisation holders can submit an electronic report regarding disruptions in the supply of medicinal products via the Agency's website.

Improvements were made also to the Medicinal Product Register of Latvia – a new icon “KZS R” was introduced to denote reference medicinal products or the cheapest medicinal product with equivalent efficacy included in the List of Reimbursable Medicinal Products (in Latvian – Kompensējamo zāļu saraksts). This means that now anyone can use the Register to find the cheapest reimbursed medicinal product that is used in the treatment of a specific disease. Furthermore, last year the Medicinal Product Register was supplemented with information regarding use of active substances in elderly patients. This was based on the Meds75+ database developed by the medicines agency in Finland, and it includes classification of almost 500 active substances or their combinations and recommendations for their use in persons above the age of 75.

Last year **we started working on a project of state significance – amendments to prescription of reimbursable medicinal products**, thus, allowing to decrease patient co-payments for medicinal products. The Agency was designated as a collaboration partner of the Ministry of Health in the informative campaign aimed at healthcare specialists, pharmacists, assistant pharmacists and the public. Parallel to the intensive work on development of informative materials for the campaign, already in November 2019 at the conference held in honour of the 25th anniversary of the Pharmacists’ Society of Latvia we informed pharmacists regarding the new requirement coming into effect on 1 April 2020 – indication of the international non-proprietary name in prescriptions for reimbursable medicinal products – and its significance and benefits to patients.



2019 was an important year for the Agency also in the context of Europe – **the Director of the State Agency of Medicines was elected as a member of the Management Group for the Heads of Medicines Agencies (HMA)**. The mission of the network for collaboration of the heads of national medicines agencies is to promote the operation of an efficient regulatory system for medicinal products, thus, ensuring strictly controlled and harmonised requirements for marketing authorisation, distribution, quality control and safety monitoring of medicinal products throughout Europe.

2019 will go down in history **as the year for initiation of medicinal product verification both in Latvia and in Europe**. From 9 February a new requirement is applicable throughout the European Union, including Latvia, for two safety elements – a unique identifier (two-dimensional barcode) and an anti-tampering device – on the outer packaging of most prescription and some non-prescription medicinal products, thus, ensuring the authenticity of medicinal products packaged by the manufacturer and that the packaging has not been opened at any stage of the distribution process until the pharmacy, healthcare institution or social care centre where patients receive medicinal products.

We have also taken another significant step towards promoting collaboration with the industry by amending the publicly available paid service pricelist of the Agency. The new pricelist was approved at the end of last year and came into effect on 1 January 2020, and includes a range of improvements aimed at making the pricelist more proportional to the costs of services and simplify administration of payments. At the same time, the impact on total revenue is estimated to be less than 1%.

Svens Henkuzens

Director of the State Agency of Medicines

About the Agency

The State Agency of Medicines is a state institution under the supervision of the Minister of Health and its operation is regulated by the State Administration Law, the Law on Public Agencies, the Pharmaceutical Law, the Medical Treatment Law, the Cabinet of Ministers Regulation No. 537 “Statutes of the State Agency of Medicines” adopted on 31 July 2012 and other normative acts. The Agency was established on 9 October 1996, based on the Cabinet of Ministers Order No. 403 “Regarding the Non-profit Organisation State Joint Stock Company “State Medicines Agency””.

Objective

The objective of Agency’s operation is to ensure qualitative and justified services in the evaluation of medicinal products used in healthcare, centres for procurement and utilisation of human blood, tissues, cells and organs, as well as pharmaceutical activity companies in accordance with the interests of the State and of the public in the field of healthcare.

It is our vision to become one of the leading authorities among equivalent national and international institutions by implementing functions delegated to the Agency and basing our development on knowledge, efficacy, quality and collaboration.

Functions

- Evaluation and authorisation of medicines, establishment and maintenance of the Medicinal Product Register
- Expertise on quality of medicines
- Pharmacovigilance of medicines
- Vigilance of medical devices
- Issuance of authorisations for conduct of clinical trials with medicines and medical devices
- Compliance evaluation of Good Clinical Practice, Good Manufacturing Practice and Good Distribution Practice
- Issuance of permits for import, export, transit, distribution and utilisation of medicines
- Assembly and provision of information regarding medicines consumption
- Issuance of licences for pharmaceutical activity
- Analysis of cost-effectiveness of medical technologies
- Approval of medical technologies utilised in healthcare
- Other functions

In 2019, the State Agency of Medicines was operating as a public agency not financed from the state budget and its operation was financed by income received from paid services in accordance with the Cabinet of Ministers Regulation No. 873 “Publicly Available Paid Service Pricelist of the State Agency of Medicines” adopted on 17 September 2013.

New functions

From 1 June 2019, the Agency started to carry out new functions after taking them over from the National Health Service on the basis of the order issued by the Ministry of Health in 2018 “On the Reorganization of Public Administration Institutions Subordinated to the Ministry of Health”. In accordance with the order, the Agency took over the following tasks:

- 1) to evaluate cost-effectiveness of medicines, medical devices and health technologies used in healthcare;
- 2) to approve medical technologies intended for use in healthcare, to authorize approved medical technologies, to develop and maintain database of approved medical technologies that are reimbursed from state budget.

Summary of results of Agency's operational strategy 2017-2019

Results achieved during this period^[1] were put forward, based on the objectives and priorities of the National Development Plan for Latvia for 2020, as well as the European Medicines Agency (EMA) and Heads of Medicines Agencies (HMA) operational strategy for 2020, and unequivocally indicate that the Agency is confidently moving towards the objective of its vision, providing a stable foundation for the aims and prioritised operational directions to be achieved during the next strategic period.

Strategic directions of the 2017 - 2019 planning period

- I. Service direction
- II. Collaboration and information direction
- III. Sustainable development direction

The Agency had put forward the following operational priorities

1. Promote availability of appropriately evaluated medicines, including minimisation of short-term and long-term shortages of medicines.
2. Increase application of risk assessment principles in compliance evaluation and ensure more efficient utilization of Agency's capacity.
3. Contribute to the public understanding of safe and rational use of medicines and promote awareness of healthcare professionals of the role of monitoring in ensuring quality, safety and efficacy of medicines.
4. Improve the use of Information and communications technology solutions in supportive and main operational processes.
5. Continuously increase the knowledge and professionalism of experts and Agency's personnel.

In the period of review, the following steps were taken to promote availability of effective, safe and qualitative healthcare products and other products utilised in healthcare on the market in Latvia:

- 1) technical solutions introduced:
 - to ensure that data regarding remaining stock of medicines at wholesaler level in Latvia is available online to general and closed-type pharmacies and healthcare institutions;
 - to decrease the time required for the Agency to issue a permit for import of unauthorised medicines in Latvia or permit for import of medicines in a packaging intended for another country in case of shortages – from 3-5 working days in 2016 to 1 working day in 2019.

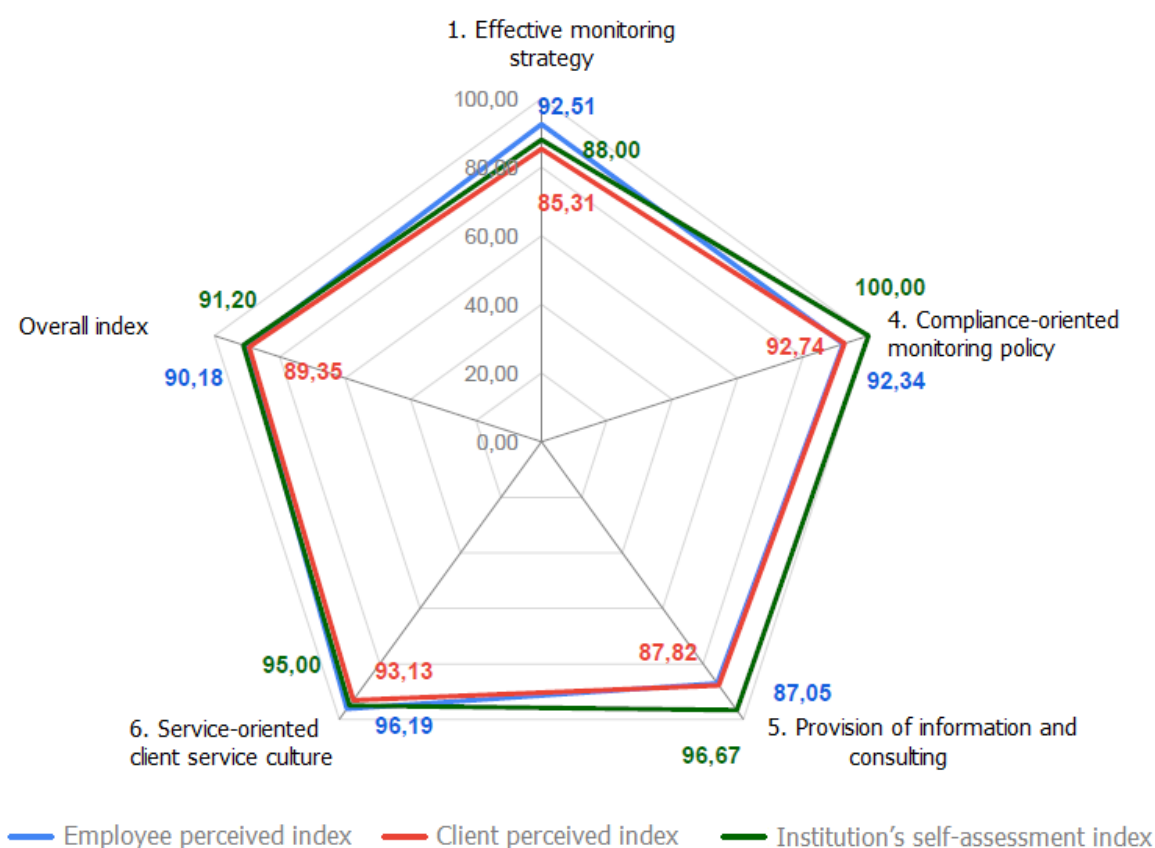
¹ A detailed overview of the most significant results is included in the Agency's mid-term policy planning document "Strategy 2020-2022". The publication is available [here](#) and on Agency's website, in the section "About us / About the Agency / Strategy."

2) Active contribution to preparation of normative acts and policy documents on a national and international level by participating in international working groups and working groups of the network of medicines agencies, including harmonisation of European Economic Area (EEA) level requirements to improve the field of surveillance

3) Amendments to normative acts and internal processes to decrease the administrative burden and facilitate quicker and more qualitative circulation of information between merchants and the Agency:

- clients have begun to utilise the benefits of e-signature and e-address in requesting services;
- digital organisation of written communication between the Agency and clients;
- in 2019, the outcome of the service, i.e. document (e.g., reference, certificate, permit, licence), was issued electronically except in cases where a paper format document was required for submission to third countries or for other reasons.

In the year of review, the Agency continued active participation in the "Consult First" initiative by the Ministry of Economics, and at the end of the year the Agency was awarded with the 1st place among 22 institutions participating in the initiative in 2019. The Agency was also awarded with the 1st place in the nomination "Merchant's Choice". The results of the assessment show that, according to clients, employees and experts, Agency's strengths include service-oriented client service culture and compliance-oriented monitoring policy (inspection policy).



RESULTS OF OPERATION OF THE AGENCY

Marketing authorisation of medicines

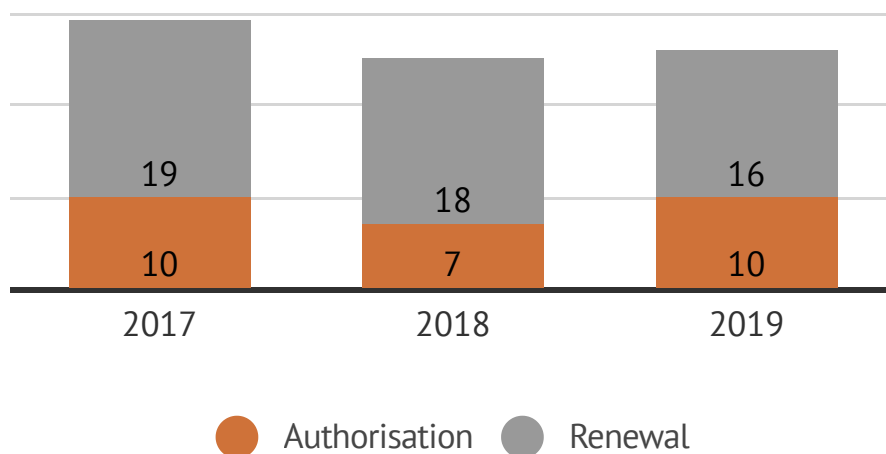
Elita Poplavska, Head of Medicines Marketing Authorization Department:

“The experience and expertise of Agency experts allows Latvia to take on the leading role in European marketing authorisation procedures for medicines more and more often.”

2019, the Agency evaluated 9822 applications for marketing authorisation, renewal and variations to marketing authorisation documentation of medicines by reviewing marketing authorisation documentation related to quality, safety and efficacy. Reviews included also administrative information, as well as chemical, pharmaceutical, preclinical and clinical sections of the documentation and pharmacovigilance documents.

Out of all the applications evaluated by Agency experts in 2019, marketing authorisations and renewals were issued to 26 medicinal products via the national procedure.

Marketing authorisations and renewals via national procedure



Last year, Latvia ensured marketing authorisation and renewal of 25 medicinal products via mutual recognition procedures (MRP) and decentralised procedures (DCP) as a Reference Member State. Latvia also participated in 348 MRP and DCP marketing authorisation and renewal procedures as a Concerned Member State.

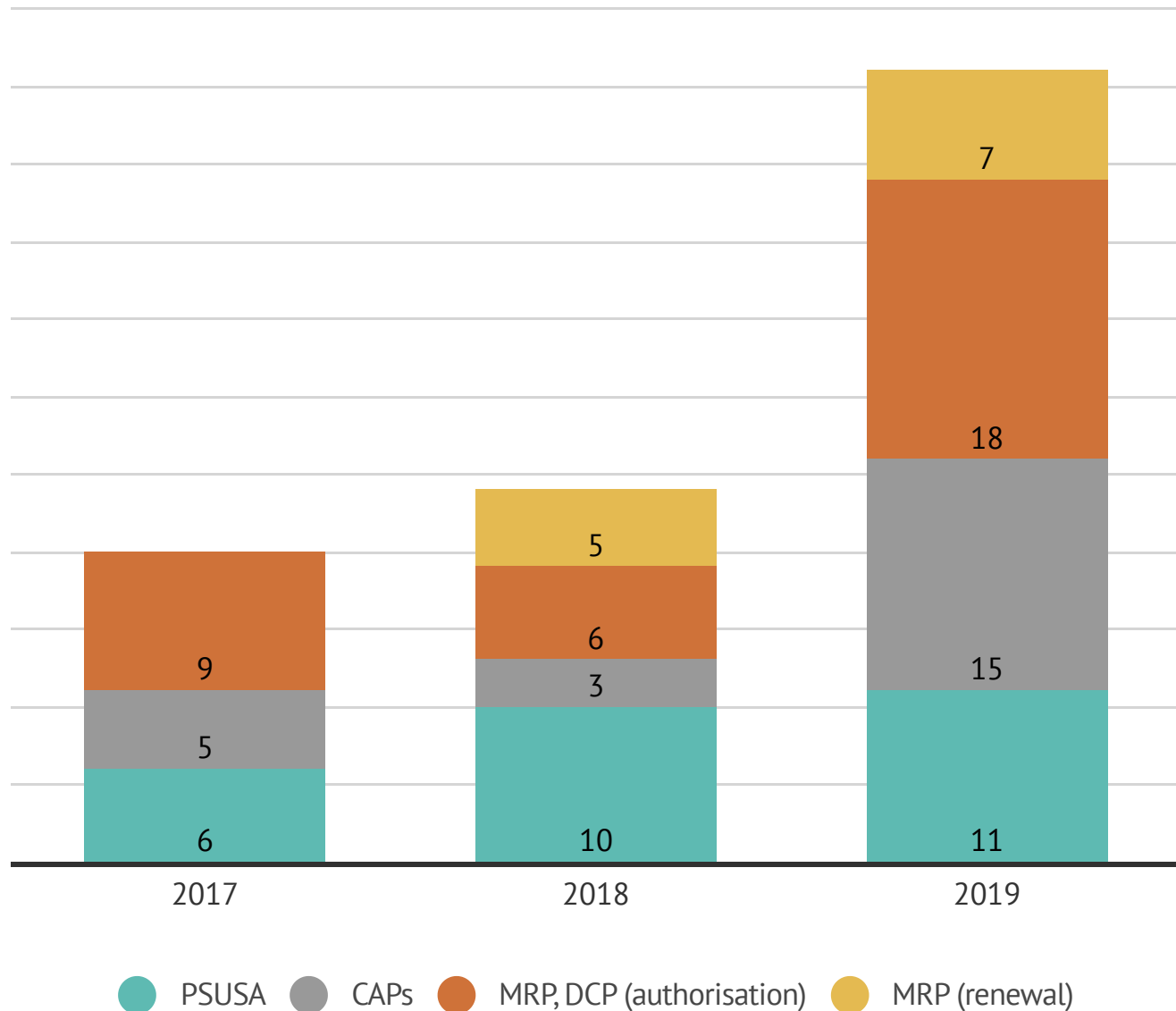
Marketing authorisation of medicines

In addition, in 2019 Agency experts prepared assessment reports for 15 centralised marketing authorisation procedures. In seven of these procedures the Agency was the responsible rapporteur and in four of these procedures – the co-rapporteur. Latvia performed peer-review in two procedures and was the responsible member state for pharmacovigilance evaluation in two other procedures.

In 2019, Agency experts also reviewed 564 translations of medicinal product information (summary of product characteristics, package leaflet and labeling) in Latvian for centrally authorised medicines in cases of new marketing authorisations or variations to authorised medicines.

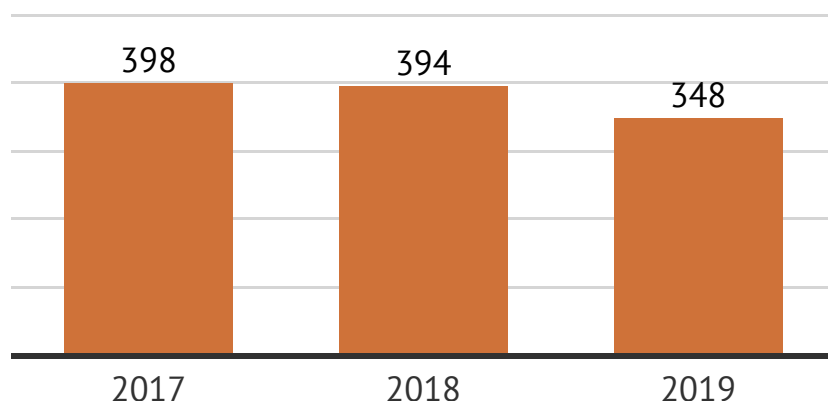
Latvia was the leading member state in European single assessment procedures of Periodic Safety Update Reports (PSUSA) for 11 active substances and the lead member state for signal monitoring for 30 active substances.

Marketing authorisation and renewal Latvia as a Reference Member State



Marketing authorisation of medicines

Marketing authorisation and renewal Latvia as a Concerned Member State



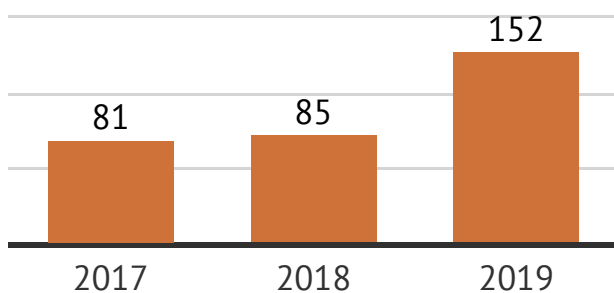
Last year, the activity of Agency experts in international procedures was very significant, similarly as in the previous years. Latvia was represented also in the European Medicines Agency's Paediatric Committee and participated in evaluation procedures for 15 primary paediatric investigation plans (PIP) and for five PIP modifications. Experts from the Medicines Marketing Authorisation Department together with external experts actively participated in the work of the Committee for Advanced Therapies (CAT), Committee on Herbal Medicinal Products and other committees. Experts from the Medicines Marketing Authorisation Department regularly participated in the work sessions of European Directorate for the Quality of Medicines as external experts.

Last year, the Agency took over 10 DCP procedures from other EU member states, including three procedures from the United Kingdom. The Agency also took over seven centralised procedures in relation to Brexit.

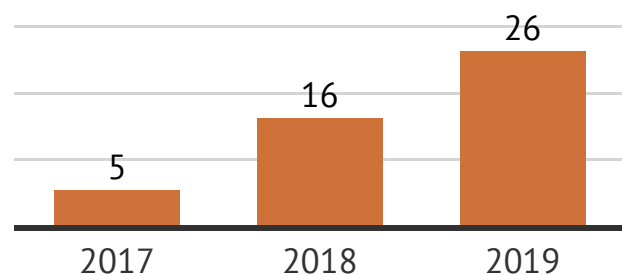
Marketing authorisation of medicines

In 2019, there was an increase in the number of variations to marketing authorisation documentation of medicines evaluated at the Agency where Latvia was the Reference Member State (an increase of 79% for type I variations and 62% for type II variations). This was related to the increased number of marketing authorisation procedures where the Agency took part as a Reference Member State.

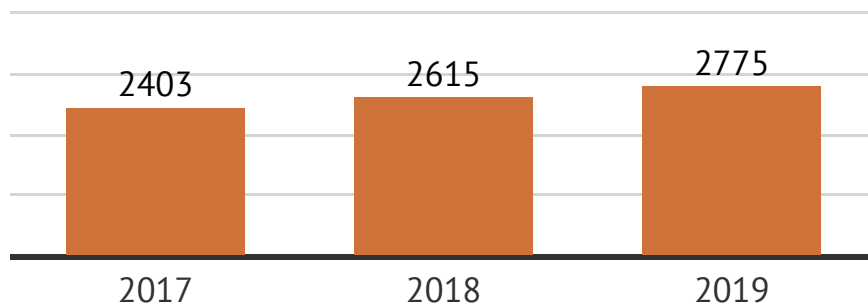
Type IA/IB variations
Latvia as a Reference Member State



Type II variations
Latvia as a Reference Member State



Variations via national procedures



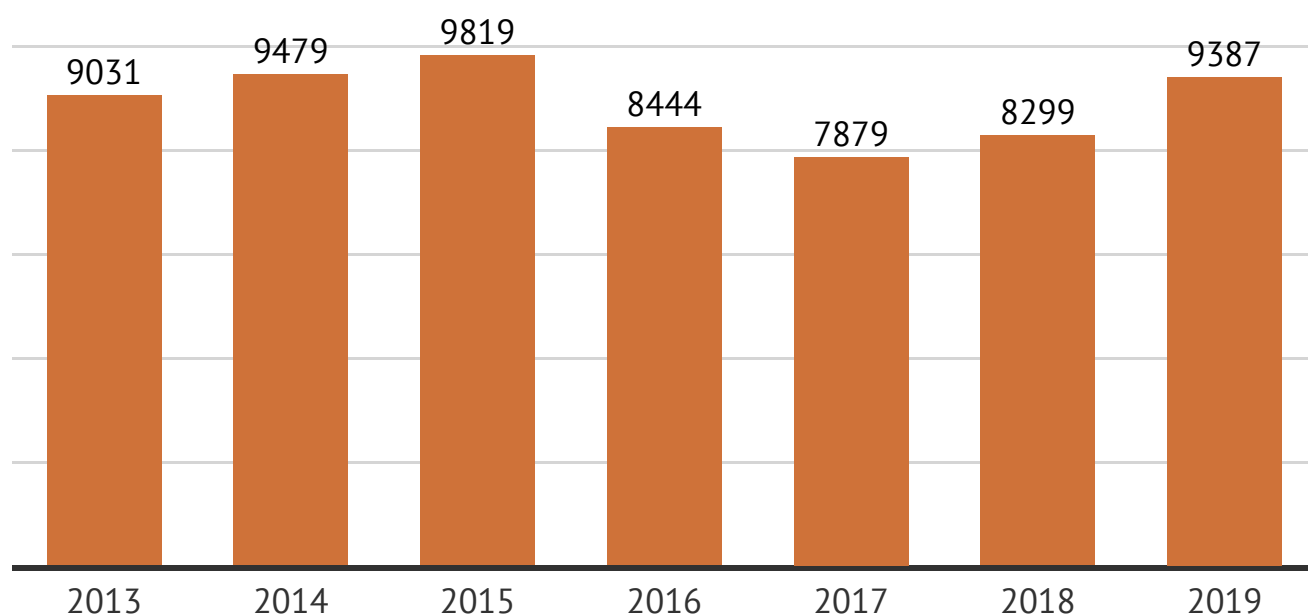
Last year, Agency experts evaluated seven applications and issued their opinion on product compliance with the definition of medicines.

By the end of the period of review, the Agency had:

- Out of all of the applications reviewed, adopted a positive decision regarding marketing authorisation of **209** medicinal products and renewal of marketing authorisation of **168** medicinal products
- Evaluated **9387** applications for variations to marketing authorisation documentation of medicines
- Performed the role of the lead member state in signal monitoring for **30** active substances
- Performed the role of the lead member state in evaluation of PSURs for **11** active substances

Marketing authorisation of medicines

Variations to marketing authorisation documentation



Last year, the Agency also issued eight Certificates of Free Sale and 180 Certificates of Pharmaceutical Products, thus, promoting export of medicinal products authorised in Latvia to countries outside of European Union. These certificates verify that companies manufacture medicines in compliance with Good Manufacturing Practice – according to strict and common quality standards and requirements.

Since 2019, all of the information regarding approved, declined or partially approved variations to marketing authorisation documentation is published on the Agency's website. Similarly, information regarding marketing authorisation, renewal or withdrawal of medicinal product marketing authorisations is also available electronically.

In 2019 as in the previous years, Agency experts voluntarily implemented the recommendation issued by the Pharmacovigilance Risk Assessment Committee (PRAC) on review of signal translations in Latvian for 29 active substances and reviewed Latvian translations of PSUR single assessment (PSUSA) procedure outcomes for 59 active substances.

Medicinal product distribution

Elma Gailīte, Head of Medicines Distribution Information Department:

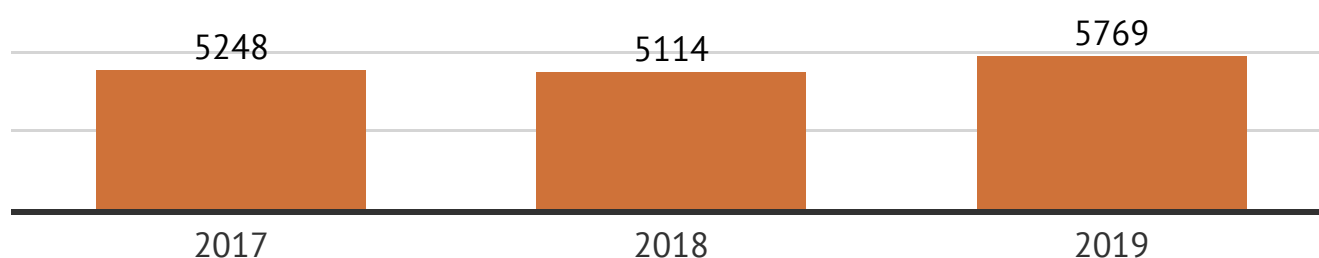
“One of the most important achievements resulting from collaboration among Agency colleagues last year was the launch of a pilot project for reporting of remaining stock of medicinal products at wholesale level. We are very grateful to all of the wholesalers that agreed to participate in this pilot project by submitting data regarding remaining stock of medicinal products to the Agency. Last year, we also designed an electronic form for reporting of unavailability of medicinal products, thus, facilitating identification of specific medicinal products mentioned in the report at the Agency and appropriate operative measures, as well as providing a convenient option for submission of information to marketing authorisation holders, pharmacies, healthcare institutions and residents and Latvia.”

In 2019, the Agency ensured expertise on applications and documentation related to distribution of medicinal products in accordance with the normative acts:

- For import and export of psychotropic, narcotic medicinal products/ substances, as well as precursors
- For distribution of unauthorised medicinal products
- For import of medicinal product samples
- For distribution of and variations to parallel imported medicinal products in Latvia

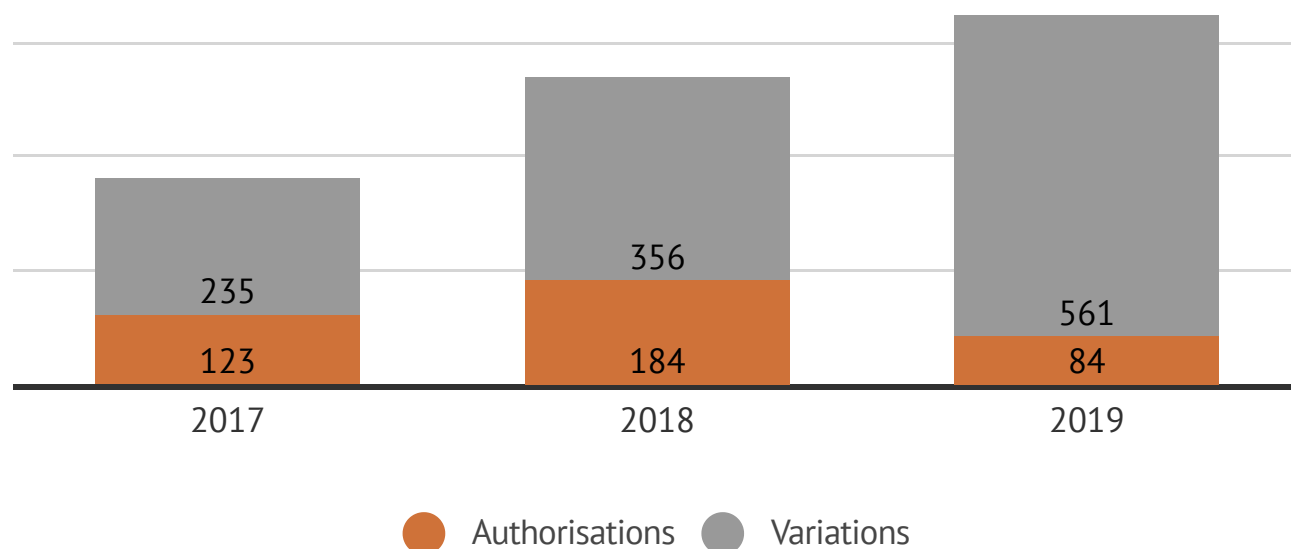
In 2019, the Agency issued 7910 permits for import, export, transit and distribution of medicinal products. In addition, the Agency performed expertise on applications and documentation, as well as issued 8 licences and registration cards to precursor operators and 1 permit for use of herbs, substances and medicinal products included in List I, II and III of narcotic substances, psychotropic substances and precursors controlled in Latvia in medical scientific research.

Authorisations for unauthorised medicines



Medicinal product distribution

Number of authorisations for parallel import/ variations



	2017	2018	2019
Authorisations for import/ export of narcotic, psychotropic medicines/ substances and precursors	1861	1837	2047
Permits for import of medicinal product samples	16	18	10

Last year, the Agency created a new solution for collecting information regarding remaining stock of medicinal products on a wholesaler level – a pilot project was launched to receive and process information regarding remaining stock of medicinal products at wholesalers. The purpose of this system is a more efficient and faster receipt of data regarding availability of specific medicinal products at wholesalers.

Prior to the start of the flu season, as well as during it, the Agency conducted monitoring of influenza vaccines. Based on the information provided by medicinal product wholesalers, the Agency published weekly updates on its website www.zva.gov.lv regarding remaining stock of influenza vaccines, indicating the number of available influenza vaccines and wholesalers where they are available.

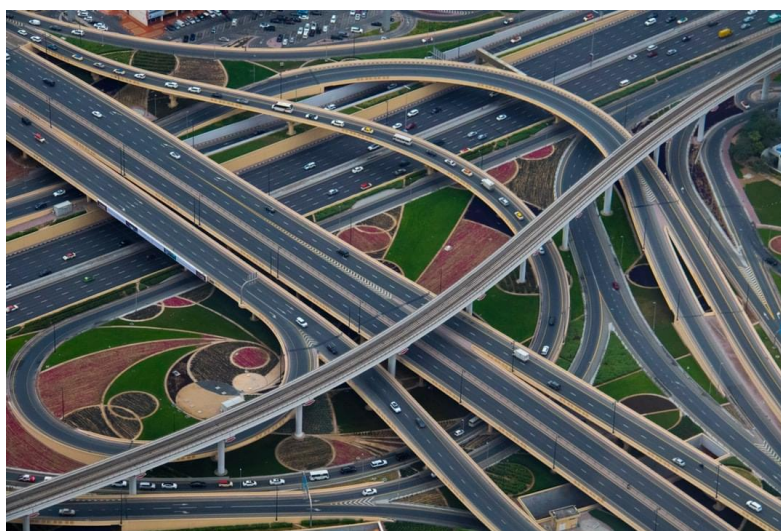
Every month the Agency collected information regarding consumption and pricing of medicinal products and published this information on its website. Based on information regarding sales of medicinal products provided by wholesalers, the Agency prepared the annual publication “Statistics on Medicines Consumption 2018”.

Medicinal product distribution

In 2019, the Agency also ensured recording and control of legal circulation of narcotic substances, psychotropic substances and precursors controlled in Latvia. A quarterly report on the import and export of narcotic substances and an annual report on the consumption of narcotic and psychotropic substances within the state was prepared and forwarded to the International Narcotics Control Board (INCB). A quarterly report on the circulation of illegal precursors and an annual report on the circulation of legal precursors was prepared and forwarded to the European Commission. In addition, the Agency participated in the expert working group on Precursors of narcotic substances, as well as in the 62nd session of the UNODC Narcotics Control Committee.

In 2019, the Medicines Distribution Information Department within its competency actively participated in the development of normative regulations in Latvia and submission of proposals to the Ministry of Health in relation to prevention of falsified medicines and implementation, operation and surveillance of the medicinal product verification system by ensuring communication with the responsible committee of the European Commission, European Medicines Agency and foreign competent authorities, as well as the Latvian Medicines Verification Organisation.

In 2019, employees of the department provided consultations regarding implementation of requirements for medicinal product verification (including parallel imported medicinal products) to Agency's administration, employees, clients and collaboration partners and participated in the training events organized by the Latvian Medicines Verification Organisation by providing regulatory insight and recommendations regarding medicinal product verification at pharmacies and institutions, as well as by responding to specialist queries.



Clinical trials with medicines

Jana Migliniece, Head of the Clinical Trials Department:

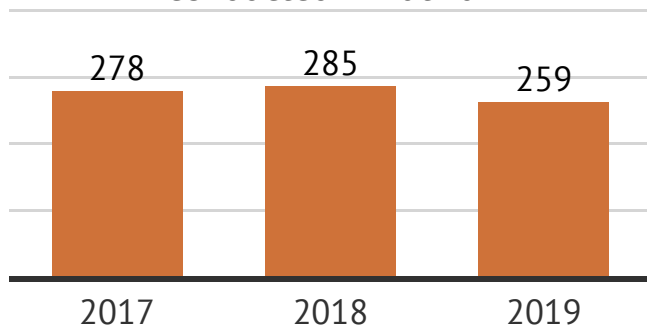
“Last year, the Agency participated in two Good Clinical Practice compliance inspections initiated by EMA which were vital in ensuring the surveillance process throughout Europe. These inspections take place before medicines receive marketing authorisation/ are approved for use in daily medical practice.”

In 2019, the Agency issued 42 authorisations for conduct of clinical trials in Latvia, including 12 clinical trials authorised as part of the Voluntary Harmonisation Procedure (VHP) in Europe.

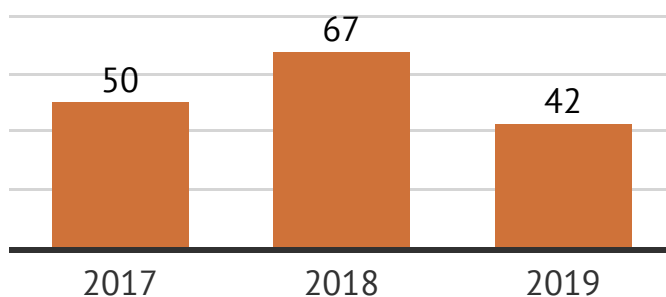
Latvia was the Reference Member State in three procedures, performing an important role in ensuring the overall evaluation process for investigational medicinal products in Europe.

In 2019, the State Agency of Medicines also authorised 333 amendments to clinical trial protocols and one observational study. Last year, there were 259 clinical trials conducted in Latvia.

Total number of clinical trials conducted in Latvia

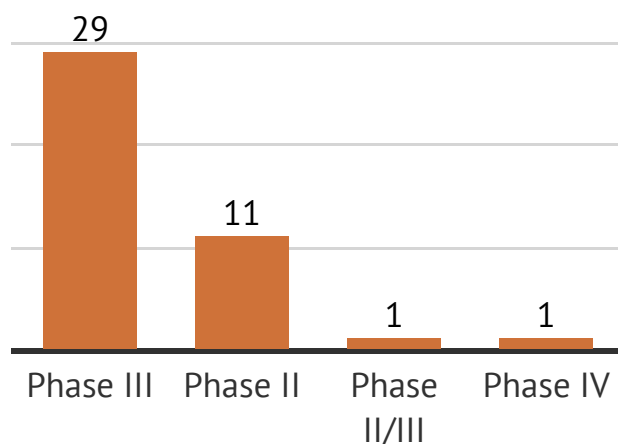


Authorisations for clinical trials



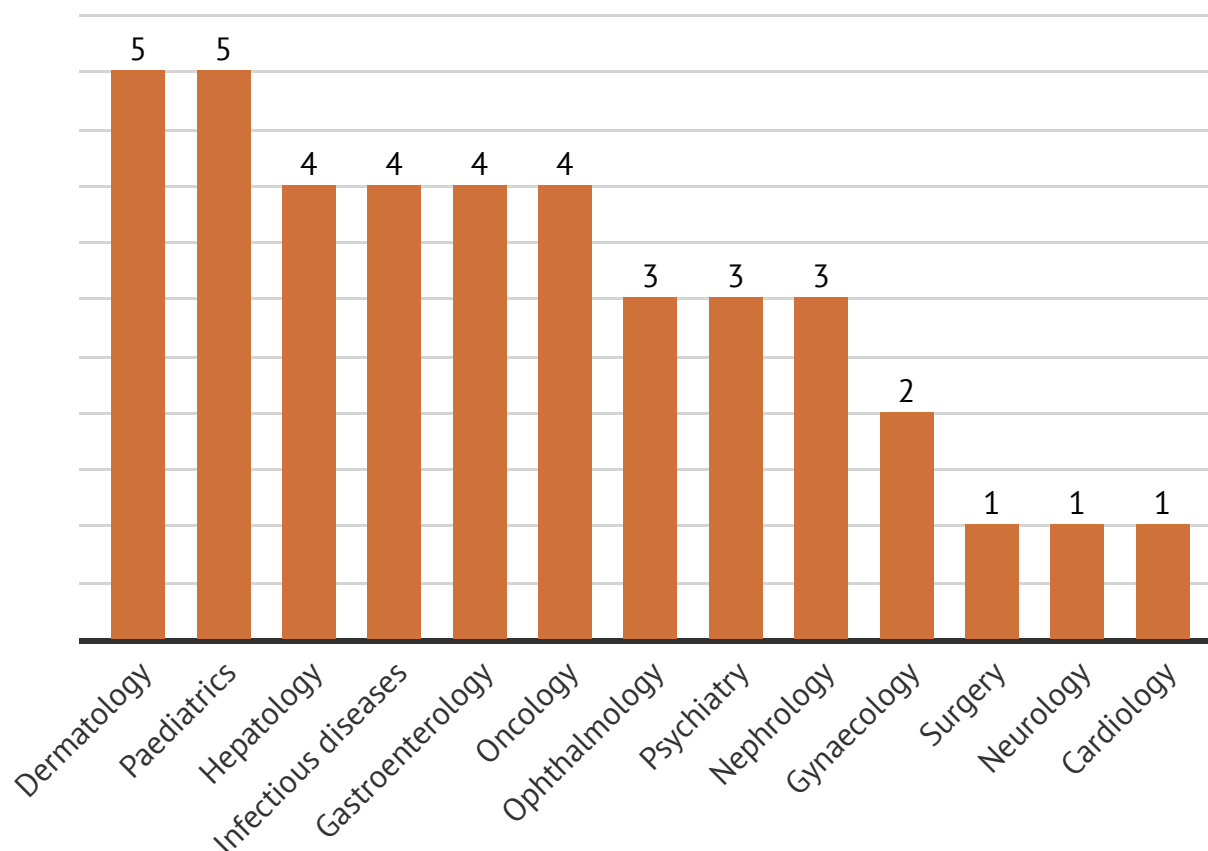
Last year, nine Good Clinical Practice compliance inspections were carried out: four inspections at sites in Latvia and four inspections at clinical trial sites in other countries, and one inspection took place at a foreign sponsor trial site

Number of clinical trials authorised in 2019, according to trial phase



Clinical trials with medicines

Number of clinical trials authorised in 2019, according to medical specialty



Trial sites of medicinal product clinical trials authorised in 2019

State LLC "Pauls Stradins Clinical University Hospital"	26
Riga Eastern Clinical University Hospital	16
LLC "Vidzeme Hospital"	7
State LLC "Children's Clinical University Hospital"	7
LLC "Daugavpils Regional Hospital"	6
LLC "J. Kisis"	6
LLC "Ventspils ambulatory centre"	5
LLC "Riga 1st Hospital"	5
Other clinical trial sites (58* in total)	1-4 trials at every site

Clinical trials with medicines

Information regarding applications for clinical trials with medicinal products, their authorisation, the dates of approval of applications for substantial amendments, opinions of ethical committees, completion of clinical trials, as well as inspections of Good Clinical Practice was regularly entered into the European clinical trial database EudraCT. Regular entry of this data is required to ensure maintenance and updating of the European Clinical Trials Register.

In the year of review, the Agency received 12 primary and 35 follow-up reports regarding serious unexpected adverse events potentially related to investigational medicinal products. The Agency received and reviewed 128 annual safety reports from sponsors related to clinical trials with medicinal products conducted in Latvia. Experts of the Clinical Trials Department together with experts from other European medicines agencies have been involved in the review of these safety reports as part of the work-sharing process. As a result, in-depth analysis of some of the annual safety reports was conducted and the assessment was reflected in the assessment form designed by the safety subgroup of the European Clinical Trials Facilitation Group.



The authorized clinical trials with medicinal products were sponsored by 42 foreign pharmaceutical companies. One of the clinical trials authorized in 2019 was sponsored by Riga Stradins University.

In 2019, thirty-seven contract research organizations were involved in the organization and quality assurance of clinical trials conducted in Latvia according to authorization issued by sponsors.

Monitoring of adverse drug reactions and risk minimisation

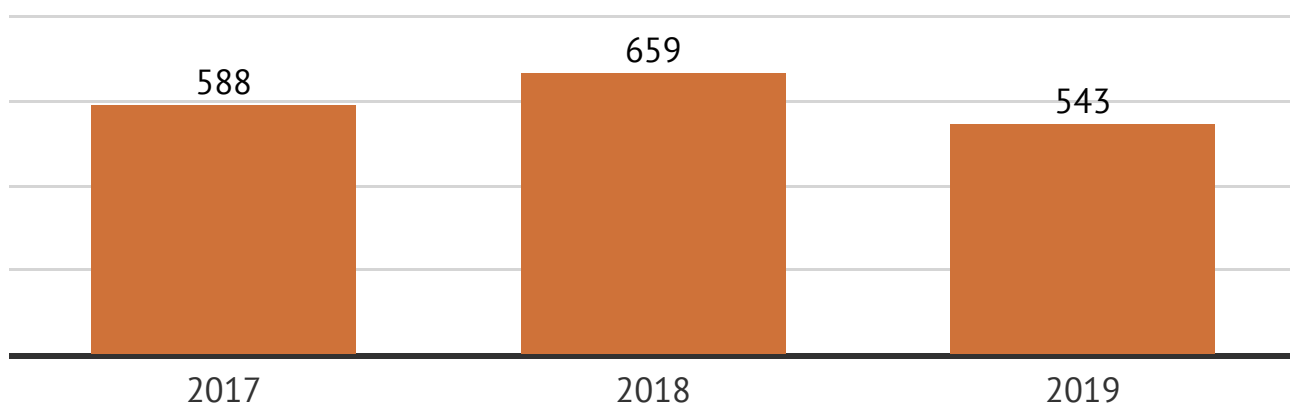
Zane Stade, Head of Pharmacovigilance Department:

“In 2019, pharmacovigilance experts actively participated in informing doctors, pharmacists and patients regarding issues related to safety of medicines and options for reporting adverse drug reactions, as well as elaborated how reporting helps ensuring safety of medicines for the public and providing more thorough information regarding potential risks of using medicines.”

In 2019, the State Agency of Medicines received 543 adverse drug reaction reports, including 16 reports related to adverse reactions to vaccines, and this information was forwarded to the EudraVigilance database in the EU. Sixty-one reports were submitted by doctors and pharmacists, but 48 reports – by patients.

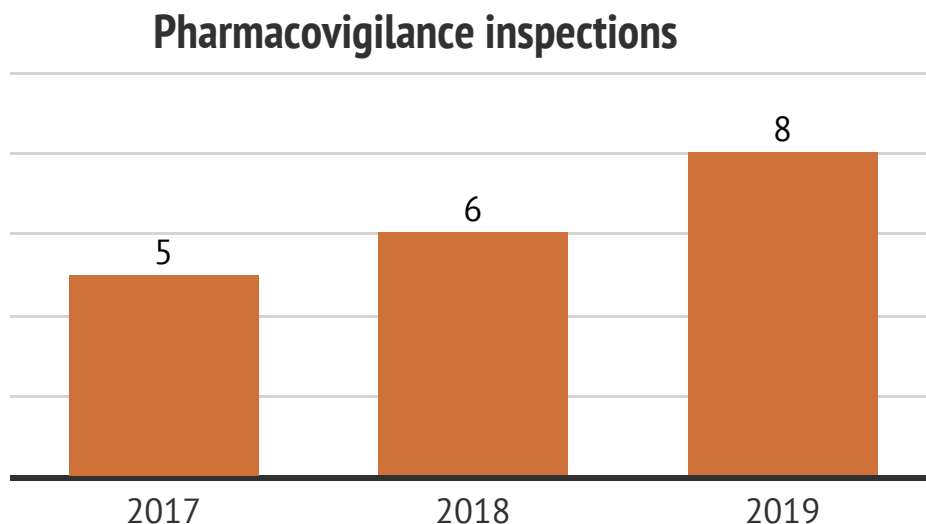
95% of the reports were submitted electronically. Last year, Agency's employees worked on improving the electronic report form to simplify and facilitate electronic report submission.

Adverse drug reaction reports



Monitoring of adverse drug reactions and risk minimisation

In 2019, Agency's experts carried out 7 Good Pharmacovigilance Practice (GVP) inspections of Marketing authorisation holders, including four national inspections, as well as one inspection as part of the international Pharmaceutical Inspection Co-operation Scheme (PIC/S).



As part of the EU single assessment procedure, Agency's pharmacovigilance experts evaluate medicinal product periodic safety update reports (PSURs) regarding active substances where EMA has delegated Latvia as a Reference Member State. Agency performed 11 evaluation procedures in 2019.

In accordance with the EMA work-sharing procedure, in 2019 Agency experts conducted monitoring for 30 active substances, i.e., regular surveillance of the safety information regarding these substances, as well as three in-depth evaluation procedures on a European level where Latvia assumed the role of the leading expert.

Last year, the Agency also evaluated risk management plans for 38 medicinal products authorised via national procedures. In addition, pharmacovigilance experts participated in centralised marketing authorisation procedures as Pharmacovigilance Risk Assessment Committee's (PRAC) rapporteurs (three procedures), as well as collaborated with clinical experts to perform safety issue assessment (six procedures).

In 2019, the Agency approved 25 Direct Healthcare Professional Communications and 93 educational materials submitted by MAHs and created with the purpose of medicinal product risk minimisation.

Monitoring of adverse drug reactions and risk minimisation

Agency's pharmacovigilance experts were also actively involved in informing healthcare specialists and MAHs by participating in 10 events related to pharmacovigilance issues.

The Agency also ensures regular exchange of pharmacovigilance-related information with EMA and European medicines agencies as reflected by the information provided in response to 45 information query documents from EU member states (NUI – non-urgent information).

A pharmacovigilance expert representing Latvia actively participated in PRAC working group meetings by regularly expressing his opinion and presenting assessments performed by experts in Latvia. Information regarding decisions adopted by PRAC in relation to safety of medicines and recommendations for risk minimisation were published on Agency's website and the specialist informative bulletin "Cito!", as well as disseminated electronically among professional associations for doctors.

In order to allow doctors and pharmacists to obtain in-depth information regarding measures required for minimisation of the risk of teratogenicity and developmental abnormalities related to valproate medicinal products and prevent foetal exposure to valproates, professional associations for doctors, MAH for the original medicinal product containing valproate ("Sanofi-Aventis Latvija") and the Agency implemented a collaboration project resulting in a module of video lectures "Valproate Pregnancy Prevention Programme" and informative materials available on the website www.evisit.eu.



Quality control of medicines

Guntars Kaspars, Head of the Medicines Examination Laboratory:

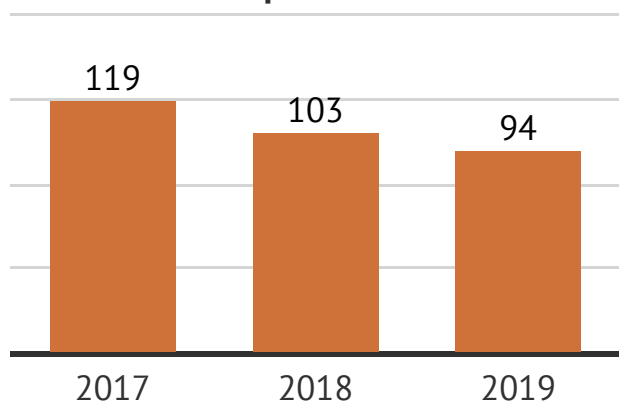
“The Medicines Examination Laboratory maintains a quality management system that is compliant with the new requirements of the LVS EN ISO/IEC 17025:2017 standard and the recommendations of the EDQM Network of Official Medicines Control Laboratories. The Laboratory is also compliant with the requirements of standards LVS EN ISO 9001 and LVS ISO/IEC 27001.”

In 2019, the Medicines Examination Laboratory of the Agency (hereinafter – Laboratory) analysed 94 samples of medicinal products.

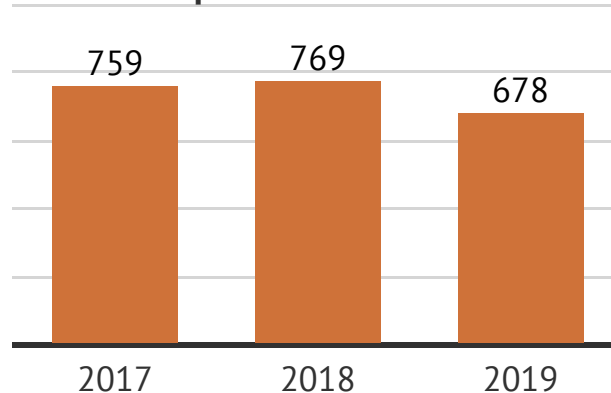
As part of the analyses, 678 quality parameters were tested. The Laboratory prepared 223 volumetric solutions, indicators and reagents upon request from pharmacies, as well as selected and tested 94 samples of purified water produced in pharmacies.



Number of medicinal product samples tested

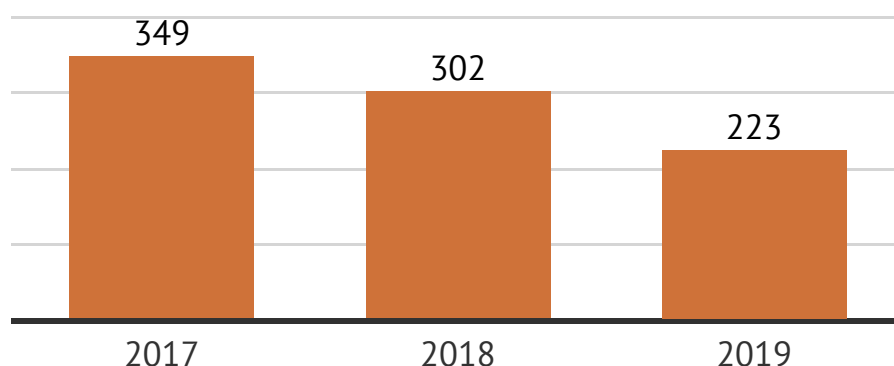


Number of medicinal product quality parameters tested

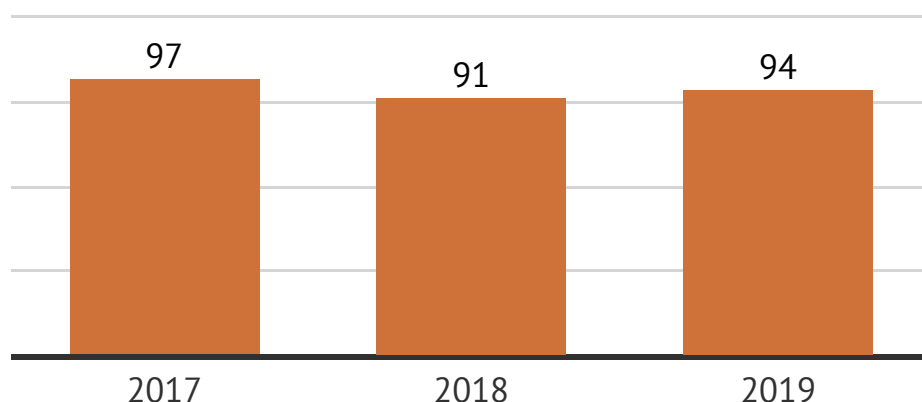


Quality control of medicines

**Number of volumetric solutions, indicators and reagents tested
upon request from pharmacies**



Number of purified water samples tested



The Laboratory conducted expertise for 28 medicinal products upon request from the Agency's Medicines Marketing Authorisation Department, assessing the methods for analysis of active substances and/ or end-products and their validation.

In 2019, Laboratory's specialists participated in international programs for quality control of medicines and professional level evaluation programs, i.e. quality control programs for medicines authorised in the CAP, MRP, DCP and national procedures.

The Latvian National Accreditation Bureau (LATAK) conducted its routing monitoring visit at the Laboratory on 29-30 May 2019. The Laboratory received accreditation in accordance with the requirements of the new version of the LVS EN ISO/IEC 17025:2017 standard across the flexible scope of accreditation.

Monitoring, clinical research and vigilance of medical devices

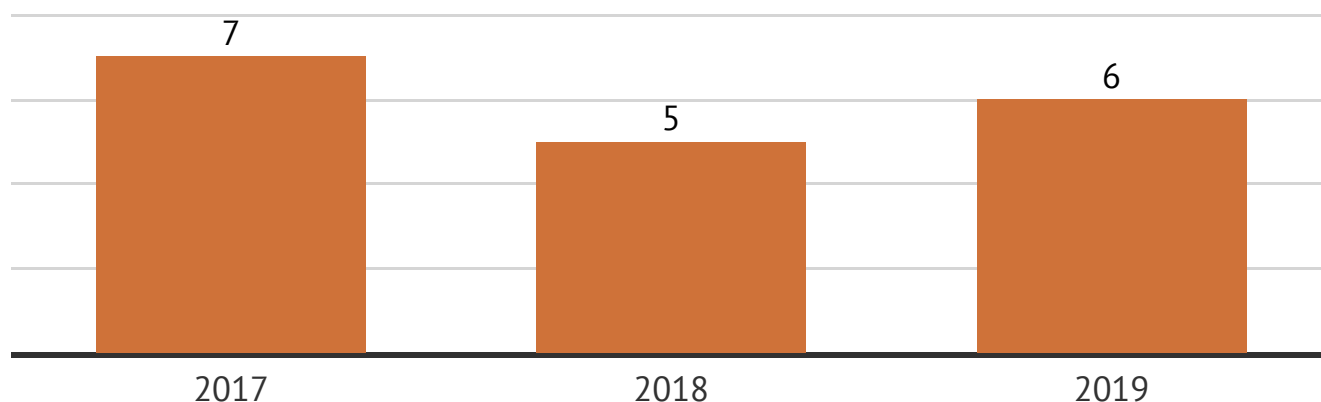
Andis Viļums, Head of Medical Devices Assessment Department:

"Last year the Agency prepared for the implementation of the new medical device Regulation (EU) 2017/745. The Medical Device Coordination Group (MDCG) prepared 14 guideline documents related to notified bodies and operation of the Eudamed database, unique identifier system, clinical evaluation of medical devices, classification of software and cyber security, as well as guidelines for manufacturers of low-risk (class I) medical devices. In order to ensure compliance of the vigilance system with the requirements of the regulation, a new incident report form was created for manufacturers."

In 2019, the Agency reviewed and entered information in the LATMED database regarding 19 medical device manufacturers in Latvia and their manufactured devices, as well as regarding 13 European Union representatives of medical device manufacturers in third countries that have registered their business activity in Latvia.

Last year, the Agency issued three authorisations for clinical trials with medical devices and three authorisations for amendments to protocols of clinical trials conducted in Latvia.

Authorisations of clinical trials with medical devices

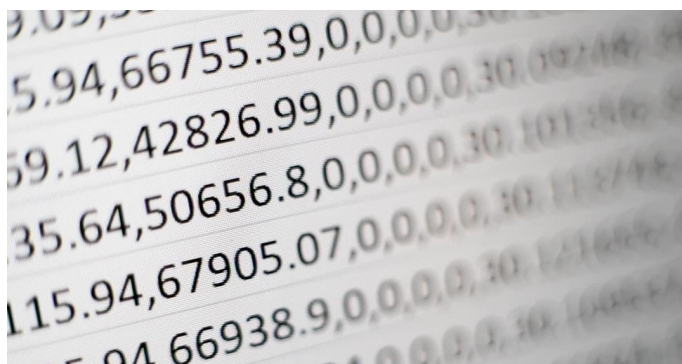
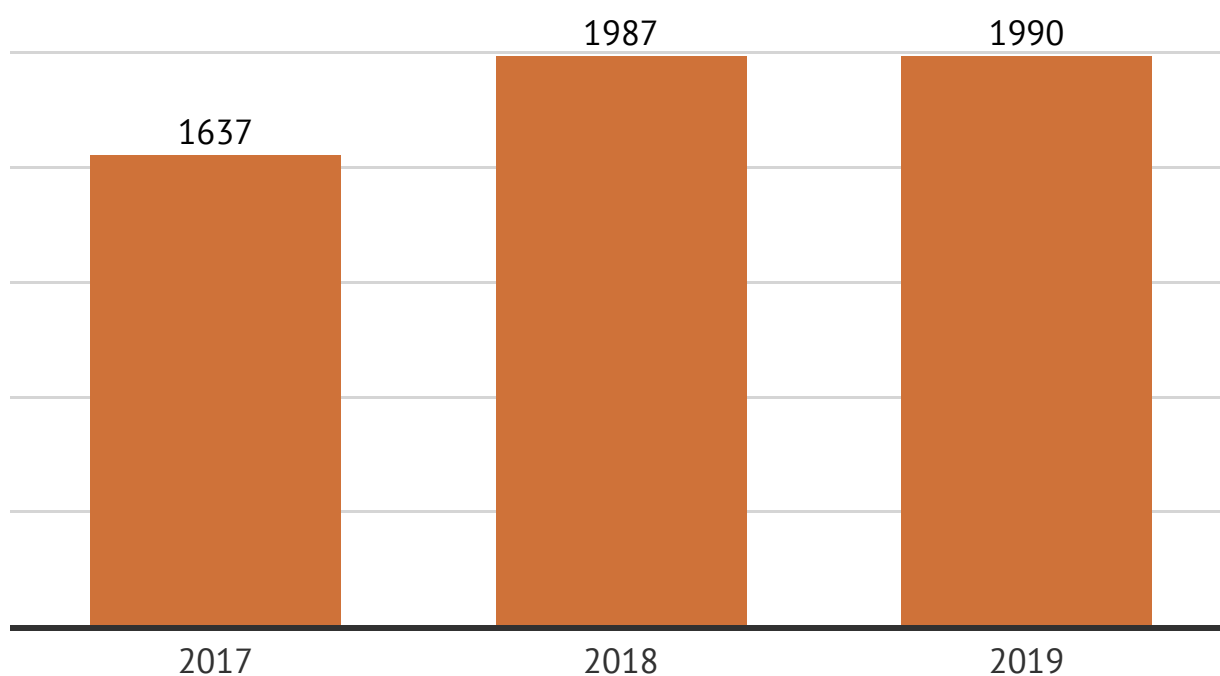


Monitoring, clinical research and vigilance of medical devices

In 2019, the Agency received 1990 primary vigilance reports regarding medical devices.

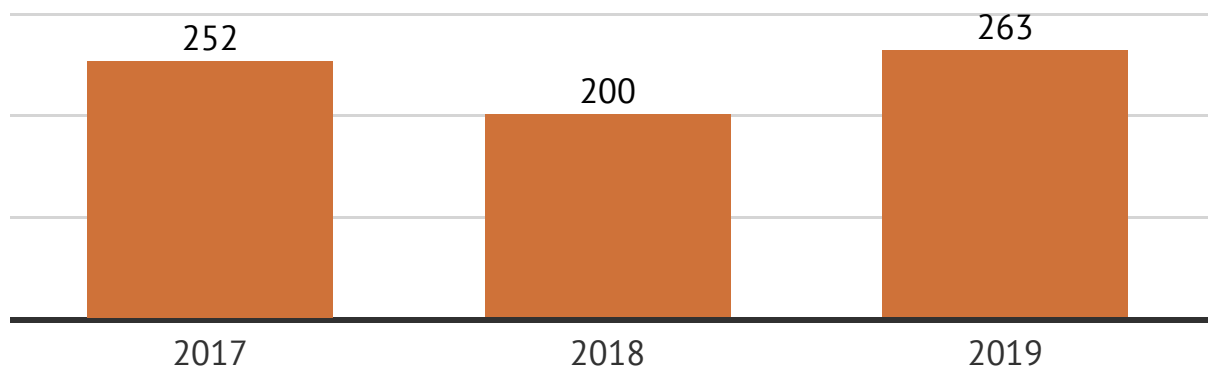
Identification of non-compliant medical devices in use in Latvia and vigilance or safety monitoring measures were ensured in 263 cases.

Primary vigilance reports regarding medical devices

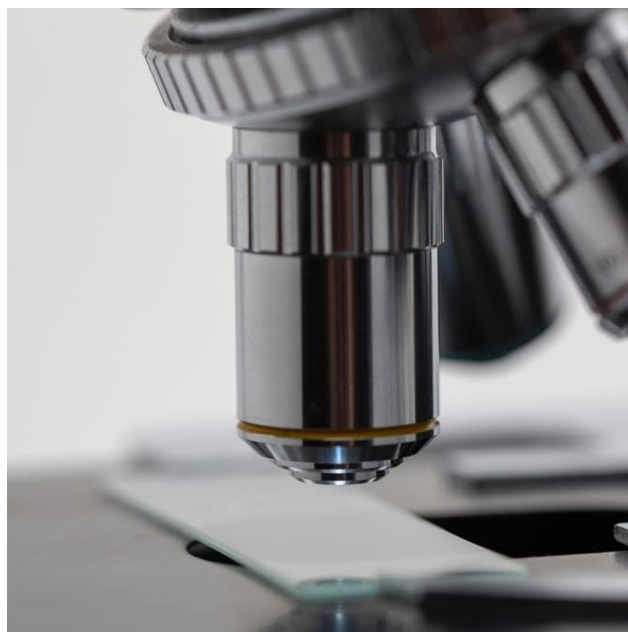


Monitoring, clinical research and vigilance of medical devices

Primary vigilance reports regarding medical devices in Latvia



To promote export capacity of Latvian manufacturers outside of the EU, last year the Agency issued 19 Certificates of Free Sale to medical devices manufactured in Latvia.



Health technology assessment

Antra Fogeles, Head of the Health Technology Assessment Department:

"The Agency as an independent institution, that does not participate in decision-making regarding inclusion of medicines in the List of Reimbursable Medicinal Products, issues its professional opinion regarding cost-effectiveness of medicines. From the middle of 2019, this became one of the documents justifying the necessity to reimburse medicines and medical devices."

From 1 July 2019, as a result of institutional reorganisation the Agency took over new functions from the National Health Service – assessment of cost-effectiveness of medicines and medical devices utilised in healthcare, as well as approval and maintenance of the database of medical technologies utilised in healthcare.

Over the course of 6 months in 2019, the Agency received 16 applications for cost-effectiveness analysis of medicines with new non-proprietary names or medicines containing new combinations of active substances. The Agency prepared three opinions on cost-effectiveness of medicines until the end of the year.

In the same time period, the Agency also received 15 applications for approval or re-assessment of new medical technologies. Two new technologies were assessed and included in the Database of Medical Technologies Utilised in Healthcare until the end of the year. Technical improvements were made to this database taken over from the National Health Service, and it was made available on the Agency's website.



Licensing of pharmaceutical activity companies

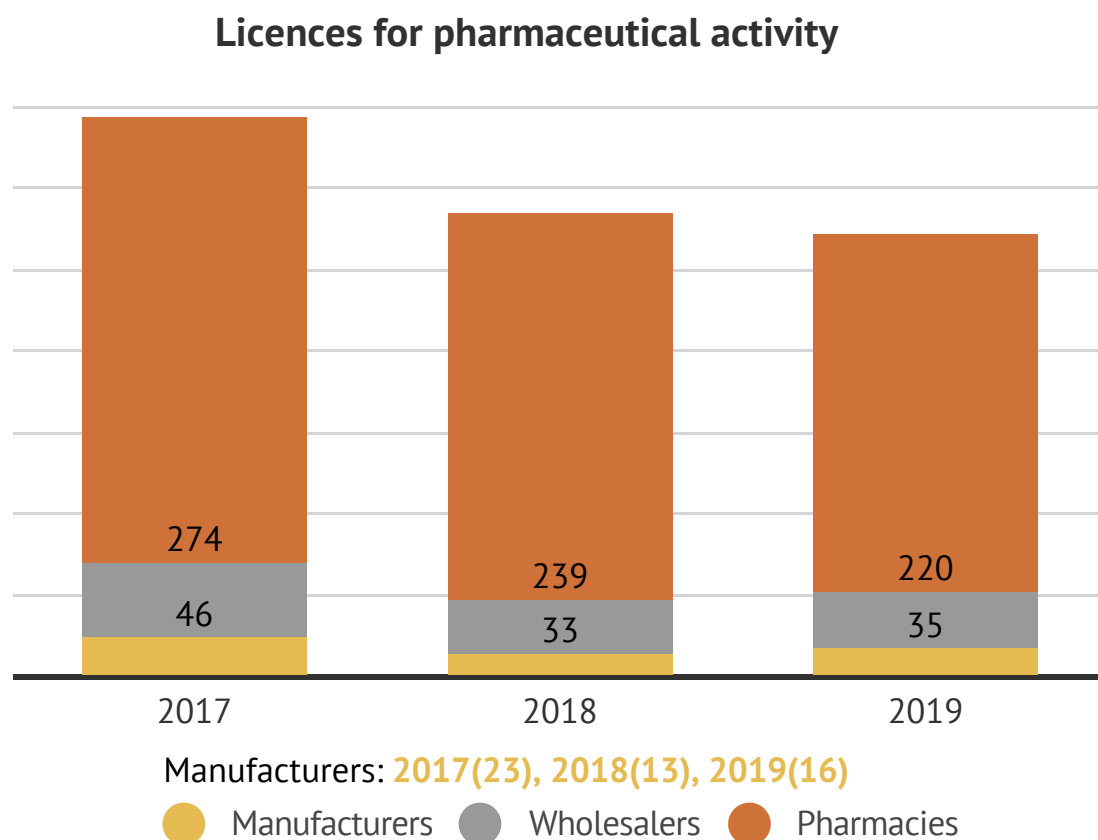
Signe Čudare, Head of Pharmaceutical Activity Company Licensing Department:

“In order to facilitate preparation and submission of pharmaceutical activity licensing documentation at the Agency and save resources in circulation of information for licence holders, as well as the Agency, from 1 August 2019 special permits (licences) for opening (operation of) general and closed-type pharmacies, operation of wholesalers, manufacturing or import of medicinal products and manufacturing of active pharmaceutical ingredients are issued in electronic format and signed with a secure electronic signature. Licences are issued together with an electronically signed decision regarding issuance or renewal of licence. In 2019, the Agency actively invited pharmaceutical activity merchants to submit documents for licence issuance in electronic format, ensuring that officials have signed these with a secure electronic signature. In collaboration with field specialists, the Agency improved submission of documents in the pharmacy sector, and licence holders supported Agency’s proposal for a unified format for electronic submission of information regarding pharmacy personnel and the conditions for special activities. Last year, there was a 50% increase in the number of documents received electronically.”

In 2019, the Agency renewed licences for pharmaceutical activity for 289 pharmaceutical activity companies:

- **220** pharmacies
- **35** medicinal product wholesalers
- **16** medicinal product manufacturing or import companies
- **2** active pharmaceutical ingredient manufacturing companies

Licensing of pharmaceutical activity companies



The Agency also assessed 56 cases related to new site (address) of operation of general-type pharmacies.

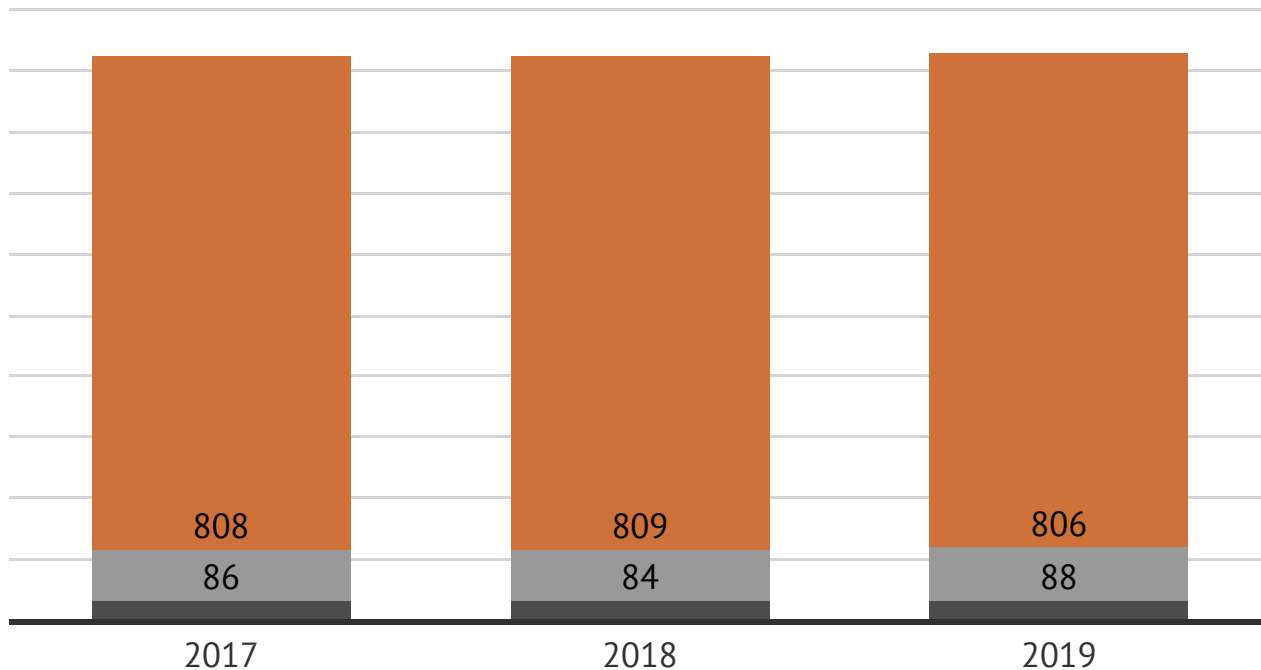
In addition, the Agency issued three licences for new general-type pharmacies, 10 licences for new medicinal product wholesalers, one licence for a new medicinal product manufacturing or import company, nine authorisations for manufacturing, import or distribution companies of active pharmaceutical ingredients.

In 2019, the Pharmaceutical Activity Company Licensing Commission held 14 meetings, reviewing issues and adopting recommendations for issuance, renewal or suspension of pharmaceutical activity licences.

Licensing of pharmaceutical activity companies

Total number of licensed pharmaceutical companies in Latvia

Data: December, 2019

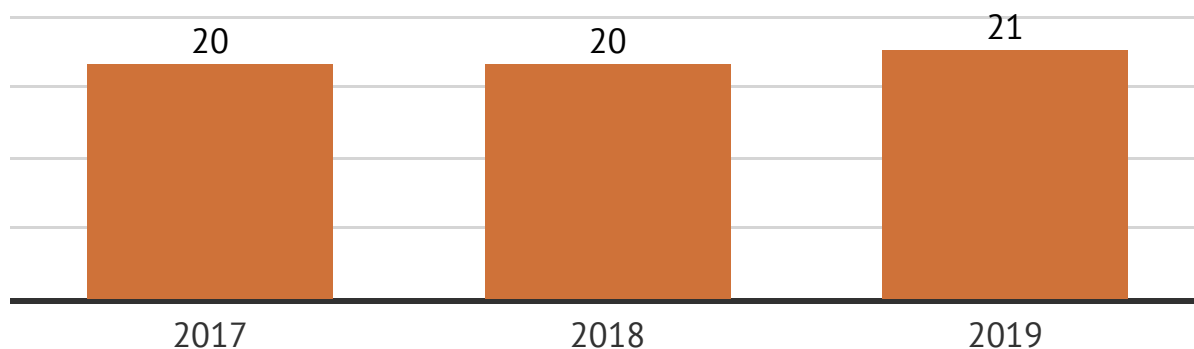


Manufacturers: 2017(29), 2018(30), 2019(31)

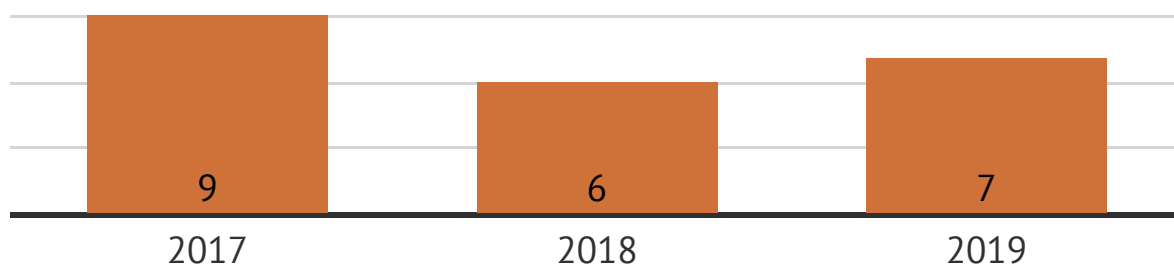
● Manufacturers ● Wholesalers ● Pharmacies*

*Not counting pharmacies' structural units (in 2019 - 76 structural units; in 2018 - 86 structural units; in 2017 - 87 structural units).

Total number of licensed of active substance manufacturers, importers and distributors in Latvia



Authorisation of active substance manufacturers, importers and distributors (including primary authorisations and renewals)



Compliance evaluation of pharmaceutical activity companies, healthcare and higher education institutions

Iveta Vilcāne, Head of Compliance Evaluation of Pharmaceutical Activity Companies Department:

"In 2019, a cycle of inspections of every blood establishment was concluded and signified the first time that implementation of the requirements of Good Practice Guidelines for blood establishments was assessed at all of the hospital blood establishments. Last year continued the collaboration program with Baltic medicines agencies in experience exchange in inspections – 2 collective Good Distribution Practice inspections were organised in Latvia with participation of Lithuanian and Estonian colleagues. As part of the memorandum on collaboration with Food and Veterinary Service, the Agency ensured exchange of inspector experience in the field of manufacturing of veterinary medicines."

In 2019, the Agency conducted Good Manufacturing Practice compliance inspections of 20 companies, including two inspections of medicines manufacturing companies outside of Latvia and two inspections of documents related to licence renewal. The Agency also conducted 40 inspections of Good Distribution Practice of medicinal product wholesalers, 23 of which were related to issuance or renewal of licences. In addition, support was provided to the Pharmaceutical Activity Companies Licensing Department in relation to issuance or renewal of special permits (licences) for wholesale and manufacturing or import of medicinal products.

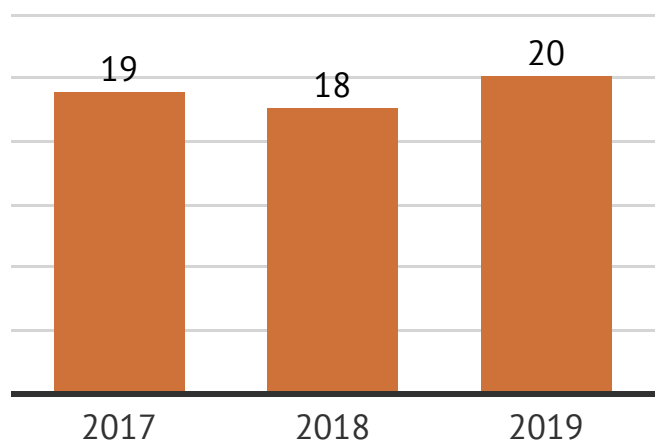
The Agency also conducted vigilance for one human biomaterial, collected data regarding the operation of tissue centres, procurement organisations/ transplantation centres of human tissues, blood establishments and State Blood Donor Centre and submitted reports to the European Commission, performed hemovigilance and biovigilance related to adverse reactions and adverse events reported to the Agency, as well as ensured exchange of information in relation to reports published as part of the Rapid Alert Systems for blood (RAB) and tissues and cells (RATC) where Latvia was indicated as a Concerned Member State. In 2019, the actual availability of accredited immunohematological compatibility testing at every certified blood bank was reviewed and recommendations were provided to healthcare institutions for expanding the field of accreditation of their laboratories or other corrective measures, if necessary.

Compliance evaluation of pharmaceutical activity companies, healthcare and higher education institutions

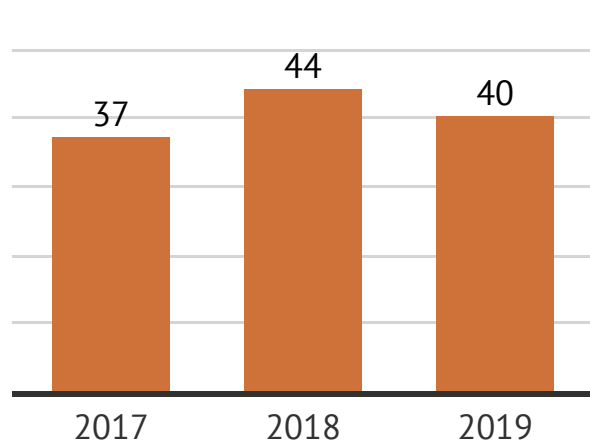
In 2019:

- The Agency received seven applications for compliance evaluation (two for blood banks, four for tissue centres, one for a higher education institution) and issuance of permit, five applications for annulment of permit (two for blood banks, two for blood establishments, one for a tissue centre);
- The Agency issued 6 permits (two for blood banks – one new permit, one related to reorganisation, three for tissue centres and one for a higher education institution in relation to changes in operation);
- Five permits were annulled (one permit for a blood bank related to discontinuation of operation, two for tissue centres – one upon request and one related to a suspended permit that was not renewed).

Good manufacturing practice inspections

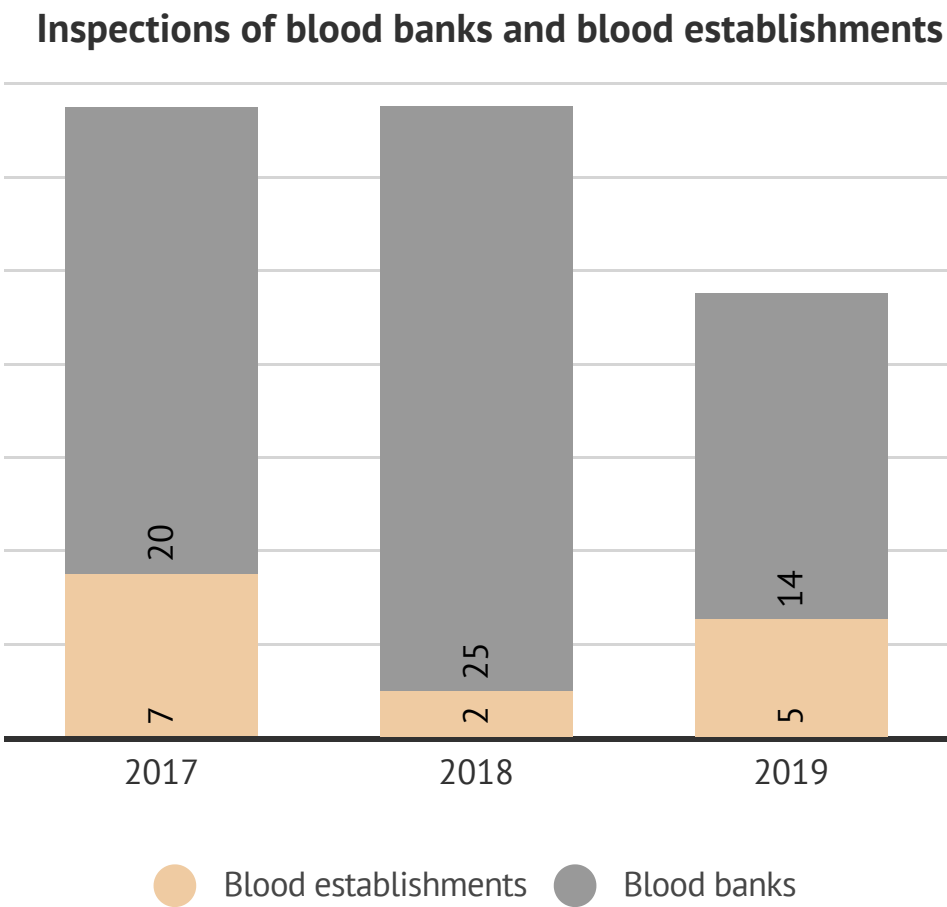
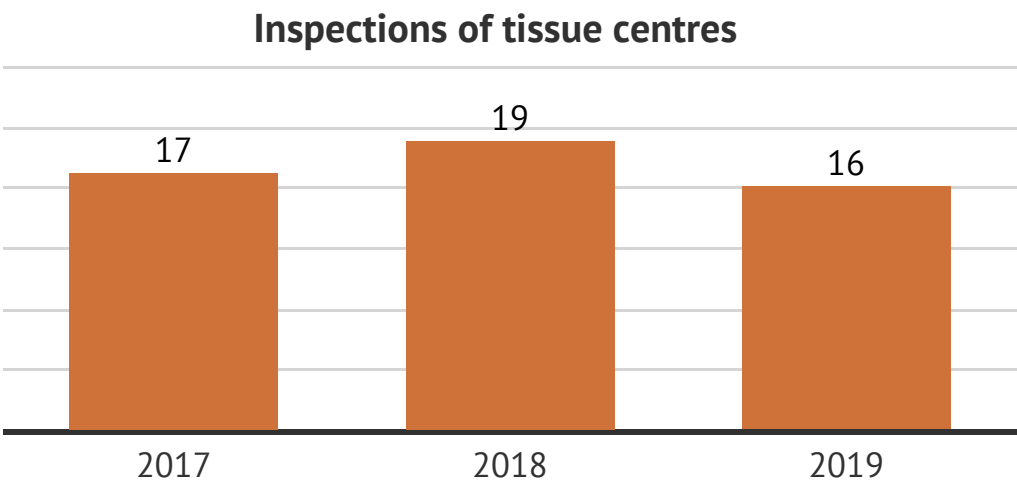


Good distribution practice inspections



Last year, the Agency also conducted five compliance inspections of human blood and blood component establishments, 14 inspections of hospital blood banks and 16 inspections of tissue centres (including four inspections of centres for procurement of tissues and cells). The Agency also conducted five compliance evaluation inspections of documentation – at four tissue centres in relation to changes in operation and one inspection related to changes in operation of a higher education institution providing a medical studies program.

Compliance evaluation of pharmaceutical activity companies, healthcare and higher education institutions



Experts from the Pharmaceutical Activity Company Licensing Department prepared annual reports regarding serious adverse reactions and serious adverse events in the field of blood, tissues and cells, and submitted them to the European Commission.

Compliance evaluation of pharmaceutical activity companies, healthcare and higher education institutions

Experts from the Department also submitted proposals to the Ministry of Health regarding amendments to normative acts in the field of medical record-keeping, epidemiology and tissues and cells (import/export, register of germ cell donors and the required improvements), as well as requested additional explanation regarding implementation of regulations by the European Commission's Directorate General for Health and Food Safety (DG-SANTE) and in the pharmaceutical field (licensing of pharmaceutical activity, manufacturing and distribution of medicinal products).

Department employees ensured representation of the Agency in the EMA Good Manufacturing and Distribution Practice Inspectors Working Group, in the activities of the Pharmaceutical Inspection Co-operation Scheme (PIC/S) and DG SANTE working groups on human blood and blood components, tissues, cells and organs, and in working group meetings organised as part of the Joint Action project (GAPP).

Last year, improvements were made to the registries of assessed institutions utilising human blood, tissues and cells and online information, including publication of a translation of EDQM informative material "Umbilical cord blood banking – information for parents".

The Agency provided information to the USA Food and Drug Administration (FDA) as part of the mutual recognition agreement (MRA) of inspection results.

International collaboration

The Agency is a member of the network of the European medicines agencies, and successful implementation of Agency's functions and tasks is closely related to participation in this network – collaboration with EMA, European Commission and more than 47 EEA authorities regulating the field of pharmaceuticals. This collaboration network gives access to a wide range of experts, thus, allowing to ensure the best possible expertise for the regulatory environment of medicines in the European Union. National experts participate in the work of EMA as members of working groups and scientific advisory groups, as well as scientific committees.

Last year, the Director of the State Agency of Medicines was elected as a member of the Management Group of the Heads of Medicines Agencies. Agency's administration also participated in meetings of the EMA Council where the agenda included EMA involvement in international projects.

Full participation in common European work procedures, which constitute additional responsibilities and duties for the Agency, undoubtedly require qualified human resources, as well as financial resources. In 2019, Agency's employees have been collaborating with EMA scientific committees, EU Commission and Council working groups, World Health Organization, European Pharmacopoeia Committee, PIC/S, EDQM, etc.

Last year, the qualification of Agency's experts was raised with the help of the International Collaboration Program established with the support of the government of Netherlands. In order to ensure and facilitate the exchange of experience between experts for quality of medicines marketing authorisation documentation and compliance inspectors of the Agency and colleagues from the competent authority of Netherlands visited the Agency.

With regard to consequences of Brexit and the increasing volume of work for reference member states, Dutch colleagues view the Agency in Latvia as an appropriate collaboration partner that can participate in evaluation of the quality of medicines marketing authorisation documentation. Therefore, the purpose of the collaboration was to agree on principles for cooperation that would be mutually beneficial to both of the competent authorities.

International collaboration

The Agency also participated in the Drug Precursor Working Group, as well as in the 62nd session of the UNODC Narcotics Control Board. For several years now, the Agency has been involved in collaboration related to surveillance of medical devices and blood and blood components. The Agency is the competent authority in Latvia for notification of medical devices, issuance of authorisations for clinical trials and safety surveillance of medical devices. Relevant Agency experts regularly participate in the meetings of representatives of national competent authorities for medical devices in Europe.

The Agency has entered into a binding agreement with the medicines agencies in Estonia and Lithuania promoting closer collaboration between the Baltic medicines agencies in the regulatory field of medicines. In 2019, a three-way meeting was organised by the medicines agency of Lithuania. During the meeting, an overview of the operation of the Baltic medicines agencies in 2018 and 2019 was presented and meeting participants discussed issues relevant to all of the medicines agencies in the Baltic States, such as introduction of safety elements on medicinal product packages, etc. Last year, Reda Bebars, the Deputy Minister of Investment and International Cooperation of Egypt, as well as representatives of the ministry regulating the pharmaceutical field in Egypt and several merchants visited the Agency in order to find out more about Agency's work in the regulatory field of pharmaceuticals. See more information about the results of international cooperation in section 2.



Implementation of and amendments to normative acts

Decisions adopted by the State Agency of Medicines are balanced, legal and compliant with the requirements of normative acts.

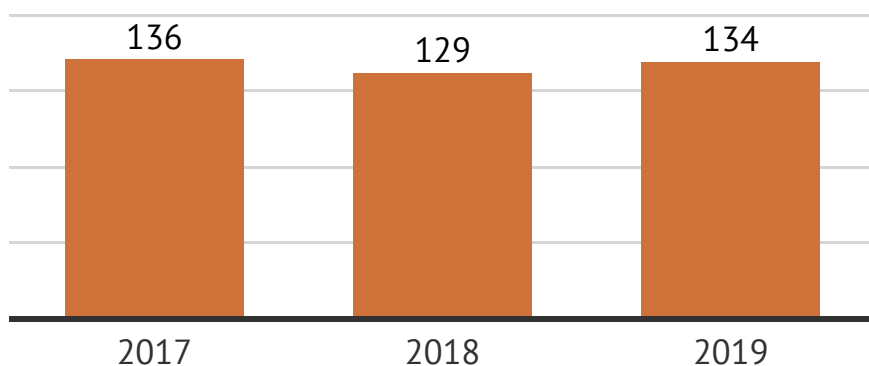
In 2019, only six out of the 8722 decisions adopted by the Agency were contested at the Ministry of Health and one of these decisions was repealed.

Last year, the Agency submitted several proposals to the Ministry of Health regarding amendments and improvements to normative acts. Mentioned below are proposals made in various areas:

- Legal circulation of unclassified substances controlled in Latvia;
- Procedure for allocation of responsibilities to persons ensuring manufacturing, storage, sale or any other form of procurement or expropriation of unclassified substances;
- Clinical research with medicinal products (except veterinary medicinal products), including non-interventional clinical trials, un procedure for non-interventional clinical trials, as well as evaluation of compliance of clinical trials with the requirements of Good Clinical Practice;
- Registration, compliance evaluation, distribution, operation and technical surveillance of medical devices related to implementation of Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC;
- Agency's publicly available paid service pricelist – purpose of proposals was to balance revenue with the cost of services, decrease the administrative burden for merchants;
- Procedure for licensing of pharmaceutical activity – proposal to introduce electronic licences and application forms, thus, improving availability of remote-access services, proposal to abandon decisions regarding approval of pharmacy sites and replace with inspections conducted by the Health Inspectorate prior to issuance/renewal of licences to pharmacies, proposal to abandon the state tax;
- Improvements to the procedure for distribution of medicinal products related to wholesaler reporting to the Agency regarding remaining stock of medicinal products and proposals to restrict export of medicinal products, based on considerations for protection of public health.

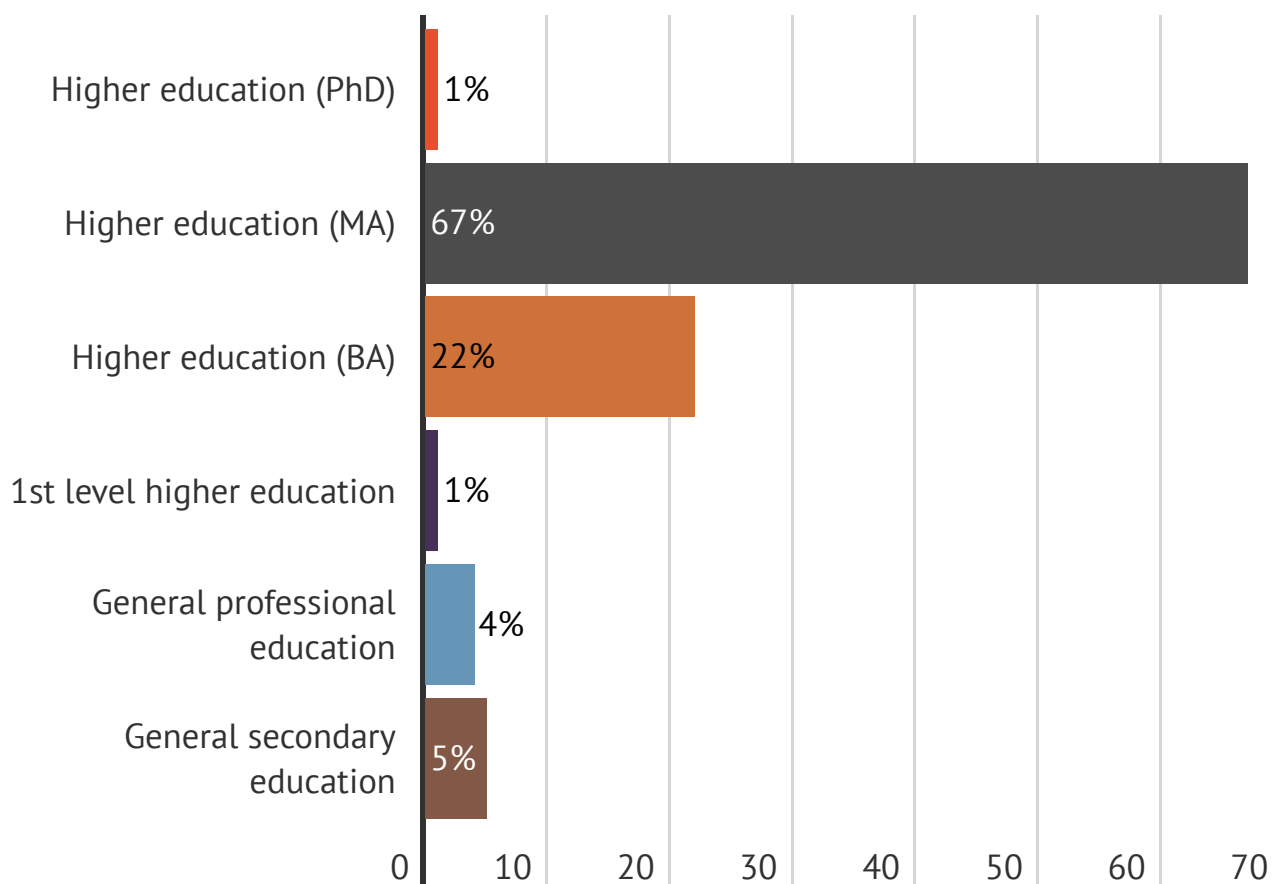
Personel management and training

Number of actual employees



Staff turnover (number of employees and civil servants, who have terminated employment, divided by the average number of staff members) – 14 %.

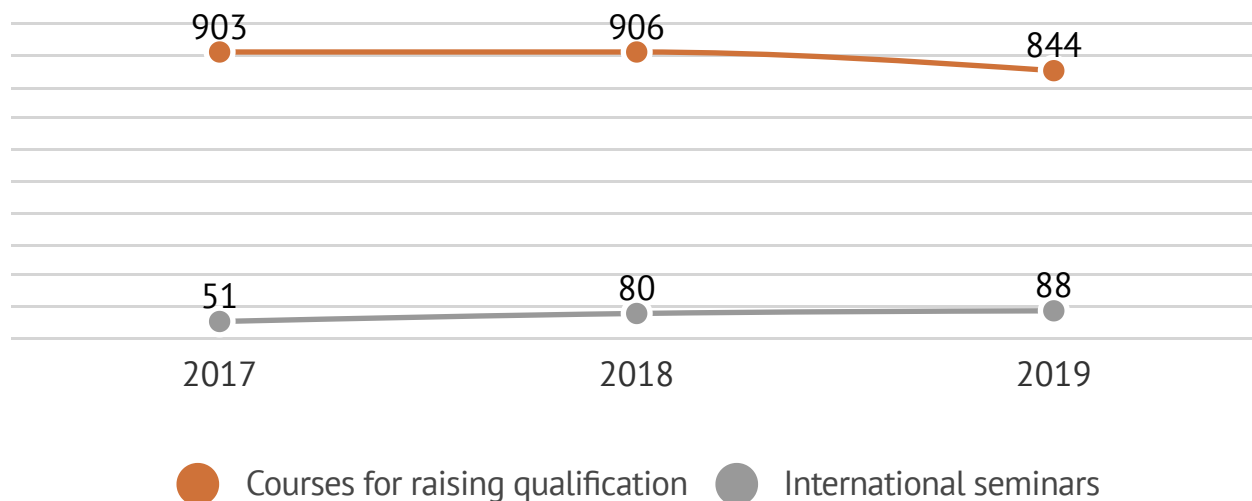
Percentage of employees according to level of education



The overall level of education among Agency's staff is high – 131 employees (91%) have a higher education and 2 of these employees have a PhD.

Personel management and training

Participation in courses for raising qualification and international seminars, conferences



Results of employee survey 2019

- The Agency is open to innovation and embodies modern thinking* – 97% of employees agree or mostly agree with the statement.
- The Agency is a workplace that I am proud of and that I would recommend to others* - 91% of employees agree or mostly agree with the statement.

**Agree or mostly agree with the statement in 2019 (%) of respondents who participated in the survey.*

Integrated management system and audits

In order to ensure compliant services to the parties interested in Agency's operation, relevant maintenance works were continued on the quality management system (QMS) in 2019. The QMS integrates the requirements of ISO 9001, ISO/IEC 27001 and ISO/IEC 17025 standards, as well as recommendations of international guidelines. Last year efforts were made towards continuous monitoring of risks included in the Risk plan of Agency's strategy in 2017-2019.

Compliance with the standard requirements was certified by compliance monitoring audits and ISO/IEC 17025:2017 accreditation visit that certified compliance of the Medicines Examination Laboratory.

Agency's QMS areas:

- Compliance with Good Clinical Practice,
- Establishment and maintenance of a pharmacovigilance system,
- Evaluation of Good Manufacturing and Distribution Practice,
- Testing of medicinal products,
- Compliance evaluation and surveillance of procurement, testing, processing, storage and distribution centres for human blood and blood components,
- Compliance evaluation and surveillance of procurement, storage and utilisation centres for human tissues and cells, as well as organs.

ISO 9001

BUREAU VERITAS
Certification



ISO 27001

BUREAU VERITAS
Certification



Integrated management system and audits

In 2019, the Agency took over the function of evaluation of healthcare technologies from the National Health Service, and in order to ensure this function a new structural unit was established and new services were integrated in the QMS.

In 2019, in order to promote the Agency as one of the leading institutions among equivalent authorities on a national and international level substantial effort was made to pursue the Sustainable development direction of Agency's strategy. As part of the strategy, a 3-month training cycle "Practical LEAN training" was ensured for 45 employees. By applying the LEAN methods, new skills and focusing on efficient resource management, employees reviewed and optimised several of the main and supportive processes.

In order to find out client opinion regarding Agency's operation in 2019, the annual client-pharmaceutical activity company survey was conducted. Survey results showed that 79% of the respondents gave a positive assessment of professionalism of the personnel and 83% of the respondents gave a positive assessment of the quality of services received.

In 2019, substantial work was put in to prepare for the audit to be conducted by European Commission delegated representatives in 2020 regarding compliance of Agency's QMS and Medicines Examination Laboratory with the requirements set for official EEA medicines examination laboratories.

Management of information and communications technology

In 2019, the Agency continued to develop and improve solutions for information systems (IS) and ICT, as well as to improve their availability and management. Last year, the Agency implemented 64 applications for ICT changes that facilitated improved work efficiency and provided substantial support to merchants, the public and employees.

Improvements were made to time schedule records on information system SAMIS, and the functionality for medicinal product synchronising was expanded. Automatic retrieval from the system and publication of information regarding marketing authorisation, renewal and withdrawal of medicines from Medicinal Product Register was ensured. Data selection was improved, ensuring that only updated medicinal product labels are available of Agency's website.

Last year, we introduced a functionality ensuring that MAHs receive reminders to submit documents for marketing authorisation renewal to the Agency at least nine months prior to the expiry of marketing authorisation. An option to receive data regarding other medicines from the reports submitted by wholesalers was introduced, i.e., regarding medicines that will not have their product number validated. The LATMED database's notification form was improved, and a functionality for data validation was integrated into the database.

Improvements to the Agency's website

Several substantial changes were to the Medicinal Product Register: a more convenient access to summaries of product characteristics and package leaflets of centrally authorised products was ensured, information regarding reference medicinal products on the List of Reimbursable Medicines was reflected on the website, a Frequently Asked Questions section was created and information regarding opinions on cost-effectiveness of medicinal products was added. Information from the Meds75+ database created by Fimea, medicines agency of Finland, regarding use of medicinal products in patients above the age of 75 was integrated into the Medicinal Product Register. The Medicinal Product Register is the most frequently visited section of the Agency's website with 262,538 views in 2019.

Database of medical technologies utilised in healthcare that was taken over from the National Health Service was integrated into Agency's website. A more convenient functionality was introduced for MAHs to report disruptions in medicinal product supplies using the Agency's website. Information regarding marketing authorisation, renewal and annulment of marketing authorisation of medicines is no longer reflected in Excel data sheets, but in a convenient list exported from SAMIS regarding the adopted decisions.

Management of information and communications technology

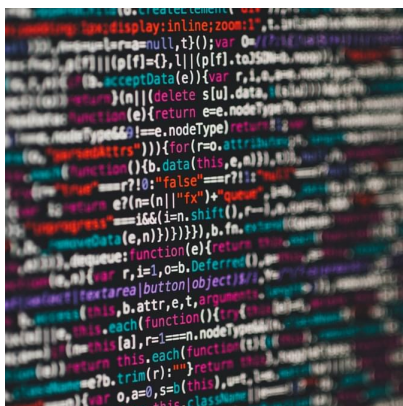
A single icon (banner) “Report adverse drug reactions, incidents with medical devices and biovigilance – for healthcare professionals and institutions” was introduced on Agency’s website by merging the three previously separate options for submission of vigilance reports:

- 1) Report adverse drug reactions;
- 2) Report incidents with medical devices;
- 3) Vigilance report regarding human blood, blood components, organs, tissues or cells.

In 2019, measures were taken to minimise IT security related risks, and regular employee training was conducted regarding IT security issues, a solution for self-training and testing of knowledge in the field of ICT security was introduced. Last year, employee knowledge on ICT security was tested using the CloudStudy.eu solution where IT security training materials are available. Based on the analysis and testing results, employees were repeatedly instructed on measures to prevent computer infection with malware and/or data leaks.

Last year, maintenance of ICT infrastructures utilised by the Ministry of Health and the institutions under its supervision was continued and support was provided to the ICT specialists of these institutions.

In 2019, collaboration continued with various European institutions and competent authorities in other countries to exchange electronic information using common ICT solutions, for example, the European clinical trial database EudraCT, the secure e-mail EudraMail and the data exchange system Eudralink, the pharmacovigilance system EudraVigilance and the data analysis system EVDAS, the European medical device database EUDAMED, the Communication and Tracking system (CTS) solution for mutual recognition procedures for medicines, the Common European Submission Platform (CESP), etc., as well as the Common Repository for marketing authorisation documentation in centralised procedures, the Periodic Safety Update Report (PSUR) Repository.



Communication and collaboration

One of the priorities of the previous year was to contribute to patient and public awareness of the safe, rational use of medicinal products and to promote healthcare professional awareness of the role of monitoring in ensuring quality, safety and efficacy of medicines. Last year, the Agency continued to expand the spectrum of external communication activities by providing clients with independent and objective information regarding the issues within the Agency's competency.

In 2019, activities in communication and public information were performed according to the "Operational Strategy of the State Agency of Medicines 2017-2019". The collaboration and information direction laid down by the strategy includes collaboration with the pharmaceutical industry, professional organisations of pharmacists and doctors, non-governmental organisations, foreign and international institutions, as well as mutual exchange of information within the areas of Agency's operation.

Collaboration with the industry

In 2019, the State Agency of Medicines was recognised as the leader of the state administration initiative "Consult First" and received an award for the nomination "Merchant's Choice"



To pursue one of the Agency's priorities in 2019 – provision of in-depth explanations of the requirements of normative acts – the Agency organised informative seminars for MAHs, manufacturers, wholesalers, retailers and other representatives of the industry and non-governmental organisations, including preparations for introduction of the verification system from February 2019. Representatives of non-governmental organisations were also invited to take part in the Medicinal Product Marketing Authorisation Commission.

Communication and collaboration

As a collaboration partner of the Ministry of Health, the Agency also planned a national informative campaign for the public regarding the new requirement coming into effect on 1 April 2020 – indication of the international non-proprietary name in prescriptions for reimbursable medicinal products.



No zālēm ar vienādu aktīvo vielu un iedarbību valsts apmaksā (kompensē) tās, kurām ir zemākā cena.

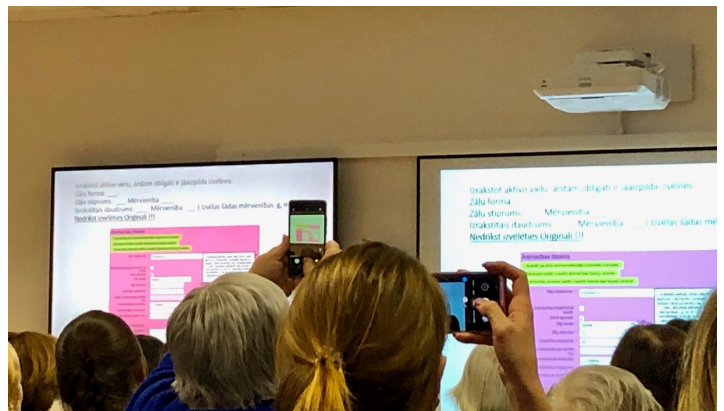
Uzticies savam ārstam – viņš izraksta Tev piemērotākās zāles!
Ja Tev rodas jautājumi, noteikti uzdod tos ārstam vai farmaceitam!

Vairāk lasi: www.esparveselibu.lv

 **NACIONĀLAIS ATĪSTĪBAS PLĀNS 2020**  **EIROPAS SAVIENĪBA**
Eiropas Sociālais
Fonds

IEGULDĪJUMS TAVĀ NĀKOTNĒ

ESF projekts „Kompleksi veselības veicināšanas un slimību profilakses pasākumi” (identifikācijas Nr. 9.2.4.1./16/V/001)



Agency's Deputy Director participated in the conference “Knowledge and ethics – basis for a pharmacist's professional decision” held in honour of the 25th anniversary of the Pharmacists' Society of Latvia, informing pharmacists about the new procedure for prescribing reimbursable medicines.



Communication and collaboration

Informative publications

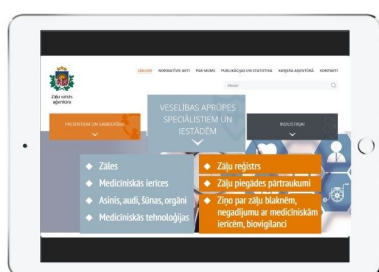
"Cito!"

The informative bulletin "Cito!" for doctors, pharmacists and other healthcare professionals has become an integral part of daily work by providing updated information regarding safety of medicines and medical devices. The main objective of the bulletin is to provide the latest science-based information and recommendations issued by the Agency, European Commission, EMA, WHO, medicines agencies of other countries and independent scientific medical publications.

In the articles of "Cito!" professionals in the field, including Agency's experts, share their experience, publish articles regarding latest issues in medicine, as well as promote exchange of opinions. Each edition of "Cito!" also includes publication of changes in the Medicinal Product Register of Latvia.

CITO!	
IZDEVUMS ĀRSTIEM UN FARMACEITIEM	
JANVĀRIS 2019./#74	
SATURS	
AKTUĀLA DROŠUMA INFORMĀCIJA	
Omega-3 taukskābes saturošas zāles vairs netiek uzskatītas par efektīvām sirds slimību novēršanā	2
Hinolonu un fluorinolonu antibiotikas: darba nespēju izraisīšu un potenciāli nestāgrizienisku blakņu dēļ daļai šīs grupas antibiotiku noteikti lietošanas ierobežojumi, bet pārējām – apturēta reģistrācijas apliecības darbība	3
BELKYRA 10 mg/ml šķīdums injekcijām (dezoksiholskābe): injekcijas vietas nekrozes risks	4
Iesaka saskāpot metamizolu saturošu zāļu informāciju par devām un lietošanu grūtniecības un krūts barošanas laikā	5
Sāk fosfomicīna vērtēšanu	6
Retinoidi ▼ (acitretinums, adapalēns, alitretinoīns, bexarotēns, isotretinoīns, tretinoīns un tazarotēns): Grūtniecības nepieļaušanas programma	7
Vēstule veselības aprūpes speciālistiem: "Valproāts ▼: jauni lietošanas ierobežojumi; jāievieš Grūtniecības nepieļaušanas programma"	9
Vēstules veselības aprūpes speciālistiem ar aktualizētu zāļu drošuma informāciju – saskaņotas ZVA: saraksts	13
Jauni brīdinājumi zāļu aprakstos	14
REĢISTRS	
Jaunums: Zāles, ko sāk izplatīt Latvijā	20
No Zāļu reģistra izslēgtās zāles	25

Bulletin with useful information for healthcare professionals on Agency's website



WWW.ZVA.GOV.LV

Ārstiem, farmaceitiem
un ikvienam veselības
aprūpes speciālistam

Informative manual in Latvian for healthcare professionals regarding biosimilars in the EU



Bioloģiski līdzīgās zāles ES

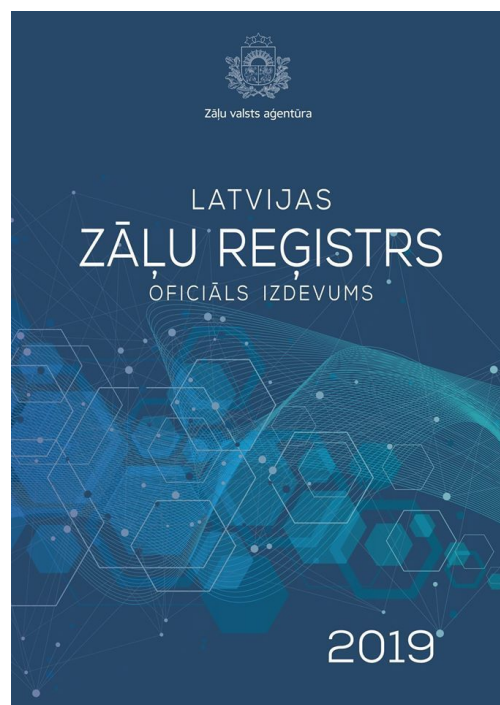
Informatīva rokasgrāmata
veselības aprūpes speciālistiem

Sagatavojusi Eiropas Zāļu aģentūra (EMA) kopā ar Eiropas Komisiju

Communication and collaboration

Medicinal Product Register 2019

The Medicinal Product Register of Latvia is an official and independent source of information for doctors and pharmacists, containing information regarding medicines authorised in the national, mutual recognition, decentralised and centralised procedures, as well as parallel imported medicines, information on medicines included in the List of reimbursable medicines, and information on maximum price of medicinal products. In addition to the book version, an electronic edition of the Medicinal Product Register is prepared in a USB data carrier format containing summaries of product characteristics and package leaflets. A convenient information search form has been developed for this format.



Statistics on Medicines Consumption 2018

To provide information regarding trends in the consumption of medicines, in 2018, the annual statistical report on the consumption of medicines in Latvia was published. The report includes information regarding total turnover of medicines in euros, number of packages sold, distribution of the turnover according to different consumer groups, dispensing status, turnover of medicines expressed in defined daily doses (DDD) per 1000 inhabitants of Latvia per day (DID). Information was also provided regarding the medicines with the highest sales in Latvia and further information was provided about the market of medicines manufactured in Latvia.

Communication and collaboration

**Informative material for future parents
regarding umbilical cord blood banking**



Annual report 2018



Last year, the Agency reinforced circulation of information on its website – 153 news articles were published on it. In addition, the Agency issued more than 150 replies to media queries.



Communication and collaboration

In 2019, the State Agency of Medicines organised the following informative campaigns:

- For the first time, the Agency had the opportunity to participate in organisation, planning and coordination of social media campaigns, including the design of campaign message and international guidelines on communication, aimed at promoting adverse drug reaction reporting. The campaign was organised in collaboration with regulatory authorities of 57 countries and the WHO in order to raise awareness of the importance of adverse drug reaction reporting and provide information on convenient adverse drug reaction reporting in electronic format. The purpose of this campaign was to provide information regarding suspected adverse drug reactions occurring with simultaneous use of several medicinal products, i.e., in case of polypharmacy. The campaign also emphasised that medicinal products may interact with each other, as well as with specific food products, resulting in adverse drug reactions.



- In support of the World Antibiotic Awareness Week activities (in November 2019), the Agency and the EMA provided information regarding the appropriate and safe use of antibiotics in order to promote awareness of bacterial resistance against antibiotics.

Antibiotiku atbildīga lietošana — par ko Jūs esat atbildīgs?

Laika gaitā **baktērijām** dabiskā ceļā **veidojas rezistence** pret antibiotikām.

Situāciju pasliktina antibiotiku **nepareiza lietošana** vai **pārdozēšana**.

Antibiotikas nedarbojas vīrusu infekciju gadījumos. Nelietojiet tās **saaukstēšanās** vai **gripas ārstēšanai**.

- Jums vienmēr ir jāpabeidz viss ārsta parakstītais antibiotiku kurss.
- Nekad nedodiet antibiotikas citiem.
- Ja Jums pēc ārstēšanas ir palikušas antibiotikas, nelietojiet tās.

#EAAD #AMR #AntimicrobialResistance

Antibiotiku atbildīga lietošana — par ko Jūs esat atbildīgs?

Jūs kā **veterinārārsts** varat aizsargāt antibiotiku efektivitāti, **nodrošinot** šo svarīgo zāļu **atbildīgu lietošanu**.

Izmantojot labo praksi, Jūs varat palīdzēt aizsargāt gan dzīvnieku, gan cilvēku veselību.

- Sekojiet līdzi jaunākajām klīniskajām vadlīnijām.
- Izmantojiet diagnostikas rīkus bakteriālu infekciju apstiprināšanai un izvēlieties atbilstošas antibiotikas.
- Ziņojiet par antimikrobiālo zāļu neefektivitāti vai samazinātu iedarbīgumu regulatorajām iestādēm.

#EAAD #AMR #AntimicrobialResistance

Communication and collaboration

- Good service initiative – in support of the Good service initiative organised by the State Chancellery in the state administration, Agency's clients and collaboration partners were invited to give feedback regarding the responsiveness and quality of client service provided by Agency's employees.
- The Agency participated in the "Trailblazer" conference on sharing experience and innovations organised by the State Chancellery and presented its initiative – collection and maintenance of medicinal product wholesaler data with business analytical tools as a solution for medicinal product availability.
- Last year, for the first time the Agency organised Career days aimed at medicinal and pharmaceutical students to allow them to obtain more information regarding job availability at the Agency. The Agency also participated in the Open Door Day and Shadow Day.
- The Agency also ensured provision of updated information on the new platform for providing information to employees – on the Intranet.



Feedback

Employee survey – objective: to obtain information regarding Agency's employees opinion on organisation of work, environment and collaboration, job satisfaction and other important aspects of work that could help to identify priorities in motivating development of personnel resources.

Client and collaboration partner survey – objective: to obtain opinion regarding Agency's work and provided services in order to improve client service and quality of services, based on this data.

Priorities and tasks for development during the next planning period

In order to strengthen the public belief in health as a value, the Agency plans to focus on the following operational direction from 2020 to 2022:

- **Public health interest direction** with the purpose of facilitating availability of appropriately evaluated medicinal products, as well as safe, effective and economically-sound pharmacotherapy
- **Readiness for future necessities and external circumstances**, considering the required competencies related to release of new and innovative medicinal products on the market, as well as opportunities provided by data in development and evaluation of medicinal products
- **Direction for sustainable and productive development of the Agency** with the purpose of organising the work environment and expand automatization of certain steps in processes in order to minimise the administrative burden and increase effective workload of highly-qualified employees in areas where their professional knowledge would provide the highest added value to public health.

The following operational priorities were put forward:

- 1) Promote availability of appropriately evaluated medicinal products, including minimisation of short-term and long-term disruptions in availability of medicinal products
- 2) Increase patient and healthcare specialist knowledge about resources providing independent and qualitative information regarding medicinal products
- 3) Purposeful professional development of employees, considering the trends in development of medicinal products and maintenance of current competencies
- 4) Promote competency and understanding of potential uses of Real World Data^[1] in decision-making
- 5) Review of processes with the purpose of maximising rational use of resources by determining risk-based priorities
- 6) Use of Agency resources in a rational and environmentally-friendly manner.

[1] Electronic medical records, registers, adverse drug reaction report data.

ANNEXES

Budget and expenses

		Budget implementation EUR	Budget implementation EUR	Budget estimate EUR	Budget implementation EUR
1.	Resources for covering expenses (income)	4832185	4873245	4934178	5161435
1.1.	Paid services and other own income	4832185	4872465	4856844	5110759
1.2.	Foreign financial assistance				10969
1.3.	Transfers from the State budget	0	780	77334	39707
2.	Expenses (total)	4109039	5610367	5888822	4814202
2.1.	Maintenance expenses	3968819	5290503	5393981	4319361
2.1.1.	Regular expenses	3968819	4249498	5193915	4205695
2.1.2.	Transfers for maintenance expenses	0	1041005	200066	113666
2.2.	Expenses for capital investments	140220	319864	494841	494841
	Financial balance	723146	-737122	-954644	347233
	Financial resources	1691766	954644	954644	1301877
	Increasing (-) or decreasing (+) change in surplus of financial resources from paid services and other independent income	1691766	954644	954644	1301877

A report by independent auditors

Zvērinātu revidentu komercsabiedrība SIA "AUDITORFIRMA PADOMS"

Bye address: Mukawila 33, Box 14-1004



A REPORT BY INDEPENDENT AUDITORS

Riga

The date of the document is the date of the electronic signature on the document

No.1/2019

To the State Agency of Medicines

Our opinion on the financial report

We have conducted an audit of the State Agency of Medicines' (hereinafter - Agency) financial report included in the annual report of 2019. The attached financial report includes:

- Report on financial situation on 31 December 2019 (balance)
- Report on the financial results of Agency operation in the year ending on 31 December 2019
- Report on the changes in own capital in the year ending on 31 December 2019
- Report on the flow of Agency's financial resources in the year ending on 31 December 2019
- Annexes of the financial report, including explanation of financial report positions, description of the principles for accounting, description of principles for preparation of annual report and description of risk management of financial instruments.

In our opinion, the attached financial report provides a truthful and clear overview of the financial situation of the State Agency of Medicines on 31 December 2019, as well as of the financial results of its operation and flow of financial resources in the year ending on 31 December 2019, in accordance with the requirements of the Cabinet of Ministers Regulation No. 344 of 19 June 2018 "Procedure for Preparation of the Annual Report".

Justification of the Opinion

In accordance with the Law on Audit Services, we conducted the audit in compliance with the International Standards of Supreme Audit Institutions (hereinafter – ISSAI) recognised in the Republic of Latvia. Our responsibilities laid down by these standards are described below in the section *Responsibility of the Auditor with Regard to the Financial Report Audit*

We are independent from the Agency in accordance with the requirements of the Code of Ethics for Professional Accountants established by the International Ethics Standards Board for Accountants (including International Independence Standards) and the independency requirements included in the Law on Audit Services applicable to the financial report audit conducted by us. We have also complied with other professional ethical standards and requirements for impartiality laid down in the Law on Audit Services and IESBA Code (including other professional ethical principles and requirements for objectivity laid down by the International Independence Standards).

We are of the opinion that the evidence obtained as a result of our audit provides sufficient and appropriate justification of our opinion.

Reporting of Other Information

The administration of the Agency is responsible for other information. Other information includes:

- Administration Report included in the annual report attached
- Budget implementation report included in the annual report attached

Other information does not include the financial report and our auditors' report regarding the financial report. Our opinion of the financial report is not applicable to such other information, and we do not provide any sort of verification for it, excluding the one indicated in the section *Other Reporting Requirements in Accordance with the Requirements of the Legal Acts of the Republic of Latvia* of our report.

In relation to the audit of the financial report, our responsibility is to familiarise ourselves with other information and, by doing so, assess whether there are no significant differences between this information and the information in the financial report or our knowledge that we obtained during this audit, and whether it does not include any other substantial discrepancies.

If, based on the work conducted and the knowledge and understanding of the Agency and its operational environment obtained during audit, we conclude that other information contains substantial discrepancies, it is our responsibility to report such circumstances. No such circumstances that would require reporting have come to our attention.

Other Reporting Requirements in Accordance with the Requirements of the Legal Acts of the Republic of Latvia

In accordance with the Law on Audit Services, it is our responsibility to provide an opinion on whether the Administration report has been prepared in accordance with the requirements of the Cabinet of Ministers Regulation No. 344 of 19 June 2018 "Procedure for Preparation of the Annual Report".

Based only on the procedures conducted as part of our audit, we are of the opinion that:

- The information provided in the Administration report on the year of review, for which the financial report is prepared, conforms with the financial report, and
- The Administration report is prepared in accordance with the requirements of the Cabinet of Ministers Regulation No. 344 of 19 June 2018 "Procedure for Preparation of the Annual Report".

Responsibility of the Administration and Persons Entrusted with the Supervision of the Agency with Regard to the Financial Report

The administration is responsible for the preparation of a financial report that is truthful and clear in accordance with the requirements of the Cabinet of Ministers Regulation No. 344 of 19 June 2018 "Procedure for Preparation of the Annual Report", as well as for the maintenance of an internal control system that, in the opinion of the administration, is necessary for preparation of a financial report, which does not contain substantial discrepancies due to fraud or error.

When preparing the report, the administration is responsible for assessing the Agency's ability to continue operation, providing information regarding circumstances related to the Agency's ability to continue operation and application of the principle of continuing operation, unless there are plans to merge the Agency with another institution or divide the Agency into parts.

Persons entrusted with the supervision of the Agency shall be responsible for the supervision of the preparation process of the Agency's financial report.

Responsibility of the Auditor with Regard to the Financial Report Audit

Our objective is to obtain sufficient certainty that the financial report as a whole does not contain substantial discrepancies due to error or fraud and provide an auditors' report expressing an opinion. Sufficient certainty is a high level of certainty but does not guarantee that the audit conducted in accordance with ISSAI shall always reveal substantial discrepancies, if such exist. Discrepancies may arise due to fraud or error and they are considered substantial, if it can be justifiably considered that any of these discrepancies alone or all of these discrepancies together could affect economic decisions made by users, based on this financial report.

Upon conducting the audit in accordance with ISSAI, during the whole audit process we make professional judgements and maintain professional scepticism. We shall also:

- Identify and assess risks of substantial discrepancies due to fraud or error being present in the financial report, establish and conduct auditing procedures for minimisation of such risks, as well as obtain audit evidence that provides sufficient and appropriate justification for our opinion. The risk that substantial discrepancies due to fraud will not be identified is higher than the risk that substantial discrepancies due to error will not be identified, because fraud may involve secret agreements, falsification of documents, intentional withholding of information, fictitious reflection of information or violations of internal control;
- Gain understanding of internal control which is important for conduct of the audit in order to establish audit procedures appropriate for the specific circumstances, but not for providing an opinion on the efficiency of the Agency's internal control;
- Assess the compliance of applied accounting policies and validity of accounting estimations and relevant information supplied by the administration;
- Draw conclusions regarding compliance with the principle of continuing operation applied by the administration and, based on the existence or non-existence of major uncertainty with regard to events and circumstances that may create significant doubts regarding Agency's ability to continue operation. If we conclude that significant uncertainty exists, the auditor report shall draw attention to the information regarding these circumstances provided in the financial report. If no such information is provided we shall provide a modified opinion. Our conclusions are justified with audit evidence obtained until the date of the auditors' report. However, the Agency may discontinue its operation due to future events or circumstances;
- Assess the overall structure and content of the financial report, including the information and explanations disclosed in the annexes, and whether the financial report truthfully reflects the transactions and events which the financial report is based on.

We shall inform the persons entrusted with supervision of the Agency of, among other things, the estimated scope and time of the planned audit, as well as important audit observations, including significant internal control deficiencies identified during audit.

LLC „Auditorfirma Padoms”
Licence No. 68

Vaira Škibele
Chairperson of the Board
Sworn Auditor
Certificate No. 24

THIS DOCUMENT HAS BEEN SIGNED WITH A SECURE ELECTRONIC SIGNATURE
AND CONTAINS A TIME STAMP

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