ANNUAL REPORT 2020

State Agency
of Medicines
Republic of Latvia

Content

Foreword

In 2020, State Agency's of Medicines (Agency) priorities were largely dictated by the Covid-19 pandemic and the challenges it posed.

In the spring, we observed a mass buy-out of various prescription and over-the-counter medicines due to the panic caused by a then unknown virus and timely restoration of medicinal product stocks was very difficult due to the closed borders between countries. **In order to find flexible solutions for ensuring medicinal product availability and minimise disruptions in their availability, we collaborated closely with representatives of medicinal product wholesalers, including facilitation of importing medicinal products in packaging intended for other countries.**

In order to monitor national medicinal product stocks and to minimise risks related to availability of medicines, in 2020, we introduced a system providing overview of remaining stocks of medicines. As a result, accounting for the remaining stocks of medicines at wholesalers has improved and become more transparent. The biggest benefactors from this system are the public and pharmacies, as they can now see in the Medicinal Product Register which wholesaler has a particular reimbursable medicinal product in stock and what is the remaining stock of the product in Latvia.

In order to prevent residents from overpaying for reimbursable medicines, last year we took an important step toward improving the affordability of medicines and in collaboration with the Ministry of Health **we introduced a new procedure – starting from 1 April 2020 healthcare specialists must indicate the active substance, not the brand name on the prescription for reimbursable medicines, and pharmacies must dispense the equivalent reimbursable medicinal product with the lowest price**. Since the introduction of the new procedure, patients have saved 1 million euros every month on patient co-payments for medicines and they have saved more than 12 million euros during the year.

We addressed individual health threats posed by the virus by taking care of the safety of our employees – we **expanded options for working remotely** already at the beginning of the pandemic and offered this to every employee, thus, allowing the Agency to quickly and successfully shift to working remotely.

In addition, we gave advice to the State Chancellery on the existing groundwork at the Agency and the best practice for implementing remote operation. As a result, the State Chancellery created unified guidelines for working remotely in the state administration. We are currently still working remotely and plan on continuing to do so after the pandemic.

By working remotely, we have substantially improved environmentally friendly use of resources by decreasing consumption of resources such as paper and electricity.

Last October **we organised the first online annual meeting of the Baltic medicines agencies**. During the meeting, discussions were held regarding the monitoring systems in place in the Baltic countries to oversee medicinal product stocks, implementation of legislative acts in the pharmaceutical field, promotion of medicinal product availability and opportunities for closer collaboration in safety monitoring of medicines, marketing authorisation procedures, manufacturing site inspections and other areas. Due to the deterioration of the epidemiological situation, for the first time the meeting was held remotely.

Last autumn, a glimmer of hope in the fight against the pandemic was provided by scientists who incredibly quickly began working in collaboration with manufacturers and regulatory authorities to create a vaccine against Covid-19.

A huge number of experts and scientists from all over the world, including the Agency, were involved in both the development and the evaluation of these vaccines and ensured a quality review process for these vaccines at an unprecedented speed according to the unwaveringly rigorous requirements for marketing authorisation.

Vaccine development and the post-authorisation period has been a substantial challenge for the whole European Union (EU) **pharmacovigilance system that has proven itself as one of the most effective systems** in the world by quickly identifying very rare adverse reactions to Covid-19 vaccines.

The previous year was remarkable not only by the fight against the pandemic, but also by Agency's strategic decisions. **Last year we approved not only the joint strategy of the Heads of Medicines Agencies (HMA) and the European Medicines Agency (EMA) until 2025, but also the operational strategy of the State Agency of Medicines until 2022**. Both strategies share common priorities and developmental directions – improving availability of medicines, big data, innovations, digital tools and digital transformation, development of competency for future needs, sustainability in terms of effective use of available human and natural resources, thus, improving general processes.

We wish to express our gratitude to our clients and collaboration partners recognising and valuing our work, and we invite you to read our annual report on Agency activities in 2020.

Svens Henkuzens,
Director of the State Agency of Medicines

"This year has been filled with various challenges that we overcame thanks to our employees, their professionality and ability to adapt to new circumstances in a short period of time and to continue to do their work at a high quality."

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

- TO EVALUATE AND AUTHORISE MEDICINES, TO ENSURE EXPERTISE ON QUALITY OF MEDICINES, TO ESTABLISH AND MAINTAIN MEDICINAL PRODUCT REGISTER
- PHARMACOVIGILANCE OF MEDICINES
- TO ISSUE PERMITS OF AUTHORISATIONS FOR CONDUCT OF CLINICAL TRIALS
- TO AUTHORISE MANUFACTURERS OF ACTIVE SUBSTANCES, IMPORTERS AND DISTRIBUTORS

- TO ISSUE PERMITS FOR IMPORT, EXPORT, DISTRIBUTION OF MEDICINES
- TO MONITOR SAFETY OF MEDICAL DEVICES
- TO ISSUE LICENCES FOR PHARMACEUTICAL ACTIVITY
- TO COOPERATE WITH EUROPEAN MEDICINES AND MEDICAL DEVICES INSTITUTIONS
- COLLECT DATA OF MEDICINES CONSUMPTION
- ETC.

Summary of implementation of Agency's strategy 2020-2022 in the year of review

Goals achieved in the planning period 2020-2022 were set considering also the joint strategy of the EMA and the Heads of HMA for the period until 2025 and they serve also as an unmistakable evidence for Agency's movement towards the objective set out in Agency's vision.

Agency's operation during the year of review

Main events affecting Agency's operation

- In order to ensure continuity of operation amidst the restrictions imposed during the Covid-19 pandemic, substantial changes were implemented in 2020 in relation to working remotely – quick amendments were made to both internal regulations and processes for document circulation, at the same time ensuring appropriate technical and information security management solutions, allowing 90% of our employees to work remotely, as well as increasing the proportion of electronic documents to 98% of the total volume of documents. Solutions for working remotely substantially decreased environmental risk factors for employees and clients.

- In order to achieve the goals laid out in the strategy of the the Agency, five working groups were established that with the help of employees from different structural units collectively planned tasks and followed-up on their completion. This allowed all the employees to participate in the implementation of Agency's strategic goals and values that became more than a formal task for a few leading employees, it became a collective and purposeful work of all the employees. For example, in 2020 we started to gather information on our current competencies and the competencies required for future needs, provided proposals for structural changes related to data analytics and opportunities for use of big data in decision making in the future, proposals were also provided for amendments to normative acts under the supervision of the Ministry of Health related to improving availability of medicines in Latvia and a tool was created for public display of information regarding remaining stock of medicines at wholesalers on the Agency's website.

- Due to the impact of Covid-19, local merchants showed increased interest in starting manufacturing or increasing the manufacturing capacity of medical devices that may be used for personal protection in healthcare.

Consultations were provided to merchants regarding the requirements of normative acts applicable to the classification, manufacturing or release of said medical devices, including requirements for medical facemasks, single-use surgical gloves and different types of medical apparel. In collaboration with other state administration institutions, we prepared informative materials on requirements for personal protective equipment and medical devices, as well as compliance evaluation procedures (certification).

- As Latvia transitioned to the indication of international non-patented names (INN) or the active substance names on prescriptions for reimbursable medicines from 1 April 2020, during the first half of the year Agency employees actively participated in the organisation of a public information campaign, in the content development of informative and explanatory materials, as well as spoke in conferences for healthcare specialists. A new version of the search form of the Medicinal Product Register was developed, changing the focus from brand names of medicines to active substances, as well as making it more convenient for use on smaller screens.

- On 1 April 2002 the requirement to provide data on remaining stock of medicines to the Agency came into effect for medicinal product wholesalers distributing medicines included in the list of reimbursable medicines. In turn, the Agency published this information on its website. In order to provide this new service, we allocated resources to develop a process for receipt of structured data and a technical solution for publication of the data of medicinal product availability submitted by wholesalers.

- As part of the authorisation of Covid-19 vaccines, management of adverse reactions and development of the vaccination process, there was a substantial increase in the workload of our employees due to participation in the following activities:
  -international working groups, as well as analysis of information on the new virus, clinical trials with vaccines and supporting experts by evaluating information and data submitted for authorisation;
  -interinstitutional working group with the aim of developing a solution for the e-health information system in Latvia to enter adverse reactions to specific vaccines and to ensure access to the adverse drug reaction report content for the Centre for Disease Prevention and Control(SPKC);
  -interinstitutional working groups and participation in the development of the vaccination strategy document for Latvia upon request from the Minister for Health.

- In 2020, the European network of medicines agencies faced various challenges related to the withdrawal of the United Kingdom (UK) from the EU. The Latvian State Agency of Medicines participated in the operational directions related to minimising risks of disruptions in supply of medicines and redistribution of UK's authorisation procedures among other member states.

- In 2020, collaboration was continued with the medicines agency in the Netherlands, including implementation of a training and experience exchange program (International Collaboration Programme – ICP) developed with the support of the Dutch government. Last year, Agency experts had the opportunity to participate in courses for raising qualification and experience exchange cycles in the Netherlands. An important aspect in 2020 was the involvement of Agency's experts in the evaluation of the presence of nitrosamine impurities in medicines containing metformin, which is one of the top priorities on an EU level.

- Continuous improvements in the services provided has remained one of Agency's objectives. In 2020, we continued to implement structured improvements and optimisation of Agency's operational processes based on the LEAN approach by utilising the knowledge and skills obtained by employees during the practical training on the LEAN method.

- We also utilised the opportunities provided by the EMA for our employees to raised their qualification by continuously learning about utilisation of data analysis tools, artificial intelligence and robotic solutions and taking self-learning courses online on various platforms to learn about new tools within the Training on Big Data program consisting of three main blocks:

  1.Utilisation of real-world evidence;
  2.Biostatistics and methodology for clinical trials;
  3.Skills for data utilisation.

RESULTS OF OPERATION OF THE AGENCY

Marketing authorisation of medicines

Elita Poplavska, Head of Medicines Marketing Authorisation Department:

"During the Covid-19 pandemic, the Agency has successfully ensured continuity of services related to marketing authorisation of medicines so that people in Latvia have access to safe and effective medicines."

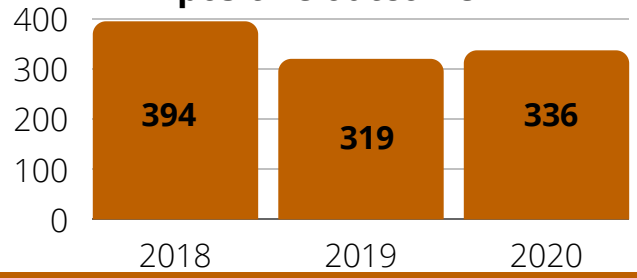
In 2020, the Agency evaluated more than eight thousand of applications for marketing authorisation, renewal and variations to marketing authorisation documentation of medicines by reviewing marketing authorisation documentation related to quality, safety and efficacy.

Reviews included also administrative information, as well as chemical, pharmaceutical, preclinical and clinical sections of the documentation and pharmacovigilance documents.

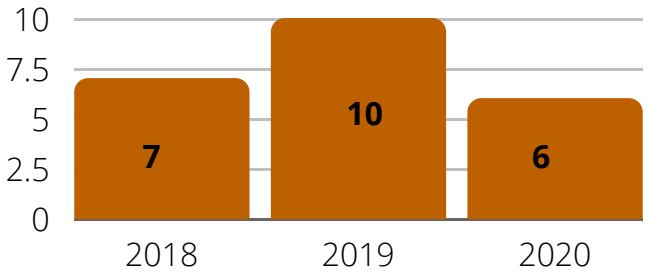
Last year, Latvia ensured marketing authorisation and renewal of 27 medicinal products via mutual recognition procedures (MRP) and decentralised procedures (DCP) as a Reference Member State. Latvia also participated in 336 MRP and DCP marketing authorisation and renewal procedures as a Concerned Member State.

In addition, in 2020 Agency experts prepared assessment reports for 18 centralised marketing authorisation procedures. In three of these procedures the Agency was the responsible rapporteur and in three of these procedures – the co-rapporteur. Latvia also performed peer-review in six procedures.

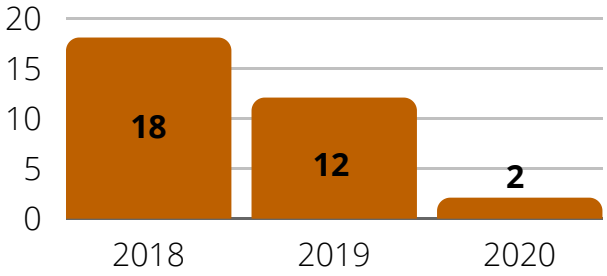
Marketing authorisations and renewals (Latvia as a Concerned Member State) with a positive outcome



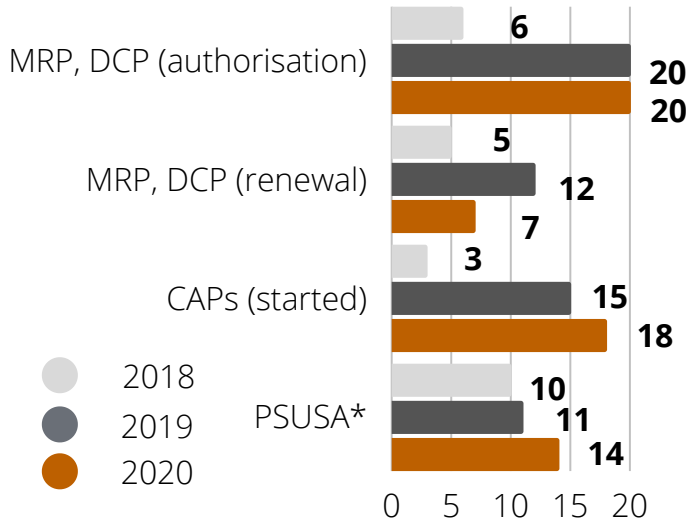
Marketing authorisations via national procedure with a positive outcome



Medicinal product renewals via national procedure



Marketing authorisations and renewals (Latvia as a Reference Member State)



*European single assessment procedures of Periodic Safety Update Reports.

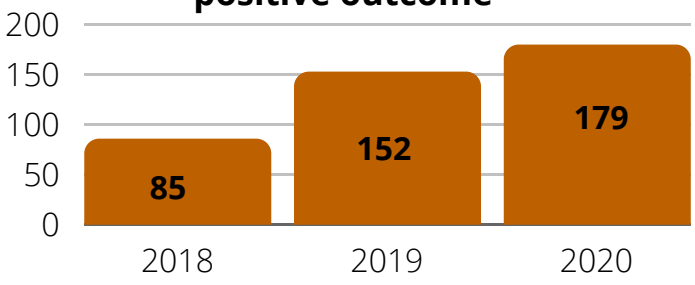
Last year, the activity of Agency experts in international procedures was very significant, similarly as in the previous years. Latvia performed the functions of the reporting member state, was represented in the EMA Paediatric Committee and participated in evaluation procedures for nine primary paediatric investigation plans (PIP) and for eight PIP modifications, conducted peer-review in seven primary PIP assessment procedures and seven PIP modification assessment procedures, as well as carried out compliance inspections in two PIP procedures. Experts from the Medicines Marketing Authorisation Department together with external experts actively participated in the work of the Committee for Advanced Therapies, Committee on Herbal Medicinal Products and other committees. Experts regularly participated in the work sessions of European Directorate for the Quality of Medicines (EDQM) as external experts.

In 2020, there was a slight increase in the number of variations to marketing authorization documentation of medicines evaluated in DCP and MRP procedures at the Agency where Latvia was the Reference Member State (an increase of 179 for type I variations and 18 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.

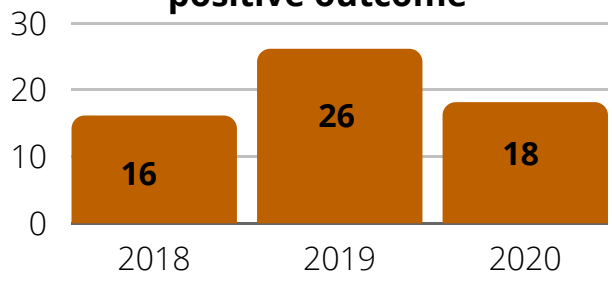
Overall, the number or variations has decreased slightly which could be related to the international restrictions related to Covid-19 that have affected operation of pharmaceutical companies.

In 2020, Agency experts also reviewed 742 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.

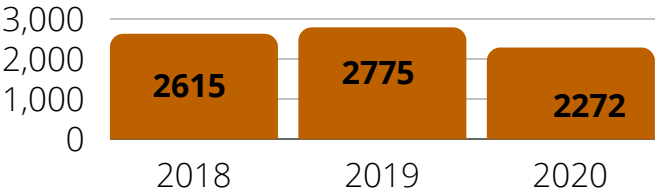
Type IA/IB variations (Latvia as a Reference Member State) with a positive outcome



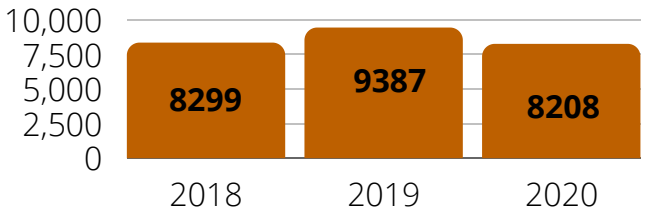
Type II variations (Latvia as a Reference Member State) with a positive outcome



Variations via national procedure



Variations to marketing authorisation documentation



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

Last year, the Agency also issued eight Certificates of Free Sale and 175 Certificates of Pharmaceutical Products, thus, promoting export of medicinal products authorised in Latvia to countries outside of EU. These certificates verify that companies manufacture medicines in compliance with Good Manufacturing Practice – according to strict and common quality standards and requirements.

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 and renewals of **371** medicinal products;
- evaluated **8208** applications for variations to marketing authorization documentation of medicines.

Medicinal product distribution

Sergejs Akuličs, Head of Information on Medicines Distribution Department

"One of the most substantial problems in the world, including Europe and Latvia, is unavailability of medicines and disruptions in their availability, therefore, one of the most important objectives of the Agency is not only to evaluate and register medicines allowing entry into the market for safe and qualitative medicines, but also to ensure swift review of applications and issuance of permits for medicinal product import and export.

It is also important to ensure useful, trustworthy and updated information regarding the availability of medicines on the market in Latvia. Therefore, one of the most notable tasks achieved last year together with Agency colleagues was the preparation of a pilot project for reporting remaining stock of medicines at wholesalers and its implementation. As a result, now pharmacies and healthcare institutions can obtain information in the Medicinal Product Register regarding both the fact of availability of a medicinal product and wholesalers where the product may be ordered from.

We commend all the wholesalers who agreed to take part in this pilot project by submit data regarding their remaining stocks of medicines to the Agency. Last year we also developed an electronic form for reporting unavailability of medicines, thus, making it easier for the Agency to identify the reported medicinal product and take rapid action and ensuring a convenient way to provide information to marketing authorisation holders, pharmacies and healthcare institutions."

2020 was marked by the Covid-19 pandemic and the global response to it. There was a substantial increase in the consumption of medicines for the treatment of Coviid-19 patients, and countries across the globe, including EU member states, activated various protective mechanisms within their internal markets, thus, affecting supply of active substances, medicines manufacturing and distribution and endangering the capacity of healthcare systems, patient health and livelihood.

Therefore, it has to be mentioned that several amendments were made to normative acts with the active participation of the Agency by provision of proposals and risk assessments, including from the Information on Medicines Distribution Department, which in reaction to the consequences and challenges posed by the Covid-19 pandemic was focusing on improving the availability of medicines by decreasing the administrative burden associated with import of medicines authorised in Latvia in packaging intended for another EU member state.

Later on, the department was focusing on issuing permits for export of medicines for which the state had signed a financial participation contract with the supplier and other types of medicines, all of this allowing to minimise the potential consequences of the Covid-19 pandemic.

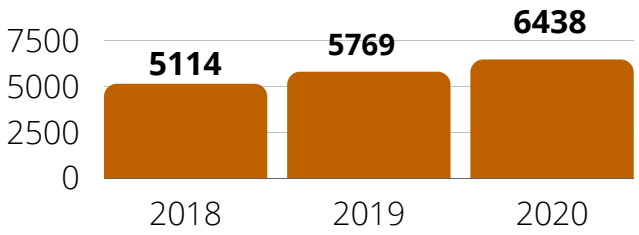
In 2020, the Agency issued 8779 permits for import, export, transit and distribution of medicinal products, thus, substantially surpassing the operational plan.

In 2020, the Agency ensured expertise on applications and documentation related to distribution of the following medicinal products in accordance with the normative acts:

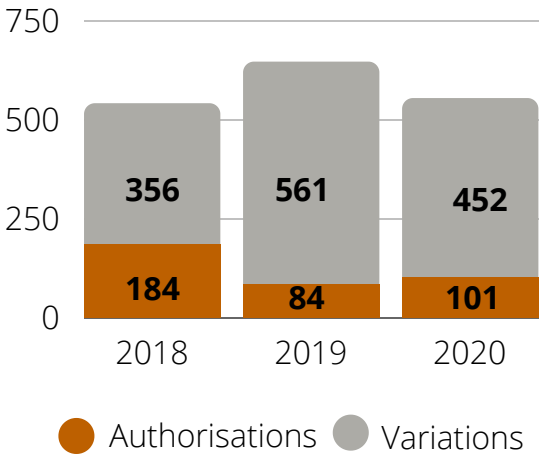
- for import and export of psychotropic, narcotic medicinal products/ substances, as well as precursor;
- for distribution of unauthorised and parallel imported medicinal products;
- for import of medicinal product samples.

In addition, the Agency performed expertise on applications and documentation, as well as issued eight licences and registration cards to precursor operators and one 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.

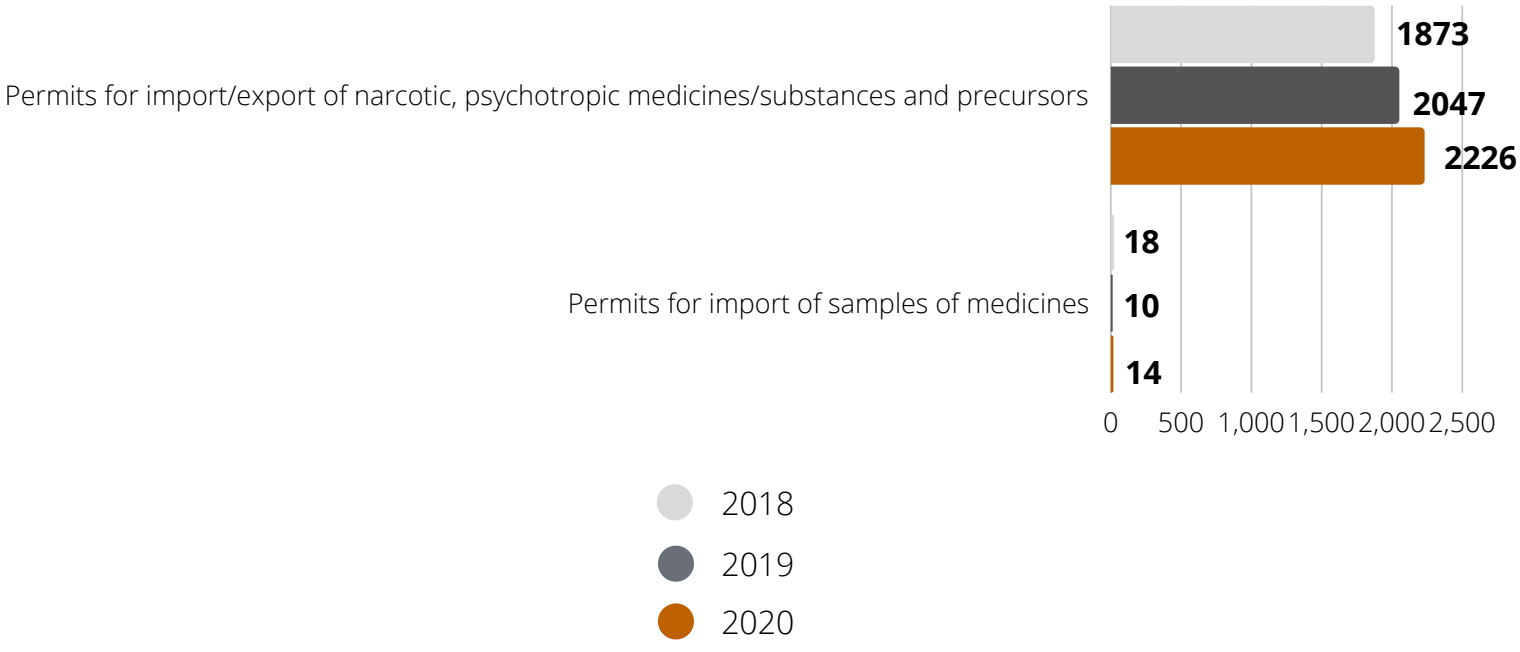
Permits for distribution of unauthorised medicines



Number of permits for parallel import/variations



Permits for import/export of narcotic, psychotropic medicines/substances and precursors and permits for import of samples of medicines



Last year, the Agency made substantial improvements to the solution for collection of information regarding remaining stock of medicines at wholesalers. The purpose of this system is to ensure a more effective and rapid collection of data regarding availability of particular medicines at wholesalers. This further decreased the need for pharmacists and healthcare specialists to report disruptions in medicinal product availability in case the Agency has already received such a report.

Prior to and during the flu season, the Agency carried out monitoring of influenza vaccines. Based on the information provided by medicines wholesalers, every week the Agency published information in the "News" section of the website www.zva.gov.lv regarding the remaining stock of influenza vaccines, indicating both the number of available influenza vaccines and the wholesalers where these vaccines were 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 its annual publication "Statistics on Medicines Consumption 2019".

In 2020, 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 2020, the Information on Medicines Distribution Department provided consultations to the Ministry of Health and institutions under its supervision, and Agency's collaboration partners regarding implementation of requirements of new normative acts (including distribution of medicines in packaging intended for another country, export of medicines, reporting remaining stock of medicines), participated in training seminars regarding amendments to normative acts related to distribution of medicines organized by the Agency for specialists in the field, as well as participated in the international training sessions on the fight against falsified medicines organized by the school of State Administration.

Proposals were submitted for amendments to normative acts regulating circulation of medicines, including the Pharmaceutical Law, the procedures for distribution and quality control of medicines, as well as for labelling of medicinal products, etc.

We also submitted to the Ministry of Health the concept and draft for the list of essential medicines, as well as the list of critical medicines required for treatment of Covid-19 patients that was based on the recommendations issued by the EMA and World Health Organization (WHO), as well as the largest state hospitals. This may serve as the basis for revising the procedure for export of medicines, organization of procurements and maintenance of stocks.

Clinical trials with medicines

Jana Migliniece, Head of the Clinical Trials Department:

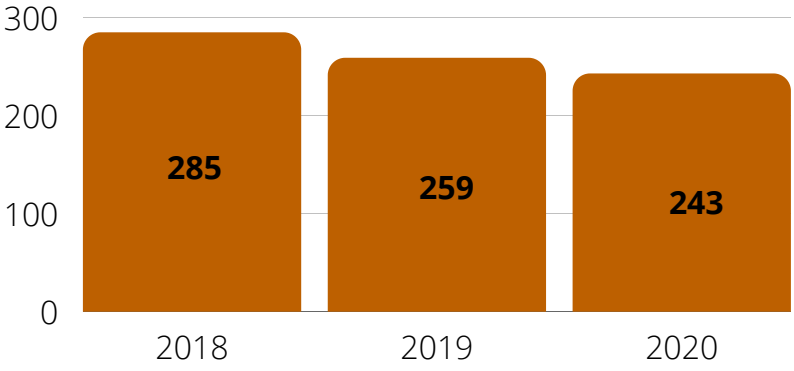
"The Clinical Trials Department got involved in the pilot project "VHP plus", meaning that Agency specialists are collaborating with independent ethics committees in order to collectively assess the risk-benefit ratio of clinical trials as part of the international voluntary harmonisation procedure. Department experts participated in the testing and auditing of the clinical trial database established by EMA by providing feedback regarding the system's convenience of use."

In 2020, the Agency issued 65 authorisations for conduct of clinical trials in Latvia, including nine clinical trials authorised as part of the Voluntary Harmonisation Procedure (VHP) in Europe.

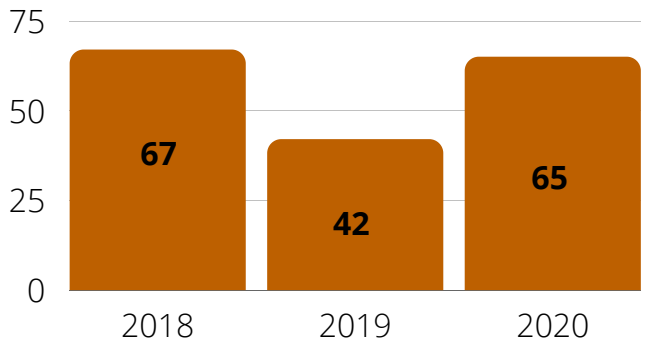
Latvia was the Reference Member State in two procedures, performing an important role in ensuring the overall evaluation process for investigational medicinal products in Europe.

Last year, five Good Clinical Practice compliance inspections were carried out.

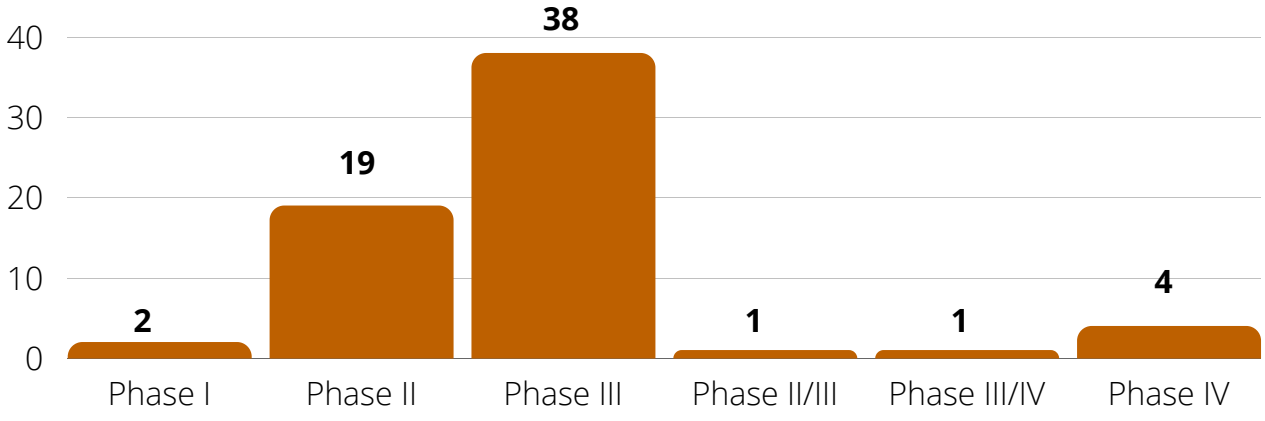
Total number of clinical trials conducted in Latvia



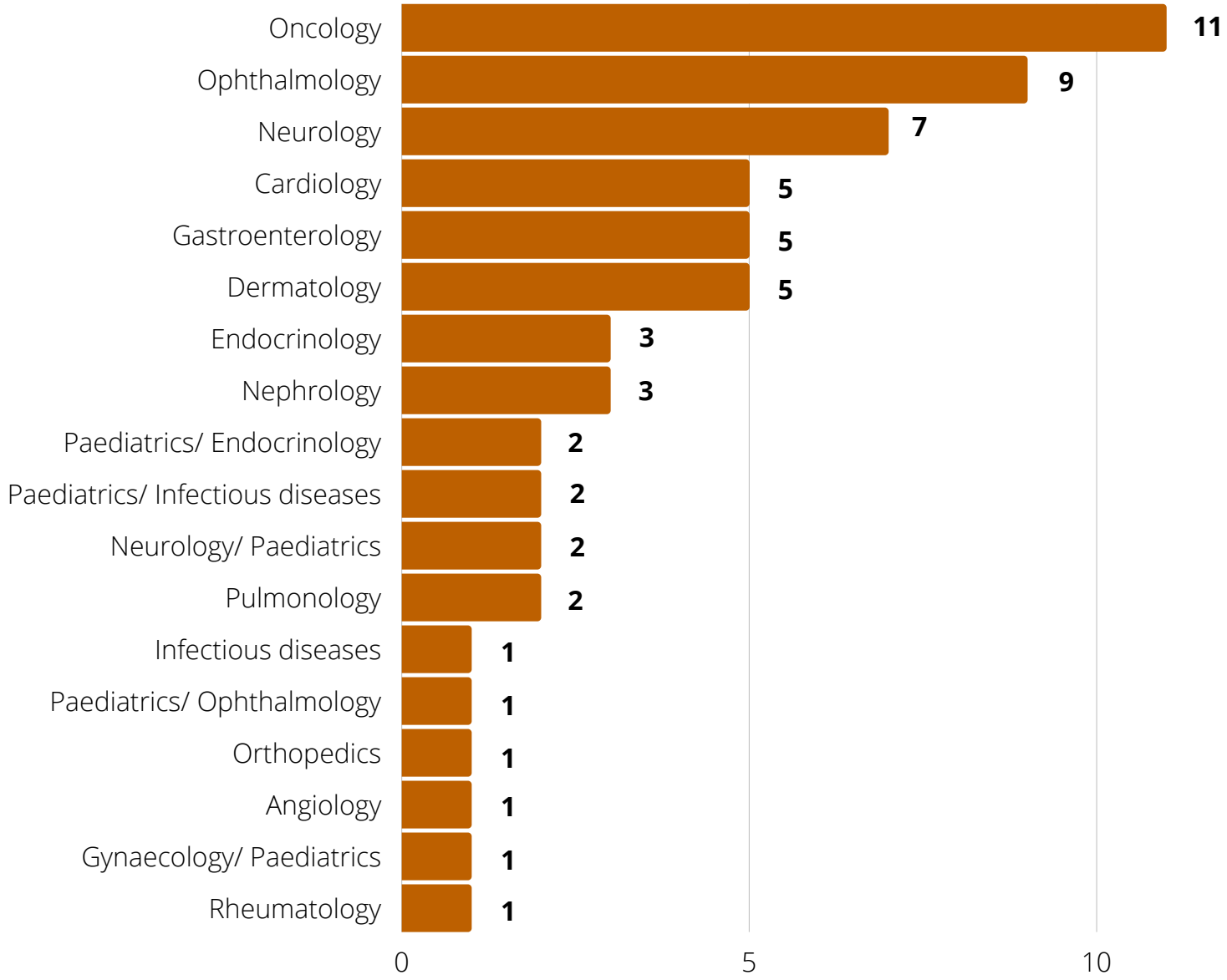
Authorisations for clinical trials



Number of clinical trials authorised in 2020, according to trial phase



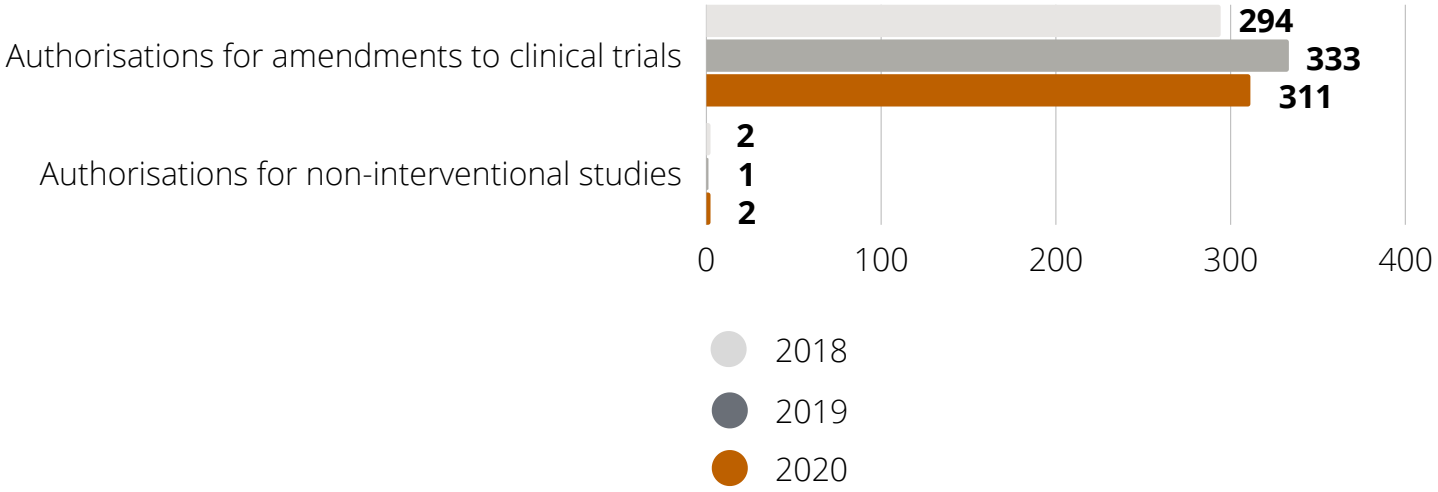
Number of clinical trials authorised in 2020, according to medical specialty



Trial sites of medicinal product clinical trials authorised in 2020

Trial site	Number of trials
State LLC "Pauls Stradins Clinical University Hospital"	43
Riga Eastern Clinical University Hospital	34
LLC "Daugavpils Regional Hospital"	10
LLC "Liepaja Regional Hospital"	8
LLC "Riga 1st Hospital" Dermatology and STS Clinic	6
State LLC "Children's Clinical University Hospital"	6
Signe Ozoliņa doctor ophthalmologist practice	5
Other clinical trial sites (73 in total)	1-4 trials at every site

Authorisations for amendments to clinical trials and authorisations for non-interventional studies in 2020



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 nine primary and 21 follow-up reports regarding serious unexpected adverse events potentially related to investigational medicinal products.

The Agency received and reviewed 126 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 51 foreign pharmaceutical companies. In 2020, 24 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 2020, a substantially greater effort was put into ensuring safety monitoring of medicines or pharmacovigilance, particularly in the field of adverse drug reaction reporting and assessment of periodic safety update reports within single EU assessment procedures.

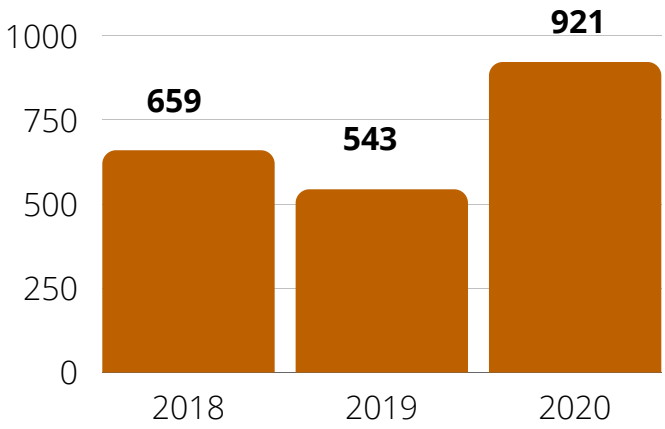
Last year the number of adverse drug reaction reports submitted to the Agency by healthcare professionals increased 10 times in comparison to 2019. In 2020, pharmacovigilance experts also assumed responsibility for regular signal monitoring in Europe related to 30 active substances. Last year, monitoring of 10 new active substances was initiated.

The Latvian representative actively participated in the work of the EMA safety committee by presenting procedures conducted by the Latvian Agency and by making valuable contributions to assessments performed by other member states, as well as by distributing updated information regarding safety of medicines to doctors and the public. Substantial work was done by the experts of the Pharmacovigilance Department by participating in the preparation of the European SCAR guidelines lead by the EMA Pharmacovigilance Risk Assessment Committee. Despite the increased workload last year, the tasks achieved constitute qualitative work based on expert experience and regular learning, as well as international collaboration."

In 2020, the Agency received 921 adverse drug reaction reports, including also reports related to adverse reactions to vaccines, and this information was forwarded to the EudraVigilance database in the EU. 594 reports were submitted by doctors and pharmacists, but 67 reports – by patients.

98 % of the reports were submitted electronically. Last year, Agency's employees worked on improving the electronic report form to facilitate the quality of data that are being submitted in electronic report, as well as made changes in the electronic reporting system in order to simplify reporting adverse drug reactions of Covid-19 vaccines for medical professionals – by submitting one report to the Agency and to Disease Prevention and Control Center.

Adverse drug reaction reports



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 14 evaluation procedures in 2020.

In accordance with the EMA work-sharing procedure, in 2020 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 47 medicinal products authorised via national procedures. In addition, pharmacovigilance experts participated in centralised marketing authorization procedures (10 procedures) as Pharmacovigilance Risk Assessment Committee's (PRAC) rapporteurs, as well as collaborated with clinical experts to perform safety issue assessment.

In 2020, the Agency approved 19 Direct Healthcare Professional Communications and 60 educational materials submitted by marketing authorisation holders (MAHs) and created with the purpose of medicinal product risk minimisation.

Agency's pharmacovigilance experts were also actively involved in informing healthcare specialists and MAHs by participating in several events related to pharmacovigilance issues un ensuring regular information by phone to MAHs and medical specialists. Actual information on medicines safety was published on Agency's website and the specialist informative bulletin "Cito!".

The Agency also ensured regular exchange of pharmacovigilance-related information with EMA and European medicines agencies as reflected by the information provided in response to 15 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.

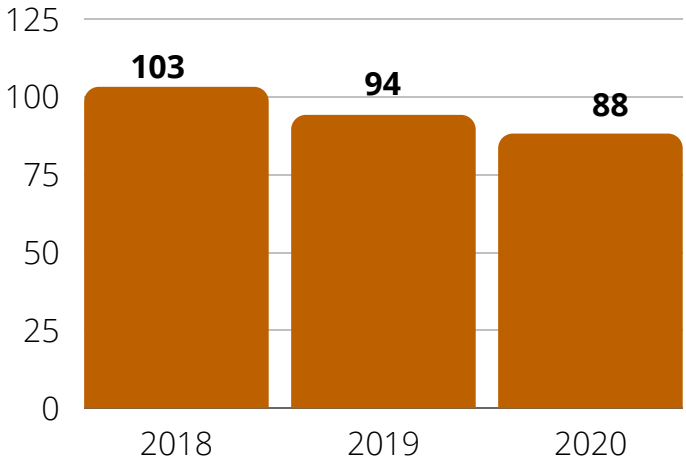
Information regarding decisions adopted by PRAC in relation to safety of medicines and recommendations for risk minimisation were provided to professional associations for doctors and to medical specialists.

Quality control of medicines

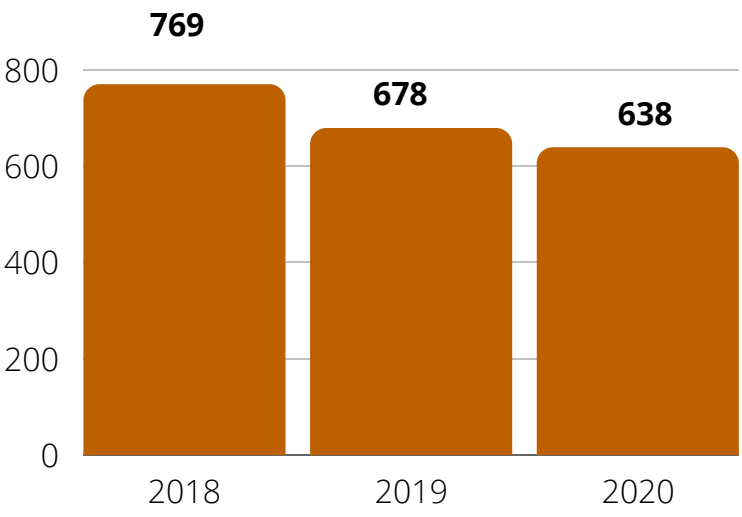
Guntars Kaspars, Head of the Medicines Examination Laboratory:

"The Medicines Examination Laboratory maintained a quality management system that is compliant with the new requirements of the LVS ENISO/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."

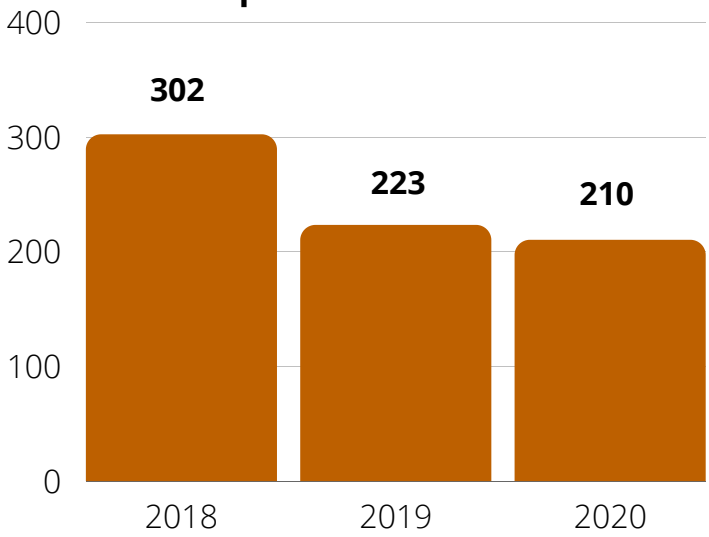
Number of medicinal product samples tested



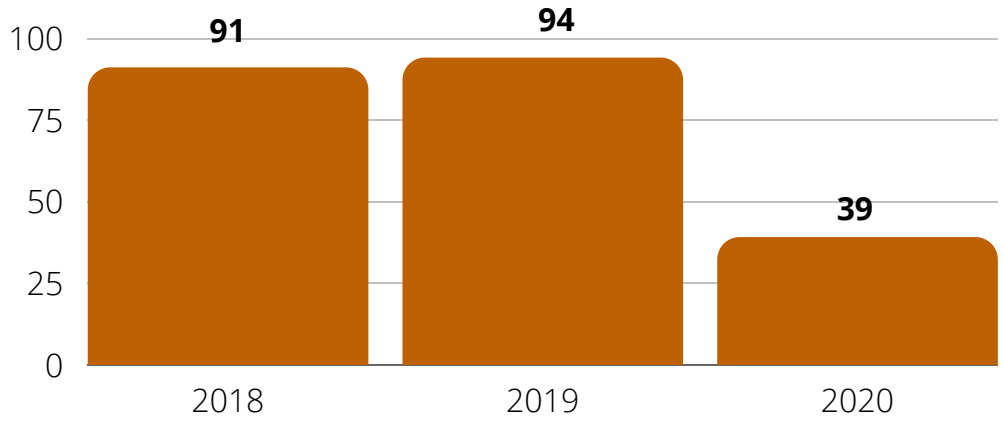
Number of medicinal product quality parameters tested



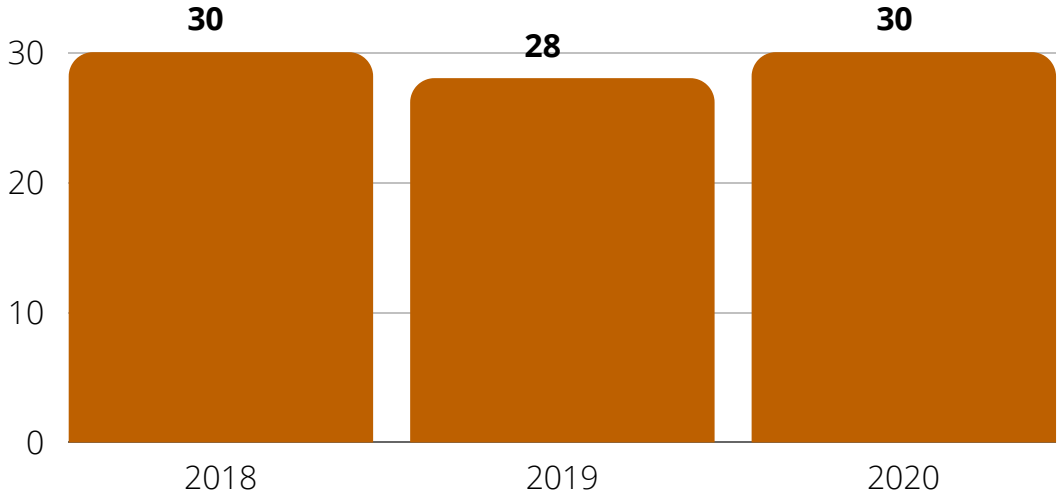
Number of volumetric solutions, indicators and reagents tested upon request from pharmacies



Number of purified water samples tested



The conducted expertise for 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 2020, 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 procedure as well as in the professional level evaluation programs provided by EDQM.

The Latvian National Accreditation Burreau (LATAK) conducted its routing monitoring visit at the Laboratory. The Laboratory maintained the accreditation in accordance with the requirements of the new version of the LVSEN 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:

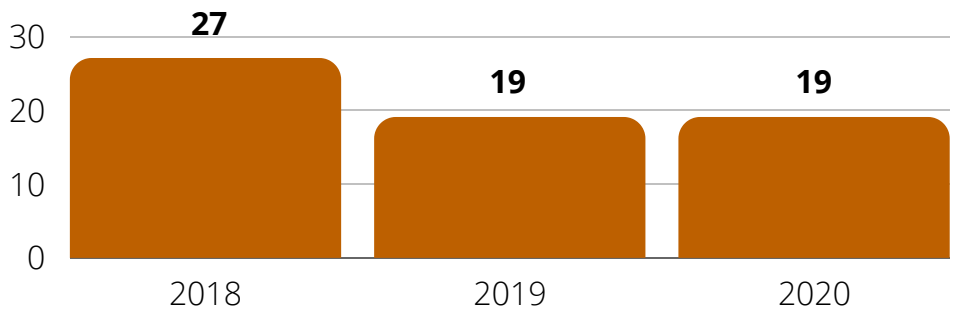
"Last year the Agency continued to prepare for the implementation of the new medical device Regulation (EU) 2017/745. A positive aspect was the fact that, in the year of the Covid-19 pandemic, local manufacturers of medical devices managed to maintain their export capacity, and the number of certificates for free sale issued by the Agency increased by a fifth in comparison to 2019."

As the Covid-19 pandemic evolved in the first half of the previous year, the Agency provided consultations for merchants and the public and prepared informative materials regarding normative requirements for single-use facemasks and disinfectants in order to ensure protection with the aim of limiting the spread of the SARS-CoV-2 virus.

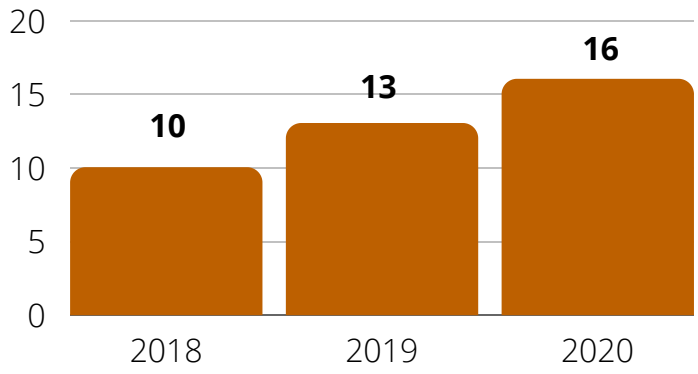
Last December, the electronic system for merchant registration in the European medical device database Eudamed was launched, thus, allowing manufacturers, authorised representatives and importers to receive a single registration number (SRN). In order to promote and facilitate reporting on serious incidents, starting from June last year an option was provided for clients to submit these reports online via the Agency's website.

To promote the export capacity of Latvian manufacturers outside of the EU, last year the Agency issued 23 certificates of free sale to medical devices manufactured in Latvia.

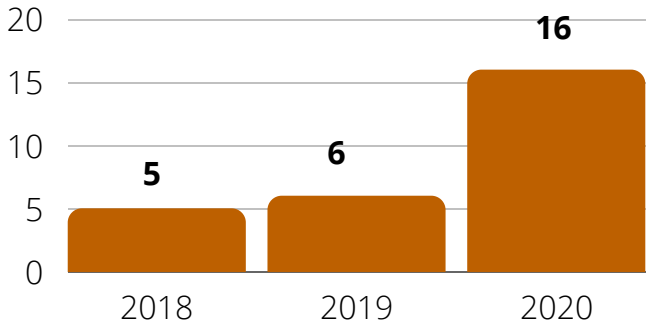
Latvian medical device manufacturers and their medical devices: information analysed and included in the Medical Device Database LATMED



Authorised representatives of third country medical device manufacturers in the EU who have registered business in Latvia: information evaluated and included in the Medical Device Database LATMED

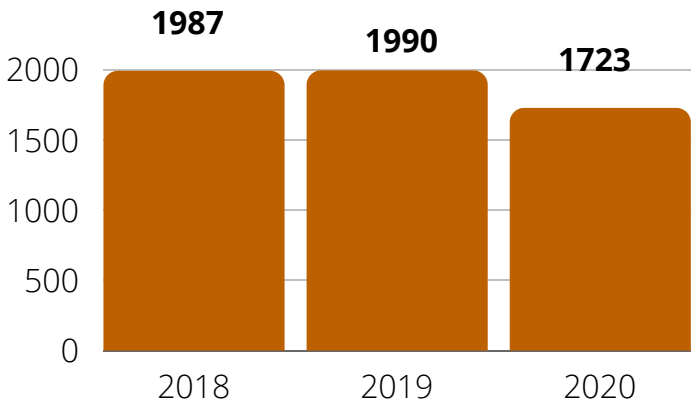


Authorisations for clinical trials with medical devices*

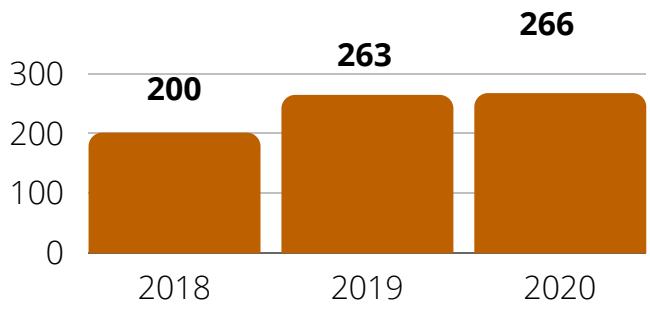


*Authorisations for conduct of clinical trials with medical devices and authorisations for amendments to the research plans of clinical trials already being conducted.

Primary vigilance reports regarding medical devices (total number)



Primary vigilance reports regarding medical devices located in Latvia and implementation of safety monitoring measures



Health Technology Assessment

Antra Fogele, Head of the Health Technology Assessment Department:
"The opinion prepared by the Agency as an independent institution on the clinical efficacy and cost-effectiveness of new non-proprietary names of medicines within the healthcare system in Latvia is a necessary step towards reimbursement of new medicines from the state budget. Last year, marketing authorisation holders and their representatives actively used this service."

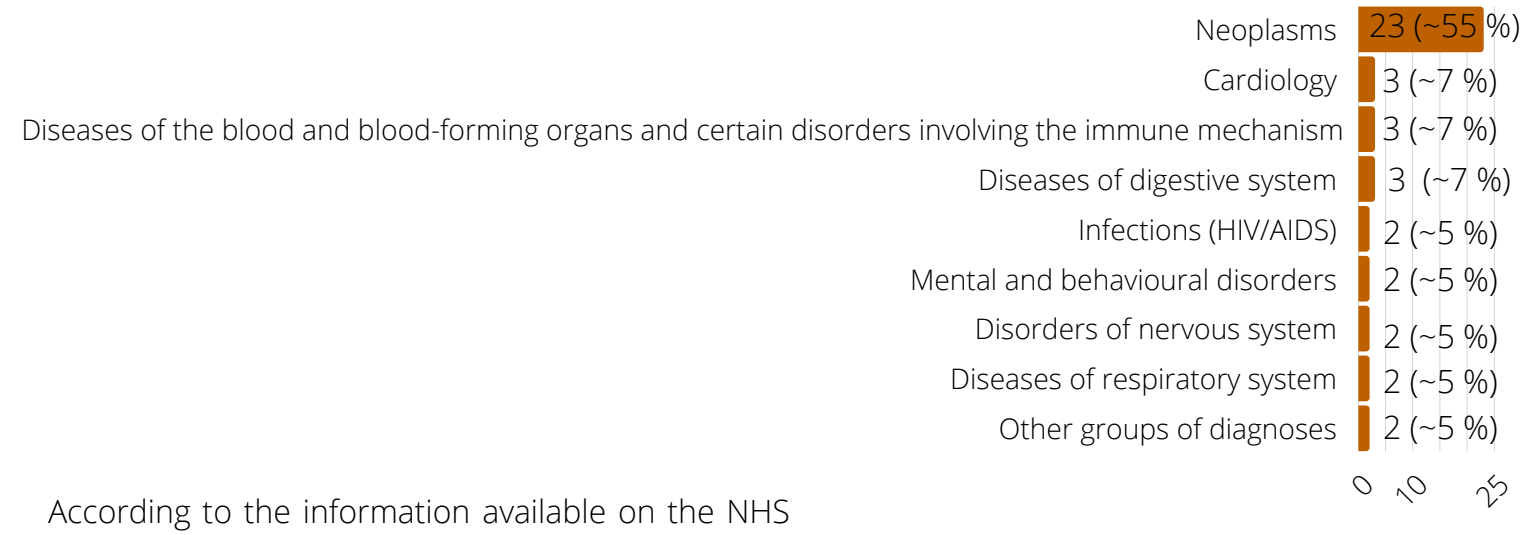
Taking into account, that the database for medical technologies utilised in healthcare was designed in 1999 and that the requirements for approval of medical technologies (MTs) have changed over time, many sections of the database need updating. In 2020, various professional organisations of healthcare workers and healthcare institutions showed initiative to start this process.

2020 was the first "complete" year since the reorganisation that took effect on 1 July 2019 when the Agency took over new functions from the National Health Service (NHS) – evaluation of cost-effectiveness of medicines and medical devices used in healthcare, approval of MT utilised in healthcare and maintenance of the database.

Opinion on clinical efficacy and cost-effectiveness of new non-proprietary names of medicines or new combinations of medicines

In 2020, the Agency received 42 applications and provided 34 opinions.

Distribution of applications according to groups of diagnoses*



*11 applications (26%) were related to the treatment orphan diseases.

According to the information available on the NHS website, in 2020, there were 24 applications submitted for medicinal product reimbursement from state budget, for which Agency's opinion was provided.

Section "Opinion on the therapeutic efficacy and cost-effectiveness of medicines" was created in the Medicinal Product Register by the relevant medicinal product, containing the publicly available information from the assessment conducted by the Agency.

During 2020, new or clarified application forms for approval, supplementation and withdrawal of MTs were prepared and approved, and a form was created for a detailed MT description serving as a template for MT applicants with the aim of ensuring preparation of standardized detailed descriptions.

Approval, supplementation and withdrawal of medical technologies and updating of the Database for Medical Technologies Utilized in Healthcare

In 2020, the Agency received 10 applications for approval, supplementation and withdrawal of new MTs and 32 decisions were prepared regarding MT approval issues

Medical technology group	Approved MTs	Supplemented MTs	Withdrawn MTs
Medical services in diagnostic and therapeutic radiology	1		
Medical services in ophthalmology and optometry	6		
Medical services in psychiatry and psychotherapy		1	
Medical services in cardiac and vascular surgery	1		
Medical services in traumatology, orthopaedics and spinal surgery	2		
Medical services in pathology	1		
Medical services in physical and rehabilitation medicine			11
Medical services in complementary medicine		1	
Medical services related to nutrition	1		
Medical services in algology (pain medicine)	1		

In 5 cases the review was closed, and there was 1 denial of approval.

In comparison, 16 applications were received and 3 opinions were provided in the six months in 2019.

In 2020, the Latvian Association of Rehabilitation Medicine Physicians took a very active part in updating the database: the approved MTs in the database were reviewed and evaluated for use in achieving therapeutic goals concerning the field of physical and rehabilitation medicine.

Such changes were largely related to the fact that until 2008 there were two separate specialties in Latvia – physical medicine specialists and rehabilitation medicine specialists with competency in physical medicine and rehabilitation. In 2008, according to the policy of the European Society of Physical and Rehabilitation Medicine and the European Society of Physical and Rehabilitation Medicine Physicians a single field of medicine, as well as a single medical specialty was established – physical and rehabilitation medicine physician. A single section for "Medical services in physical and rehabilitation medicine" was established in the database.

Licensing of pharmaceutical activity companies

Signe Čudare, Head of Pharmaceutical Activity Company Licensing Department:

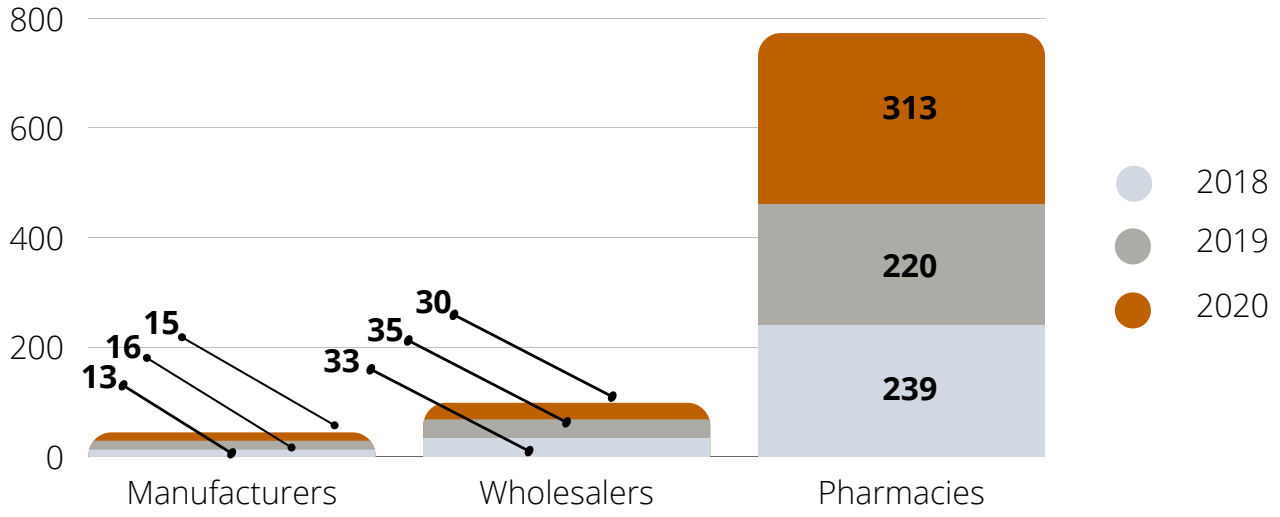
"2020 was mostly spent working remotely due to the state of emergency in Latvia. As a result, swift action had to be taken to adjust performance of work tasks and provision of services. The fact that circulation of pharmaceutical activity licencing documents between the clients and the Agency is mostly ensured in an electronic format allowed to speed up the provision of services in the field of licencing of pharmaceutical activity delegated by the Pharmaceutical Law – issuance of special permits (licences) for opening (operation) of general and closed-type pharmacies, operation of medicines wholesalers, manufacturing or import of medicines and manufacturing of active pharmaceutical ingredients. In 2020, documents were received in an electronic format for 82% of all the pharmaceutical activity licencing services requested by clients.

Based in the client survey data, in 2020, pharmaceutical activity companies that have requested Agency services related to the field of pharmaceutical activity licencing gave a positive assessment for services provided in an electronic format. Many clients collaborating with the Agency have switched receipt and submission of documents to electronic channels. We have a very positive view on this form of collaboration which is much faster and resource-sparing."

In 2020, the Agency renewed licences for pharmaceutical activity for 363 pharmaceutical activity companies:

- 313 general-type pharmacies;
- two closed-type pharmacies;
- 30 medicinal product wholesalers;
- 15 medicinal product manufacturing or import companies;
- three active pharmaceutical ingredient manufacturing companies.

Changes in licences for pharmaceutical activity

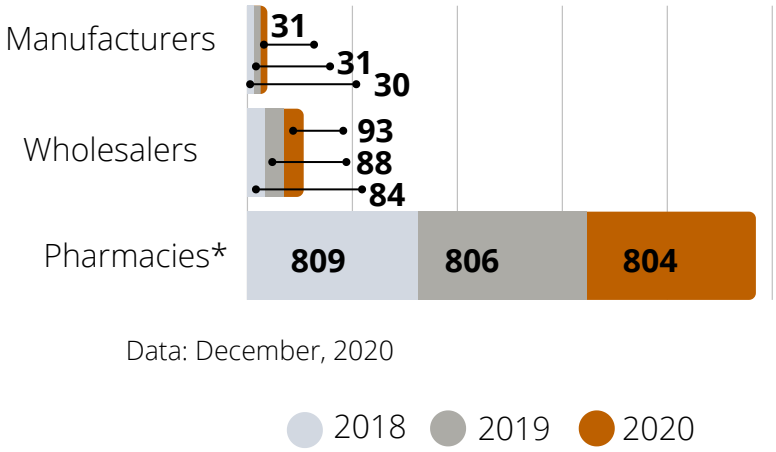


The Agency also assessed 37 cases related to new site (address) of operation of general-type pharmacies.

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

In 2020, the Pharmaceutical Activity Company Licensing Commission held 15 meetings, reviewing issues and adopting recommendations for issuance, renewal or suspension of pharmaceutical activity licences.

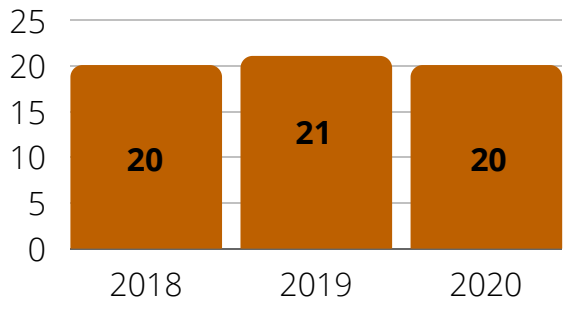
Total number of licensed pharmaceutical companies in Latvia



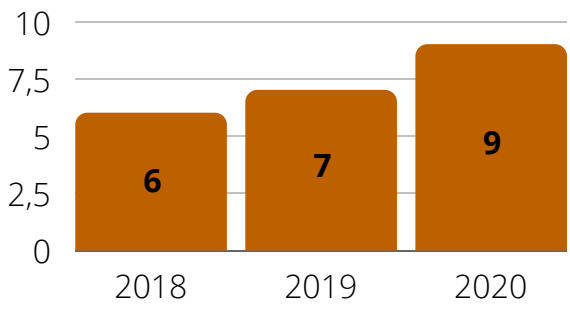
Data: December, 2020

*Not counting pharmacies' structural units (in 2020 – 77 structural units; in 2019 – 76 structural units; in 2018 – 86 structural units).

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



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



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

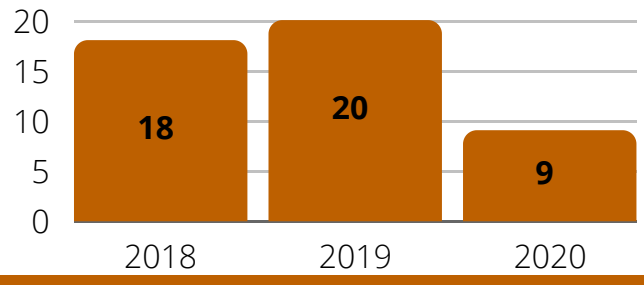
Iveta Vilcāne, Head of Pharmaceutical Activities Compliance Evaluation Department:

"In 2020, we initiated planning of compliance inspections according to the risk assessment criteria designed specifically for each supervisory field. Agency professionals ensured substantial reorganisation of inspection activities during the Covid-19 pandemic and the related state of emergency.

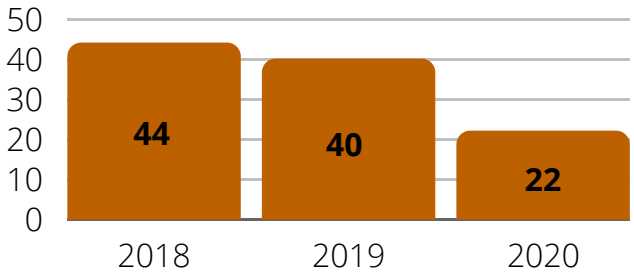
Despite the idle period that lasted more than three months, all of the most important inspections were carried out as was possible in this complicated situation filled with various challenges due to the restrictions applicable to the Agency's and merchant activity put in place during the state of emergency and the Covid-19 pandemic."

In 2020, the Agency conducted Good Manufacturing Practice compliance inspections of nine companies and one additional inspection of documents related to licence renewal. Due to the Covid-19 pandemic and the related travel restrictions, there were no inspections outside of Latvia in 2020. The Agency also conducted 22 inspections of Good Distribution Practice of medicinal product wholesalers, nine of which were related to issuance or renewal of licences. In addition, support was provided to the Pharmaceutical Activities Company Licensing Department in relation to issuance or renewal of special permits (licences) for wholesale and manufacturing or import of medicinal products, as well as registration of manufacturers, importers and distributors of active substances.

Good Manufacturing Practice inspections



Good Distribution Practice inspections



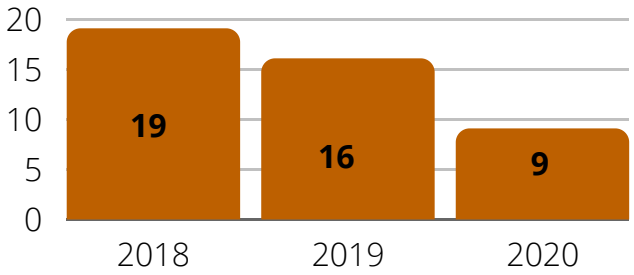
The Agency also conducted vigilance for utilisation of human biomaterial, collected data regarding the operation of tissue centres, procurement organisations/ transplantation centres of human tissues, blood establishments and State Blood Donor Centre and submitted reports to the European Commission, performed hemovigilance and biovigilance in relation 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 a concerned member state.

In 2020:

- The Agency received six applications for compliance evaluation (one for a blood bank, one for the State Blood Donor Centre, four for tissue centres) and issuance of permits related to variations;
- The Agency issued four permits (one for a blood bank, three for tissue centres in relation to changes in operation);
- Six permits were annulled (for two blood banks and two blood establishments according to the information received in 2019 and 2020 regarding discontinuation of operation, for two tissue centres – one upon request and one related to the end of the Brexit transition period).

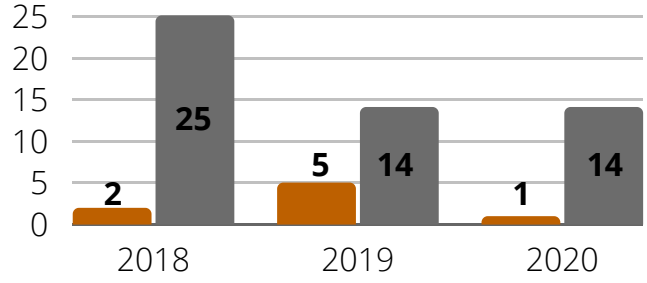
Last year, the Agency also conducted one compliance inspection of a human blood and blood component establishment (conducting on-site inspections of two blood procurement sites in Riga and two regional structural units), 14 inspections of hospital blood banks and eight inspections of tissue centres (including two inspections of centres for procurement of tissues and cells), one inspection of a transplantation centre for human organs, one in a higher education institution providing a medical studies program. The Agency also conducted six compliance inspections of documents - at five tissue centres in relation to changes in operation and one inspection related to changes in operation of a blood bank.

Inspections of tissue centres (and an organ transplantation centre*)



* In 2020, one tissue transplantation centre was inspected, but the remaining eight inspections were conducted at tissue centres. In 2018 and 2019, no organ transplantation centres were inspected.

Compliance inspections of human blood banks and blood establishments



- Blood establishments/ State Blood Donor Centre
- Blood banks

Experts from the Pharmaceutical Activities 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.

Experts from the Department also submitted proposals to the Ministry of Health regarding amendments to normative acts related to improvement of work organisation of blood banks and delegation of responsibilities regarding maintenance of tracking data and submission of reports regarding discontinuation of operation of healthcare institutions, as well as prepared proposals for amendments to the Cabinet of Ministers Regulation No. 1176 and No. 70 due to the amendments to the Law "On the Protection of the Body of Deceased Human Beings and the Use of Human Tissues and Organs in Medicine" related to professional development programs for healthcare professionals. Proposals were prepared for amendments to normative acts on manufacturing and distribution of medicinal and veterinary medicinal products and active substances related to adjustments in supervisory functions during the pandemic.

Department experts ensured communication with the Ministry of Health and healthcare institutions regarding issues related to the Covid-19 infection, including the use of Covid-19 convalescent donor plasma, informed various institutions, as well as prepared and approved documents related to annulment of authorisations due to the end of the Brexit transition period and ensured communication with the field of logistics regarding licensing of customs storage facilities and temporary product storage facilities.

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).

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

As part of vigilance activities, hyperlinks to the vigilance information published on Agency's website were added to the website of the Centre for Disease Prevention and Control, vigilance rapid alert forms in the field of human blood were supplemented with the information required by the State Blood Donor Center, principles for analysis and collection of vigilance and report data were established, thus, initiating a new approach to the circulation of information related to RATC/RAB rapid alert notification systems and decreasing the administrative burden on the Agency and other institutions.

International collaboration

The Agency is a member of the network of the European medicines agencies. 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 European Economic Area authorities regulating the field of pharmaceutics. 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 EU. National experts participate in the work of EMA as members of working groups and scientific advisory groups, as well as scientific committees.

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 2020, Agency's employees have been collaborating with EMA scientific committees, EU Commission and Council working groups, WHO, European Pharmacopoeia Committee, PIC/S, EDQM, etc. Last year, the Director of the Agency participated in the Management Group of the HMA.

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 components. The Agency is the competent authority in Latvia for 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 2020, a three-way online meeting was organised by the Agency of Latvia. See more information about the results of international cooperation in section "Results of the operation of Agency" and in other sections.

Implementation of and amendments to normative acts

Decisions adopted by the Agency are balanced, legal and compliant with the requirements of normative acts. In 2020, only two out of the 9223 decisions adopted by the Agency were contested at the Ministry of Health, and none of the decisions adopted by the Agency in 2020 was repealed.

In 2020, the Agency in collaboration with the Ministry of Health prepared amendments to several normative acts that were reviewed and approved in 2020, for example:

- amendments to the Law "On the Protection of the Body of Deceased Human Beings and the Use of Human Tissues and Organs in Medicine";
- in relation to the Covid-19 pandemic, the Agency urgently prepared several proposals for amendments to normative acts (e.g., Cabinet of Ministers Regulation No. 416 of 26 June 2007 "Procedures Regarding the Distribution and Quality Control of Medicinal Products", Cabinet of Ministers Regulation No. 57 of 17 January 2006 "Regulations Regarding Procedures for the Labelling of Medicinal Products and the Requirements to Be Set for the Package Leaflet of Medicinal Products" and others) in order to ensure availability of medicines during the pandemic;
- the Agency prepared proposals for amendments to the Cabinet of Ministers Regulation No. 376 of 9 May 2006 "Procedures for the Registration of Medicinal Products" (hereinafter – Regulation No. 376) related to the extension of the validity of marketing authorisations of medicinal products in the renewal process in order to prevent disruptions of medicinal product supply. As a result, on 14 July 2020 the Cabinet of Ministers Regulation No 443 was adopted amending the Regulation No. 376 and supplementing it with a new paragraph. The amended regulation facilitates protection of public health interests by ensuring availability of medicines, including medicines in the list of reimbursable medicinal products whose renewal procedure is ongoing, but the marketing authorisation has expired;
- amendments to the Cabinet of Ministers Regulation No. 416 of 26 June 2007 "Procedures Regarding the Distribution and Quality Control of Medicinal Products" laying down that starting from 1 April 2020 medicinal product wholesalers distributing medicines included in the list of reimbursable medicinal products are obligated to submit daily data reports to the Agency on remaining stock of every medicinal product. The Agency automatically reflects the information on remaining volume of medicinal product stock and specific wholesalers where the medicines are available in the Medicinal Product Register on the Agency's website;

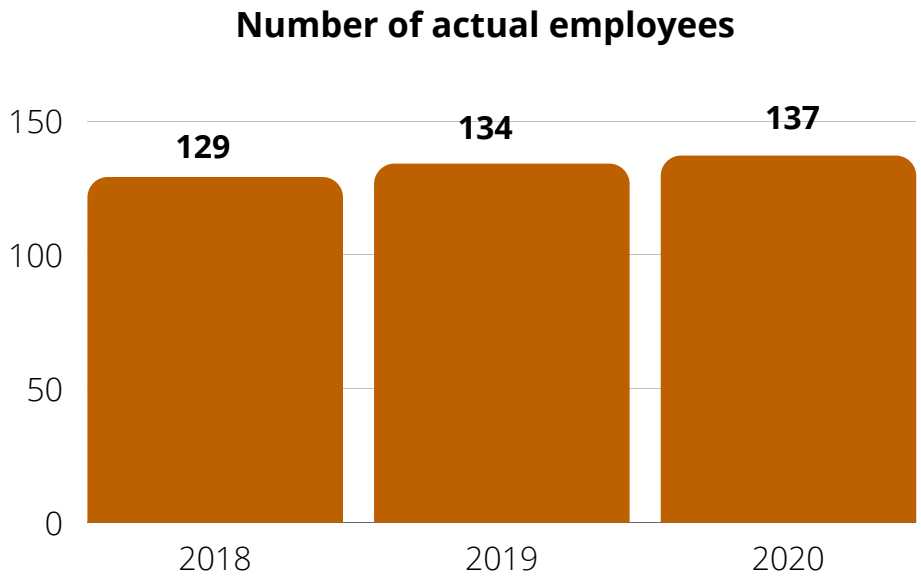
- amendments to the Cabinet of Ministers Regulation No. 899 of 31 October 2006 “Procedures for the Reimbursement of Expenditures for the Acquisition of Medicinal Products and Medical Devices Intended for the Outpatient Medical Treatment”;

- amendments to the Cabinet of Ministers Regulation No. 175 of 8 March 2005 “Regulations Regarding Manufacture and Storage of Prescription Forms, as well as Writing out and Storage of Prescriptions”;

- amendments to the Cabinet of Ministers Regulation No. 689 of 28 November 2017 “Procedures for Registration, Compliance Evaluation, Distribution, Operational and Technical Surveillance of Medical Devices”;

- on 1 January 2020, the Cabinet of Ministers Regulation No. 641 of 10 December 2019 “State Agency of Medicines Paid Service Pricelist” came into effect, including the revised paid services offered by the Agency and their fees, as well as new services, procedure for payment, rates and waived fees.

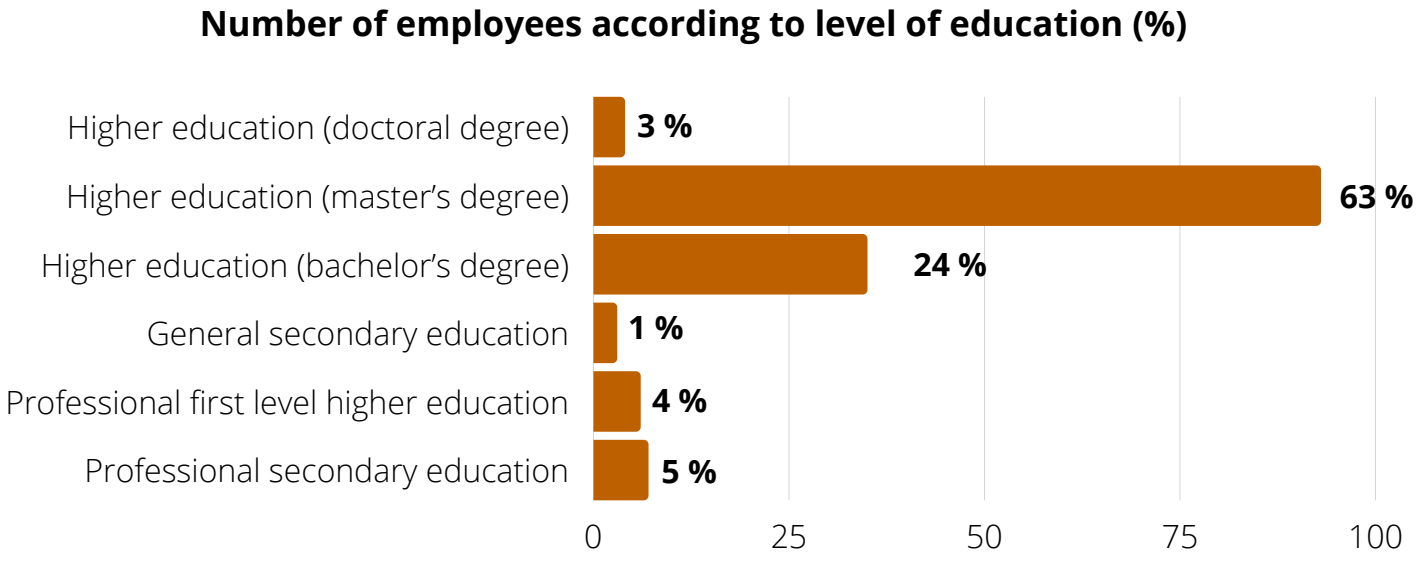
Personel management and training



In total, last year there were 148 persons in a civil service or an employment relationship with the Agency.

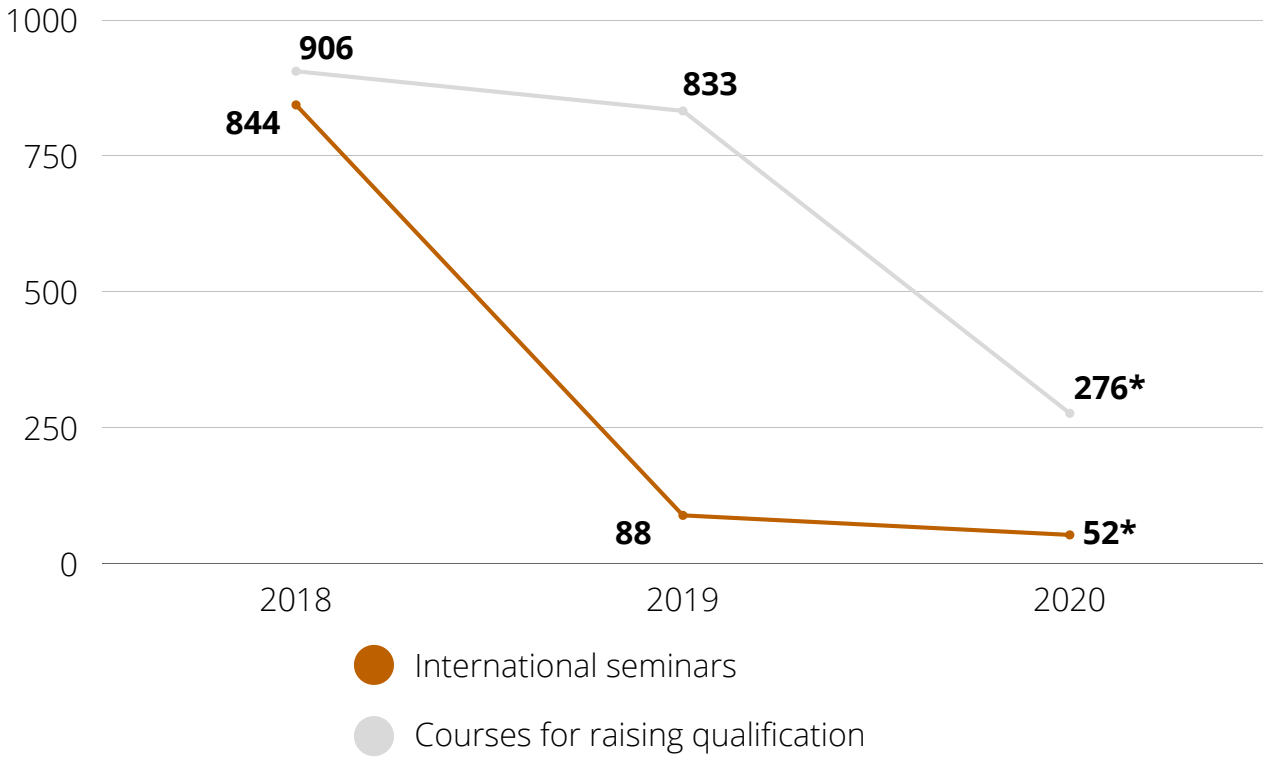
Staff renewal* – 4 %.

*Number of new employees and civil servants divided by the average number of staff members.



The overall level of education of Agencys' staff members is high – 145 or 91 % of Agency's employees have completed higher education, four of these staff members have a doctoral degree.

Participation in courses for raising qualification and international seminars, conferences



*In 2020, personnel participation in training and international events was ensured according to the plan with some deviations due to objective reasons as during the state of emergency (and during the Covid-19 pandemic as such) majority of events, including training and international collaboration events were organized remotely and were free of charge. Employees had plenty of opportunities to use the available resources independently and without taking leave or requesting additional financial resources from the Agency.

Results of employee survey 2020

- **88.5 %** of employees were satisfied with the process of solutions to personnel management issues and the availability of relevant information (applying for vacation and other absences, arranging business trips, consultations and support for resolving various personnel issues);

- **91.3 %** of employees were satisfied with working environment and solutions regarding facilities support service issues (work environment, technical condition of the rooms, transport provision).

Management of the integrated quality management system

Principles of quality management:

- client focus
- management
- employee recruitment
- orientation and improvement of processes
- knowledge-based decision making
- management of relationships

In order to implement the principles and fulfil the aims set out in the Agency's quality policy, in 2020 we continued maintenance and improvement of the quality management system by ensuring compliance with the requirements of the ISO 9001 "Quality Management System", ISO/IEC 27001 "Information Technology. Security Measures. Information Security Management System", ISO/IEC 17025 "General Requirements for the Competence of Testing and Calibration Laboratories" standards, as well as international guidelines and recommendations.

Overall review and improvement of the documentation and processes was carried out in the structural unit Medicines Examination Laboratory.

The quality management system helped to coordinate and manage Agency's operations to comply with the requirements of clients and normative acts and to continuously improve Agency's organisational efficacy.

Review of the completion of parameters within the quality management system indicated that they were completed and that changes in the work environment did not adversely affect timely provision of services.

We noted some instances of exceeded terms due to limited human resources within the Agency that in some cases directly affect the Agency's capacity to provide services during unscheduled employee absences.

It is important to note the following:

- IS operational availability to clients and employees was ensured 99 % of the total time during working days.
- in the annual employee survey, 91.3% of employees indicated satisfaction with the work environment and their job in the Agency which is high appraisal of the operation of Agency's administrative and support functions ensuring and organising remote working and regular mutual communication.
- 0.02% of the adopted Agency decisions (i.e., 2 decisions) were contested and none were repealed which reflects maintenance and assurance of a high level of professionalism.

Changes were made also to the priorities of internal audits with the focus redirected to active performance of internal control, primarily to the management of information security, taking in account Agency employee substantial workload by involvement in the management of the pandemic, as well as changes in the work schedule and limitations in the means for communication.

After analysis of client satisfaction as part of the "Consult first" project of the Ministry of Economics, as well as the Agency's annual client survey, it can be concluded that the overall rating has remained high.

Professionalism, independence and quality of services received the same high appraisal (reaching even 93%), however, "provision of information and consulting" was identified as an area for improvement. Currently Agency provides clarifications for the content of normative acts, has identified solutions for improvement to the contents of the Agency's website and started working on a client portal which could ensure a more efficient mutual flow of information in receiving the service.

However, as the functions delegated to the Agency are surveillance and compliance evaluation, employees performing surveillance have limited capacity to simultaneously perform both roles and the professional knowledge required for providing consultations, a significant increase in client satisfaction with consulting is not achievable in the short term.

Activities planned during the next period of review:

- improvement of process documentation and remote solutions;
- improvement of documentation for ensuring continuity of operation considering the updated guidelines of the network of medicines agencies in the context of the pandemic;
- preparations for the 2022-2023 benchmarking of the members of the European network of medicines agencies and other inspections by third parties.

Management of information and communications technology

In 2020, the Agency continued to develop and improve solutions for IS and information and communications technologies (ICT), as well as to improve their availability and management. Last year, the Agency implemented 35 applications for ICT changes that facilitated increase in work efficiency and provided substantial support to merchants, the public and employees.

Process improvement was done in the information system ZVAIS to allow issuance of annual fee invoices for parallel imported medicines and changes were made related to the amendments to the Agency's pricelist. In addition, coordinate storage of pharmaceutical activity companies or pharmacies was improved.

Improvements were also made to the medical device notification form regarding data validation and verification in the LATMED database.

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 2020, 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) for marketing authorisation documentation, as well as the Common Repository for marketing authorisation documentation in centralised procedures, the Periodic Safety Update Report (PSUR) Repository.

Improvements to the Agency's website

Agency's website underwent several substantial changes:

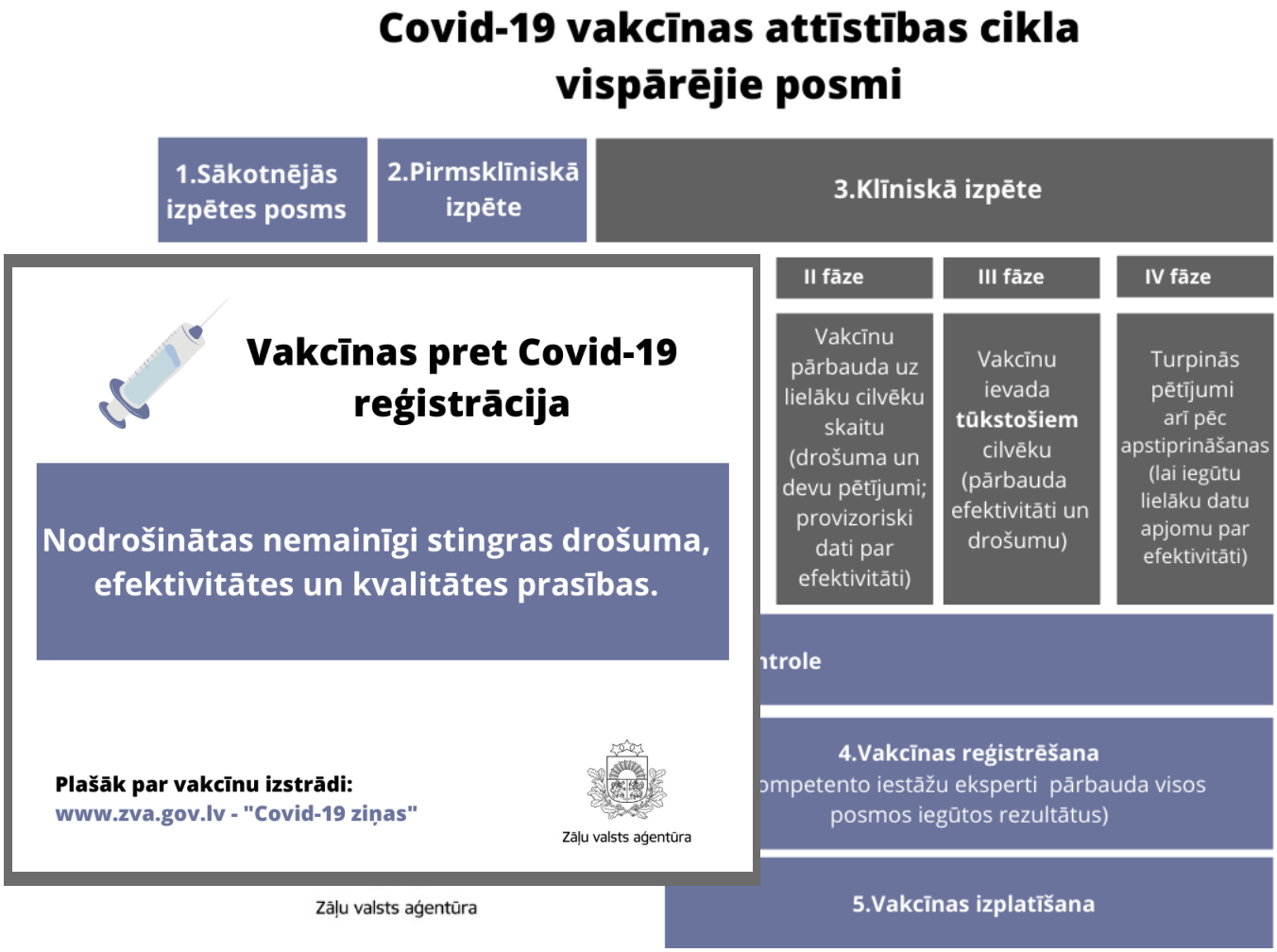
- a more updated version of the Medicinal Product Register was introduced to increase convenience of use on screens of different sizes. This new version allows displaying unauthorised and withdrawn medicines, exporting list of selected medicines, as well as comparing several medicines on a single page. The Medicinal Product Register shows information regarding medicinal product availability at wholesalers, as well several criteria related to the list of reimbursable medicines that are useful in the everyday work of pharmacists;
- improvements were made also to the visual appearance, comprehensibility and user convenience of pharmacy maps, adverse drug reaction report form and other report forms. We added a functionality for reporting of adverse reactions following Covid-19 vaccination which has improved the exchange of information with the Centre for Disease Prevention and Control.

In 2020, 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 used. 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.

Communication and collaboration

In 2020, activities in communication and public information were performed according to the "Operational Strategy of the State Agency of Medicines 2020-2022". The objective of providing independent information regarding medicines, as defined in Agency's strategy, is to promote safe, effective, economically justified pharmacotherapy. The Agency contributed to patient and public awareness of the safe, rational use of medicinal products and to promoted healthcare professional awareness of the role of monitoring in ensuring quality, safety and efficacy of medicines.

One of the main priorities in the second half of the last year was to ensure evidence-based and reliable information on Covid-19 vaccine research, development and authorisation, including informing the public that the evaluation of these vaccines is carried out according to the same rigorous quality, safety and efficacy standards as in the case of any other medicinal product. The Agency regularly provided the latest EMA information on progress made in vaccine evaluation and approval or authorisation process of Covid-19 vaccines and the role of regulatory authorities in vaccine approval, evaluation and safety monitoring.



Publications

Last year, the Agency significantly reinforced circulation of information on its website – 249 news articles were published on it. In addition, the Agency issued more than 150 replies to media queries.

Collaboration with the industry

To pursue one of the Agency's priorities in 2020 – provision of in-depth explanations of the requirements of normative acts – the Agency during the year organised informative seminars for MAHs, manufacturers, wholesalers and other representatives of the industry and non-governmental organisations.

The Agency organised seminars regarding the following topics

- seminar for MAHs on requirements for medicinal products with a new general name with regard to information required by the Agency to analyse cost-effectiveness and provide an opinion;
- seminar for pharmacists (responsible persons at pharmacies, wholesale and manufacturing companies) regarding latest developments in the circulation and surveillance of narcotic, psychotropic substances and precursors in Latvia and a new requirement to indicate the international non-proprietary name (INN) on prescriptions for reimbursable medicines;
- seminar for clinical trial sponsors and representatives of contract research organisations regarding evaluation of clinical trials within the voluntary harmonization procedure and good clinical practice;
- seminars for representatives of medicinal product wholesalers regarding export of medicinal products to EU member states and export restrictions;
- discussions with merchants and responsible state administration institutions in the field of customs warehouses, temporary storage facilities of medicinal products and cargo services in relation to the requirement coming into effect on 1 January the following year to receive a special permit from the Agency to open a medicinal product wholesale facility applicable to merchants involved in distribution of medicinal products.

Campaigns

In 2020, the Agency carried out the following information campaigns:

- from March 2020, the Agency carried out a public information campaign on TV, radio, printed and online media, as well as using environmental advertising spaces all over Latvia to provide useful information for patients regarding the procedure for receipt of reimbursable medicines coming into effect on 1 April.

  The Agency also distributed printed info sheets for patients in pharmacies, hospitals and medical practices, as well as prepared other electronic informative campaign materials summarising the most important information for patients. Informative materials intended for doctors, pharmacists and patients were provided to general practitioners, hospitals and pharmacies in Latvia in both electronic and printed format. In total, approximately million informative materials were distributed to 1286 general medical practices, 37 hospitals, 7 pharmacy networks all over Latvia, as well as professional organisations and associations.

In order to inform healthcare professionals and pharmacists regarding the new INN prescription procedure, Agency experts participated in conferences for doctors and pharmacists, explaining and presenting the procedure for INN prescription. As part of the campaign, the Agency prepared informative and explanatory materials for healthcare professionals, pharmacists and pharmacy assistants:

- digital bulletin;
- expanded informative material including answers to frequently asked questions by healthcare professionals, pharmacists and pharmacy assistants regarding the new procedure;
- explanatory video regarding prescribing of active substances on the E-health portal;
- explanatory video regarding prescribing medicines containing several active substances on the E-health portal;
- digital info sheet summarising important information for patients.

As part of the campaign, we also designed a visual identity that was applied to all of the informative and explanatory campaign materials, and all of the campaign materials were also published on the Agency's website www.zva.gov.lv, in a designated section for healthcare specialists and pharmacists, pharmacy assistants "Healthcare professionals and institutions" and section "Patients and public".

Due to the amendments to the procedure for prescribing reimbursable medicines that were implemented last year, patients saved more than 1 million euros on co-payments for reimbursable medicines each month starting from April, thus, saving 12 million euros in total last year.

- last year the Agency also participated in implementation of a social media campaign regarding promotion of adverse drug reaction reporting. The campaign was organised in collaboration with regulatory authorities of several dozens of 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 use of medicines;

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

"Cito!"

During the year of review the informative bulletin "Cito!" for doctors, pharmacists and other healthcare professionals has been issued thus 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, 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.

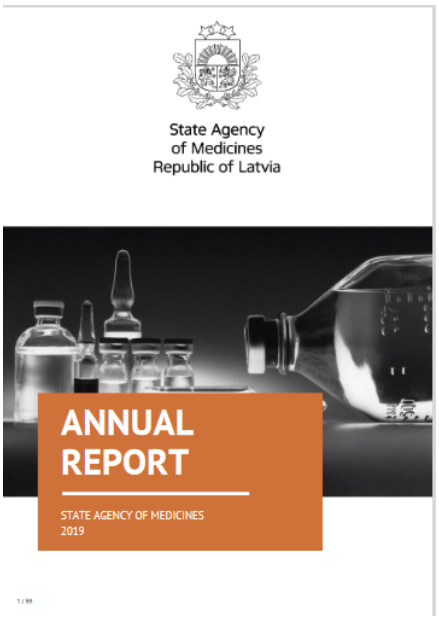
Annual publication "Statistics on Medicines Consumption" and Annual report

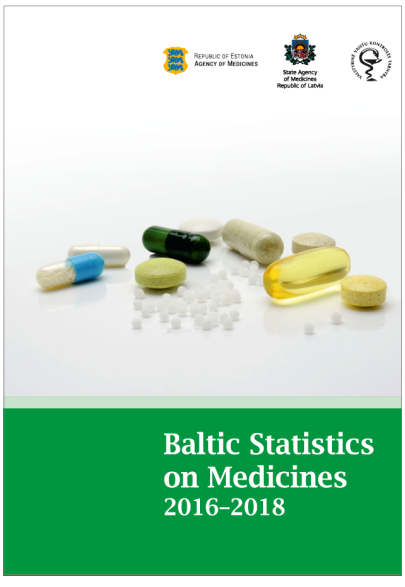
To provide information regarding trends in the consumption of medicines, in 2020, the annual statistical report on the consumption of medicines in Latvia in 2019 was published. The report includes information regarding total turnover of medicines in euros, number of packages sold, distribution of the 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 and further information was provided about the market of medicines manufactured in Latvia. Last year, the Agency's annual report for 2019 was also published.

Publication "Baltic Statistics on Medicines 2016-2018"

The publication contains data on the consumption of medicines in three Baltic States over a three-year period, as well as description of the pharmaceutical market, regulatory requirements, medicinal product reimbursement systems in all three countries. All three Baltic countries were also compared by other aspects: statistics of various licences, wholesalers and many other aspects (including the most consumed medicines). The publication also included conclusions of experts on consumption changes in concrete groups of medicines during 2010-2018 period in connection with reimbursement changes and changes in treatment guidelines.


CITO!
Zāļu valsts aģentūra
IZDEVUMS ĀRSTIEM UN FARMACEITIEM
AUGUSTS 2020/#77
SATURS
AKTUĀLA DROŠUMA INFORMĀCIJA
Pirmais Covid-19 ārstēšanas līdzeklis "Veklury" (remdesivirs) ieteikts reģistrācijai ES 4
Sāk vērtēšanu par deksametazona lietošanu pieaugušiem ar COVID-19 5
COVID-19: EMA atgādinājums par hlorohīna un hidroksihlorohīna nopietnu blakņu risku 6
Jaunākie dati atbalsta AKE inhibitoru un ARB preparātu lietošanas turpināšanu COVID-19 pandēmijas laikā 7
Ieteikumi par pārbaudēm un ārstēšanu ar fluoruracilu, kapecitabīnu, tegafūru un flucitozīnu 8
Saistībā ar meningiomas risku ierobežo ciproterona lietošanu 9
Ieteikumi par nesteroīdo pretiekaisuma līdzekļu lietošanu COVID-19 infekcijas gadījumā 10
Apstiprina augsta stipruma estradiola krēmu lietošanas ierobežojumu līdz 4 nedēļām 11
Sāk ifosfamīdu saturošu pretvēža zāļu vērtēšanu 12
Jauna informācija par jau zināmo krūts vēža risku saistībā ar hormonu aizstājterapiju 13
Ieteikts ierobežot zāļu "Lemtrada" (alemtuzumabs) lietošanu pacientiem ar recidivējoši remitējošu multiplu sklerozi 13
"Picato" (ingenola mebutāts) lietošanas risks pārsniedz guvumu 14
Leiproreltna depo preparāti: jauni pasākumi kļūdu novēršanai 15
Pēc vērtēšanas netiek mainītas pretvēža zāļu "Yondelis" reģistrētās indikācijas 16
Lēmums par nitrozamīnu klātbūtni zālēs 17
Aknu bojājuma riska dēļ vērtēšana laikā aptureta ulipristāla acetāta lietošana dzemdes fibroīdu ārstēšanai 18
Metokarbamola un paracetamola kombināciju saturošu zāļu guvumi joprojām atsver risku 19
"Xeljanz" (tofacitinib): jāievēro piesardzība pacientiem ar augstu trombu risku 20





Bulletins, infographics and videos

- in collaboration with the Dutch Medicines Evaluation Board, the Agency prepared an informative bulleting providing answers to frequently asked questions from patients and the public regarding generic or patent-free medicines, including information on the safety of such medicines and the equivalent efficacy and quality of patented (original) and patent-free medicines;
- infographic aimed at patients with a confirmed coronavirus infection inviting them to report any suspected adverse reactions to any medicinal product they may have used;
- infographic aimed at healthcare professionals inviting them to report any suspected adverse reactions to any medicinal product used in patients with a confirmed coronavirus infection. This included both medicines used for treatment of Covid-19 and medicines used by patients to treat concomitant chronic diseases, as well as medicines used for off-label treatment of Covid 19;
- infographic regarding the procedure for reporting incidents with medical devices;
- infographic regarding consumption of medicines in 2019 and 2018, including the total consumption, as well as consumption of original and patent-free medicines;
- infographic inviting the public not to purchase medicines from unlicensed websites;
- infographic regarding research and authorisation of Covid-19 vaccines;
- infographic "Arrival of the first Covid-19 vaccines in Latvia";
- infographic "Timeline for public vaccination against Covid-19";
- last year, the Agency prepared an informative video regarding completion of an adverse drug reaction form to facilitate completion of adverse drug reaction forms by healthcare professionals.

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.

Last year for the second year in a row the Agency participated in the initiative "Officials shadowing merchants" organised by the Ministry of Economics in collaboration with the Latvian Chamber of Commerce and Industry, Employers' Confederation of Latvia and Junior Achievement Latvia. The initiative prototype was developed by the State Chancellery's innovation laboratory for decreasing the administrative burden of state administration and involved collaboration of experts from all stakeholders.

The Agency also ensured provision of updated information on the new platform for providing information to employees – on the Intranet.

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 work-load 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* 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.

* Electronic medical records, registers, adverse drug reaction report data.

Annexes
Budget and expanses

		2018	2019	2020	
		Budget implementation, EUR	Budget implementation, EUR	Budget estimate, EUR	Budget implementation, EUR
1.	Resources for covering expenses (income)	4 873 245	5 161 435	5 200 492	6 102 023
1.1.	Paid services and other own income	4 872 465	5 110 759	4 903 201	5 265 476
1.2.	Foreign financial assistance		10 969	228 900	763 393
1.3.	Transfers from the State budget	780	39 707	68 391	73 154
2.	Expenses (total)	5 610 367	4 814 202	5 911 353	5 229 171
2.1.	Maintenance expenses	5 290 503	4 319 361	5 477 036	4 920 943
2.1.1.	Regular expenses	4 249 498	4 205 695	5 370 621	4 814 528
2.1.2.	Transfers for maintenance expenses	1 041 005	113 666	106 415	106 415
2.2.	Expenses for capital investments	319 864	494 841	434 317	308 228
	Financial balance	-737 122	347 233	-710 861	872 852
	Financial resources	954 644	1 301 877		2 174 729
	Increasing (-) or decreasing (+) change in surplus of financial resources from paid services and other independent income	954 644	1 301 877		2 174 729

SIA AUDITORFIRMA ŠĶIBELE UN PARTNERI
Reģ.Nr.40103374852; LZRA komercsabiedrības licence Nr.164
Juridiskā adrese: Ķekavas nov., Ķekavas pag., Lapenieki, "Bērzavoti k-3" - 24C, LV-2111
Biroja adrese: Mūkusalas iela 33, Rīga, LV-1004
Tālr.: +37167627940, Fakss: +37167627941, Mob.tālr.: +37129239651

A REPORT BY INDEPENDENT AUDITORS

Riga

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

No.01/2020

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 2020. The attached financial report includes:

- Report on financial situation on 31 December 2020 (balance);
- Report on the financial results of Agency's operation in the year concluded on 31 December 2020;
- Report on the changes in own capital in the year concluded on 31 December 2020;
- Report on the flow of Agency's financial resources in the year concluded on 31 December 2020;
- 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 2020, as well as of the financial results of its operation and flow of financial resources in the year concluded on 31 December 2020, 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 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 in the Code of Ethics for Professional Accountants (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 this 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 review 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 as required, unless there are plans to merge the Agency with another institution or to divide the Agency.

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 also do the following:

- 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 the internal control which is important for conduct of the audit in order to establish audit procedures appropriate for the specific circumstances, but not to provide an opinion on the efficiency of 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 adequacy of the principle of continuing operation applied by the administration and, based on the audit evidence obtained, also regarding the existence or non-existence of major uncertainty with regard to events and circumstances that may create substantial concerns regarding Agency's ability to continue operation. If we conclude that substantial 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 Šķibele un Partneri”
Licence No. 164

_____

Līga Šķibele
Member of the Board
Sworn Auditor
Certificate No. 197

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

Līga Šķibele 26523462
info@skibeleunpartneri.lv

Contacts:

State Agency of Medicines
Jersikas iela 15, Riga, LV-1003
Phones: 67078424, 29447659
E-mail: info@zva.gov.lv

www.zva.gov.lv

https://www.facebook.com/ZVALatvija

https://twitter.com/ZVALatvija