State Agency
of Medicines
Republic of Latvia

STATE AGENCY OF MEDICINES

ANNUAL REPORT

2022

CONTENTS

FOREWORD

Indra Dreika,
Director of the State Agency of Medicines

Welcome to the 2022 annual report of the State Agency of Medicines!

This report will allow you to see the numbers collected in 2022 characterising the pharmaceutical industry and its regulation, as well as what the State Agency of Medicines has achieved and planned for the future. I am truly proud of what my colleagues have achieved, particularly, considering the challenges of the previous year.

Since I have joined the State Agency of medicines only in 2023, my contribution to the results in 2022 is only indirect as for someone working in the industry. It allows me to assess the current operation of the Agency and its ability to give the necessary contribution to the healthcare system in the future without bias. I want to briefly characterise the three main aspects - resources, employees and functions.

The Agency, being a state administration institution, performs work that are expected from it by the public, the state, its residents and – in case of the Agency – also by the European Union and even the world.

Agency's **resources** are skilfully utilised and its budget allows it to ensure successful regulatory operation and invest in the future. There are, of course, plenty of challenges, however, the status of the Agency allows it to ensure its own operation almost without any contributions from the state budget, whereas the experience and professionalism of its employees guarantee that the Agency can fully respond to requests from the European Medicines Agency and is considered as a trustworthy partner among other national medicines agencies.

I am truly delighted about the modern and organised work environment and processes, constantly caring about what we see around

us, how we feel and what is the ecological footprint of our institution. I fully support both waste sorting and use of solar batteries, as well as measures allowing employees to express their opinion openly and to feel valued. There is a great need for innovations in technical tools and the technologies applied. One of the short-term goals is to establish a client portal within the information system of the State Agency of Medicines.

Now about the **colleagues**: the Agency has cultivated and maintained a professional environment that has allowed it to attract and keep highly qualified personnel – most of the employees have a pharmaceutical or medical degree and have obtained many additional skills and knowledge allowing them to become experts in the pharmaceutical field operating on a European level. Low staff turnover and an established training program for new colleagues allow to ensure the minimum number of required experts, but if we plan development according to the current demand of services, then the current number of employees will not be enough.

My job as the director of this institution will be to continue to create and maintain infrastructure, work environment and institutional culture where people can do their job well. And by doing their job I mean – achieving their goals, feeling content and valued, promoting personal and collective development, as well as challenging oneself with new goals. At the same time, it is no less important to feel good as a human being – to be together with loved ones, to develop oneself as a personality and to simply live life. To this day, this balance has been maintained at the Agency even in the face of great challenges, and I will strive to continue to maintain it.

There have been substantial changes in the **work tasks** over the last few years. The pandemic and the resulting need for new medicines and vaccines, the idea of an all-encompassing state protection and challenges within it, lists of critically necessary and important medicines, new solutions to problems in logistics and supply chains, and a great challenge – new regulations and directives passed in Europe and intent to substantially change the regulation of the pharmaceutical industry – have all created new tasks to complete.

In these conditions, the Agency has shown its stability and resiliency, ability to adapt to change, take on new functions and adapt its operation to changing conditions corresponding to the needs and demands of the public. The most important thing is to make rational choices about priorities.

The responsibility of the director after these challenging times – to bring Agency's achievements into the world, to inspire its employees and to maintain the course so that everyone at the State Agency of Medicines heads in the same direction and holds the same values. This year we will renew closer collaboration with the industry and the priority will be a client-oriented approach. We will aim to identify and prioritise the needs of the companies operating in Latvia that manufacture and distribute medicines. We are on the same side aiming to ensure medicines and medical devices necessary to the public.

With respect and gratitude for the opportunity to be here,
Indra Dreika
Director of the State Agency of Medicines

Ilze Bude,
Acting Director of the State Agency of Medicines in 2022

For the State Agency of Medicines, as well as the whole world 2022 came with concerns about the end of the COVID-19 pandemic, with anxiety regarding Russia's attack on Ukraine, with uncertainty how to find the energy to work, inner peace and joy for life amidst this rapidly changing environment.

Looking back on what has been achieved, today we can be proud that, regardless of these anxietyfilled times, the Agency has found strength and has successfully caried on with daily tasks, as well as taken on new challenges. One of these was the introduction of a new function – evaluation of and reimbursement for harm caused by adverse reactions to COVID-19 vaccines. Another mentionable achievement was the effort put into implementation of EU regulation requirements in the fields of evaluation of clinical trial authorisations and medical devices. In addition, as part of recertification last year we received validation that the Agency operates in compliance with the requirements of ISO 9001 and 27001 standards.

In order to implement the state administration remuneration system reform at the Agency, in 2022, we introduced a competency-based remuneration system that gives incentive for continuous improvement of knowledge and competencies. Acknowledging that working at the Agency allows to obtain unique competencies on a national level, one of the tasks in the nearest future is to implement amendments to the budget in order to ensure motivation for the most competent specialists in the field to work in state admnistration and the Agency.

Despite the considerable amount of work that has been done, we are facing new initiatives, challenges and unknown issues in the ever-changing and rapidly developing environment. I am very thankful to everyone working at the Agency for the work we have achieved collectively and I wish everyone to have resilience, perspective and open-mindedness about future opportunities.

Have peace of mind and pride for your achievments!

Best regards

Sergejs Akuličs,
Deputy Director

The State Agency of Medicines is an institution comprised of professionals and experts. Behind every mention of the word "Agency" in this foreword are the names and surnames of colleagues and their full devotion to their work. The people, who choose the Agency as their workplace, care about the people in Latvia having access to safe medicines, medical devices, health technologies, about an organised and safe environment in the field of healthcare and pharmaceutics that is oriented towards the interests of the people, public, the state and the economy. Further details regarding the different areas of Agency's responsibilities will be outlined in the following sections of this report, but I would like to highlight some of the challenges and achievements in 2022.

2022 was full of challenges for the Agency: a state of emergency was declared throughout the country due to the SARS-CoV-2 pandemic, which was compounded by the monkey-pox emergency situation in the middle of the year, the early onset of the influenza epidemic and rapid spread of the respiratory syncytial virus (RSV) and other infectious diseases at the end of the autumn, truly testing the resilience of the system. In addition to other issues, we were shocked by the attack on Ukraine initiated by Russia on 24 February 2022. The extent of the economic consequences of this war continues to increase, affecting both the normal supply chains and the financial resources of every resident of Latvia, as well as the state as a whole. This affects both the price of resources and the cost and availability of medicines and medical devices.

In 2022, shortages of medicines became even more pronounced both globally and in Europe, including Latvia. We were especially affected by the shortage crisis of antibiotics containing amoxicillin and its combination with clavulanic acid and antifever medications for children that started at the end of autumn of 2022 due to the rapid spread of seasonal infections and a substantial increase in the demand for these medicines. Since it is our mission to ensure that residents of Latvia have timely access to safe and verified healthcare products, the Agency closely followed the situation in Latvia and Europe, as well as participated in the EMA Executive Steering Group on Shortages and Safety of Medicinal Products and proactively sought solutions for the medicinal product availability problems: urgently issued permits for distribution of unauthorised and parallel imported medicines, approved delivery of medicines intended for the market of another country, actively invited marketing authorisation holders and other merchants to utilise all the legal solutions to ensure supply of medicines.

The pandemic, war and crises do not allow the Agency to postpone other work, so it continued to evaluate the compliance of medicines, medical devices and health technologies with the relevant requirements, and to evaluate clinical research, pharmaceutical activity and activity

with biological materials of human origin. In addition to its main functions, the Agency actively participated in the development of the unified European Clinical Trails Information System (CTIS), EMA scientific committees and working groups, participated and prepared assessment reports in centralised authorization procedures for medicines, continued monitoring the safety of medicines, including vaccines, participated in implementation of the new medical device regulation and development of the European Medical Device database EUDAMED, participated or organised international work events and informative campaigns and underwent audits, reviews and inspections.

Furthermore, in May 2022 legislators entrusted the Agency with a new and atypical function – to evaluate requests for compensation due to severe or moderately severe harm to patient health or life as a result of adverse effects caused by an approved COVID-19 vaccine, to determine the amount of compensations, approve and disburse them.

The Agency's three-year strategy for 2020-2022 was established according to Latvia's national priorities and goals in public health, as well as international priorities included in the collective strategy of EMA and HMA and their multiannual working plan for 2020-2025. Agency's strategy included directions for public health interests, sustainable and productive Agency development and preparedness for future needs and external conditions.

Specific structural units of the Agency, as well as designated working groups were responsible for achieving Agency's strategic goals and made substantial progress in 2022 in solving different issues:

- Gathered information about options for streamlining the medicinal product authorisation process and overcoming hurdles for establishing a multilingual packaging by participating in the work of EMA Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), as well as in the multilingual packaging working group, providing commentary and opinions regarding specific situations, and in the meetings of medicines agencies of the Baltic states.
- Contacted marketing authorisation holders to identify medicines that are not included in the Medicinal Product Register of Latvia, but are necessary to ensure treatment and are regularly imported in Latvia as unauthorised medicines.
- Continued to implement a structured and LEAN-based approach to streamlining and optimisation of Agency's operational processes, utilising the knowledge and skills obtained by employees in the practical LEAN methodology training.
- Streamlined the employee competence tool that allows accumulation of information regarding current and predicted competence requirements in order to ensure purposeful competence training based on future needs and a competence continuity process.
- Improved and maintained an environmentally friendly policy by substantially reducing the amount of paper utilised and ensuring that circulation of documents was done by using digital solutions in more than 90% of the cases, by increasing energy efficiency and decreasing the CO2 footprint.

The turbulent conditions of 2022 forced us to focus even more on ensuring progress and optimisation of an increasing work amount. In 2022, adaptations and developments in the field of healthcare and pharmaceutics were continued, and in addition to is functions and strategic goals, the Agency worked on the development and implementation of new national and European regulations with Agency experts actively helping and supporting policy makers. Work will have to be continued, and at the time of publishing of this annual report Agency's strategy for the next time period is being developed with the participation of every Agency employee and drafts of normative acts regulating the field of pharmaceutics and healthcare, including our proposals, are lying on the table of policy makers. No one can foresee becoming the next "black swan", but the Agency did and will continue to do everything within its power to find solutions to future challenges.

Best regards.

ABBREVIATIONS

Agency	State Agency of Medicines, SAM
BEMA	Benchmarking of European Medicines Agencies
CAP	Centralised authorisation procedure
CHMP	Committee for Medicinal Products for Human Use
CM	Cabinet of Ministers
CTIS	Clinical trials information system
DCP	Decentralised authorisation procedure
EC	European Commission
EDQM	European Directorate for the Quality of Medicines and Healthcare
EEA	European Economic Area
EMA	European Medicines Agency
EU	European Union
HI	Health Inspectorate
HMA	Heads of Medicines Agencies
ICT	Information and communications technology
ISO	International Organization for Standardization
IT	Information technology
LATMED	Electronic database of the Registers of Medical Devices
MH	Ministry of Health
MRP	Mutual recognition procedure
NHS	National Health Service
NP	National procedure
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PSKUS	Pauls Stradins Clinical University Hospital
SAMIS	State Agency of Medicines information system
SBDC	State Blood Donor centre
SoHO	Substances of human origin
UNODC	United Nations Office on Drugs and Crime

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"".

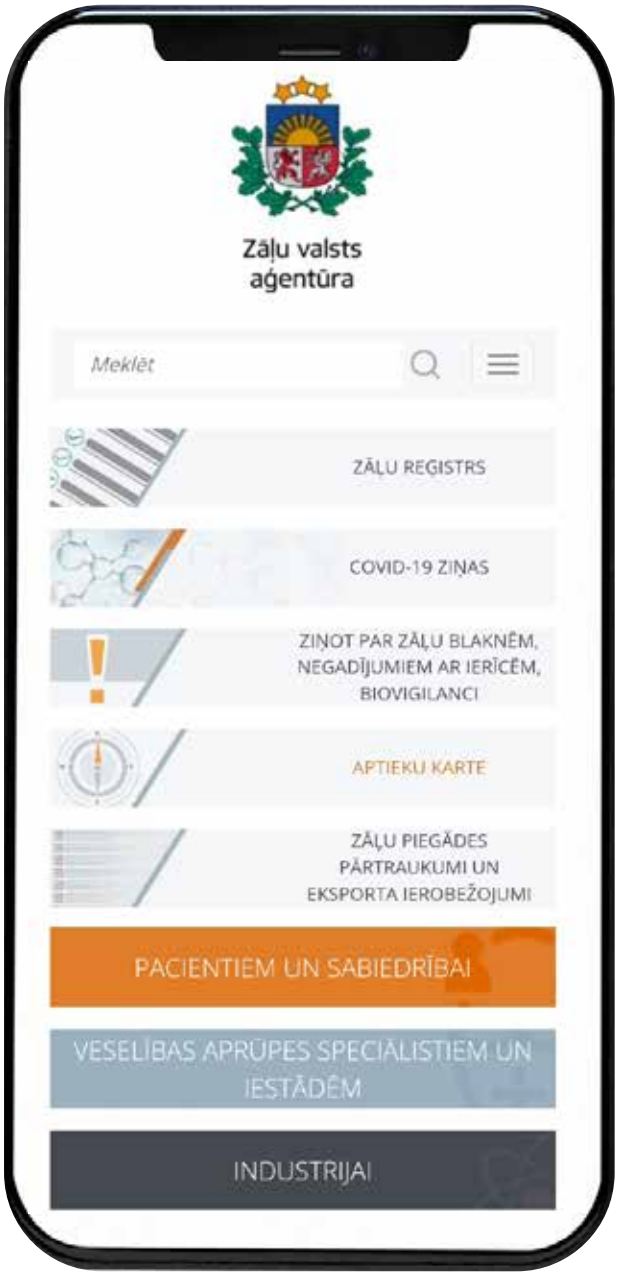
THE MISSION OF THE AGENCY

The mission of the Agency has been included in the objective of its activities determined by the Cabinet of Ministers of the Republic of Latvia 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.

VISION

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

FUNCTIONS



- evaluation and authorisation of medicines
- establishment and maintenance of the Medicinal Product Register
- expertise on quality of medicines
- pharmacovigilance of medicines
- vigilance of medical devices
- issuance of authorisations for conduct of clinical trials with medicines and medical devices
- compliance evaluation of Good Clinical Practice, Good Manufacturing Practice and Good Distribution Practice
- issuance of permits for import, export, transit, distribution and utilisation of medicines
- assembly and provision of information regarding medicines consumption
- issuance of licences for pharmaceutical activity
- analysis of cost-effectiveness of medicines and medical devices
- approval of medical technologies used in healthcare
- other functions

In 2022, the State Agency of Medicines was operating as a public agency and its operation was mostly financed by income received from paid services in accordance with the Cabinet of Ministers Regulation No. 641 "Publicly Available Paid Service Pricelist of the State Agency of Medicines" adopted on 10 December 2019.

SUMMARY OF IMPLEMENTATION OF THE AGENCY'S STRATEGY 2020-2022 IN THE YEAR OF REVIEW

Results achieved in 2022 as set forth for the planning period 2020-2022, taking into account nationally identified priorities and objectives in ensuring public health, and considering also the operational strategy of the EMA and Heads of Medicines Agencies (HMA), may be taken as a confirmation of the Agency's movement towards attaining the objective set out in its vision.

AGENCY OPERATION IN THE YEAR OF REVIEW

The main factors affecting Agency's operation in the year of review were the nationwide state of emergency due to the SARS-CoV-2 pandemic, developments in the field of healthcare and the pharmaceutical industry, including introduction of new EU/EEA regulations, and Russia's attack on Ukraine. As a result of the aforementioned:

- In May 2022, a new function was delegated to the Agency, and, in order to ensure this, a COVID-19 Vaccine Adverse Reactions Damage Compensation Division was estab-

lished. Its main task is to evaluate requests for compensations for serious or moderate harm to patient health or life as a result of adverse reactions to authorised COVID-19 vaccines, and to determine the amount of compensation and make compensation payments.

- The Agency participated in the development of the Clinical Trial Information System for EU member states and EEA countries. Starting from 31 January 2023, this information system is the only place where clinical trial sponsors submit applications for clinical trials and where regulatory authorities evaluate the submitted trial information.
- Proactive solutions were implemented to ensure availability of medicines – the Agency issued permits for distribution of unauthorised medicines, for parallel import and allowed supply of medicines to Latvia in packaging intended for other countries and actively communicated with marketing authorisation holders in cases of potential disruptions in supply of medicines to ensure supply of the necessary medicines to the market in Latvia.
- The Agency ensured participation in the EMA Executive Steering Group on Shortages and Safety of Medicinal Products that was established to coordinate actions across the EU in case of medicinal product supply disruptions caused by major events or public health emergencies.
- The Agency also ensured participation in EMA scientific committees and working groups, where the Agency evaluated information and data to ensure availability of medicines, including vaccines, as well as participated and prepared assessment reports in centralised authorisation procedures.
- We continued safety monitoring of medicines, including vaccines, evaluation of adverse drug reaction reports and increasing awareness of healthcare professionals regarding management of medicinal product use and adverse reactions. In 2022, the Agency conducted in-depth evaluation of the causal relationship in cases where suspected serious adverse reactions resulting in death were reported after receiving a COVID-19 vaccine.
- We continued to work on implementation of the European Parliament and Council Regulation (EU) 2017/745 and preparation for implementation of the new regulation on in vitro diagnostic medical devices – European Parliament and Council Regulation (EU) 2017/746 – from 26 May 2022, providing a robust, transparent, sustainable and internationally recognised legal regulation for in vitro diagnostic medical devices, improving the clinical safety of these devices and ensuring fair access to market for medical device manufacturers.
- We ensured participation in the development of the new European medical device database EUDAMED that will improve information transparency and coordination with respect to medical devices available on the EU market. The new database includes various electronic systems for medical device registration and unique identifiers, for merchant registration, for notified bodies and certificates, for clinical trials, vigilance, post-marketing surveillance and monitoring of the medical device market.
- The Medicines Examination Laboratory organised an international meeting in Riga in collaboration with EDQM regarding quality and quality testing of medicines authorised via mutual recognition, decentralised and centralised procedures.
- We also participated in the development of a framework for implementation of the Regulation (EU) 2021/2282 on health technology assessment in order to promote availability of innovative technologies, including medicines and certain medical de-

vices, to patients in the EU.

- We have developed a draft strategy for 2023-2027 by involving all employees in strategy working groups that analysed Agency's strengths and weaknesses, opportunities and threats (SWOT analysis).
- In relation to Russia's attack on Ukraine, the Agency worked on monitoring of and providing information on alternatives to medicines manufactured in Ukraine, Russia and Belarus, as well as invited people not to create unnecessary stock of medicines, worked on minimising the impact of the war in Ukraine on clinical trials, pharmaceutical company inspections, etc.
- We provided independent information based on scientific data regarding COVID-19 vaccines and medicinal products authorised in the EU, their safety and approval process, as well as the latest information regarding vaccine research and evaluation progress, role of regulatory authorities in vaccine approval, thus, improving understanding among the general public in Latvia regarding safe and rational use of medicines. As part of this, the Agency provided monthly updates regarding safety of COVID-19 vaccines in Latvian and regularly published statistics regarding the number of suspected adverse reaction reports for COVID-19 vaccines on Agency's website.
- The Agency ensured publications and prepared information for doctors, the public and residents regarding latest news on COVID-19 vaccines and medicines (including development of a dedicated section on Agency's website "For patients and public > Medicines > COVID-19 vaccines"). We regularly provided EMA news regarding medicines and vaccines in Latvian and established intense collaboration with the media and organisation in the field of health, providing information regarding COVID-19 vaccines and medicines, particularly regarding COVID-19 vaccines adapted for the omicron strain, regarding vaccine approval for infants, regarding issuance of standard marketing authorisations for COVID-19 vaccines, etc. We also provided information regarding the vaccine against monkeypox.
- We have implemented international informative campaigns in Latvia regarding use of antibiotics, adverse reactions to medicines and disposing of expired medicines, as well as prepared informative materials for the general public regarding oocyte (egg cell) donation, preservation of fertility, COVID-19 vaccines and medicines, receipt of medicines from foreign countries, informative materials regarding mutual substitution of biosimilars, use of biomaterials of human origin, etc.
- In 2022, we have continued actively working on improving SAMIS and developing a client service platform, evaluating the optimal solution to connect the SAMIS information system with the new platform.
- We have improved our work environment and maintained solutions for working remotely in order to ensure continuity of operation and substantially decrease health risks for our employees and clients.
- As part of the state administration remuneration reform, the Agency developed a new remuneration system, recategorizing every office position at the Agency according to the changes in the Office catalogue. The new remuneration system is based on employee competence assessment, as well as increasing the level of motivation with improving personnel competencies.
- The Agency ensured the conduct of a compliance evaluation audit (ISO 9001, ISO/IEC 27001, ISO/IEC 17025) in order to verify compliance of Agency's operational activities with national and EU requirements, as well as quality and safety standards.

MARKETING AUTHORISATION OF MEDICINES

Ineta Popēna,
Head of Medicines Marketing Authorisation Department:

"The main responsibility of the Medicines Marketing Authorisation Department is the scientific evaluation of marketing authorisation documentation submitted by merchants to ensure that in Latvia we authorise and patients have access to medicines that are manufactured in compliance with the high quality standards applied in the EU and whose efficacy and safety has been proven with certainty, and that have an appropriate safety surveillance plan in place. Despite various challenges, in 2022, department employees continued to fulfil this task with a great sense of responsibility, actively participating in both international and national authorisation and variation procedures, including carrying out the role of a reference member state in international authorisation procedures for pharmaceutical companies in Latvia and other EU member states. Since the qualitative performance of the aforementioned tasks and responsibilities requires knowledgable and highly qualified experts, part of the work was focused on developing competencies, streamlining and knowledge exchange in order to ensure regulatory capacity in the longterm.

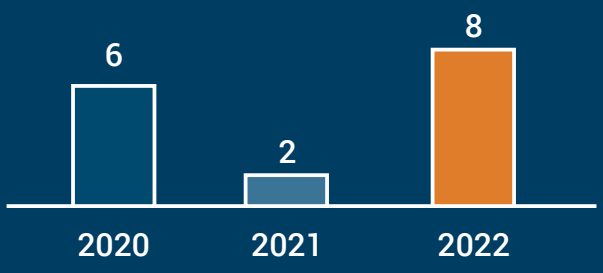
Agency's participation in the collective work-sharing procedures, scientific committees and working groups of EMA is one of our duties and an important additional responsibility, that is largely provided by the employees of the Medicines Marketing Authorisation Department. Operation is largely focused on the scientific evaluation and safety surveillance of new medicines in the EU that are critically needed for the patients. Similarly to the previous period of review, in 2022, department experts continued participating in the evaluation and safety monitoring of COVID-19 vaccines and treatments, thus, contributing to the fight against the pandemic."

Last year, Latvia ensured marketing authorisation and renewal of 20 medicinal products via mutual recognition procedures (MRP) and decentralised procedures (DCP) as a Reference Member State.

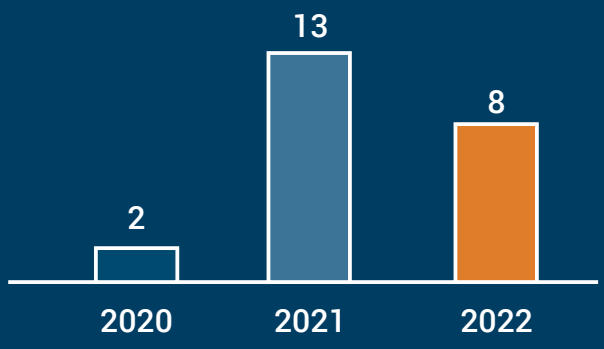
Latvia also participated in 374 MRP and DCP marketing authorisation and renewal procedures as a Concerned Member State.

Overall, in 2022, in comparison to the previous

Marketing authorisations via national procedure

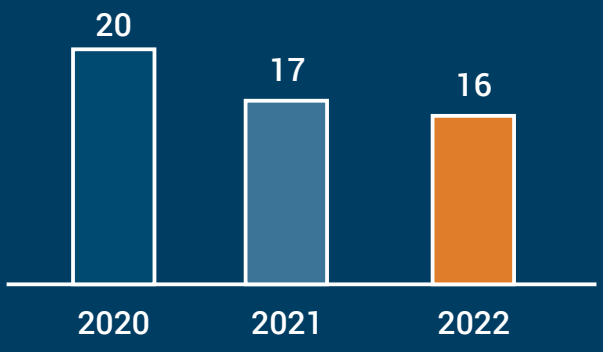


Medicinal product renewals via national procedure

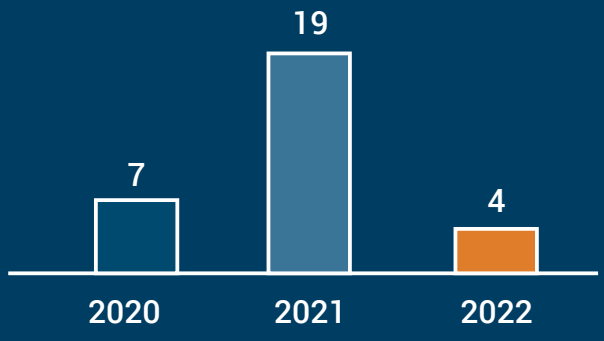


Marketing authorisations and renewals (Latvia as a Reference Member State)

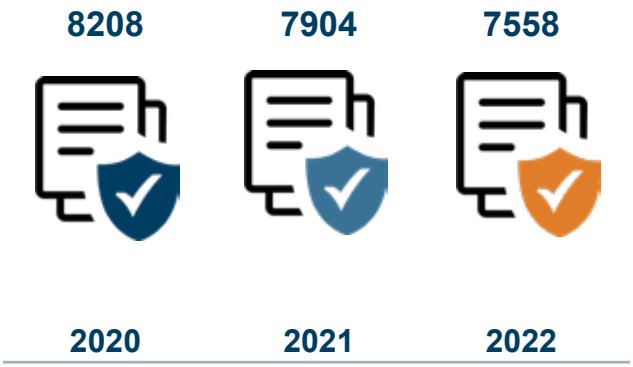
DCP, MRP (authorisation)



MRP (renewal)



VARIATIONS TO MARKETING AUTHORISATION DOCUMENTATION



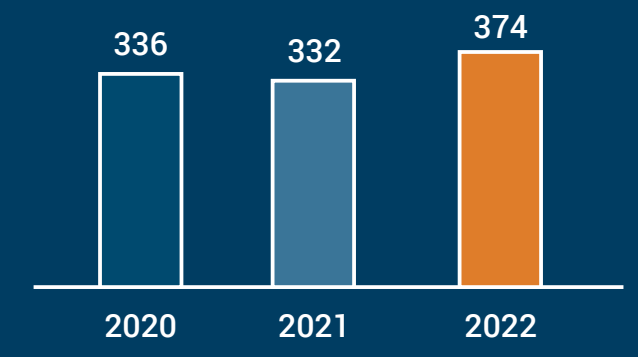
years there was a decrease in the number of marketing authorisation variations evaluated by the Agency, which could be explained by international restrictions due to COVID-19 and by geopolitical processes that have in turn affected the operation of pharmaceutical companies.

Agency experts evaluated 13 applications and issued their opinion on product compliance with the definition of medicines.

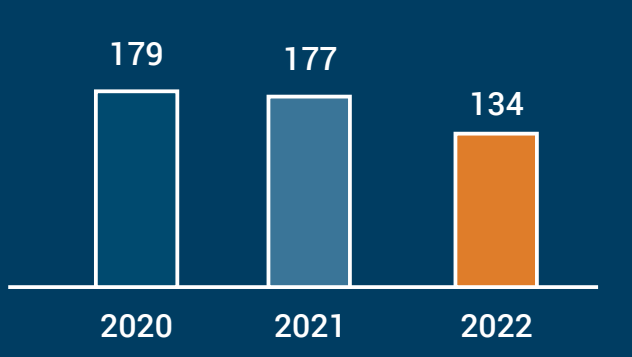
Last year, the Agency also issued 2 Certificates of Free Sale and 238 Certificates of Pharmaceutical Products, thus, promoting export of medicinal products authorised in Latvia to countries outside of EU. These certificates verify that companies manufacture medicines in compliance with Good Manufacturing Practice – according to strict and common quality standards and requirements.

Last year, the activity of Agency's experts in international procedures of European medicines regulatory network was very significant, similarly as in the previous years. In addition, the experts of the Agency carried out scienti-

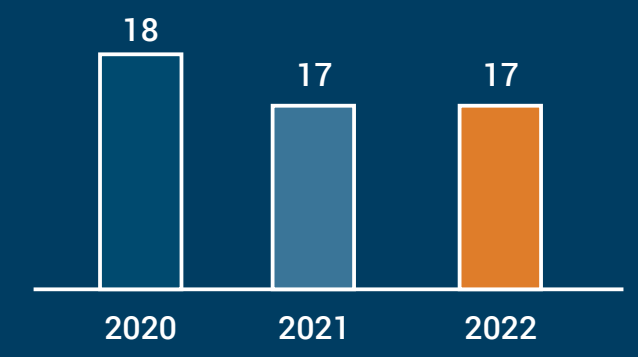
Marketing authorisations and renewals (Latvia as a Concerned Member State)



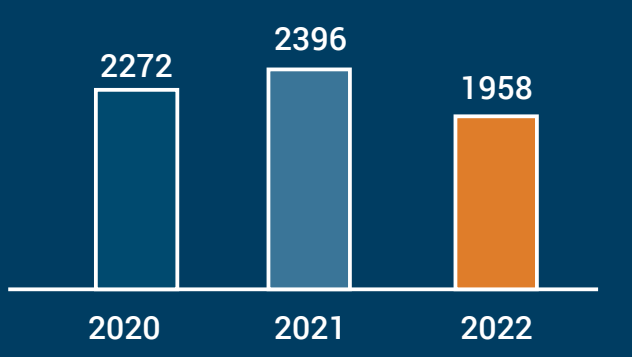
Type IA/IB variations (Latvia as a Reference Member State) with a positive outcome



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



Variations via national procedure



fic evaluation for 5 centralised marketing authorisation procedures (CAP) which were started in 2022, as well as for variations of CAP authorised medicines.

Latvia was represented in the EMA Paediatric Committee and participated in evaluation procedures for 18 primary paediatric investigation plans (PIP) and for 24 PIP modifications, as well as in 4 PIP compliance check. A representative delegated by the Agency to the EMA Paediatric committee is heading the Neonatology working group and acts as a rapporteur in the process of reviewing guidelines on medicines intended for neonates.

Experts from the Medicines Marketing Authorisation Department together with external experts actively participated in the work of the Committee for Advanced Therapies (CAT), Committee for Orphan Medicinal Products, Committee on Herbal Medicinal Products and other committees. Experts regularly participated in the work sessions of EDQM as external experts.

By participating in the EMA Scientific consulation working group, Agency's marketing authorisation experts in collaboration with outsourced experts have provided scientific consultations regarding 25 aspects of medicinal product development, research and authorisation.

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

- carried out a scientific evaluation of more than 8000 applications for marketing authorisation, renewal and variations to marketing authorisation documentation of medicines by reviewing data and evidence included in medicines marketing authorisation documentation that confirm quality, safety and efficacy of medicines. Reviews included also administrative information, as well as chemical, pharmaceutical, preclinical and clinical sections of the documentation and pharmacovigilance documents.
- out of all the applications evaluated, the Agency has taken a positive decision on authorisations and renewals of 410 medicinal products;
- evaluated 7283 applications for variations to marketing authorisation documentation of medicines with a positive outcome.

MEDICINAL PRODUCT DISTRIBUTION

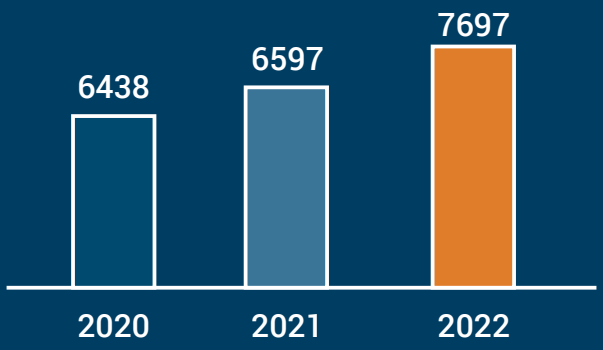
Katrīna Lukša,
Head of Information on Medicines Distribution Department:

"In 2022, one of the biggest problems globally, in Europe and Latvia remained the unavailability and disruptions in the availability of medicines. This dictated that one of the most important objectives of the Agency is to not only evaluate and authorise medicines, thus, allowing safe and qualitative medicines to enter the market, but also to ensure prompt review of applications and issuance of permits for import and export of medicines. This was particularly relevant and challenging at the end of the year when there was insufficient supply of antibiotics throughout the world. The disruption in supply was caused by manufacturing delays, manufacturing capacity issues (shortages of personnel and packaging), as well as increased demand. During this situation it was particularly important to ensure useful, truthful and updated information regarding the availability of medicines on the market in Latvia. This reaffirmed the relevance and importance of the previously implemented project regarding remaining stock of medicines at medicinal product wholesale facilities."

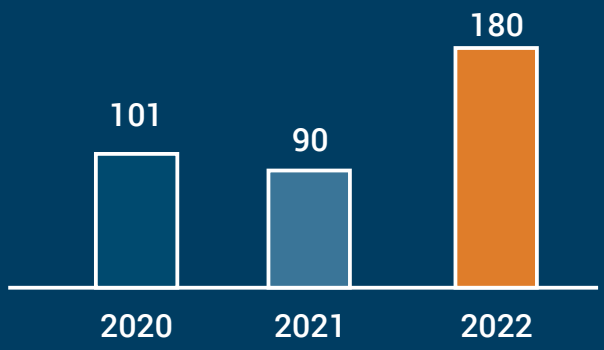
To resolve this situation countries all over the globe, as well as EU member states, including Latvia, took various measures aimed at improving availability of medicines:

- Actively monitored the situation of availability of antibiotics in Latvia on a daily basis;
- Every working day the Agency requested medicinal product wholesalers to submit information regarding antibiotics delivered to pharmacies on the previous day and increased monitoring of antibiotic availability data;
- The Agency ensured daily communication with marketing authorisation holders and wholesalers, as well as issued additional per-

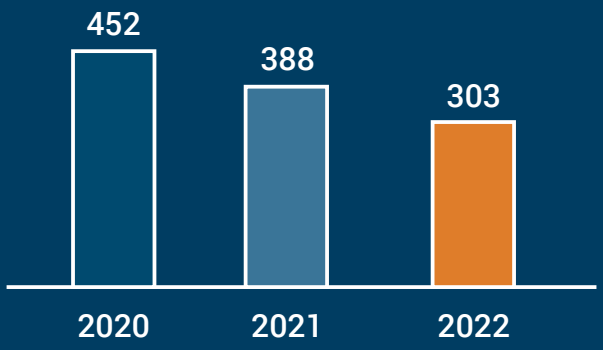
Permits for distribution of unauthorised medicines



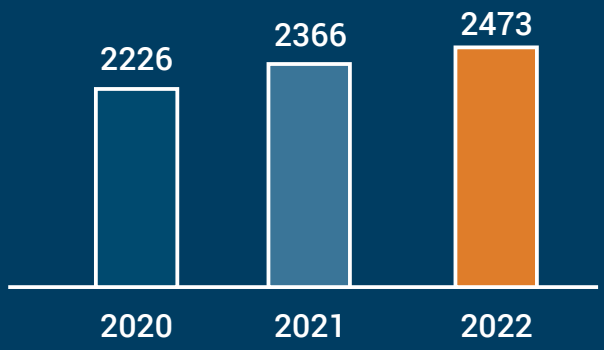
Number of permits for parallel import



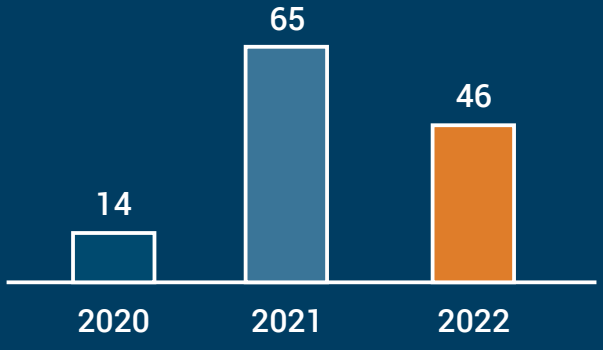
Number of variations to permits for parallel import



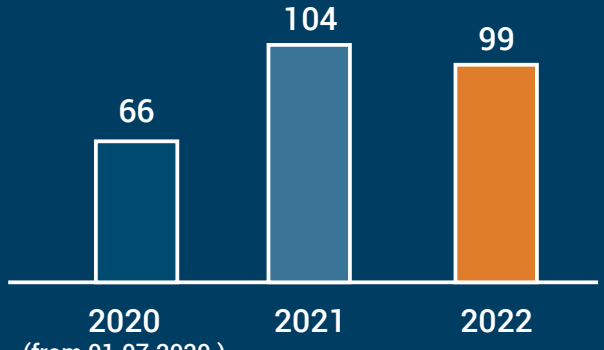
Permits for import/ export of narcotic, psychotropic medicines/ substances and precursors



Permits for import of samples of medicines



Permits for supply of medicines to other EU member states or export of medicines



mits for distribution of antibiotics to ensure availability of medicines for patients as soon as possible;

- To solve this issue, in 2022, the Agency issued 5 permits for distribution of parallel imported medicines containing Amoxicillinum, Acidum clavulanicum un Amoxicillinum. In addition, the Agency approved additional supply of medicines in packaging intended for the market of another country.

In 2022, the Agency issued 10,396 permits for import, export, transit and distribution of medicines, keeping up with the average timeline for issuance of permits (for example, 2 days for import/export permits for narcotic, psychotropic substances and precursors controlled in Latvia), thus, ensuring prompt issuance of permits to merchants who have submitted all of the required documentation.

The Agency ensured expertise on applications and documentation relaed to distribution of the following medicinal products in accordance with the normative acts:

- for import and export of psychotropic, narcotic medicinal products/substances, as wel as precursor;
- for distribution of unauthorised and parallel imported medicinal products
- for import of medicinal product samples;
- for supply of medicines to other EU member states or export of medicines.

In addition to the aforementioned, the Agency performed expertise on applications and documentation and issued 6 registration cards for precursor operators and 5 authorisations for medical scientific research on herbs, substances and medicinal products included in the I, II and III list of narcotic substances, psychotropic substances and precursors controlled in Latvia. In 2022, the Agency received 206 applications and notifications to authorise distribution of medicines in packaging intended for a market of another EU/EEA member state. For notifications, the response time was 1 day in 100% of the cases, whereas for applications – in 15% of cases response was given within 1 day, in 73% of cases – within 3 days (for cases not eligible for the notification procedure), thus, ensuring prompt action, giving priority to notifications/ applications regarding medicines currently affected by supply disruptions.

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 2022''. To facilitate receipt of permits for import and export of narcotic and psychotropic substances or medicines, we established and published on the Agency's website a form "Application for import/export permit of narcotic, psychotropic substances and precursors controlled in Latvia" including information stipulated by Article 19 of the "Law on the Legal Trade of Narcotic and Psychotropic Substances and Medicinal Products, and also Precursors". Thus, the number of incorrectly completed applications and the amount of additional information requested from merchants has been decreased. We have also updated, translated into English and supplemented other information related to our department, for example, import and export of medicines, receipt of medicines via postal mail, and clients have been informed regarding amendments to legal acts and were reminded of relevant norms stipulated by such acts.

In 2022, 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 pre-

cursors 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 65th session of the UNODC Narcotics Control Committee.

The Agency continued to ensure monitoring of the availability of medicines regarding which the National Health Service and the marketing authorisation holder or wholesaler have made a cofinancing agreement, and performed expertise on applications for medicinal product export, thus, ensuring that the medicines remain available to patients in Latvia and are not exported to other countries.

The Agency continued to collaborate with other institutions to create a list of critically important medicines including medicines that are necessary to ensure priority needs in the healthcare system in terms of treatment and prevention of diseases, foreseeing special conditions for distribution of these medicines in legal acts.

We also provided proposals for amendments to legal acts regulating circulation of medicines, including acts regulating the circulation of narcotic and psychotropic substances and medicines, as well as precursors, the procedure for import and export of medicines, distribution and quality control of medicines, labelling of medicines, etc.

CLINICAL TRIALS WITH MEDICINES

Jana Migliniece,
Head of the Clinical Trials Department:

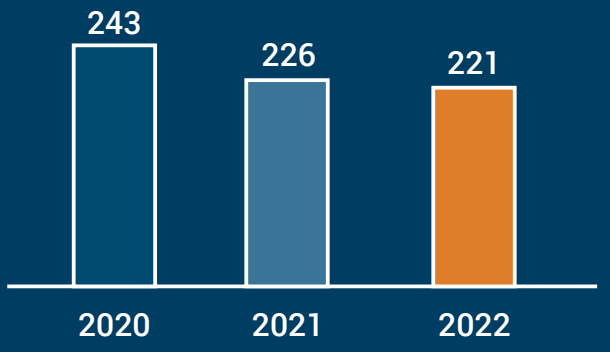
"On 31 January 2022, the Clinical Trials Department began working in the unified European Clinical Trials Information System (CTIS) by reviewing two and allowing the conduct of one transitional clinical trial* in Latvia. The trials were reviewed in collaboration with the Ethics Committee of the Development Society of Pauls Stradins Clinical University Hospital and other EU competent authorities. Last year, the Agency participated in three international expert working groups – working groups for clinical trial experts established by the EC and HMA, by contributing to the harmonisation of clinical trial approval in Europe, and in the EMA working group for Good Clinical Practice inspectors in order to harmonise the procedure for inspections."

In 2022, the Agency issued 40 authorisations for conduct of clinical trials in Latvia.

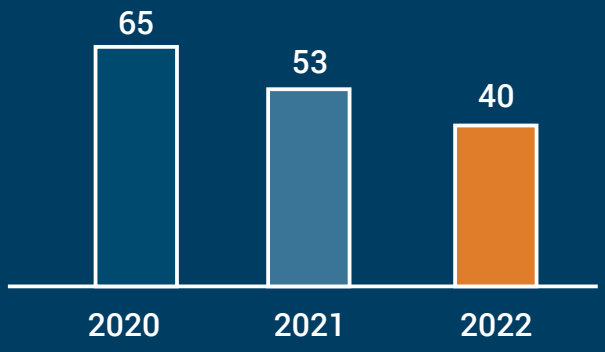
Last year, 5 Good Clinical Practice compliance inspections were carried out.

* Transitional clinical trials are trials that have been approved in accordance with the requirements of the Clinical Trials Directive 2001/20/EC and whose sponsor has decided to modify documentation as stipulated by the requirements of the EU Regulation 536/2014 by submitting it in CTIS.

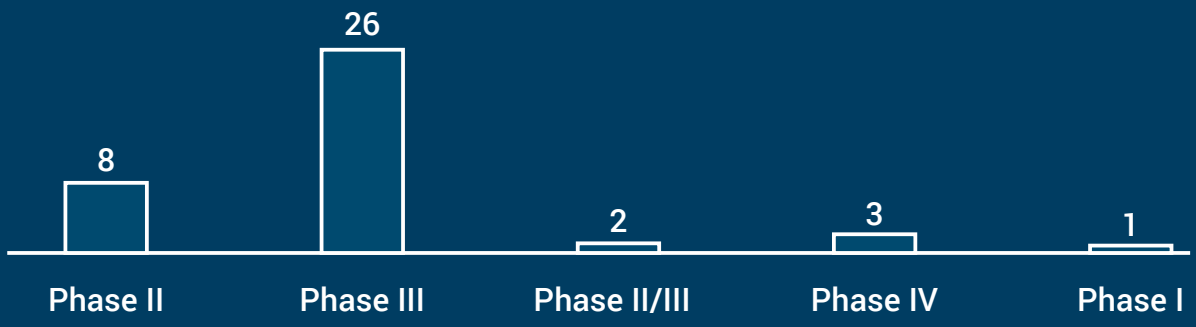
Total number of clinical trials conducted in Latvia



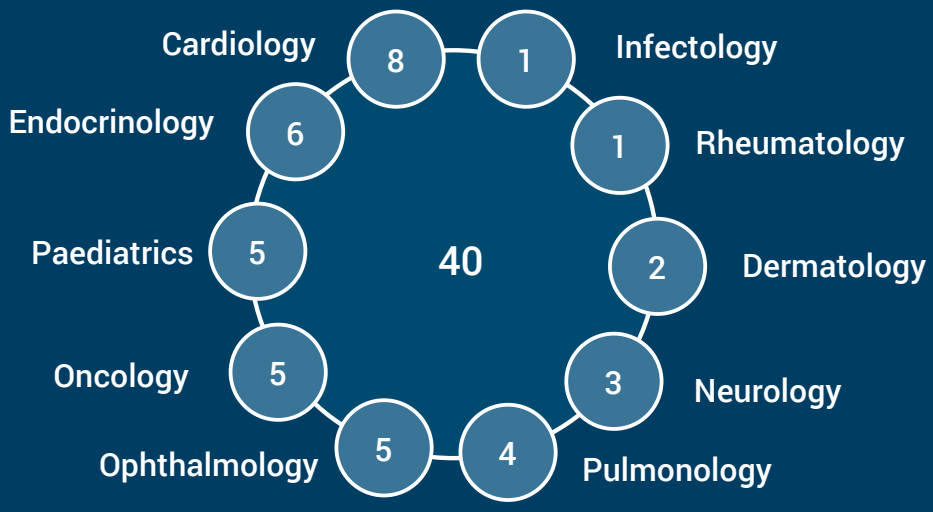
Authorisations for clinical trials



Number of clinical trials authorised in 2022, according to trial phase



Number of clinical trials authorised in 2022, according to medical specialty



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 11 primary and 15 follow-up reports regarding serious unexpected adverse events potentially related to investigational medicinal products.

The Agency received and reviewed 125 annual safety reports from sponsors related to clinical trials with medicinal products conducted in Latvia.

The authorized clinical trials with medicinal products were sponsored by 41 foreign pharmaceutical companies. In 2022, 32 contract research organizations were involved in the organization and quality assurance of clinical trials conducted in Latvia according to authorization issued by sponsors.

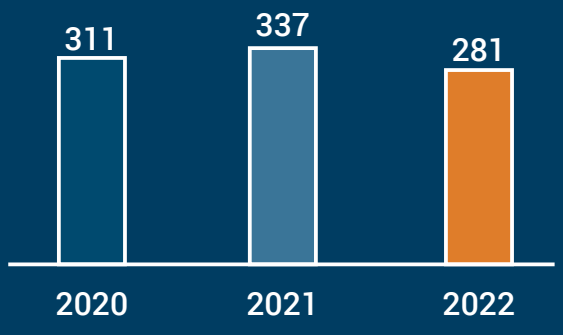
Last year, proposals were submitted to the Ministry of Health regarding amendments required to national legal acts.

In order to promote synchronised safety evaluation of investigational medicinal products throughout the EU, we began the SAFE-CT project supported by EU4Health. As part of this project, a new safety evaluation expert was hired in order to establish competence and experience through the learning process and a mentoring program that is required for evaluation of investigational medicinal products in clinical trials, thus, also establishing a sustainable procedural framework for safety evaluation of clinical trials in the future.

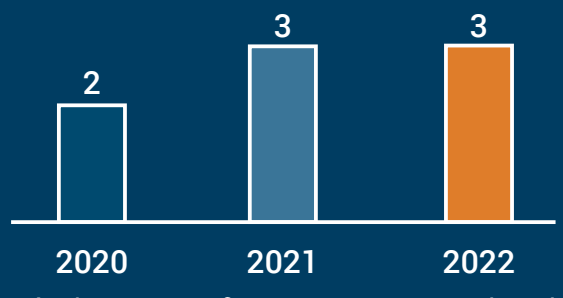
Trial sites of medicinal product clinical trials authorised in 2022

Trial site	Number of trials
State LLC "Pauls Stradins Clinical University Hospital"	28
Riga Eastern Clinical University Hospital	20
LLC "Daugavpils Regional Hospital"	15
LLC "Riga 1st Hospital"	7
LLC "Liepaja Regional Hospital"	7
"Veselības Centrs 4"	6
Ltd. "Adoria"	6
State LLC "Children's Clinical University Hospital"	5
Other clinical trial sites (59 in total)	1-4 trials at every site

Authorisations for amendments to clinical trials and authorisations for non-interventional studies in 2022



Authorisations for amendments to clinical trials



Authorisations for non-interventional studies

MONITORING OF ADVERSE DRUG REACTIONS AND RISK MINIMISATION

Zane Stade,
Head of Pharmacovigilance Department:

"In 2022, experts of the Pharmacovigilance Department have put substantial effort in in-depth evaluation of reports of serious adverse drug reactions. A total of 69 assessments have been prepared, of which a large proportion was prepared as part of requests for compensation for harm caused by COVID-19 vaccines. Active collaboration took place with clinicians of various specialties in order to arrive at objective conclusions regarding the potential causal link with the use of medicines or vaccines. The experts also prepared response letters to submitters of these reports regarding the results of the in-depth evaluation of their cases, as well as informed doctors who provided additional information upon Agency's request. In 2022, there was active exchange of information with specialists in the field. Based on the professional opinion of practicing doctors, it is possible to adopt objective regulatory decisions."

In 2022, the State Agency of Medicines received 802 adverse drug reaction reports, including reports related to adverse reactions to vaccines, and this information was forwarded to the EudraVigilance database in the EU. Last year, 58% of the reports were submitted by healthcare professionals and pharmacists, but 42% reports – by patients.

Almost all adverse drug reaction reports were received in an electronic format. Agency's pharmacovigilance experts and IT specialists regularly worked on improving the electronic report form in order to facilitate data entry for doctors and improve the quality of submitted reports. The improved Adverse drug reaction report information system is now easy to use in daily work and for collection of statistical data.

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. The Agency performed 12 single assessment procedures in 2022.

In accordance with the EMA work-sharing procedure, in 2022, Agency experts conducted monitoring for 31 active substance, i.e., regular surveillance of the safety information regarding these substances, as well as one in-depth evaluation procedure on a European level where Latvia assumed the role of the leading expert.

Last year, the Agency also evaluated risk management plans for 59 medicinal products authorised via national procedures. In addition, pharmacovigilance experts participated in centralised marketing authorisation procedures: 8 procedures as rapporteur for the Pharmacovigilance Risk Assessment Committee (PRAC) and 7 procedures in collaboration with clinical experts to provide safety issue assessment.

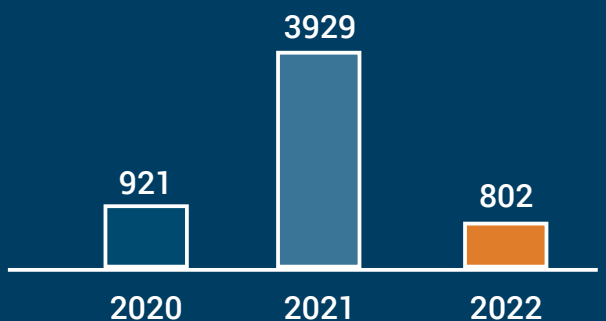
In 2022, the Agency approved a total of 92 additional risk minimisation materials intended for doctors and patients prepared with the purpose of risk minimisation for specific medicines. Twenty-nine of these were Direct Healthcare Professional Communication (DHPC) letters including important information on safety of medicines.

Agency's pharmacovigilance experts also actively participated in informing the public and healthcare specialists regarding the field of adverse drug reaction reporting and safety issues of medicines. Healthcare specialists regularly received updated information following meetings of the European Pharmacovigilance Risk Assessment Committee (PRAC). A representative of Latvia participated in the monthly meetings of the PRAC working group meetings, expressing their opinion and presenting assessments performed by pharmacovigilance experts. Information regarding decisions adopted by PRAC in relation to safety of medicines and recommendations for risk minimisation was provided to professional associations of doctors and medical specialists in Latvia. Agency's pharmacovigilance experts also participated in online events organised by professional associations of healthcare specialists and have given a substantial contribution in providing the latest information regarding safety of medicines and explaining the importance of submitting reports, as well as in the development of the new electronic format of the bulletin "Cito!".

Information exchange was also ensured with EMA and European medicines agencies regarding pharmacovigilance issues, as reflected by responses to 22 information query documents to EU member states (NUI – non-urgent information).

In 2022, we planned and organised research regarding the efficacy and distribution of risk minimisation materials. We have initiated preparation of survey forms to obtain the opinion of healthcare specialists and pharmacists and to clarify the most effective and convenient form of communication with respect to safety issues of medicines. We also worked on preparing an international publication regarding efficacy assessment of risk minimisation measures and trends in prescription of valproates in Latvia.

Adverse drug reaction reports



COMPENSATION FOR DAMAGE FROM ADVERSE REACTIONS TO COVID-19 VACCINES

Inārs Švarcs,
Head of COVID-19 vaccine adverse reactions damage compensation division

"On 3 May 2022, the government approved a Cabinet Regulation on issuance of compensation for cases when a person has suffered from a moderately severe or severe harm to health or life as a result of an adverse reaction to a COVID-19 vaccine. Last year, the Agency evaluated 112 requests for compensation and paid out compensations in 6 cases."

In 2022, the Agency received a total of 122 requests for compensation for moderately severe or severe harm to a person's health or life as a result of an adverse reaction to a COVID-19 vaccine. Last year, we evaluated 112 requests and compensation was paid out in 6 cases, whereas evaluation of 4 cases is being continued in 2023.

QUALITY CONTROL OF MEDICINES

Guntars Kaspars,
Head of the Medicines Examination Laboratory:

"In 2022, the Latvian National Accreditation Bureau (LATAK) conducted its routine monitoring visit, as a result of which the Agency maintained its accreditation for compliance with the requirements of the LVS EN ISO/IEC 17025:2017 standard in the following fields: physical and physicochemical testing of medicinal products, pharmaceutical active ingredients and excipients (fixed and flexible scope), physical testing of purified water (fixed scope).

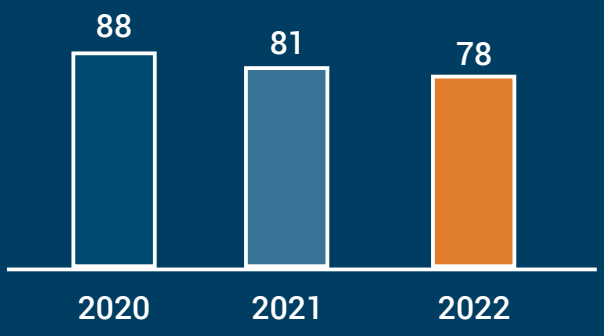
In 2022, the Medicines Examination Laboratory had an audit of the EDQM MJA, where EDQM assessed the compliance of Medicines Examination Laboratory with the requirements of LVS EN ISO/IEC 17025:2017, the implementation and use of the guidelines developed by the EDQM, and the fulfilment and compliance with the conditions of the European Pharmacopoeia.

Successful audits are important validation of the quality of Agency's professional operation. This annual confirmation of certification compliance ensures that our clients can have confidence in our work – industry professionals, collaboration partners in Latvia and other countries and the residents of Latvia may rely on the quality of the Agency operation."

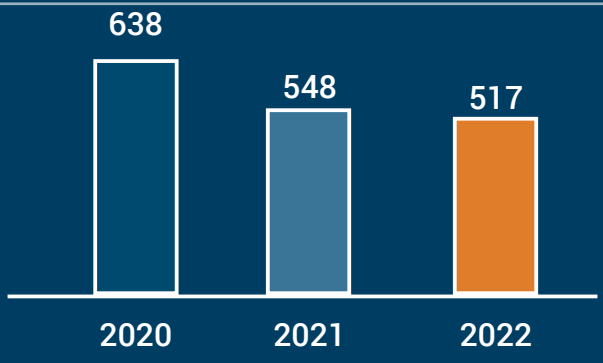
Laboratory's specialists participated in international programs for quality control of medicines and professional level evaluation programs, i.e. quality control programs for medicines authorised in the CAP, MRP/DCP and national procedure as well as in the professional level evaluation programs provided by EDQM and Royal Dutch Pharmacists Association.

In November 2022, the annual meeting of the CAP and MRP/DCP was held in Riga, which was organized by the Medicines Examination Laboratory in collaboration with other departments of the Agency. The event was organized at a very high level, for which a certificate of appreciation was received from the EDQM.

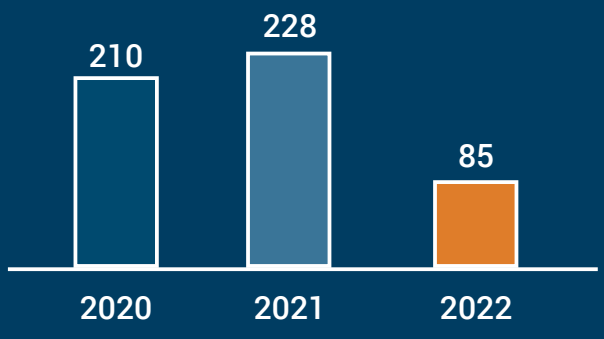
Number of medicinal product samples tested



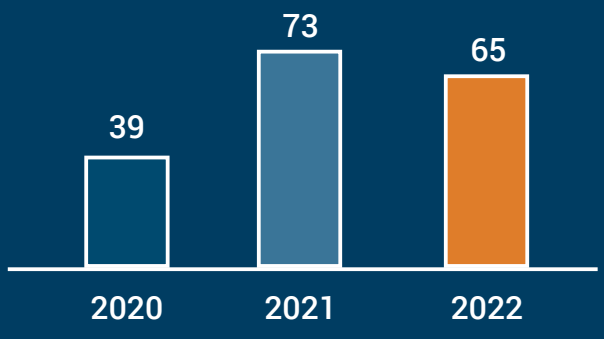
Number of medicinal product quality parameters tested



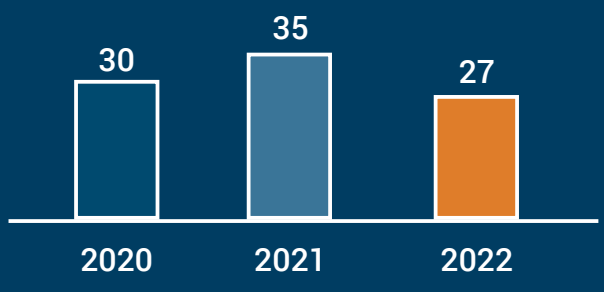
Number of volumetric solutions, indicators and reagents tested upon request from pharmacies



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



MONITORING, CLINICAL RESEARCH AND VIGILANCE OF MEDICAL DEVICES

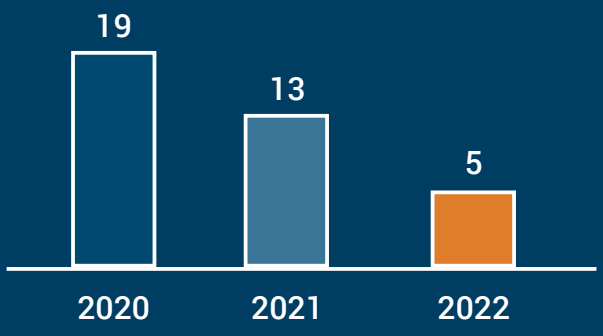
Andis Viļums,
Head of Medical Devices Assessment Department:

"In order to ensure uninterrupted internal market activity in the field of in vitro diagnostic medical devices with a focus on the high level of protection of patient and user health and considering the interests of the average company operating in this field, on 26 May 2022 we began implementation of the new Regulation (EU) 2017/746 on in vitro diagnostic medical devices. Due to concerns that healthcare institutions, notified bodies, merchants and other stakeholders will not be able to ensure full implementation of this Regulation starting from the aforementioned date, thus, creating a risk of disrupted supply of in vitro diagnostic medical devices throughout the EU, the transition periods for the Regulation (EU) 2017/746 were pre-emptively extended (on 26 January 2022). The length of a transition period depends on the risk class of an in vitro diagnostic medical device. Thus, it will ensure that critically important in vitro diagnostic medical devices continue to be available and safe and guarantee a seamless transition from the Directive on in vitro diagnostic medical devices to the Regulation."

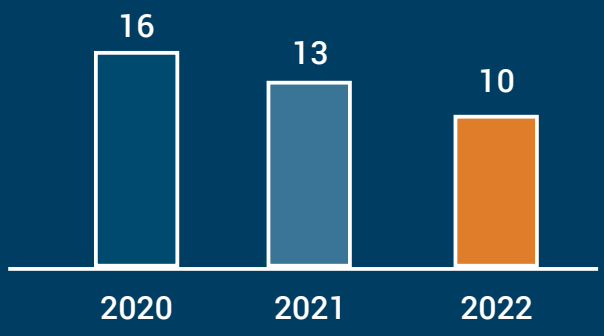
To promote the export capacity of Latvian manufacturers outside of the EU, last year the Agency issued 37 certificates of free sale to medical devices manufactured in Latvia.

In 2022, the number of free sales certificates issued to local medical device manufacturers in Latvia was 25% higher than in 2021, indicating a growth in the export of medical devices manufactured in Latvia.

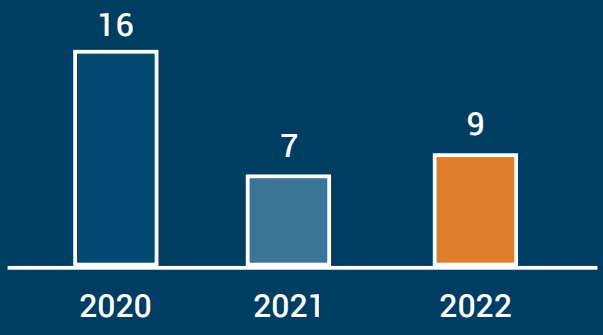
Latvian medical device manufacturers and their medical devices: information analysed and included in the Medical Device Database LATMED



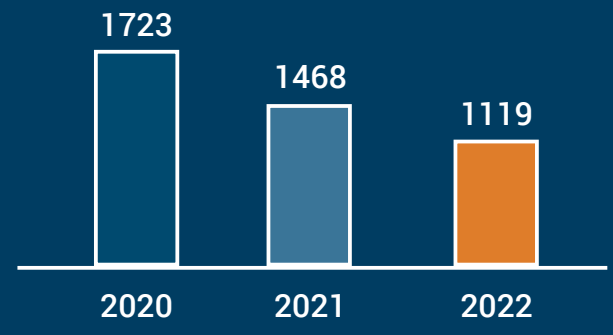
Authorised representatives of third country medical device manufacturers in the EU who have registered business in Latvia: information evaluated and included in the Medical Device Database LATMED



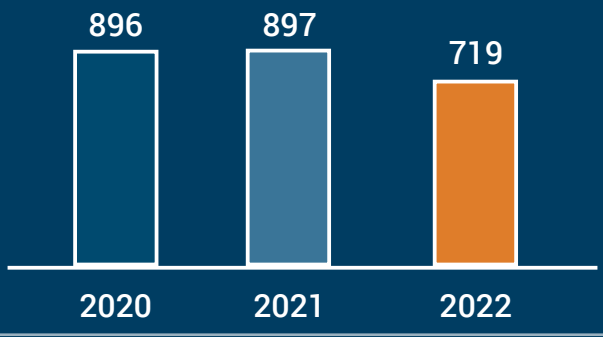
Authorisations for clinical trials with medical devices (permits issued)[1]



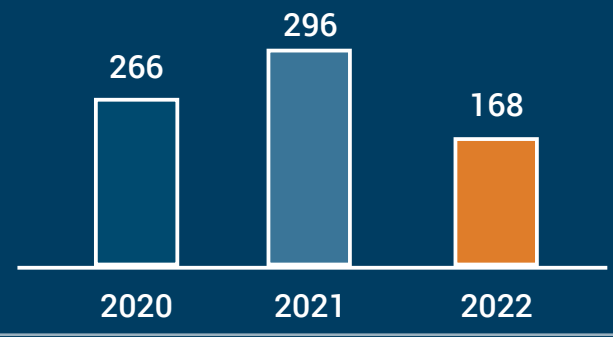
Vigilance[2] reports regarding medical devices (total number of reports received by the Agency)



Primary vigilance[2] reports regarding medical devices (number of primary reports received by the Agency)



Primary vigilance[2] reports regarding medical devices located in Latvia and implementation of safety monitoring measures



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

[2] The medical device vigilance system is a unified EU reporting system for incidents involving medical devices, corrective measures taken by manufacturers or competent authorities and for evaluation of reports and information. The objectives of the vigilance system are 1) to prevent repeat incidents, 2) to protect patients by using the medical device incident reporting system in all EU member states, 3) to ensure that member states may simultaneously identify non-compliant medical devices on the market and in use.

HEALTH TECHNOLOGY ASSESSMENT

Antra Fogele,
Head of the Health Technology Assessment Department:

"In 2022, the Regulation 2021/2282 of the European Parliament and of the Council on health technology assessment came into effect, stipulating that starting from 2025 a unified clinical evaluation will be conducted for new medicinal products intended for treatment of neoplasms, as well as for advanced therapy medicinal products. Agency experts are involved in the coordination group for implementation of this Regulation and are working on preparing detailed procedural regulations and documents. The implementation of the aforementioned Regulation in the future will affect specific steps in the evaluation process for new medicines established in Latvia."

OPINION ON CLINICAL AND COST-EFFECTIVENESS OF NEW NONPROPRIETARY NAMES OR NEW COMBINATIONS OF MEDICINES

In 2022, the Agency received 50 applications and prepared 49 opinions.

Opinions provided according to diagnostic groups (according to the International Classification of Diseases (ICD-10)):

- Neoplasms – 22 opinions (45%)
- Endocrine, nutritional and metabolic diseases – 7 opinions (14%)
- Diseases of the musculoskeletal system and connective tissue – 4 opinions (8%)
- Diseases of the circulatory system – 3 opinions (6%)
- Diseases of the nervous system – 3 opinions (6%)
- Diseases of the digestive system – 2 opinions (4%)

- Factors influencing health status and contact with health services – 2 opinions (4%)
- Diseases of the genitourinary system – 2 opinions (4%)
- Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism – 1 opinion (2%)
- Diseases of the skin and subcutaneous tissue– 1 opinion (2%)
- Diseases of the respiratory system – 1 opinion (2%)
- Mental and behavioural disorders – 1 opinion (2%)

24 of all the opinions provided in 2022 (49%) were related to the treatment of orphan (rare) diseases. In comparison, in 2021, the Agency prepared 44 opinions, including 17 (39%) on orphan diseases.

As the Agency's opinion is a required step towards the opportunity for reimbursement of new medicines from the state budget, according to the information available on the website of the National Health Service, 37 applications, for which Agency's opinion was issued, have been submitted for inclusion in the system for reimbursement of medicinal product expenses.

Starting from 2021, we have initiated public participation in the evaluation process of medicines. After gathering information about experience in other countries and consulting with patient organisations and professional associations of doctors, we have established separate survey forms for healthcare professionals and patients where the interested parties may express their opinion regarding the role of the new medicinal product in the treatment process of a specific disease, the expected benefits and unmet needs. Completion of this survey by patients and specialists is voluntary, but it may provide important information for the evaluations performed by the Agency. Initially during the pilot project, surveys were created only for medicines for the treatment of oncological diseases, but from 1 September 2021 such survey forms are being prepared and disseminated for every new application. Out of the 49 opinions prepared in 2022, 41 survey was disseminated to patient organisations via the Patient organisation network. Surveys regarding 44 new non-proprietary names of medicines or new diagnoses/patient groups were sent to professional associations of doctors. Replies were received from specialists in 15 cases, and from patient organisations – in 6 cases. Information from these surveys was included in the opinion prepared regarding the clinical and cost effectiveness of medicines.

APPROVAL, SUPPLEMENTATION AND WITHDRAWAL OF MEDICAL TECHNOLOGIES (MT) AND UPDATING OF THE DATABASE OF MEDICAL TECHNOLOGIES FOR THERAPEUTIC USE

In 2022, the Agency received 13 applications for approval, supplementation or withdrawal of MTs and adopted 14 decisions, including 2 decisions on refusal to review application due to incorrectly submitted documentation:

In comparison, in 2021 the Agency received 30 applications for approval, supplementation or withdrawal of MTs and adopted 37 decisions on approval of MTs.

Utilising the opportunity provided by normative acts, we have asked for the opinion of the Latvian Medical Association regarding a medical technology submitted for approval.

Preparation and submission of applications at the Agency is the competence and choice of healthcare institutions and professional associations of doctors. The Agency regularly invites different organisations to review the approved technologies already included in the Database of Medical Technologies for The-

Name of MT group	Approved MTs	Supplemented MTs	Withdrawn MTs
Medical services in internal medicine and functional diagnostics	1		
Medical services in anaesthesia, reanimatology, transfusiology and intensive care	1	3	1
Medical services in physical medicine and rehabilitation	2	2	1
Medical services related to nutrition	1		

rapeutic Use, update them as required and consider to approve new MTs. The most active communication has been established with the State Blood Donor Centre and the Latvian Physiotherapists' Association.

In 2022, we continued to work on improving the content and updating of the Database of Medical Technologies for Therapeutic Use:

Majority of adopted decisions were related to the following medical technology groups: "Medical services in anaesthesia, reanimatology, transfusiology and intensive care" (5) and "Medical services in physical medicine and rehabilitation" (5);

In collaboration with the Latvian Physiotherapists' Association, updates were made to the section "Physiotherapy technologies" of the medical technology group "Medical services in physical medicine and rehabilitation";

Updating of the medical technology group "Medical services in laboratory examination" was initiated;

Methodical review of sections of the database was conducted to prevent overlap of extended MT descriptions;

11 specialist associations were invited to review and update as required the list of registered MTs in the medical technology group "Medical services in neurology".

The Medical technology assessment commission, whose responsibility is to evaluate the compliance of documentation submitted to the Agency regarding approval, supplementation or withdrawal of medical technologies with the requirements stipulated by legal acts and to provide an opinion to the Director of the Agency, held 3 meetings in 2022. Representatives from the National Health Service and the Health Inspectorate participate in the commission alongside Agency specialists.

LICENSING OF PHARMACEUTICAL ACTIVITY COMPANIES

Signe Čudare,
Head of Pharmaceutical Activity Company Licensing Department:

"In 2022, the Agency provided services stipulated by the Pharmaceutical Law: issued (renewed) special permits (licences) for opening (operation) of general and closed-type pharmacies, for operation of medicinal product wholesale facilities, manufacturing or import medicinal products and manufacturing of active pharmaceutical ingredients, authorisations for manufacturers, importers and distributors of active substances, evaluated documentation for a medicinal product broker and authorised the first medicinal product broker in Latvia.

Last year, 94% of all client applications for pharmaceutical activity licensing services (issuance of permits/authorisations) were received as electronic documents.

As part of the ongoing administrative reform, the Agency took measures related to updating and renewal of legal addresses of licensed pharmaceutical activity subjects, synchronising address data with the data indicated in the State Address Register and the Enterprise Register of the Republic of Latvia. This data is reflected in the Pharmaceutical Activity Company Register on Agency's website.

We highly appreciate the collaboration of Agency's clients with our employees in providing the necessary information in order to ensure legal services in the field of pharmaceutical activity. It is also in the Agency's interest to provide the requested services to clients as quickly as possible to minimise and optimise the use of resources."

In 2022, the Agency renewed licences for pharmaceutical activity for **246** pharmaceutical activity companies (including **10** new companies):

- **190** generaltype pharmacies (including 1 licence for new general-type pharmacy)
- **2** closed-type pharmacies
- **36** medicinal product wholesalers (including 2 licences for new medicinal product wholesalers)
- **14** medicinal product manufacturing or import companies (including 2 licences for medicinal product manufacturers/importers)
- **3** active pharmaceutical ingredient manufacturing companies (including 1 licence for new active substance manufacturer)
- **1** veterinary medicinal product wholesaler.

In 2022, the Agency issued athorisations:

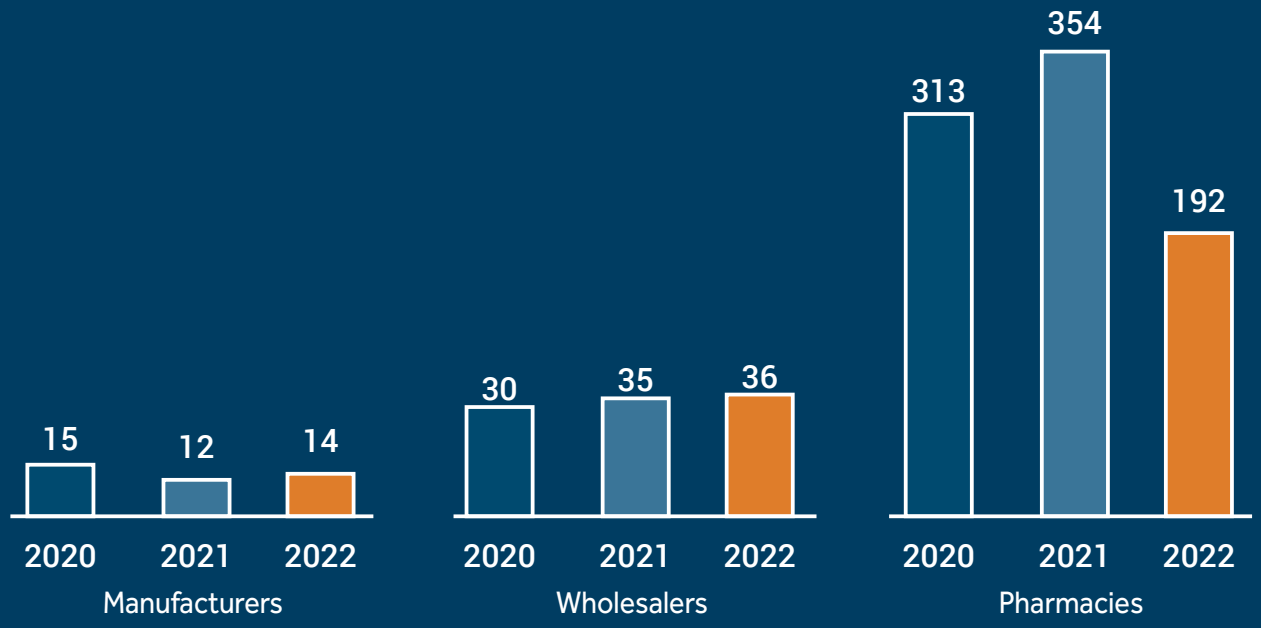
- **17** authorisation for manufacturing, import or distribution company of active pharmaceutical ingredients (including 3 new companies)
- **1** authorisation for a medicinal product broker

In 2022, the Agency renewed or authorised 17 active pharmaceutical ingredient manufacturing, importing or distribution companies and 1 authorisation for a medicinal product broker.

In 2022, 34 cases of new pharmaceutical activity location for general type pharmacies (pharmacy branches) were evaluated.

In 2022, Agency's Pharmaceutical Activity Company Licensing Commission (hereinafter – Commission) held 13 meetings where issues were reviewed and recommendations were adopted regarding issuance, renewal and

Changes in licences for pharmaceutical activity



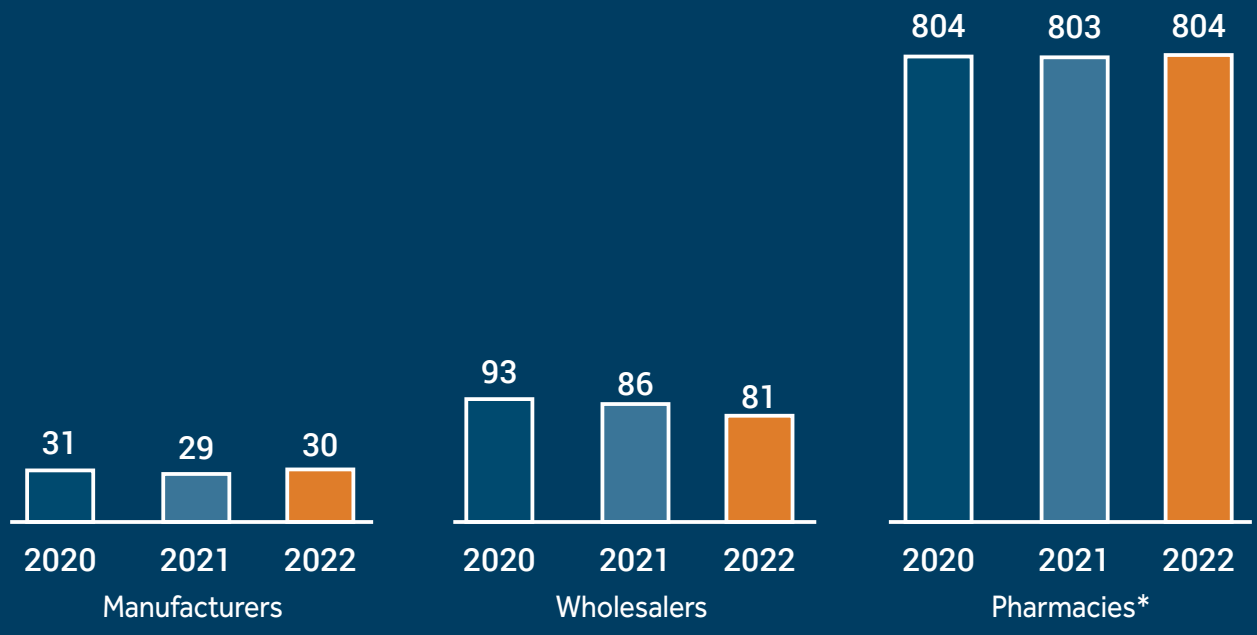
suspension of pharmaceutical activity licences and special activity permits in compliance with the procedure for reviewing such issues stipulated by the Commission's regulation.

The national state of emergency in the previous period of review, as well as the global situation due to the war in Ukraine in 2022 was a factor in the decision made by several licensed merchants to discontinue pharmaceutical activity.

In 2022, the following special permits (licences) were annulled:

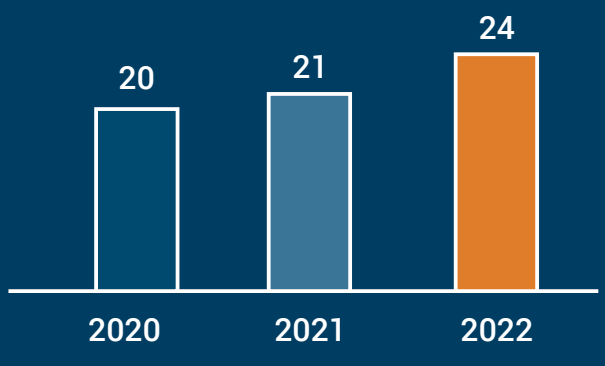
- **1** licences for opening a general pharmacy (activity);
- **7** licences for medicinal product wholesaler operation;
- **1** licences for manufacturing or import companies.

Total number of licensed pharmaceutical companies in Latvia (Data: December, 2022)

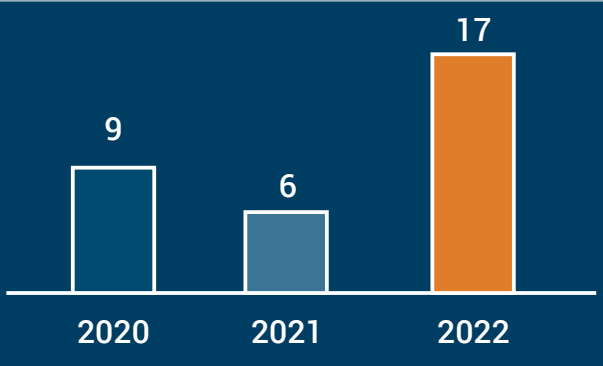


*Not counting pharmacies' structural units (in 2022 – 72 structural units; in 2021 – 73 structural units; in 2020 – 73 structural units; in 2019 – 77 structural units).

Total number of licensed of active substance manufacturers, importers and distributors (API) in Latvia (Data: December, 2022)



Authorisation of API (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 2022, we successfully continued on-site inspections, utilising also remote evaluation of documentation where possible – implementing EMA recommendations on principles of regulatory flexibility. Inspections in countries outside of EEA were not resumed."

In 2022, the Agency conducted Good Manufacturing Practice compliance on-site inspections of 14 companies (including 3 inspections related to issuance or renewal of licence) and 3 additional inspections of documents related to licence renewal. Within the framework of the cooperation agreement between the medicines agencies of the Baltic States, support was provided to the Estonian Medicines Agency by Agency's participating in the conduction of 1 inspection. Taking into account the significant reduction in expert resources and restrictions of travel abroad (including due to the war and COVID-19 pandemic) and safety risks in 2022,

Good Manufacturing Practice compliance inspections in manufacturing companies outside of EEA were not planned and not conducted.

The Agency also conducted 29 inspections of Good Distribution Practice of medicinal product wholesalers, 7 of which were related to issuance or renewal of licences and 3 additional inspections of documents related to licence renewal and 1 inspection related to authorisation of a medicinal product broker.

In addition, support was provided to the Agency's 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 authorisation of manufacturers, importers and distributors of active substances.

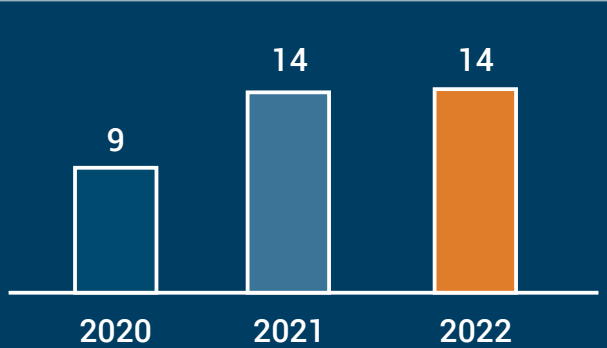
The Agency also conducted vigilance for utilisation of human biomaterial, collected data regarding the operation of tissue centres, procurement organisations/ transplantation centres of human organs, blood establishments and the State Blood Donor Centre (SBDC) and submitted reports to the EC, performed hemovigilance and biovigilance in relation to serious 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 2022:

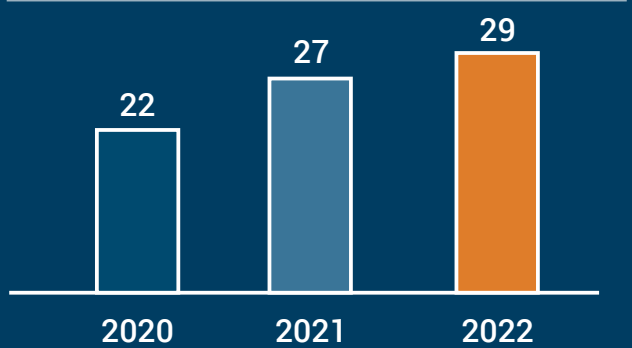
- The Agency received 3 applications for tissue centres compliance evaluation and issuance of permits related to variations, as well as received 1 applications for tissue centre compliance evaluation and issuance of new permit;
- The Agency issued 4 permits for tissue centres;
- The Agency annulled 4 permits for blood banks, suspended the permit for 1 blood bank.

Last year, the Agency also conducted 1 compliance inspection of a human blood and blood component establishment (on-site inspections were also conducted of 2 blood collection points in Riga and 2 regional units), 17 inspections of hospital blood banks and 8 inspections of tissue centres (including 2 inspections of centres for procurement of tissues and cells). The Agency also conducted 3 compliance inspections of documents – at 3 tissue centres in relation to changes in operation.

Good Manufacturing Practice inspections



Good Distribution Practice inspections



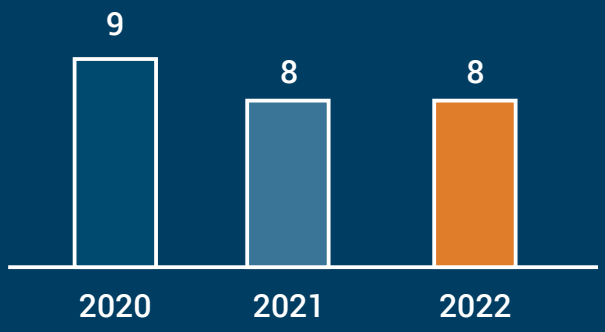
In 2022 inspections in transplantation centres of human organs and in higher education institutions providing a medical studies program were not planned and not conducted.

Experts from the Pharmaceutical Activities Compliance Evaluation Department prepared annual reports for EC regarding serious adverse reactions and serious adverse events in the field of blood, tissues and cells. Agency also ensured communication with healthcare treatment institutions regarding Urgent reports of serious adverse reactions and events received online, as well as reports in the Rapid alert systems maintained by the EC in the fields of tissues and cells (RATC) and blood (RAB).

Agency ensured representation in the EMA Good Manufacturing and Distribution Practice Inspectors Working Group, in the activities of PIC/S and European Commission 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 (JA11).

The Pharmaceutical Activities Compliance Evaluation Department specialists actively participated in the preparation of normative acts and amendments, including participation in the preparation of the national position on the EC's proposal for the regulation in the field of substances of human origin, and, in this context, the Agency participated as a technical expert in meetings organised by the Council of Europe and the Presidency on regulatory reviews in the field of human substances and pharmaceutical field and also submitted proposals. Department experts also submitted proposals to the Vigilance Expert Subgroup of National Competent Authorities regarding vigilance issues related to the review of blood and tissue/cell regulation.

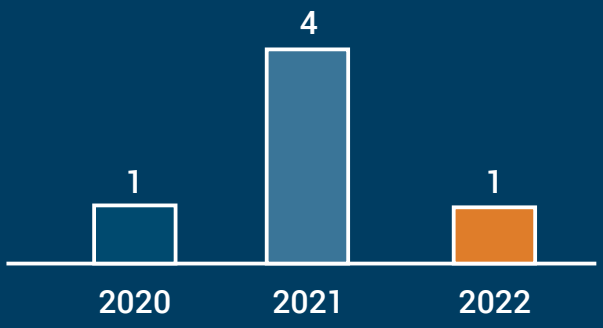
Inspections of tissue centres (and an organ transplantation centre*)



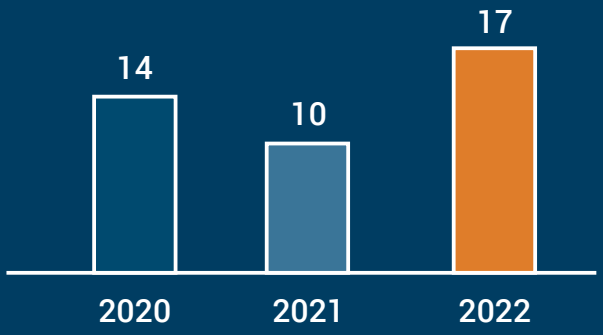
* In 2020, 1 tissue transplantation centre was inspected, but the remaining 8 inspections were conducted at tissue centres.

Compliance inspections of human blood banks and blood establishments

Blood establishments/ State Blood Donor Centre



Blood banks



INTERNATIONAL COLLABORATION

The Agency is a member of the network of the European medicines agencies. 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.

In 2022, Agency employees have collaborated with **EMA scientific committees, the European Commission and Council working groups, as well as working groups established by EDQM and Heads of Medicines Agencies (HMA), etc.**

EMA committees with Agency representation

- Committee for Medicinal Products for Human Use (CHMP)
- Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh)
- Pharmacovigilance Risk Assessment Committee (PRAC)
- Committee for Advanced Therapies (CAT)
- Committee for Orphan Medicinal Products (COMP)
- Committee on Herbal Medicinal Products (HMPC)
- Pediatrics Committee (PDCO)

The Agency participates in more than 30 international working groups, including EMA working groups dedicated to specific regulatory issues, for example, EMA CHMP Biologics Working Party, EMA Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG) and EMA Medical Devices Shortages Steering Group (MDSSG), EMA Working Group on Quality Review of Documents, Pharmacovigilance Inspectors Working Group, GMP/GDP Inspectors Working Group, International Cooperation Platform etc. The management of the Agency participated in the Management Group of the HMA.

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 2022, Agency's employees have been collaborating with EMA scientific committees, European 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.

See more information about the results of international cooperation in the report.

COMMUNICATION AND COLLABORATION

One of the main Agency's priorities last year was to ensure evidenceba-sed and reliable information regarding COVID-19 vaccines, their safety monitoring and adverse reactions, as well as availability of medicines.

Last year, the Agency provided regular and prompt updates in Latvian to the general public in Latvia about EMA news on COVID-19 vaccines and medicines, providing explanation that these vaccines are evaluated ac-cording to the same strict quality, safety and effectiveness standards as any other medicinal product.

PUBLICATIONS AND MEDIA

Last year, the Agency **published 181 articles** on its website's News section (in 2021 – **251 published news articles**).

In 2022, the Agency had intense collabora-tion with the media and all year round gave answers to media queries, providing scientific evidencebased and clarifying information.

Last year, an important part of providing information was reporting on suspected adverse reaction reports received in Lat-via after COVID-19 vaccine administration and evaluation of these reports. In 2022, in-creased informative activities were focused on raising awareness about medicinal prod-uct safety and adverse reactions.

The Agency published monthly information regarding the number of adverse reaction reports regarding COVID-19 vaccines and

overviews of safety of authorised COVID19 vaccines in Latvian. These overviews provided a summary of results from EMA safety committee's latest global safety data evaluation and included information from reports on suspected adverse reaction reports received in the EU that the EMA took into account in the evaluation process.

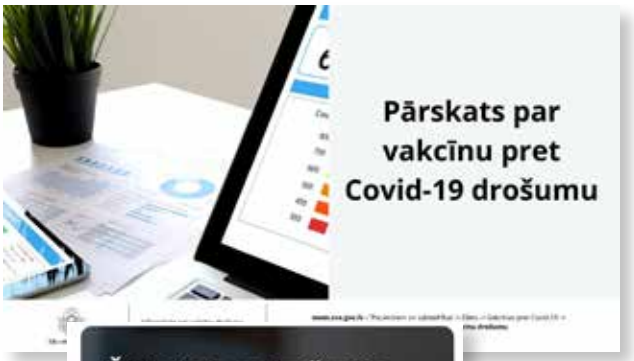
Examples of publications:

- First adapted COVID-19 vaccines recommended for approval in the EU
- EMA gives recommendations on use of monkeypox vaccine
- The Agency has finalised evaluation of 22 fatal cases after COVID-19 vaccine administration
- The Agency recommends first contacting your doctor in case of suspected adverse reactions to a COVID-19 vaccine
- The Agency recommends not to stockpile medicines and not to make individual donations of medicines to Ukraine

INFORMATION ON AGENCY'S WEBSITE

In order for the general public and healthcare professionals to have easy access to reliable and science-based information on authorisation and safety monitoring of COVID-19 vaccines, the Agency regularly updated and published the latest information regarding vaccines and their approval process, including reliable and science-based facts on vaccines.

Reliable and non-commercial information sources about COVID-19 vaccines and medicines were provided to the public in the dedicated sections "Patients and Public" and "COVID-19 News". In addition, reliable and qualitative information regarding COVID-19 vaccines was provided



to healthcare professionals in the website section "Healthcare Professionals".

Website traffic parameters:

- In 2022, Agency's website **had 1 120 876 visits**, excluding visits to the Medicinal Product Register and other Agency's databases that are regularly utilised mainly by the industry. In 2021, Agency's website **had almost 7.8 million visits**.
- In 2022, the Agency's website was used by 313 095 unique users.

BROCHURES, INFOGRAPHICS AND VIDEOS

- Informative brochure "Oocyte donation. A guide for women in making informed decisions"
- Informative brochure "Preserving fertility. A guide for persons affected by disease or life events affecting their fertility."
- Monthly report "COVID-19 vaccine safety update"
- Public report on Agency's operation in 2021
- Informative material regarding utilisation of biomaterials of human origin
- Informative brochure for the public and healthcare professionals "Compensation for harm to health caused by adverse reactions to COVID-19 vaccines" and infographics
- Infographic "Differences between a COVID-19 vaccine adverse reaction report and application for compensation for serious or moderate harm to patient health or life"

* Last year, the Medicinal Product Register was the most frequently used the Agency database/ register and had more than 4.5 million visits (4 560 039 visits).

- Infographic “Medicines safety monitoring”
- Infographics during “Medicines safety week (7-13 November 2022)”
- Infographic about evaluation of COVID-19 vaccine marketing authorisation applications
- Infographic “Update on COVID-19 vaccine adverse reaction reports”
- Infographic “COVID-19 vaccines in Latvia: marketing authorisation”
- Infographic “Medicines for COVID-19”
- Infographics during World Antimicrobial Awareness Week (“Do not use antibiotics for the flu or the common cold”, “Decrease of antibiotic use over the last 10 years”, “Rational use of antibiotics for protection of vulnerable groups”, “Antibiotic-resistant bacteria are here”, “Antimicrobial resistance is one of the biggest threats to public health worldwide”, “Talk to your children about antimicrobial resistance”)
- Infographic “What are biosimilars?”
- Infographic “Biosimilars in the European Union”
- Infographic “Medicines from other countries for personal use: how to carry into and out of the country, how to receive via postal mail?”
- Infographic “Achievements in 2021”
- Infographics “Consumption of generic and original medicines in 2021”
- Infographic “Monthly medicinal product consumption data”
- Infographic “Important information regarding COVID-19 vaccines”
- Video “How is vaccine safety monitored in the EU and how are adverse reaction

reports evaluated?"

- Video "Clinical trial conduct in the European Union"
- Video and infographics as part of the campaign "The nature needs no pill!"

CAMPAIGNS

- **Social media campaign during Medicines Safety Week**

In November 2022, the Agency together with 82 medicines agencies across the world carried out a public information campaign as part of Medicines Safety Week (#MedSafetyWeek2022) inviting to report suspected adverse drug reactions, i.e., health problems observed after administration of any medicine or vaccine that might be an adverse reaction to such medicine or vaccine.

In order to promote reporting of suspected adverse reactions, the Agency distributed informative videos and infographics on its social media profiles.

- **World Antimicrobial Awareness Week**

In support of World Antimicrobial Awareness Week activities, the Agency informed about the correct and safe use of antibiotics in order to increase awareness of bacterial resistance to antibiotics.

- **Campaign for vaccination against COVID-19,** providing information from a vaccine regulatory perspective in collaboration with EMA and the European Center for Disease Prevention and Control (ECDC) on an international level

As a result of this collaboration, regulatory information and explanations were provided regarding vaccines and medicines against COVID-19, their evaluation, development, effectiveness and use.

Last year, the Agency conducted informative activities within two projects. One of these projects was the **pilot project of Baltic medicines agencies for implementation of electronic package leaflets for medicines used in hospitals**. In 2022, the Agency also initiated distribution of informative materials for the project conducted by Lithuanian and Latvian experts "Pharmaceutical substances in waste water – amount, impact and options for minimisation" (MEDWwater).

SOCIAL NETWORKS

Every press release regarding vaccines and medicines against COVID-19 and other important information for raising public awareness was published on Agency's sites on social networks Facebook and Twitter.

The Agency also fought against disinformation, including on social media, to dispel the prevalent myths among the public regarding vaccines and their adverse reactions.

INFORMATION FOR HEALTHCARE PROFESSIONALS AND PHARMACISTS

Last year, we increased informative materials to healthcare professionals and persons performing vaccination regarding COVID-19 vaccines and their potential adverse reactions. Information was provided in seminars for healthcare professionals, informative articles and letters.

In 2022, we also released the publication "Cito!" for doctors, pharmacists and other healthcare professionals.

COLLABORATION WITH THE INDUSTRY

As part of implementing one of the Agency's priorities in 2022 – provide explanations of legal act requirements, last year the Agency organised informative seminars for the in-

dustry, covering the following topics:

- Health technology assessment
- Clinical and cost-effectiveness of medicines
- Latest amendments to normative acts
- Implementation of the new Regulation on *in vitro* diagnostic medical devices starting from 26 May 2022
- Clinical trial regulation

Explanatory regulatory information was also provided in informative news articles, letters and frequently asked questions, including explanatory information regarding requirements of normative acts. Last year, participation of industry representatives was ensured in various public discussions.

FEEDBACK

- **Employee survey** – aim: to find out employee opinions regarding work organisation, environment and collaboration, job satisfaction and other relevant aspects that would help to determine priorities in motivational aspects of personnel resource development;
- **Client and collaboration partner survey** – aim: to find out assessment of Agency's work and services provided in order to improve client service and quality of services based on these data.

Updated information was provided on the informative employee platform – the Intranet. More information regarding different achievements is available in the corresponding section of this public report.

IMPLEMENTATION OF AND AMENDMENTS TO NORMATIVE ACTS

Decisions adopted by the State Agency of Medicines are balanced, legal and compliant with the requirements of normative acts. In 2022, only 17 out of the 10 382 decisions adopted by the Agency were contested at the Ministry of Health, where one of the decisions adopted by the Agency in 2022 was repealed.

In 2022, the State Agency of Medicines in collaboration with the Ministry of Health prepared amendments to several normative acts that were reviewed and approved in 2022, for example:

- Amendments to the "Law on the Rights of Patients" to stipulate for Agency's rights to process patient data when adopting decisions regarding compensation in case of serious or moderately serious harm to health or life as a result of adverse reactions to authorised COVID-19 vaccines;
- Cabinet Regulation No. 272 of 3 May 2022 "Regulations Regarding Compensation for Serious or Moderately Serious Harm to the Health or Life of a Patient Inflicted due to Adverse Effects Caused by Vaccination against COVID-19 Infection". Justification for development – Part 1 of Section 49.7 of the Law on the Management of the Spread of COVID-19 Infection. Aim of regulation – to stipulate for the opportunity to receive compensation, if an adverse reaction to a COVID-19 vaccine has caused serious or moderately serious harm to a patient's health or life. Proposals for the changes required to other relevant external normative acts (Law on the Management of the Spread of COVID-19 Infection, Cabinet Regulation No. 537 of 31 July 2012 "Bylaws of the State Agency of Medicines") were prepared accordingly in order to harmonise them with the requirements of the new regulation;
- Cabinet Regulation No. 433 of 14 July 2022 "Amendments to Cabinet Regulation No. 436 of 26 June 2007 "Procedures for the Importation and Exportation of Medicinal Products"". The aim of these amendments was to clarify in the Cabinet Regulation No. 436 of 26 June 2007 "Procedures for

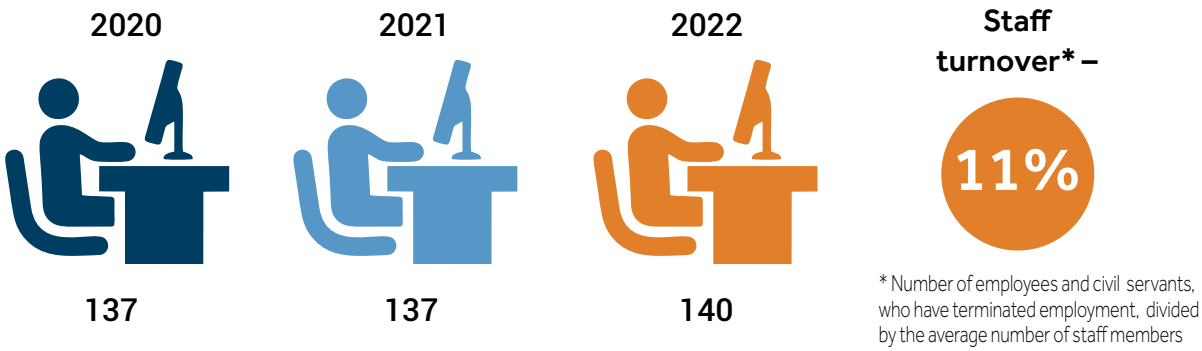
the Importation and Exportation of Medicinal Products" the procedure for import and export of investigational medicines and samples of medicines, surveillance of customs storage facilities and temporary storage sites in relation to other normative acts, as well as to make other required changes and technical amendments;

- Cabinet Regulation No. 46 of 18 January 2022 "Amendments to Cabinet Regulation No. 1037 of 27 December 2005 "Regulations Regarding Quality and Safety Standards for the Collection, Testing, Processing, Storage, and Distribution of Human Blood and Blood Components, Import and Export Conditions, and also Compensation for Expenditures for the Renewal of the Lost Volume of Blood"". The objective of these amendments was to improve the legal regulation and to better transpose the requirements of directives related to organisation and coordination of healthcare institutions in terms of supply with blood components and blood preparations compliant with quality requirements, as well as to clarify that the State Blood Donor Centre shall establish and submit to the Agency technologies for preparation and utilisation of blood and blood components.

In 2022, proposals and opinions regarding more than 35 normative acts were reviewed, prepared and provided to both the Ministry of Health and other state administration institutions.

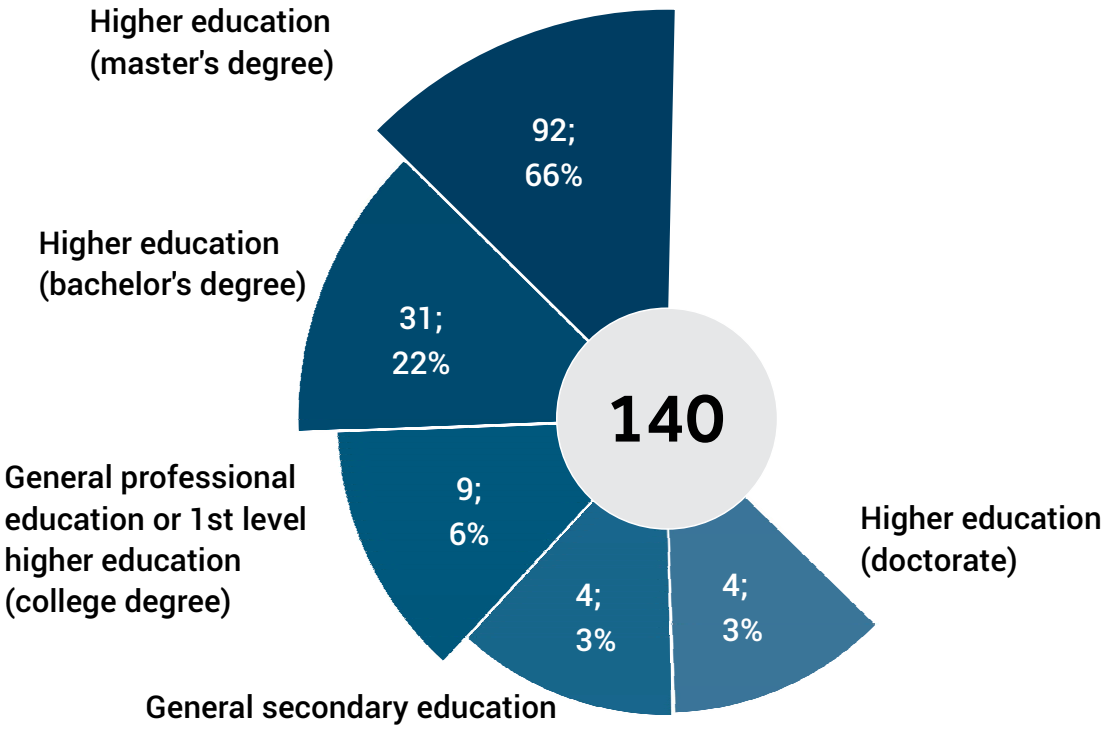
PERSONNEL MANAGEMENT AND TRAINING

ACTUAL NUMBER OF EMPLOYEES



There were a total of 147 employees under employment or civil service at the Agency.

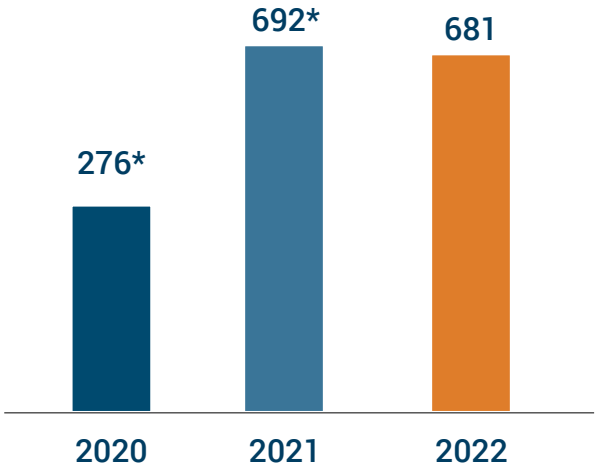
STAFF MEMBERS ACCORDING TO THE LEVEL OF EDUCATION (%)



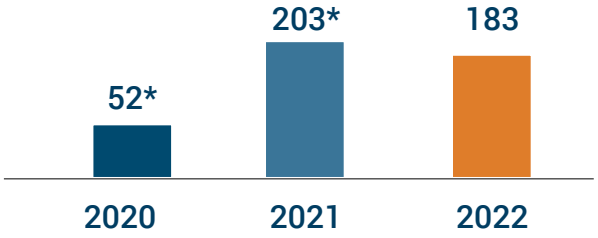
The overall level of education among Agency's staff is high – 136 employees (97%) have a higher education, and 4 of these employees have a doctorate degree.

PARTICIPATION IN COURSES FOR RAISING QUALIFICATION AND INTERNATIONAL SEMINARS, CONFERENCES

Courses for raising qualification



Seminars organised by international organisations



*In 2022, staff participation in training and international events was ensured according to demand. Most of the events, including training and international collaboration events, were organised remotely and free of charge. Employees had a wide range of opportunities to utilise the available resources independently without absence or additional financial expenses for the Agency.

RESULTS OF THE EMPLOYEE SURVEY IN 2022:

96%
of employees

were satisfied with the solutions for personnel management issues and the availability of relevant information (applications for vacations and other absences, business trip organisation, consultations and support for other personnel management issues);

96,5%
of employees

were satisfied with the work environment and solutions for household issues (work environment, technical condition of facilities, transport coverage).

MANAGEMENT OF INFORMATION AND COMMUNICATIONS TECHNOLOGY

In 2022, we continued to work on developing and streamlining our information systems and ICT solutions, as well as on improving accessibility and management. Last year, we executed 26 applications for ICT changes that facilitated improved work efficiency and provided substantial support to merchants, the public and employees.

Substantial changes were made to Agency's website:

- Changes to the publicly available Medicinal Product Register by allowing marketing authorisation holders to have access to the work versions of medicinal product summaries of product characteristics and package leaflets in Word format.
- Improvements were made to the preparation of open data in the Medicinal Product Register in order to ensure prompt corrections of inaccurate information and provide broader options for data publication in the future. At the same time, we have supplemented the missing information regarding medicinal product labelling and preparation of open data in JSON format.

In 2022, 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.

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 2022, 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.

A new EURS next generation program EURSnext was introduced in the medicinal product documentation evaluation system and user migration to its use in daily operation is taking place, allowing for more convenient and faster use of the necessary data.

ENERGY EFFICIENCY AT THE AGENCY

The Agency has a heating system with efficient gas heating devices that provide both hot water and heating of our facilities, as well as a diesel fuel generator with 270 kW of power that ensures continuity of Agency operation in case of disruption of electrical supply. On Agency's grounds we have also set up a solar power microgeneration station that ensures a minor electrical energy economy and energy supply autonomy.

The Agency continuously looks after the efficient use of its resources, ensuring sorting of glass, metal and PET materials, as well as batteries. In addition, the current lighting means are gradually being replaced with more energy efficient lighting solutions, and it has been ensured that employees use recycled paper in printing out work materials.

Currently we have initiated the project implementation for reconstruction of Agency's archive facility that we aim to finish by 2025, thus, increasing the building's energy efficiency to achieve an annual heating consumption of 33 kWh/m^2.

AGENCY'S STRATEGIC PRIORITIES IN 2023

1. **Authorise medicines in the interest of public health**;
2. **Provide professional services to clients, including national medicinal product manufacturers;**
3. **Availability of medicines to residents in Latvia: provide solutions and take action to ensure uninterrupted supply of medicines** (in collaboration with companies that authorised medicines and wholesalers);
4. **Provide updated information and data regarding availability and consumption of medicines;**
5. **Create national regulation in the pharmaceutical and healthcare field** by submitting proposals for the required amendments to normative acts;
6. **Represent Latvia in the preparation of an international (European) regulation in the fields of pharmaceutics and healthcare (SOHO);**
7. **Ensure implementation of new regulations:**
   - Establish a plan for implementation of Regulation (EU) No. 2021/2282 **on health technology assessment**, start the development of normative basis;
   - Implement the requirements of **Clinical Trial Regulation** (EU) No. 536/2014;
   - Implement Regulation (EU) 2017/745 on **medical devices** and Regulation (EU) 2017/746 on ***in vitro* diagnostic medical devices**;
   - **new regulation in the pharmaceutical field in Europe** and **on quality and safety standards for substances of human origin intended for human use,** participate in the development of regulation.
8. Implement in Latvia the common Baltic state project on use of electronic package leaflets (e-PIL) in healthcare institutions;
9. Ensure that **SAM participates in at least 30 EMA scientific committees and working groups of EU institutions;**
10. Improve the functionality of SAM information system by creating a **unified client portal;**
11. Ensure the conduct of EMA mutual benchmarking process (**BEMA V**) at SAM in order to ensure further improvements at SAM.

TASKS

1. Lead the working group on the necessity of artificial intelligence regulation, prepare proposals;
2. Establish a **list of critical medicines in Latvia;**
3. Establish a **minimal list of critical medicines** for state of emergency;
4. Create a **collaboration platform for pharmaceutical industry companies ensuring supply of medicines during crises;**
5. **Safety of medicines**: clarify the level of awareness of residents and healthcare professionals in Latvia, its changes over time;
6. **Promote patient compliance, participate in preparation of compliance programs** that may be implemented in the following planning period;
7. **Collaborate with the pharmaceutical industry**, establishing the following goals:
   - **Manufacturers in Latvia primarily choose DCP with Latvia as a reference member state;**
   - **Are informed** about the documents required for authorisation and the authorisation process.
8. **Provide support to national medicinal product manufacturers with respect to market expansion** (ensure scientific consultation, involvement of international experts, provide product certificates, etc.);
9. Hold at least **two informative client days** per year;
10. **Increase client survey representation** to at least 30% of participants within the field.

Appendix 1

BUDGET AND EXPENSES

		2020	2021	2022	
		Budget implementation, EUR	**Budget implementation, EUR**	**Budget estimate, EUR**	**Budget implementation, EUR**
1.	Resources for covering expenses (income)	6 102 023	6 733 920	6 681 007	6 741 347
1.1.	Paid services and other own income	5 265 476	5 364 714	4 994 313	5 369 016
1.2.	Foreign financial assistance	763 393	1 300 815	1 318 723	1 003 525
1.3.	Transfers from the State budget	73 154	68 391	367 971	368 806
2.	Expenses (total)	5 229 171	5 654 977	8 221 564	6 798 660
2.1.	Maintenance expenses	4 920 943	5 189 700	7 742 931	6 383 183
2.1.1.	Regular expenses	4 814 528	5 176 040	6 722 840	5 361 805
2.1.2.	Transfers for maintenance expenses	106 415	13 660	720 511	720 511
2.1.3.	Social payments and compensations			299 580	300 867
2.2.	Expenses for capital invesments	308 228	465 277	478 633	415 477
	Financial balance	**872 852**	**1 078 943**	**-1 540 557**	**-57 313**
	Financial resources	**2 174 729**	**3 253 672**	**1 540 557**	**3 196 359**

Appendix 2

A REPORT BY INDEPENDENT AUDITORS

Riga

The date of the document is the date of the electronic signature on the document **No.01/2023**

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 2022. The attached financial report includes:

- Report on financial situation on 31 December 2022 (balance);
- Report on the financial results of Agency's operation in the year concluded on 31 December 2022;
- Report on the changes in own capital in the year concluded on 31 December 2022;
- Report on the flow of Agency's financial resources in the year concluded on 31 December 2022;
- 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 for 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 2022, as well as of the financial results of its operation and flow of financial resources in the year concluded on 31 December 2022, 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 on public sector auditing (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 ethics 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 ethics 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 discrepancies 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 provides a truthful and clear impression 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 an internal control system that, in the opinion of the administration, is required for preparation of a financial report, which does not contain substantial discrepancies due to fraud or error.

Upon preparation of 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 in place 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 opin-

ion. 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 conduct of 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.

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Baiba Jēkabsone
Sworn Auditor
LZRA Certificate No 195
LLC „Auditorfirma Šķibele un Partneri"
Licence No 164

Līga Šķibele
Member of the Board
LLC „Auditorfirma Šķibele un Partneri"
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THIS DOCUMENT HAS BEEN SIGNED WITH A SECURE ELECTRONIC SIGNATURE AND INCLUDES A TIME STAMP

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