State Agency of Medicines of the Republic of Latvia

STATE AGENCY OF MEDICINES

ANNUAL REPORT

2014

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INTRODUCTION

Dear readers!

I am truly honoured to present you the report on the achievements of the staff of the State Agency of Medicines in 2014. Even though the previous period is marked by political changes, as well as amendments to the legislation regulating the field, the Agency has been able to successfully ensure the continuous process of change and maintain rigorous regulatory requirements and professional neutrality. Our task is not simple, because the clients of the Agency are very diverse and sometimes they have competing interests. First and foremost, the clients are the patients and the interests of the public that need to be balanced with the position of the State. However, the needs of the merchants are also important, as pharmaceutics is a strategically important field for both local and foreign merchants not only in the context of ensuring public health, but also for the development of the national economy.

By assessing the tasks of the Agency and the daily work in the present geopolitical context, it is clear that we have fully integrated in the network of European medicines agencies and in the common procedures of the scientific committees and working groups of the European Medicines Agency. It is also shown by the fact that in 2014 the Heads of the Medicines Agencies and the European Medicines Agency took the decision to create a unified strategy for the next period from 2016 until 2020, and the first meeting holding discussions on the strategy took place in Riga as part of the Latvian Presidency of the Council of the European Union. It was the Heads of the Medicines Agencies meeting on 5th February 2015, where we had planned a special work session for this purpose. It is important for the public to be informed and assured that the requirements for the quality, effectiveness

and safety of medicines are equal throughout Europe, including Latvia, and that they are ensured not only by the knowledge and experience of separate experts, but by a stable system with internationally recognised standards, common procedures and transparent adoption of decisions. In order to maintain the trust of the public and professionals the Agency's experts have to continue to be highly professional, independent and neutral, and any kind of pressure on the adoption of decisions guided by political or selfish motives is unacceptable.

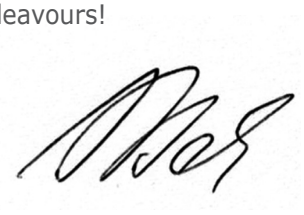
This is the second year when the State Agency of Medicines operates as a public agency that is not financed from the State budget. Its financial resources are ensured by the paid services provided in accordance with the price list approved by the Cabinet of Ministers. In other words, at the beginning of the year the institution does not receive financial resources from the State budget to ensure its primary functions. It also means that we are a State institution that has to actually earn and receive financial resources by providing qualita-

tive services to clients, and after that we can cover planned expenses. This is an even more complicated task, if you take into account that a large proportion of our clients are not residents of Latvia. In addition, it should be noted that our income is directly dependent on the amount of work, that is, requests for services, we have. Analysis shows that the income provided for by the Cabinet of Ministers regulation regarding paid services is overall sufficient, but it is not balanced with regard to ensuring separate functions. Therefore, we have requested a repeated evaluation of the proposal to provide budget grants to ensure specific tasks where the income will never be able to cover the costs. The establishment of this principle would correspond to the Good Management Practice and would ensure finances for the fulfilment of functions essentially important for the State. Consequently, it would be possible to decrease the amounts laid down in the paid service price list.

We are now working in a dynamically changing environment, in conditions, where patients and professionals, as well as merchants have considerable expectations with regard to the possibilities of using and developing new and innovative products. Agency's experts are involved in complex expertises and procedures also in the European Medicines Agency. International experience proves that the current conditions require acceptance of higher risk, accelerated marketing authorisation process or conditional marketing authorisations. We also consult our clients regarding innovative products, methods, new companies and the application of current legislation as soon as possible. Sometimes such issues cannot be managed by the Agency alone, but can be managed only in close collaboration with other institutions and scientific organisations. These are interdisciplinary tasks that require social intelligence and can be solved in multinational teams with a creative organisational and an adaptive approach. It is a significant added value to the economy and, therefore, support from the Ministry and the government is required.

Sustainable development, adequate capacity and motivated capability - these are the three main tasks of the Agency in the implementation of the annual work plan, as well as in the establishment of long-term strategic directions.

Best of luck in our endeavours!



Director of the State Agency of Medicines,
Inguna Adoviča

ABBREVIATIONS USED IN THIS REPORT

ADR	Adverse drug reaction
BEMA	Benchmarking of European Medicines Agencies
CDPC	Center for Disease Prevention and Control
CHMP	European Medicines Agency Committee for Medicinal Products for Human Use
CM	Cabinet of Ministers
CPP	Certificate of Pharmaceutical Product
CRP	Centralised registration procedure
DCP	Decentralised procedure
EMA	European Medicines Agency
EU	European Union
GCP	Good clinical practice
GDP	Good distribution practice
GMP	Good manufacturing practice
GVP	Good pharmacovigilance practice
IMS	Integrated Management System
INCB	International Narcotics Control Board
ISO	International Organization for Standardization
LATMED	Electronic database of the Register of Medical Devices
MAH	Marketing authorisation holder
MD	Medical device
MH	Ministry of Health
MRP	Mutual recognition procedure
NP	National Procedure
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PRAC	European Medicines Agency Pharmacovigilance Risk Assessment Committee
RMP	Risk management plan
SAM	State Agency of Medicines
SAMIS	State Agency of Medicines information system
VIC	Vaccine induced complications
WHO	World Health Organization

1. ABOUT THE STATE AGENCY OF MEDICINES

1.1. Legal Status of the State Agency of Medicines

The State Agency of Medicines (hereinafter also SAM) is a state institution under the supervision of the Minister of Health. The Minister of Health supervises the Agency through the Ministry of Health. SAM operation is regulated by the State Administration Law, the Law on Public Agencies, the Pharmaceutical Law, the Cabinet of Ministers Regulation No. 537 "Statutes of the State Agency of Medicines" adopted on 31st July 2012 and other normative acts.

SAM was established on 9th October 1996, based on the Cabinet of Ministers of the Republic of Latvia (hereinafter - CM) Order No. 403 "Regarding the Non-profit Organisation State Joint Stock Company "State Medicines Agency"". Jānis Ozoliņš was appointed as its first Director. Since 2nd November 2005 Inguna Adoviča has been the Director of SAM.

1.2. Functions of the State Agency of Medicines

The operational objective of SAM is to ensure qualitative and justified services in the evaluation of medicinal products used in healthcare, procurement and storage (utilisation) organisations 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.

SAM performs the following tasks:

- Evaluation and authorisation of medicines, expertise on quality of medicines, development and updating of the Medicinal Product Register of the Republic of Latvia.
- Pharmacovigilance.
- Issuance of authorisations for conduct of clinical trials with medicinal products, compliance evaluation of clinical trials with good clinical practice requirements, as well as evaluation of applications for non-interventional studies of medicines.
- Issuance of authorisations for import, export, transit, distribution and purchase (to ensure own operation) of medicines, as well as authorisations for use of plants, substances and medicines included in the lists of narcotic, psychotropic substances and precursors controlled in Latvia for medical and veterinary medical scientific research or training, as well as determining their physical and chemical properties.
- Regular assembly and distribution of information regarding consumption of medicines.
- Issuance of authorisation cards for precursor operators and special permits (licences) for operation with precursors.
- Authorisation of medical devices manufactured in Latvia, issuance of authorisations for placing specially supplied medical devices on the market, as well as vigilance for medical devices.
- Issuance of authorisations for conduct of clinical trials with medical devices.
- Issuance of compliance certificates to procurement and storage (utilisation) organisations of human tissues, cells and organs, blood establishments, hospital blood banks and the State Blood Donor Centre.
- Issuance of special permits (licences) for pharmaceutical activity.
- Issuance of good manufacturing practice compliance certificates.
- Evaluation and inspection of compliance of active substance manufacturers and

importers with the requirements of good manufacturing practice and issuance of good manufacturing practice certificates.

- Evaluation and inspection of compliance of active substance distributors with the requirements of good distribution practice and issuance of good distribution practice certificates.
- Registration of manufacturers, importers and distributors of active substances.
- Registration of persons conducting international business transactions with medicines for human use.
- Participation in the unified systems of medicines and medical devices agencies in the member states of the European Economic Area, cooperation with European institutions and international organisations by participating in work-sharing and complying with the collective standards and procedures.
- Collaboration with professional organisations of doctors and pharmacists, non-governmental organisations in the field, foreign and international institutions, as well as ensuring mutual exchange of information in the areas of operation of SAM.
- Fulfilment of the tasks of the competent authority in accordance with the requirements laid down in the normative acts of the European Union.
- Operation in the European medicines network by participating in work-sharing and complying with the collective standards and procedures, cooperation with other European and international organisations.

1.3. Main Objectives of the Year of Review

- The Work Plan of the Agency for 2014 was approved on 14th February 2014. The Work Plan lays down specific tasks for each structural unit and for the institution as a whole taking into account the functions and tasks delegated to SAM. In addition to the primary operation of SAM, in 2014 the following priority tasks were set for the year of review:
- Strengthen the capacity by participating in MRP/DCP authorisation processes as the Reference Member State, in EMA coordinated procedures and in expertise on master files of medicinal products as delegated by the European Directorate for the Quality of Medicines and Healthcare (EDQM).
- Implement the new pharmacovigilance normative acts, as well as carry out compliance inspections of pharmacovigilance systems.
- Develop the circulation of e-applications (e-CTD, CESP, LATMED) and electronic documents.
- Improve the internal audit system; complete the BEMA audit and ISO re-certification.
- Introduce the project management system.
- Ensure active communication also in social media.
- Prepare for the events planned as part of the Latvian Presidency of the Council of the European Union.

2. RESULTS OF OPERATION OF THE STATE AGENCY OF MEDICINES

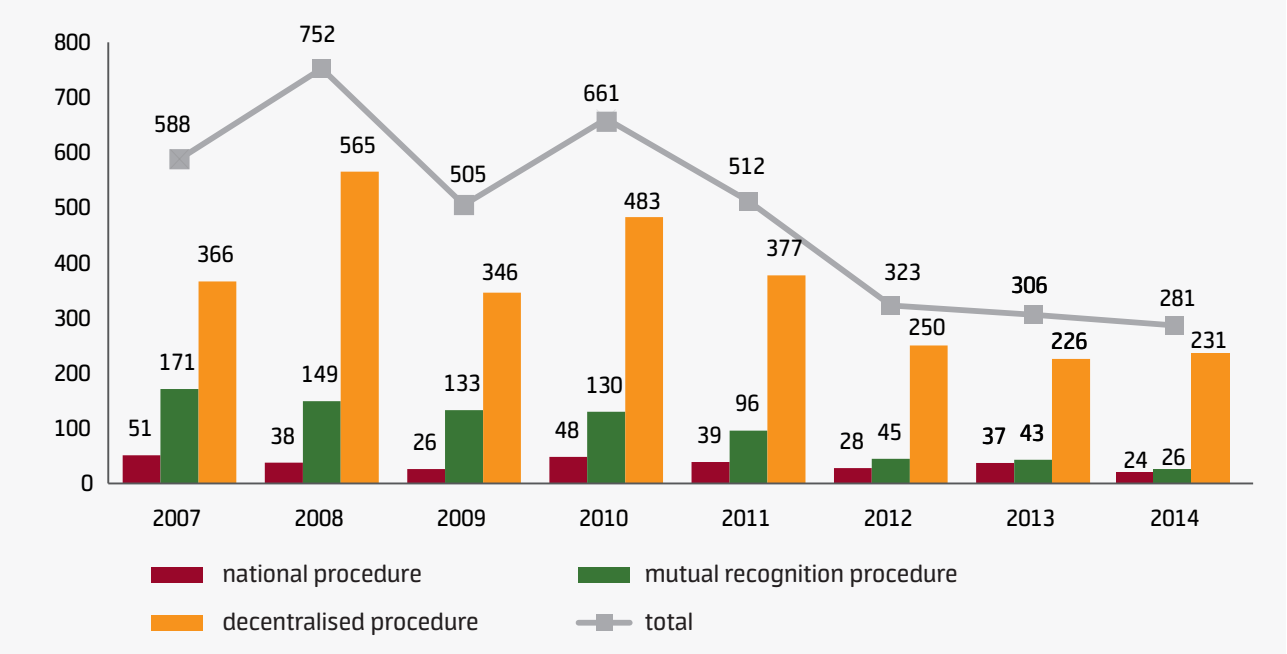
2.1. Marketing Authorisation of Medicines

To allow the State Agency of Medicines to provide more qualitative services and to utilise pharmacovigilance resources and the scientific resources of clinical experts in a more effective way, in 2014 the Human Medicines Evaluation Department and the Adverse Drug Reactions Monitoring Department were merged into a single structural unit.

In 2014 by evaluating documentation on quality, safety and effectiveness of medicines SAM has carried out expertise more than 2000 times on general, chemical and pharmaceutical, as well as preclinical and clinical sections of the documentation of medicines. Assessment reports on 48 medicines have been prepared for the SAM Commission on Marketing Authorisation of Human Medicines for adoption of a decision regarding marketing authorisation and renewal of medicines in the national procedure. In 2014 Latvia has successfully led one mutual recognition procedure (MRP) and five decentralised procedures (DCP) as a Reference Member State. Also in 2014 Latvia has taken over five DCP procedures from other member states, thus, becoming the Reference Member State for these procedures. In 2014 Latvia initiated three DCP and one MRP marketing authorisation procedure, and two MRP renewal procedures. 257 DCP/MRP authorisation procedures and 215 renewal procedures have been carried out in 2014.

In the year of review SAM expert activity in international procedures has been higher than in the previous year. In 2014 Latvia participated in the EMA Committee for Medicinal Products for Human

MARKETING AUTHORISATION OF MEDICINES



Use (CHMP) by evaluating five centralised marketing authorisation procedures. In two of those centralised marketing authorisation procedures the team from the State Agency of Medicines was the responsible rapporteur of the medicinal product documentation.

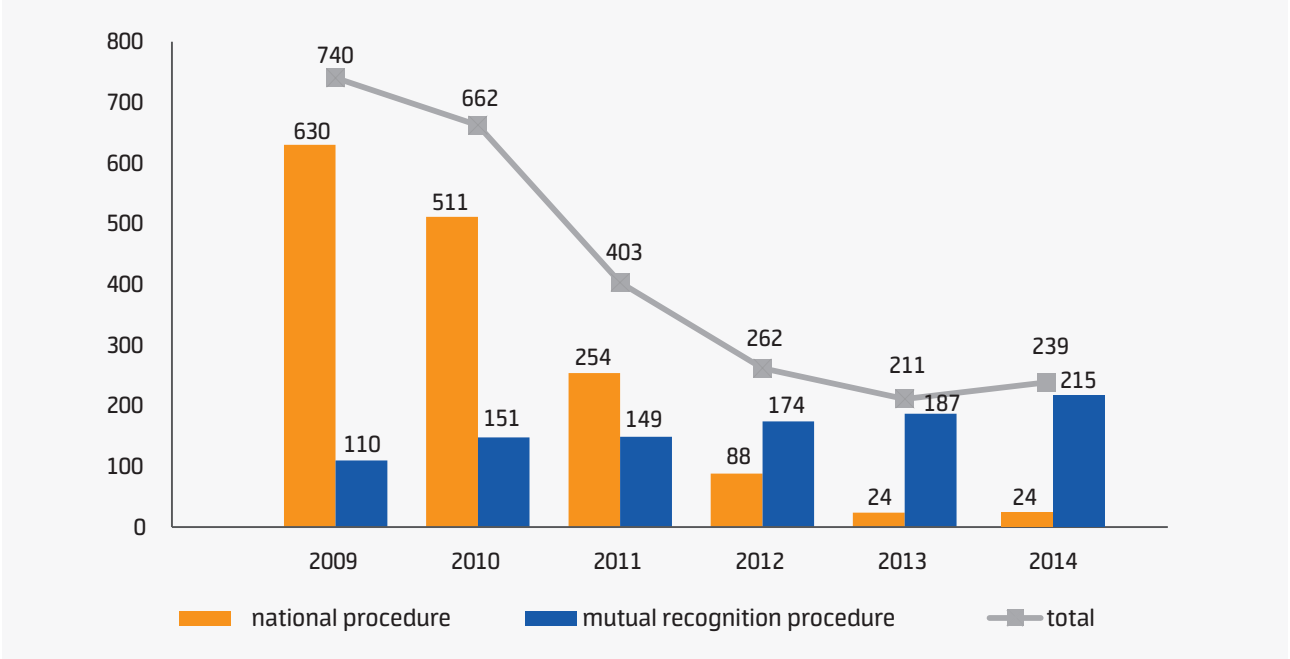
Latvia is represented in the EMA Paediatric Committee and has participated in 10 PIP (Paediatric Investigation Plan) procedures as a rapporteur, and in 3 procedures - as a co-rapporteur, as well as in 4 PIP modification evaluations as a rapporteur.

SAM internal and external experts successfully led a paediatric work-sharing procedure of the MRP and DCP coordination work group for the varicella vaccine by evaluating the documentation in accordance with Article 46 of the Paediatric Regulation.

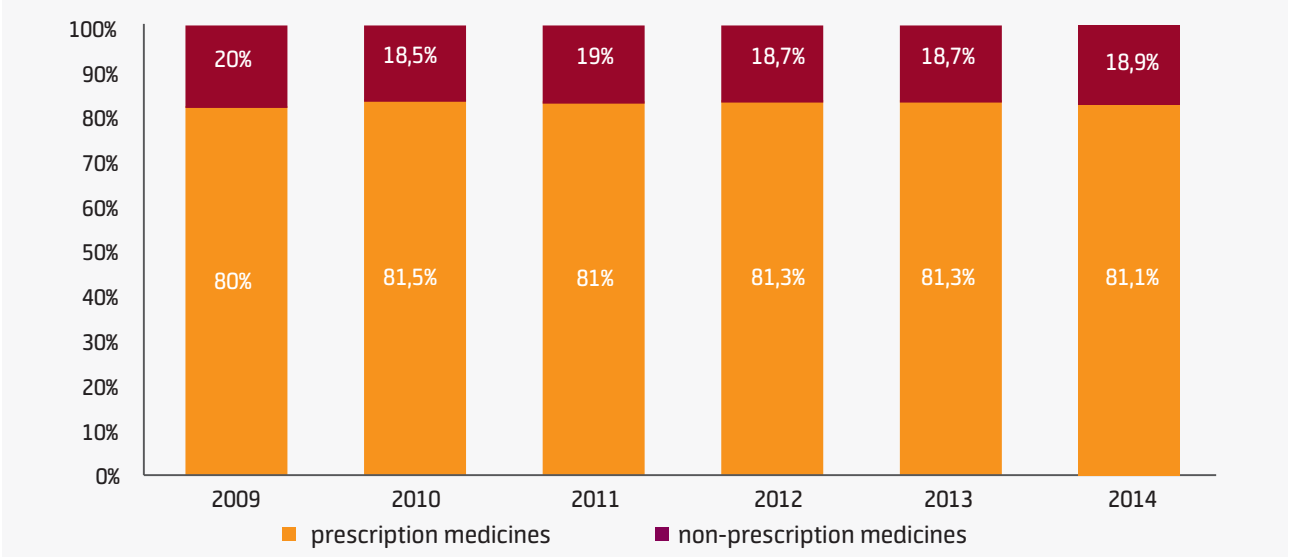
Experts from the Human Medicines Evaluation Department together with external experts actively participated in the work of the Committee on Herbal Medicinal Products. In 2014 the 5-year review procedure for the Union monograph on *Eleutherococcus senticosus (Rupr. et Maxim.) Maxim., radix* was successfully led and the development of a new Union monograph on *Ononis spinosa L. Radix* was completed. Also a new evaluation procedure for the Union monograph on *Polygoni avicularis herba* was initiated.

Even though there is a decreasing trend in the

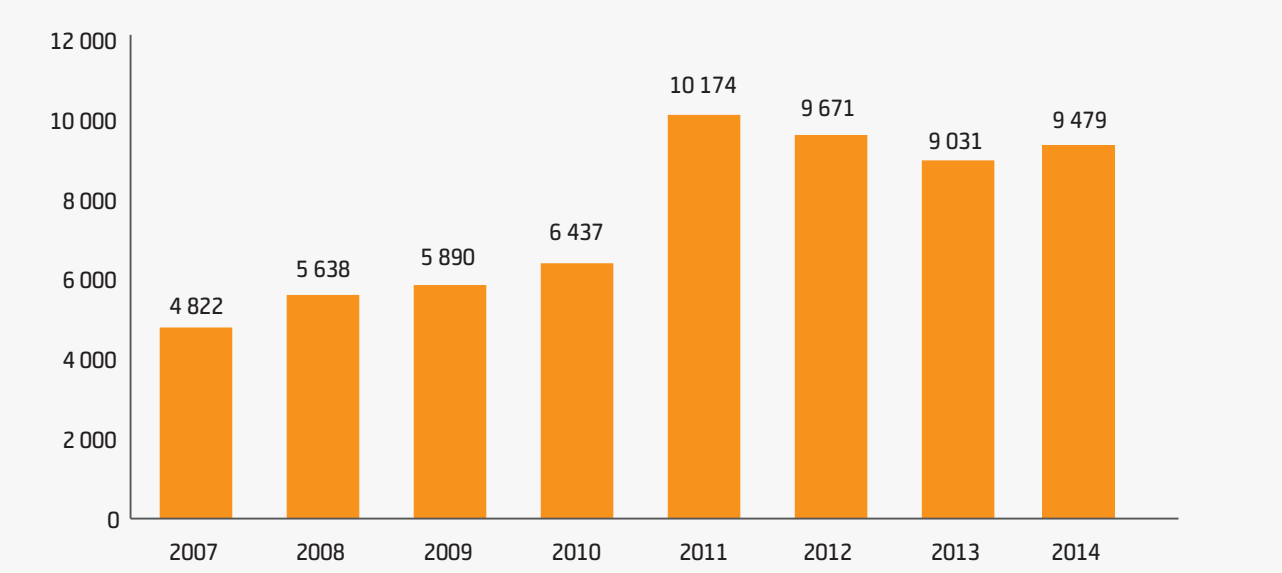
RENEWAL PROCEDURE OF MEDICINES



PROPORTION OF PRESCRIPTION AND NON-PRESCRIPTION MEDICINES



VARIATIONS TO THE MARKETING AUTHORISATION DOCUMENTATION



total number of medicines in the Medicinal Product Register of the Republic of Latvia, the proportion of prescription and non-prescription medicines has remained the same.

9479 variations to the documentation of authorised medicines were submitted and evaluated in 2014.

In the year of review 39 applications were received for the evaluation of compliance with the definition of medicinal products and SAM issued its opinion regarding the status of these products. 148 periodic safety update reports were evaluated in 2014. 8 public assessment reports for nationally authorised medicines were prepared, coordinated with marketing authorisation holders and published in 2014.

2.2. Issuance of Authorisations for Distribution of Medicines

In 2014 within its competency SAM ensured monitoring of distribution of medicines in Latvia, provided consultations to clients and collaboration partners regarding distribution of medicines and carried out expertise on applications and documentation regarding:

- Import and export of psychotropic, narcotic medicines/substances and precursors.
- Distribution of unauthorised medicines.
- Import of samples of medicines.
- Distribution of remaining stock of medicines.
- Distribution of parallel imported medicines in Latvia and their variations.

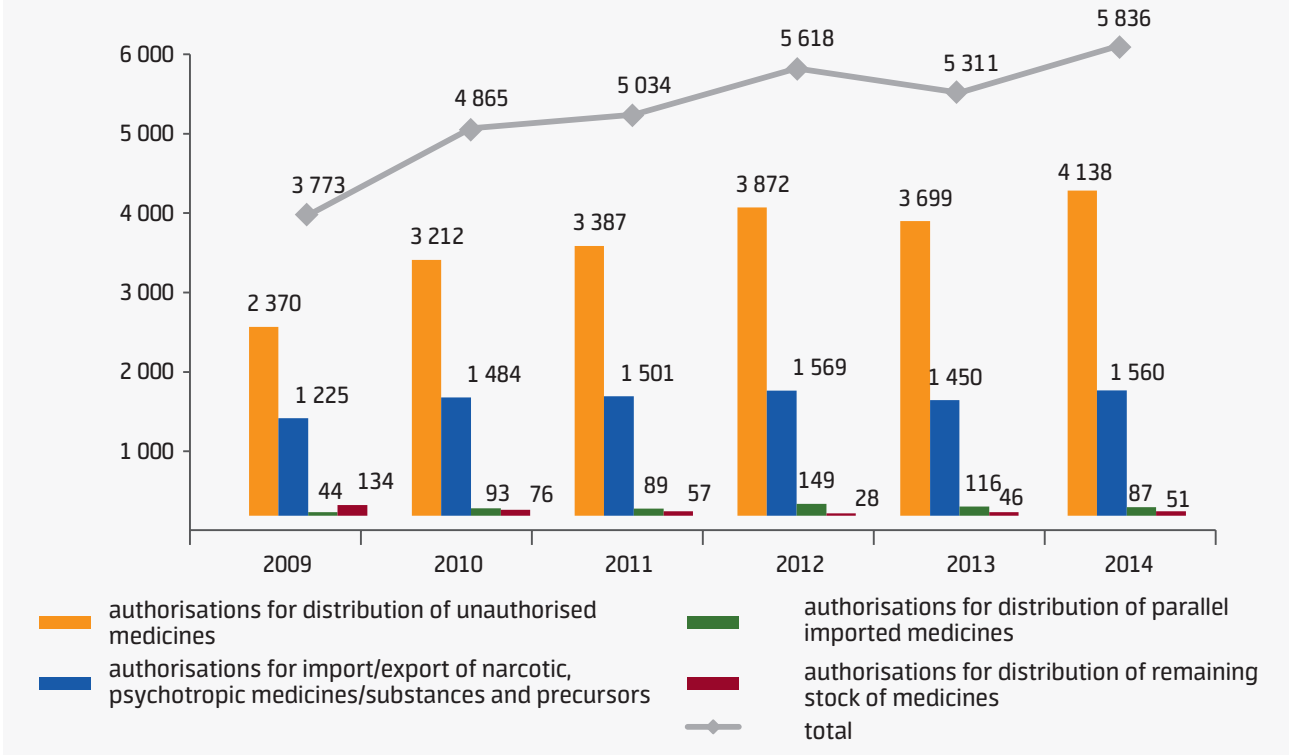
In 2014 SAM issued 5849 authorisations for import, export and distribution of medicines. This includes 4138 authorisations for distribution of unauthorised medicines, 87 authorisations for distribution of parallel imported medicines and 51 authorisations for distribution of remaining stock of medicines after the withdrawal of the medicinal product from the Medicinal Product Register of the Republic of Latvia.

In addition to the aforementioned functions SAM carried out expertise on applications for:

- Special permits (licences) for operation with precursors and issuance of precursor operator cards.
- Use of plants, substances and medicines included in the I, II and III list of narcotic, psychotropic substances and precursors controlled in Latvia for medical and veterinary medical scientific research or training, as well as determining their physical and chemical properties.
- Purchase of medicines (to ensure own operation).

In the year of review four precursor operator authorisation cards were issued to precursor operators and four authorisations were issued for use of plants, substances and medicines included in the I, II and III list of narcotic, psychotropic substances and precursors for medical and veterinary medical scientific research or training, as well as determining their physical and chemical qualities. Variations were made to marketing authorisations of 185 parallel imported medicines.

NUMBER OF AUTHORISATIONS FOR MEDICINES IMPORT, EXPORT AND DISTRIBUTION 2009 - 2014



SAM ensures the recording and control of legal circulation of narcotic substances, psychotropic substances and precursors controlled in Latvia. SAM prepares 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 and forwards them to the International Narcotics Control Board (INCB). SAM also prepares a quarterly report on the circulation of illegal precursors and an annual report on the circulation of legal precursors and forwards them to the European Commission.

SAM regularly assembles and updates the information in the Medicinal Product Register regarding availability and prices of medicines, collects and processes data regarding the turnover of pharmacies, wholesalers and manufacturing companies. Every month SAM compiles statistical information regarding consumption of medicines submitted by wholesalers and once a year prepares a publication "Statistics on Medicines Consumption" that is published on SAM website.

It has to be noted that SAM continuously prepares and provides recommendations to the Ministry of Health and via its mediation also to the European Commission for amendments to normative regulations regarding distribution of medicines. SAM provides routine consultations to clients regarding availability and prices of medicines, as well as interpretation of regulatory requirements.

2.3. Clinical Trials with Medicines

In 2014 SAM received 56 applications for clinical trial projects for medicines, including 15 clinical trial applications in the international harmonisation procedure (in accordance with the European guidelines regarding the voluntary harmonisation procedure for the assessment of multinational clinical trials). After carrying out expertise on application documentation and after evaluating the benefits and risks SAM employees from the Clinical Trials Department adopted decisions regarding the approval of clinical trials in 26 department meetings. In 2014 SAM issued a total of 53 authorisations for initiation of clinical trials in Latvia. An authorisation was denied for one clinical trial, but it was granted after a repeated application was submitted with a significantly modified trial design. Applications of twelve authorised clinical trials were evaluated in the international voluntary harmonisation procedure before they were submitted nationally.

Three clinical trials (in the field of neurology and infectology) planning to involve children and adolescents were authorised in 2014.

Out of all the clinical trials authorised in 2014, 12 clinical trials planned to investigate medicinal products obtained with recombinant DNA technology (monoclonal antibodies, hormones) and intended for the treatment of various autoimmune,

oncological, hematologic and cardiac diseases.

217 authorisations were issued for significant amendments to clinical trial protocols or other clinical trial related documentation. 33 variation applications were received in the international voluntary harmonisation procedure.

Information regarding applications for clinical trials with medicinal products, the time of their authorisation, the dates of approval of applications for significant 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*. It is necessary to regularly ensure the aforementioned data for the maintenance and updating of the European Clinical Trials Register.

Department employees ensured electronic data exchange in the *EudraVigilance* system by forwarding confirmation of receipt of safety reports concerning clinical trials in Latvia to clinical trial sponsors that had submitted safety reports in the Clinical Trial Module of the *EudraVigilance* database according to European and local normative requirements. 60 reports were received in the year of review regarding serious adverse drug reactions observed at clinical trial centres in Latvia. These reports were analysed and included in a register established by SAM. In total SAM received, reviewed and registered 152 annual safety reports prepared by sponsors regarding clinical trials conducted in Latvia. Separate annual safety reports were deeper analysed and the assessment is reflected in an established appropriate format.

10 external experts were involved in the evaluation of documentation of authorised projects, conducting expertise on a total of 13 cases.

A total of 267 clinical trials were conducted in Latvia in 2014. 47 projects were completed.

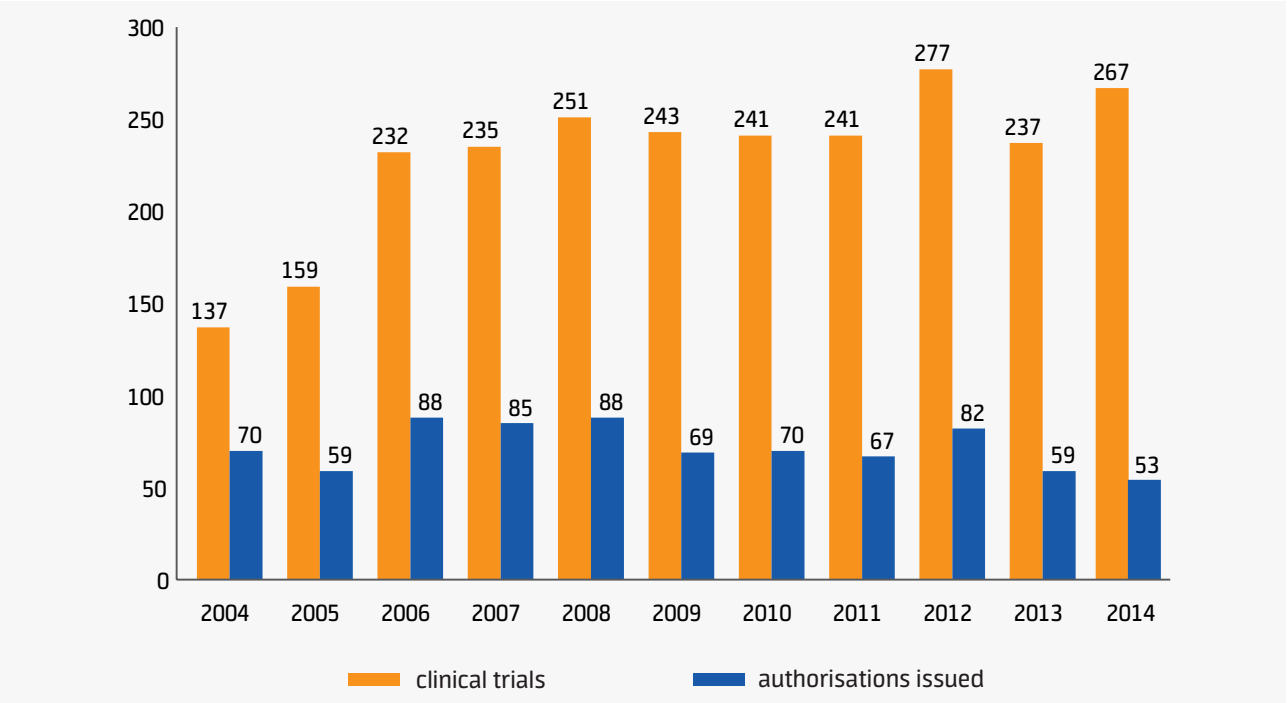
The authorised clinical trial projects were sponsored by 38 foreign pharmaceutical companies. In accordance with the power of attorney from the sponsors, the following contract research organisations were involved in organising and ensuring the quality of conduct of clinical trials in Latvia in 2014: *Amber CRO* (6 projects), *Quintiles* (5 projects), *Pharm-Olam International* (4 projects), *Parexel International* (3 projects) and 11 other contract organisations (1-2 projects each).

Four inspections of clinical trial compliance with good clinical practice were carried out in 2014. Two inspections were conducted in trial centres in Latvia, but two other inspections - in other countries. Both high importance and other deficiencies were disclosed during the inspections.

Two applications for non-interventional studies were submitted in 2014 and an authorisation was granted for one of them.

In the year of review employees of the SAM Clinical Trials Department participated in the development of the regulation of the European Parliament and of the Council, as well as of the European

NUMBER OF AUTHORISATIONS ISSUED AND CLINICAL TRIALS WITH MEDICINES (2004-2014)



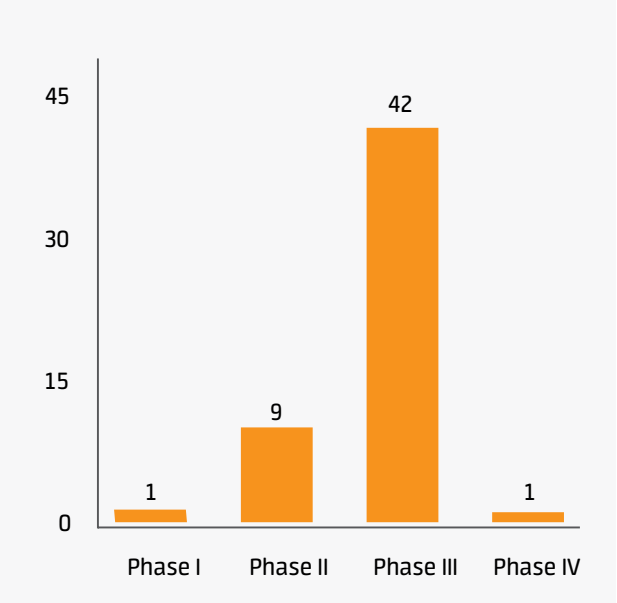
NUMBER OF CLINICAL TRIALS WITH MEDICINES AUTHORISED IN 2014 ACCORDING TO MEDICAL SPECIALITY

Medical speciality	Number of clinical trials
Gastroenterology	8
Rheumatology	7
Pulmonology/Allergology	6
Oncology	6
Infectology	6
Cardiology	5
Urology/Nephrology	4
Psychiatry/Neurology	4
Dermatology	3
Endocrinology	2
Reproductive Health	2

CLINICAL TRIAL CENTRES OF THE CLINICAL TRIALS WITH MEDICINES AUTHORISED IN 2014 (79 TRIAL CENTRES)

Clinical trial centre	Number of clinical trials
P. Stradins Clinical University Hospital	29
Riga Eastern Clinical University Hospital	21
• Clinical hospital „Gailezers"	11
• Latvian Oncology Center	6
• Clinic "Bikernieki", State Burn Centre	3
• Clinic "Tuberculosis and Lung Disease Centre"	1
Daugavpils Regional Hospital	14
Liepaja Regional Hospital	11
Latvian Maritime Medicine Centre	8
LLC "Riga 1st Hospital"	7
JSC "Health Centre Union", medical centre "OLVI"	6
Digestive Diseases Centre "Gastro"	6
Health Center 4	5
LLC "Vidzeme Hospital"	5
Clinic "ORTO"	5
Other clinical trial centers (64 in total)	1 - 4 trials at each centre

NUMBER OF CLINICAL TRIALS AUTHORISED IN 2014 ACCORDING TO PHASE



Commission on clinical trials with medicinal products and the related normative acts and portal.

On 11th November 2014 an informative seminar took place at SAM for collaboration partners regarding clinical trials in Latvia and the new clinical trials regulation. 54 persons attended the seminar.

2.4. Monitoring of Adverse Drug Reactions and Risk Minimisation

SAM has been maintaining the database for adverse drug reactions observed in Latvia since 2001 and since 2004 the reported information is being forwarded to the European Union database *EudraVigilance* for identification of new risks with medicines. Each year SAM analyses the information entered in the database in Latvia and the reporting activity in Latvia.

The adverse drug reaction reporting activity in Latvia decreased in 2014. The number of clinical cases reported to the State Agency of Medicines also decreased.

Doctors and pharmacists submitted fewer reports than in the previous years. The Centre for Disease Prevention and Control (CDPC) also submitted less data regarding adverse reactions to vaccines. This could be explained by the clarification of reporting criteria for the data exchange regarding serious adverse reactions between the CDPC and SAM.

The reporting activity among marketing au-

thorisation holders (MAHs) remained stable in comparison with the previous year.

In 2014 SAM carried out 8 good pharmacovigilance practice inspections of MAHs.

In 2014 pharmacovigilance experts carried out evaluations of periodic safety update reports regarding 2 active substances as part of work-sharing procedures where Latvia was the Reference Member State. This was done in accordance with the EU work-sharing procedure (Periodic Safety Update Reports Worksharing), which includes the assessment of periodic safety update reports for the necessities of the whole European Union.

During the year periodic safety update reports were evaluated for 148 nationally authorised medicines and their assessments with recommendations regarding necessary actions were forwarded to the marketing authorisation holders.

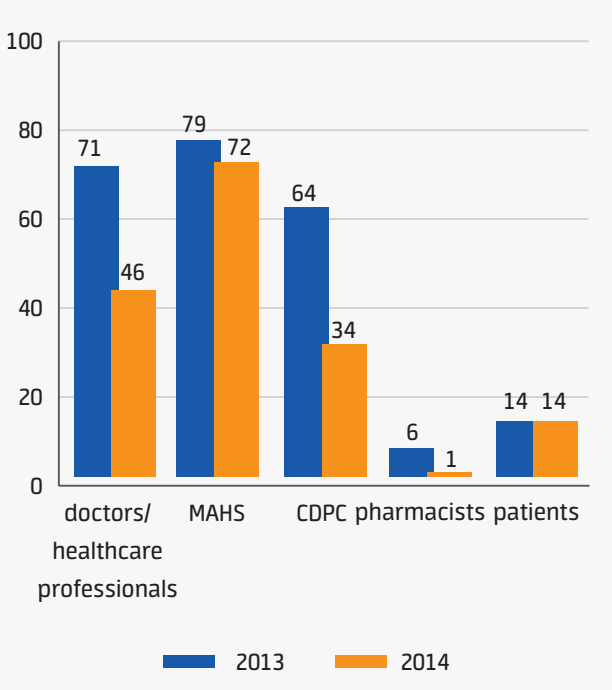
The number of risk management plans (RMPs) submitted for evaluation was greater than in the previous year. RMP related documentation was evaluated for a total of 43 MAH applications.

SAM operates in collaboration with the Qualified Persons Responsible for Pharmacovigilance for MAHs. This also ensures that the MAH developed risk minimisation measures are implemented in Latvia, including the necessary communication with healthcare professionals, patients and the public regarding the safe use of medicines. SAM approves all of the projects for "Direct Healthcare Professional Communication" letters (DHPCs) and the educational material projects for risk minimisation submitted by MAHs.

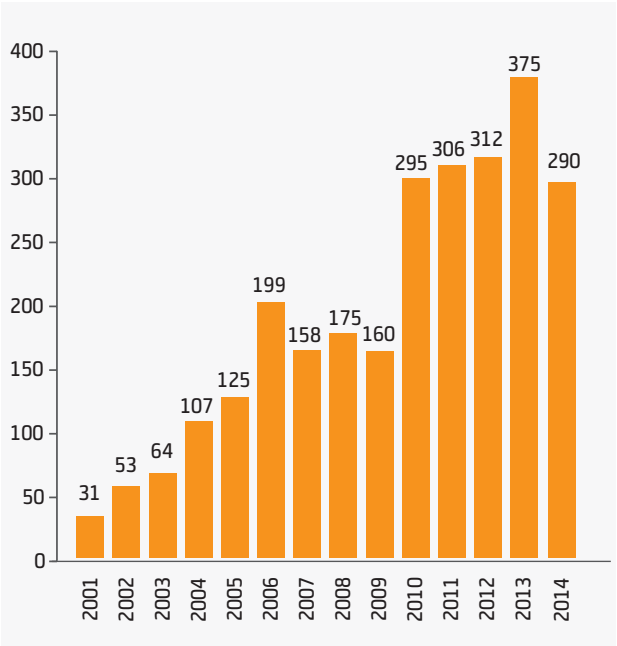
In the period of review expertise was carried out on 70 educational materials for risk minimisation in relation to the use of medicines and 30 MAH submitted DHPCs were approved.

Information regarding safety of medicines in-

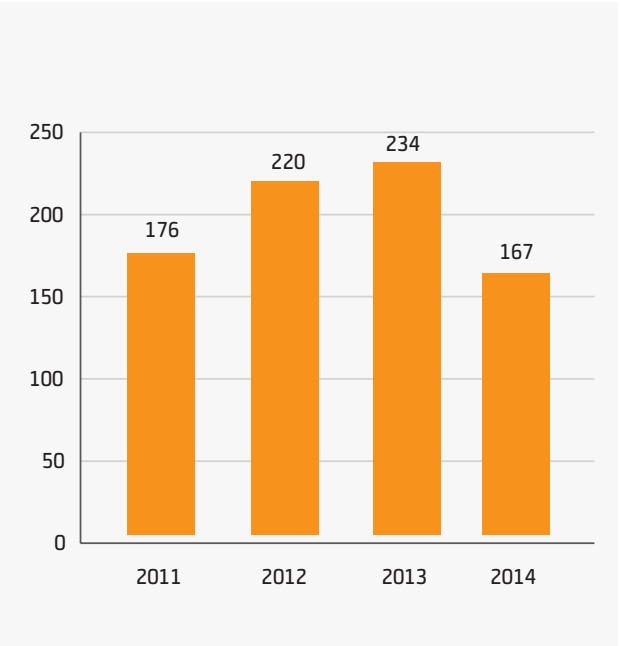
ADVERSE DRUG REACTION REPORTS ACCORDING TO PROVIDER OF INFORMATION IN 2013 - 2014



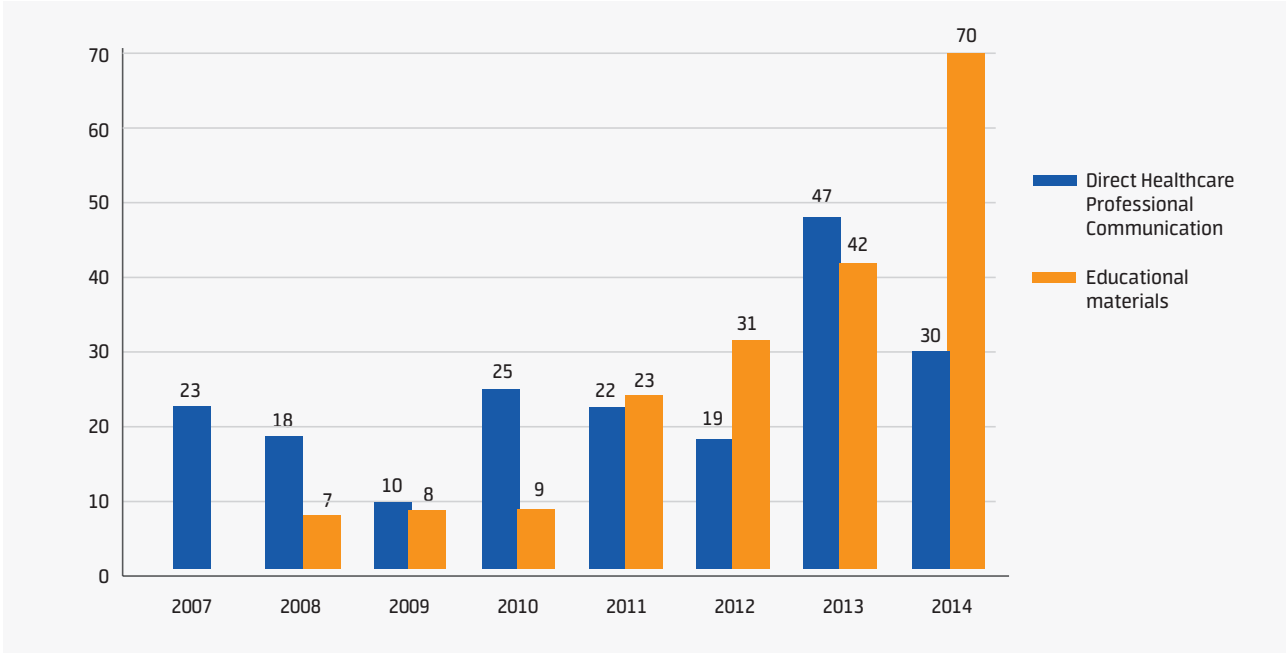
ADVERSE DRUG REACTION REPORTS 2001-2014



CLINICAL CASES OF ADVERSE EVENTS WITH MEDICINES



APPROVAL OF INFORMATIVE RISK MINIMISATION MEASURES



tended for doctors, patients and the public, as well as for MAHs was published on SAM website in collaboration with Public Relations specialists. This included five announcements regarding safety issues with medicines raised by EMA, two announcements regarding approval of medicines safety information, two announcements regarding new pharmacovigilance normative acts, 12 informative announcements for MAHs, 30 SAM approved "Direct Healthcare Professional Communication" letters, information regarding additional educational materials for 70 medicinal products approved by SAM.

Information about current issues regarding safety of medicines and recommendations regarding necessary risk minimisation measures are regularly provided in the SAM informative bulletin *"Cito!"* for healthcare professionals and pharmacists.

2.5. Quality Control of Medicines

In 2014 SAM Laboratory carried out analysis of 135 samples of medicines. In the process of analysis 844 quality criteria were tested. 760 volumetric solutions, indicators and reagents were prepared upon request from pharmacies. 106 samples of purified water produced in pharmacies were selected and tested in 2014. Non-compliance with the requirements of the European Pharmacopoeia was discovered in two samples of purified water. Upon request from the Human Medicines Evaluation Department expertise was carried out on 15 names of medicinal products evaluating the methods of analysis of the active substance and/or final product and their validation.

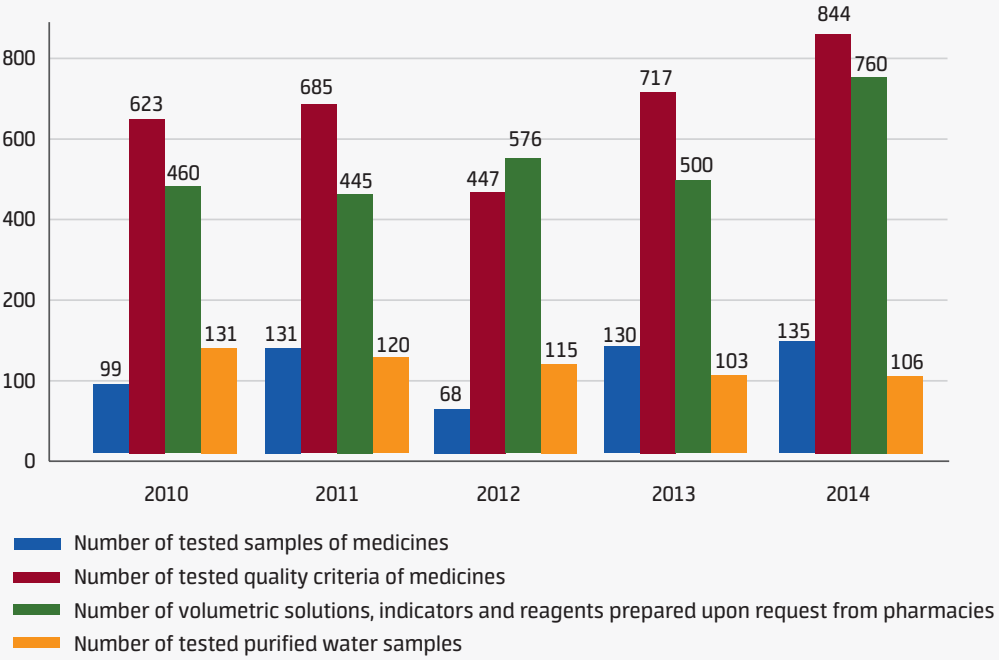
Amendments to the CM Regulation Nr. 416 of 26th June 2007 "Procedures Regarding the Distribution and Quality Control of Medicinal Products" came into force on 1st October 2012 (determining regular quality control of non-sterile pharmaceutical forms of medicinal products). Because of this amendment, in 2014 the emphasis was on the quality control of non-sterile pharmaceutical forms of medicinal products, similarly as in 2013.

The criteria for selecting medicinal product samples for testing were based on the potential risk to public health, that is:

- A great quantity of the medicinal product on the market.
- Medicinal products for which samples had not been tested in the last five years.
- Medicinal products with a low level of active substance.
- Medicinal products for long-term use.
- Parallel imported medicinal products.
- Unauthorised and patent-free medicinal products.
- Medicinal products where samples had previously shown quality deficiencies.

SAM Laboratory regularly participates in international programs for quality control of medicines and professional level evaluation programs. In 2014 SAM Laboratory specialists participated in quality control programs for medicines authorised in the centralised authorisation procedure (CAP), mutual recognition procedure and decentralised procedure (MRP/DCP) and the national procedure

RESULTS OF OPERATION OF THE MEDICINES EXAMINATION LABORATORY

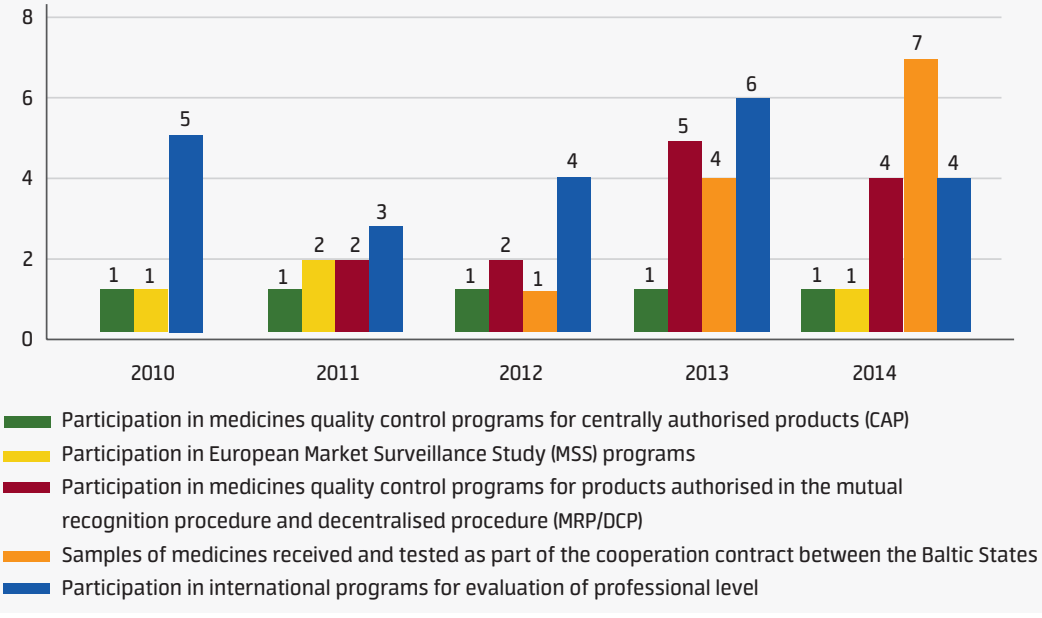


(in accordance with the collaboration agreement between the Baltic states), as well as in the European Market Surveillance Study (MSS) program.

A routine monitoring visit by the Latvian National Accreditation Bureau took place on 10th June 2014. The Laboratory maintained the accreditation regarding compliance with the requirements of the LVS EN ISO/IEC 17025:2005 standard: physical and physical-chemical testing of medicines, pharmaceutical active ingredients and excipients (fixed and flexible field), physical testing of purified water (fixed field). The expiration date of the accreditation of the Laboratory is 16th June 2018.

A project was initiated in 2014 with the objective of implementing the measures necessary for ensuring the sterility testing in the laboratory, including the construction of class D cleanrooms, purchasing and setting up an isolator and other relevant equipment and training. Laboratory employees are involved and actively participating in the implementation of the project.

PARTICIPATION IN INTERNATIONAL PROGRAMS FOR QUALITY CONTROL OF MEDICINES AND PROFESSIONAL LEVEL EVALUATION PROGRAMS

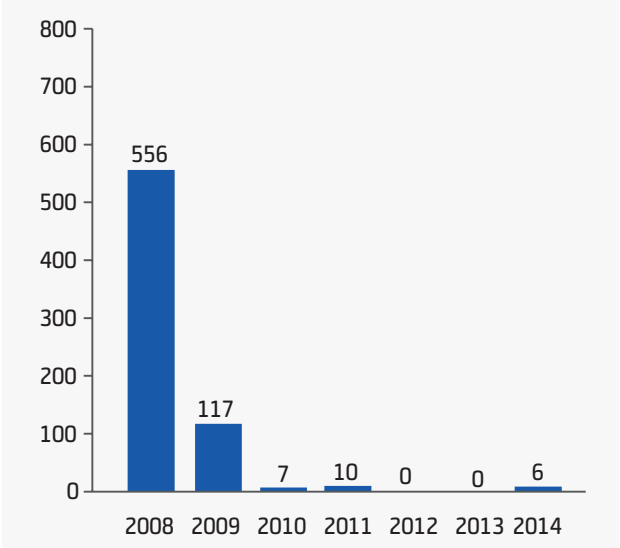


2.6. Authorisation, Clinical Trials and Safety Monitoring of Medical Devices

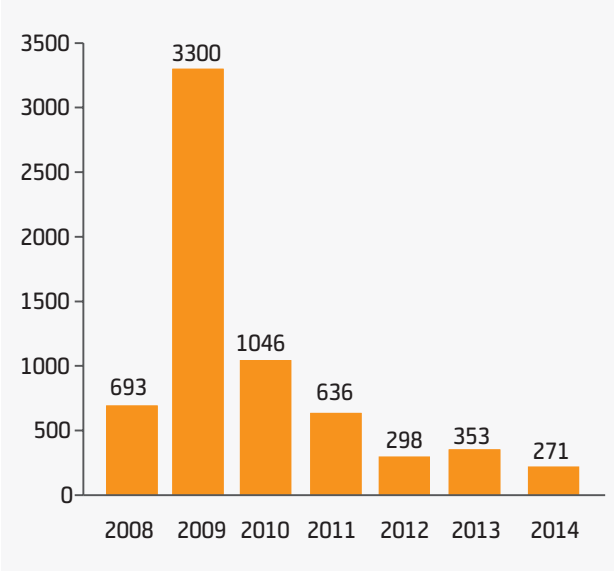
In 2014 seven applications were submitted for authorisation of medical devices in Latvia and 271 notifications were added to the LATMED database regarding placement of medical devices on the market in the Republic of Latvia. 1020 primary reports about accidents with medical devices were received within the vigilance system from competent institutions for medical devices in the EU member states, as well as from manufacturers, distributors and users of medical devices. In 185 of these cases it was found that the medical device involved in the accident is or possibly is available in Latvia and appropriate safety measures were taken.

In the year of review expertise was carried out on documentation for grant of authorisation to 11 clinical trials with medical devices, excluding expertise on documentation submitted for amendments to clinical trial plans (protocols) that have already received authorisation from SAM.

NUMBER OF AUTHORISATIONS ISSUED FOR MEDICAL DEVICES IN THE REPUBLIC OF LATVIA



ANNOUNCEMENTS OF MEDICAL DEVICES ENTERING CIRCULATION IN THE REPUBLIC OF LATVIA (INCLUDING MEDICAL DEVICES FOR IN VITRO DIAGNOSTICS)



AUTHORISATION, CLINICAL TRIALS AND SAFETY MONITORING OF MEDICAL DEVICES

Criteria	Number
Expertise on authorisation documentation of MDs manufactured in the Republic of Latvia	10
Expertise on authorisation documentation of MDs without CE mark	0
Expertise on documentation for issue of authorisation to specially supplied MDs	1
Registration of information submitted within the notification procedure in the LATMED database	271
Registration of information provided by MD holders regarding purchase of safety group I and II MDs in the LATMED database	4111
Registration of information provided by MD holders regarding changes in use of safety group I and II MDs in the LATMED database	2389
Acceptance of reports received within the Vigilance system, analysis and processing of information and registration of data in the LATMED database	1020
Identification of non-compliant MDs utilised in Latvia and implementation of safety measures	185
Expertise of documentation submitted for authorisation of clinical trials with MDs	11
Expertise of documentation submitted for approval of amendments to a clinical trial with MDs	12
Applications for variations to previously issued MD authorisations	1

Consultations were regularly provided to clients regarding the procedure for authorisation of medical devices, preparation of documentation and normative acts regulating the field. SAM specialists participate in European Commission working parties in the fields related to SAM functions, organise seminars and perform other activities to provide information regarding news in the field of medical devices.

2.7. Compliance Evaluation of Pharmaceutical Activity

In 2014 the Pharmaceutical Activities Compliance Evaluation Department conducted 20 inspections in manufacturing/ importing companies and one inspection in a contract laboratory that carries out testing for authorised manufacturing companies. In total it required 69.5 person-days. Two of the inspected manufacturing companies were located in countries outside of the European Economic Area, but three inspections were related to the inspection of manufacturing of active substances initiated upon request from the manufacturers themselves. Overall, manufacturing of 14 chemically synthesised pharmaceutical ingredients was inspected (four of these ingredients are used in veterinary medicine). One inspection of an active substance manufacturer was carried out in relation to the authorisation of a new active substance manufacturer. Department employees in cooperation with the Pharmaceutical Activities Company Licensing Department authorised 8 active substance manufacturers, importers and distributors.

36 (medicinal) product samples were selected during inspections of manufacturing companies. In the year of review 22 good manufacturing practice certificates were issued to medicinal product manufacturing/ import companies.

Upon request from the Latvian medicines manufacturers and wholesalers 51 certificates of pharmaceutical products and 47 certificates of free sale were issued in 2014 in order to promote export of medicines manufactured in Latvia and their marketing authorisation in countries outside of the European Union/European Economic Area.

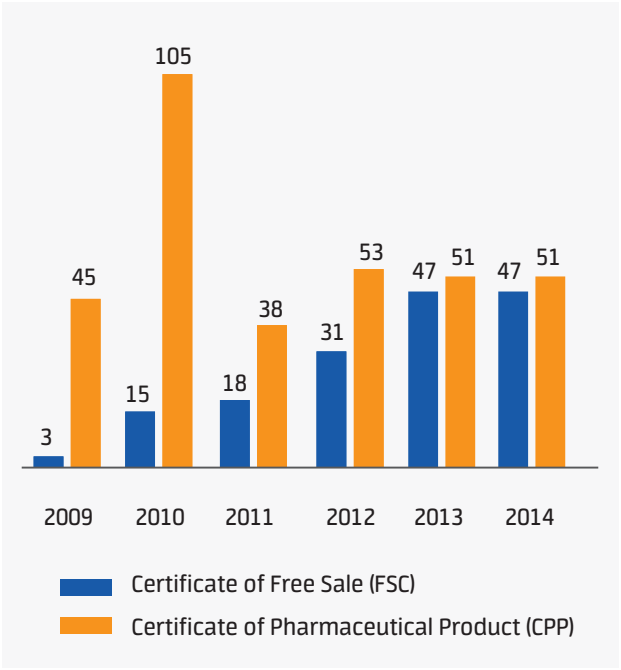
In 2014 department experts participated in an inspection of a manufacturing company in another EU member state and it was conducted together with other agency inspectors involved in PIC/S as part of an experience exchange visit.

30 compliance evaluations of medicines wholesalers, as well as good distribution practice inspections of medicines wholesalers were carried out in 2014 requiring a total of 39.5 person-days. One inspection was carried out in relation to distribution of active substances.

26 compliance evaluations of human blood and blood component establishments and hospital blood banks, as well as 20 surveillance procedures were performed in 2014. Five compliance evaluations and two surveillance procedures of tissue/cell procurement and storage centres were conducted. Evaluation was conducted for one transplantation centre, which operates in the field of human organ procurement and transplantation. Compliance evaluation was carried out in a higher education institution that provides a medical study program and an authorisation was issued for use of human tissues and cells. Department specialists prepared information for the surveys received from the European Commission Directorate General for Health and Consumers (DG-SANCO) regarding the current practice in Latvia in relation to voluntary and unpaid donation of tissues and cells, as well as blood.

Department employees ensured SAM representation in the European Medicines Agency (EMA) GMP Inspectors Working Group, in the activities of the Pharmaceutical Inspection Co-operation Scheme (PIC/S), as well as in the working groups organised by the European Commission Directorate General for Health and Consumers (DG-SANCO) regarding human blood and blood components, tissues, cells and organs.

DYNAMICS OF THE NUMBER OF CERTIFICATES ISSUED TO NATIONAL MANUFACTURERS



2.8. Licensing of Pharmaceutical Activity Companies

The main task of the Pharmaceutical Activities Company Licensing Department is to address pharmaceutical activity company licensing issues in order to ensure the issuance of special permits (licences) to pharmaceutical activity companies in accordance with the current normative acts.

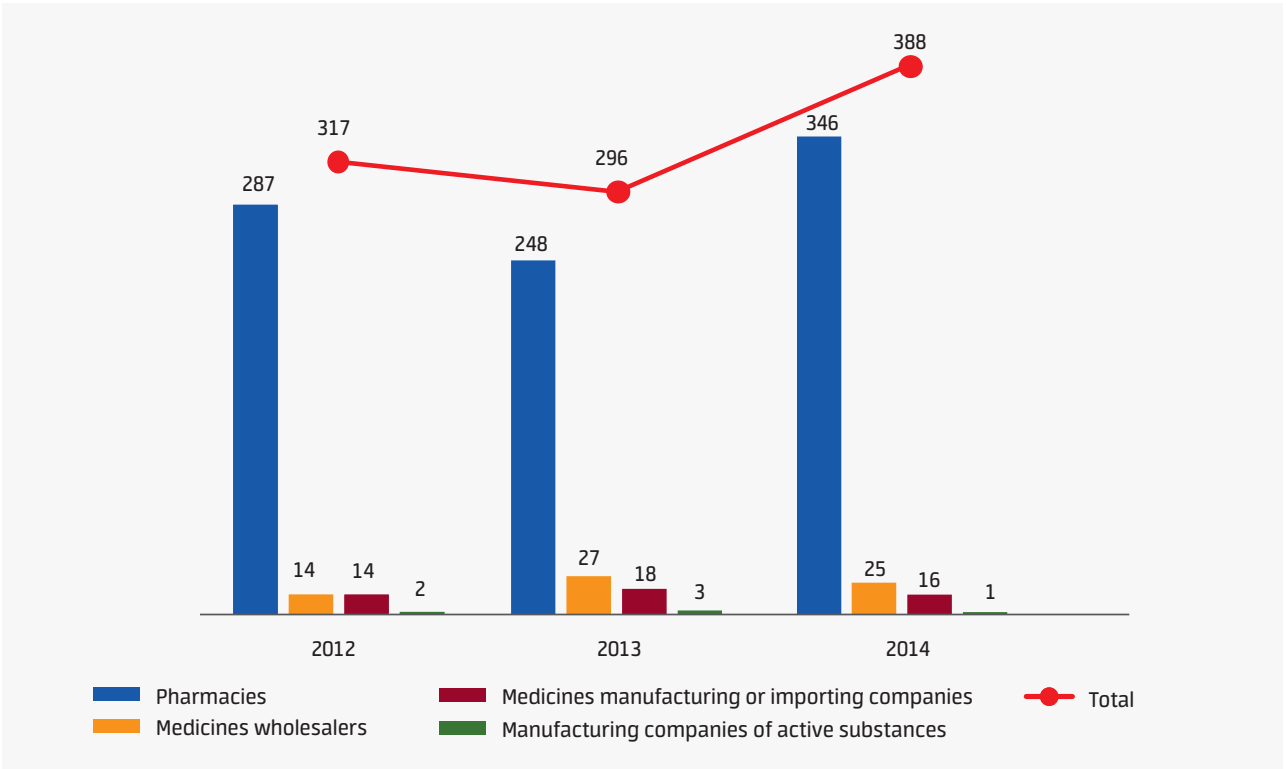
The procedure for licensing of pharmaceutical activity and for review of documentation and adoption of decisions in SAM regarding issuance, renewal, suspension and annulment of special permits (licences) is laid down in the CM Regulation No. 800 of 19th October 2011 "Procedure for Licensing of Pharmaceutical Activity" (hereinafter - Regulation No. 800).

The competency of the department is to perform evaluation of the documentation submitted by pharmaceutical activity companies - medicines wholesalers, medicines manufacturing or import companies, manufacturing companies of active pharmaceutical ingredients, general or closed type pharmacies. The department carried out evaluation of plans for premises of general and closed type pharmacies in accordance with the requirements of normative acts, prepared opinions on pharmacy compliance evaluations and projects for decisions on issuance, renewal, suspension or annulment of special permits (licences).

In cooperation with experts from the Pharmaceutical Activities Compliance Evaluation Department, the department ensured the performance of the functions laid down in Section 10, Articles 12, 12^1, 12^2, 12^3, 16 of the Pharmaceutical Law and in Article 4.10 of the CM Regulation No. 537 of 31st July 2012 "Statutes of the State Agency of Medicines", that is, evaluated the compliance of pharmaceutical activity companies, evaluated the compliance of the qualification and experience of the responsible person for companies manufacturing or importing medicines and manufacturing active pharmaceutical ingredients, and for medicines wholesalers with the requirements of normative acts regarding manufacturing and distribution of medicines, reviewed submitted documents and prepared decisions for authorisation of manufacturers, importers and distributors of active substances.

In 2014 the direct responsibilities of the department included assembly of the documentation related to compliance evaluation and licencing of pharmaceutical activity companies, storage of information submitted by licenced pharmacies, medicines wholesalers, medicines manufacturing or import companies, manufacturing companies of active pharmaceutical ingredients, preparation of special permits (licences) for pharmaceutical activity, regular updates to the data on special permits (licences) issued for pharmaceutical activity after adoption of decision in the Agency, regarding cas-

LICENCES FOR PHARMACEUTICAL ACTIVITY COMPANIES



es of establishment and relocation of general type pharmacies, special activity initiation cases (preparation of medicines in the pharmacy or 24-hour operation), publication of this information on SAM website www.zva.gov.lv. The department provided regular reports regarding the issued, renewed, suspended, annulled licences for pharmaceutical activity to the Health Inspectorate, Pharmacists' Society of Latvia, Food and Veterinary Service and the State Revenue Service.

Before the Agency adopts a decision on the issuance, renewal, suspension or annulment of a special permit (licence) the Commission on Licencing of Pharmaceutical Activity (hereinafter - the Commission), which is a structural unit established by the Agency, reviews the issues related to licencing. Commission decisions have the nature of a recommendation. The Commission operates in accordance with the regulations approved by the Agency Director. Organisational preparations and recording minutes for Commission meetings are in the competency of the department. 14 Commission meetings were held in 2014.

Review of applications for opening of new general type pharmacies or pharmacy branches or relocation of pharmacies is carried out in accordance with the requirements of the CM Regulation No. 610 "Criteria for Location of Pharmacies and Pharmacy Branches" adopted on 2nd August 2011 (hereinafter - Regulation No. 610) and Regulation No. 800. In 2014 merchants (licence holders) continued to submit applications for new general type pharmacies or pharmacy branches, or relocation of pharmacies, so that the Agency could carry out inspections and approve the new pharmaceutical activity sites in accordance with the criteria for location of pharmacies. The Agency adopted 99 decisions regarding approval of new pharmaceutical activity sites for general type pharmacies. In the year of review the Agency continued cooperation with the State Agency "Latvian Geospatial Information Agency" in order to precisely measure the distance between general type pharmacies and also requested regional building authorities to provide information regarding the planned initiation of exploitation of the premises of general type pharmacies. Regulation No. 610 stipulates that, upon carrying out evaluation of the availability of pharmaceutical care, the local authority can submit an application to SAM regarding the necessity of a general type pharmacy or a 24-hour pharmacy in a populated area where there are enough general type pharmacies, but there is no general type 24-hour pharmacy or other pharmacies are located further than 3 kilometres away. Following a request from City Council of Kuldiga and Jelgava, SAM evaluated the availability of pharmaceutical care in those specific populated areas where a general type 24-hour pharmacy was necessary.

The department continued to issue authorisations and enter data into the *EudraGMDP* database in accordance with the CM Regulation No. 344 of 25th June 2013 "Procedure for Import and Distribution of Active Substances" (hereinafter - Regulation No. 344) laying down a new authorisation procedure for manufacturers, importers and distributors of active substances. The department cooperated with experts from the Pharmaceutical Activities Compliance Evaluation Department to assess these issues. In 2014 the Agency adopted 9 decisions regarding authorisation of manufacturers, importers and distributors of active substances, issued authorisations, published the information on SAM website www.zva.gov.lv and entered the data into the *EudraGMP* database.

In 2014 SAM received 1303 applications and additional documentation, provided 124 response (information query) letters, carried out compliance evaluation of documentation of 75 general and closed type pharmacies, in cooperation with the Pharmaceutical Activities Compliance Evaluation Department conducted compliance evaluation of 15 medicines wholesalers, 16 medicines manufacturing or import companies and their documentation, prepared 75 opinions regarding pharmacy compliance assessments, 466 decisions regarding issuance, renewal, suspension, annulment of special permits (licences) and extension of case review term. During the year of review 388 special permits (licences) for pharmaceutical activity were renewed and issued to pharmaceutical activity companies (including 346 licences for pharmacies, 25 - for medicines wholesalers, 16 - for medicines manufacturing or import companies, one for a company manufacturing active pharmaceutical ingredients). In 2014 the Agency adopted decisions regarding issuance of special permits (licences) for 9 new general type pharmacies and 8 medicines wholesalers.

The Agency's interactive map of pharmacies available on SAM website ww.zva.gov.lv is regularly supplemented with updated information regarding general type pharmacies in the territory of Latvia.

3. BUDGET AND EXPENSES OF THE STATE AGENCY OF MEDICINES

3.1. Budget and expenses of the State Agency of Medicines

No.	Financial Resources	Budget utilization in 2012 EUR	Budget utilization in 2013 EUR	2014	
				Budget estimate EUR	Budget utilization EUR
1.	Financial resources for covering expenses (total)	6 207 599	5 420 582	4 609 718	6 130 863
1.1.	Income from paid services and other independent income	6 187 399	5 419 404	4 609 718	5 704 553
2.	Expenses (total)	6 870 098	5 770 129	6 202 724	4 862 979
2.1.	Maintenance expenses (total)	6 557 445	5 467 844	5 440 978	4 594 276
2.1.1.	Regular expenses	3 273 123	4 306 641	4 827 862	3 985 773
2.2.	Transfers of maintenance expenses	3 284 322	1 161 203	613 116	613 116
2.3.	Expenses for capital investment	312 653	302 285	761 746	264 090
	Financial balance			-1 593 006	
	Financing			1 593 006	
	Financial Resources			1 593 006	
	Increasing (-) or decreasing (+) change in surplus of financial resources from paid services and other independent income			1 593 006	

3.2. The Opinion of a Certified Auditor

A Report from Independent Auditors to the State Agency of Medicines.

A report on the financial report

We have conducted an audit of the State Agency of Medicines' financial report of 2014. The audited financial report includes:

- An account of the financial situation of the institution on 31st December 2014 - form No. 1 "Balance".
- An account of the financial results of operation in 2014 - form No. 4-3.
- An account of the changes in own capital (net assets) in 2014 - form No. 4-1.
- An account of the financial resources flow in 2014 - form No. 2-NP.
- Annexes of the financial account laid down in Article 4.5 of the Cabinet of Ministers of the Republic of Latvia Regulation No. 1115 of 15th October 2013 "Procedure for Preparation of the Annual Account", description of the principles for keeping accounting records, explanation of the financial account.

Responsibility of the Administration regarding the preparation of the financial account

The Administration is responsible for the preparation of this financial report and the truthful reflection of the information provided in this report in accordance with the requirements of the Cabinet of Ministers of the Republic of Latvia Regulation No. 1115 of 15th October 2013 "Procedure for Preparation of the Annual Account", as well as for an internal control that the Administration implements to ensure the preparation of a financial report, which does not include major discrepancies due to fraud or errors.

Responsibility of the Auditors

We are responsible for the opinion that we provide on this financial report based on the audit we have conducted. We conduct the audit in accordance with the International Standards on Auditing. These standards determine that we shall comply with ethical requirements and we shall plan and conduct the audit in a way that allows obtaining sufficient proof that the financial report does not contain major discrepancies.

The audit includes procedures that are conducted to obtain audit evidence regarding the amounts indicated in the financial report and the information disclosed in the account. The procedures are selected based on the professional evaluation of the auditors, including an assessment of the risk of major discrepancies due to fraud or errors in the financial report. Upon conducting this assessment auditor take into account the internal control, which is established to ensure preparation of the financial report and the truthful reflection of the information in the report, in order to determine the appropriate audit procedures for the conditions, but not to form an opinion regarding the effectiveness of the control. The audit also includes a general evaluation of the suitability of the utilised accounting principles and of the justification for the conjectures made by the Administration, as well as an evaluation of the general layout of the financial account.

We consider that the evidence obtained in our audit is sufficient and appropriate for the preparation of the opinion of our auditors.

Opinion

In our opinion the aforementioned financial report provides a truthful and clear view on the financial situation of the State Agency of Medicines on 31st December 2014, as well as of the financial results of its operation and of the financial resources flow in 2014 in accordance with the requirements of the Cabinet of Ministers of the Republic of Latvia Regulation No. 1115 of 15th October 2013 "Procedure for Preparation of the Annual Account".

Report on the compliance of the Administration report

We have also viewed the Administration report for the year of 2014 that is reflected in the "Administration report" section of the annual account and we have not discovered any major discrepancies between the financial information included in this Administration report and in the financial account of 2014.

Emphasis on conditions

Not providing an opinion with objections:

- We point out that 114 343 EUR from the amount indicated in the expenses of the following periods will not be written off in 2015, but in the following periods of operation.

LLC "REVUSS", Licence No. 49

Māra Zabrauska

Member of the Board, LR certified auditor

Certificate No. 23

Riga, 25th February 2015

4. GENERAL MANAGEMENT OF THE STATE AGENCY OF MEDICINES

The Operational Strategy of the State Agency of Medicines for 2014-2016 is a document for operational planning and it is established, maintained and published in accordance with the requirements of the Law on Public Agencies and Cabinet of Ministers Instruction No. 3 of 28th April 2015 "Procedure for Preparation and Updating of the Operational Strategy of An Institution and for Evaluation of its Implementation". The strategy indicates Agency's:

- Operational authorisation
- Objective
- Implemented operational directions and the related services
- Priorities
- Other characteristics in accordance with the requirements.

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

The Agency has set three priorities that are important for the public health in the period of planning and implementation of the strategy, as well as for the development of the Agency and the improvement of services:

- Promotion of sustainable development of the national market of medicines.
- Ensuring the prerequisites for the safe and rational use of medicines, medical devices, tissues, cells, organs, blood and its components.
- Improving the efficiency of the operation of the Agency.

4.1. Ensuring Public Procurement and Economic Activities

Public procurement and the economic activity of the State Agency of Medicines are ensured by the Department of Public Procurement and Infrastructure Provision. The operational objective of the department is to ensure the prerequisites and conditions necessary for the successful operation of all of the structural units of the Agency.

The most important functions of the SAM Department of Public Procurement and Infrastructure Provision:

- Organisation of public procurements
- Management of material assets and organisation of work safety measures
- Maintenance of the building complex and the territory on Jersikas Street 15 owned by the Agency and of other rented properties
- Maintenance of the stock of automobiles of the Agency and provision of related services
- Ensuring continuous operation of the infrastructure of the Agency (electricity, water supply, sewage and heating system, communication network, ventilation system, security and fire safety alarm)

In 2014 SAM announced 18 procurement procedures. There were 57 candidates in those procedures. Contracts for supply and services were developed and signed for the conducted public procurement procedures. The most significant contracts were signed for ensuring infrastructure and primary functions:

- Reconstruction of a part of the building and renovation of the ventilation system in the building area of the Medicines Examination Laboratory
- Ensuring security
- Safety testing of the information systems and consultation services
- Establishment and maintenance of infrastructure for accessing network resources
- Solution for two-factor authentication.

4.2. Legal Provisions and the Development of Normative Acts

The objective of the operation of the Legal Department of the State Agency of Medicines is to improve and promote compliance with the administrative process and its implementation in the Agency so that the decisions adopted by SAM would be justified, legal and compliant with the requirements of normative acts, as well as to ensure the interests of the Agency in courts so that the decisions adopted by SAM within the administrative process would stay in effect. Only 15 decisions (less than 0.1 %) of the total of 16 111 decisions adopted by SAM in 2014 were contravened in the Ministry of Health. Three of the Agency decisions contravened in 2014 were reviewed at the highest judicial authority - the Supreme Court of the Republic of Latvia, which took the decision that the Agency decisions were legal and should be in force.

In 2014 the Agency in cooperation with the Ministry of Health prepared and submitted its proposals for more than ten normative acts. In order to improve the surveillance of the distribution of medicines, the requirements for labelling and for manufacturing of medicines, the Agency submitted proposals to the Ministry of Health regarding the following normative acts:

- Cabinet of Ministers Regulation No. 57 of 17th January 2006 "Regulations Regarding Procedures for the Labeling of Medicinal Products and the Requirements to Be Set for Package Leaflets of Medicinal Products".
- Cabinet of Ministers Regulation No. 416 of 26th June 2007 "Procedures Regarding Distribution and Quality Control of Medicinal Products".
- Cabinet of Ministers Regulation No. 803 of 25th October 2005 "Regulations regarding the Principles for the Determination of the Price of Medicinal Products".
- Cabinet of Ministers Regulation No. 436 of 26th June 2007 "Procedure for Import and Export of Medicinal Products".
- Cabinet of Ministers Regulation No. 175 of 8th March 2005 "Regulations for Manufacture and Storage of Prescription Forms, as well as Writing out and Storage of Prescriptions".
- Cabinet of Ministers Regulation No. 304 of 18th April 2006 "Regulations Regarding the Procedures for the Manufacture and Control of Medicinal Products, the Requirements for the Qualification and Professional Experience of a Qualified Person and the Procedures for the Issuance of the Certificate of Good Manufacturing Practice to a Medicinal Products Manufacturing Site".

The Agency submitted proposals regarding the Cabinet of Ministers Regulation No. 376 of 9th May 2006 "Procedures for the Registration of Medicinal Products" in relation to primary expertise, evaluation of medicines documentation, as well as requirements stemming from the Commission Regulation (EU) No. 712/2012 of 3 August 2012 amending Regulation (EC) No. 1234/2008 concerning the examination of variations to the terms of the marketing authorisations for medicinal products for human use and veterinary medicinal products.

In 2014 the Agency also submitted proposals for the Cabinet of Ministers Regulation No. 288 of 23rd March 2010 "Regulations Regarding Operating of Pharmacies" in relation to the requirements for ensuring premises for receiving clients and the pharmacy sticker label, as well as for the Cabinet of Ministers Regulation No. 1176 of 22nd October 2013 "Procedure for Utilisation of Human Tissues and Cells" in relation to the environmental indicators of the premises of tissue centres and the improvement of the procedure for import/export of tissues and cells.

The following amendments to the Cabinet of Ministers regulations, for which the Agency had provided its proposals, were adopted in 2014:

- Cabinet of Ministers Regulation No. 70 of 29th January 2013 "Regulations Regarding Use of Human Organs in Medicine, as well as Use of Human Organs and Body of Deceased Human Being for Medical Studies" (adopted with the amendments of 08.07.2014.).
- Cabinet of Ministers Regulation No. 873 of 17th September 2013 "The State Agency of Medicines Publicly Available Paid Service Pricelist" (adopted with the amendments of

02.09.2014.).

- Cabinet of Ministers Regulation No. 47 of 22nd January 2013 "Procedure for Pharmacovigilance" (adopted with the amendments of 30.09.2014.).
- Cabinet of Ministers Regulation No. 800 of 19th October 2011 "Procedure for Licensing of Pharmaceutical Activity" (adopted with the amendments of 16.12.2014.).

SAM employees participated and ensured representation of the interests of Latvia in the meetings of the European Union Council Working Group on Pharmaceutical Products and Medical Devices where the new European Commission proposals were reviewed for regulations of the European Parliament and of the Council regarding medical devices and medical devices for *in vitro* diagnostics.

4.3. Staff and Human Resources Management

Human resources management is ensured by the Administrative Resources Management and Documents Management Department, which resolves issues of human resources management, ensures the work processes for recruitment, selection, assessment and development of personnel, as well as processes the documentation related to personnel issues.

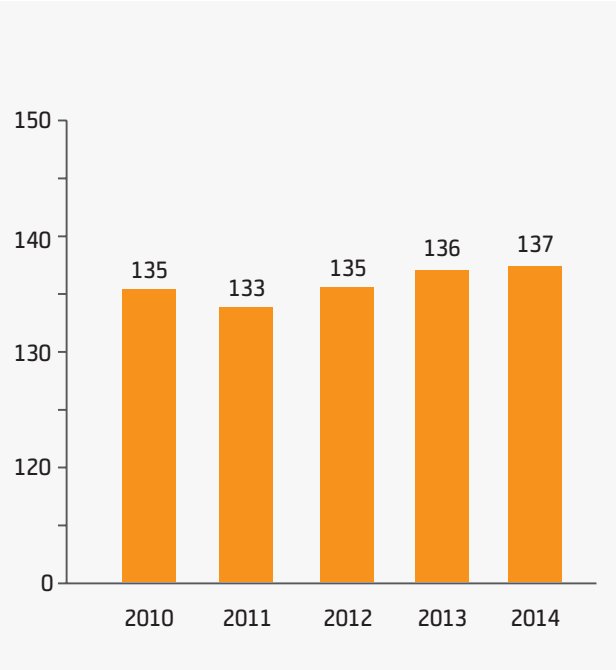
At the end of the 2014 there were 137 civil servants and employees (hereinafter - employees) actually working at SAM. In total 154 persons were in a civil service or an employment contract with SAM in 2014. The figure below shows the number of employees from 2010 until 2014.

During the year of review 19 new employees (4 civil servants and 15 employees) began their employment at the Agency and 16 persons (6 civil servants and 10 employees) terminated their civil service or employment. The average staff turnover was 10% (*staff turnover = number of terminated staff members in a definite time period/ average number of staff members in the same definite time period*).

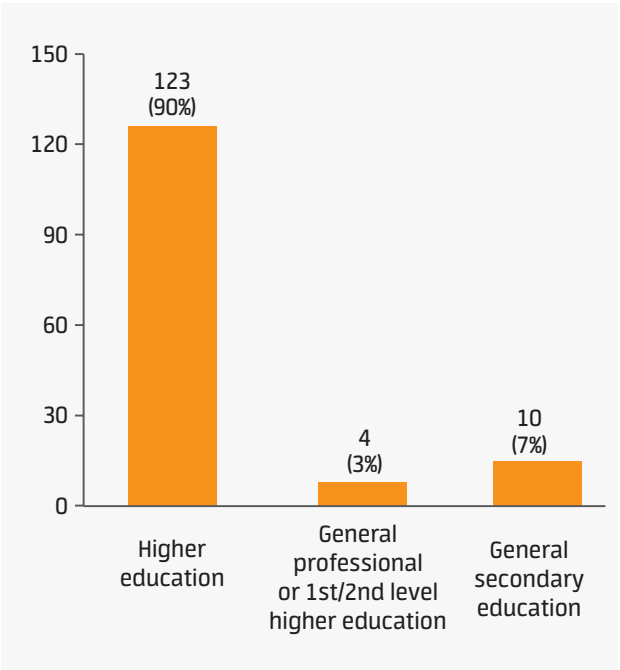
Well-educated, competent and highly qualified specialists are necessary to successfully ensure the functions assigned to SAM. The division of SAM employees according to their level of education is shown in the diagram. Overall the education level of SAM staff members is high - 123 (90%) of SAM employees have a higher education, of these 3 civil servants have a doctorate degree and 1 civil servant is a Doctor of Science.

One of the basic principles of SAM staff policy is to motivate staff members to raise their qualification. During 2014 in order to raise their qualification SAM civil servants and employees attended 540 training sessions and seminars and 22 confer-

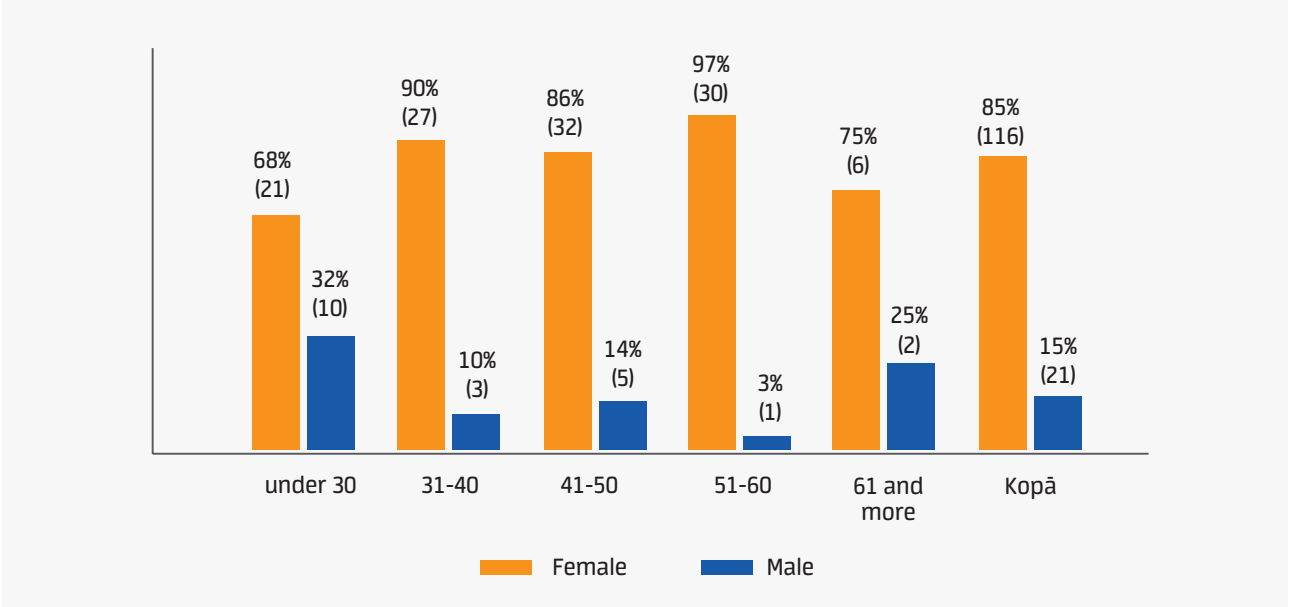
NUMBER OF AGENCY STAFF MEMBERS 2010 - 2014



STAFF MEMBERS ACCORDING TO LEVEL OF EDUCATION IN 2014



STAFF MEMBERS ACCORDING TO THE AGE GROUP AND GENDER IN 2014



ences and forums.

In the year of review 562 training events were ensured for Agency employees (including 96 seminars, courses and conferences organised by international organisations; centrally organised training for all employees: use of the work-hour accounting system - 104 employees were trained; practical and theoretical training regarding fire safety - 92 employees were trained; ordering and accepting changes in the information systems - 47 employees were trained; newest issues regarding information security management (implementation of the ISO 27001 requirements) - 103 employees were trained).

Senior employees, who were involved in the organisation of the events for the Latvian Presidency of the Council of the European Union, regularly attended the training organised by the General Secretariat of the Council of the European Union and the School of Public Administration for heads and deputies of working groups, as well as the training on issues related to event coordination, communication and document management organised for supporting specialists. 25 SAM employees attended training related to the Latvian Presidency of the Council of the European Union, 8 employees participated in training on using State information

RAISING OF QUALIFICATION OF STAFF MEMBERS 2010 - 2014

systems to work with European Union documents (ESVIS).

4.4. Integrated Management System

- At the end of 2014 surveillance audits were conducted at the Agency in accordance with the international standards ISO 9001:2008 and ISO/IEC 27001:2013. The certifications included the following functions: expertise on marketing authorisation and post-authorisation documentation of medicinal products and medical devices, expertise on quality of medicinal products, pharmacovigilance and vigilance of medical devices, issuance of special permits (licences), authorisations and marketing authorisations according to authorisation of the institution, expertise on related documentation, gathering and publishing of information according to authorisation.
- SAM Medicines Examination Laboratory received accreditation for compliance with the requirements of the LVS EN ISO/IEC 17025:2005 standard (surveillance visit by the Latvian National Accreditation Bureau on 10th June 2014).
- Audit of the pharmacovigilance system in accordance with the requirements of the Directive 2010/84/EU of the European Parliament and of the Council of December 15th 2010 and GVP requirements - the first report was sent to the European Commission on 19.09.2013, the next report is to be sent until 19.09.2015.
- The State Agency of Medicines continuously improves the integrated management system by involving as many SAM employees as possible in the process.
- Once in every 4 years Benchmarking of European Medicines Agencies is carried out in accordance with previously defined criteria in the following areas: organisation and management, quality management system, process of marketing authorisation of medicinal products, pharmacovigilance, cooperation with stakeholders, compliance evaluation and others. The III BEMA auditor visit at the State Agency of Medicines took place on 24-28 February 2014 and it resulted in a positive assessment.
- By implementing the strategic audit plan of SAM, internal and external audits were carried out in various areas during the year of review - staff management, pharmacovigilance, import, export of medicines, maintenance of information on the website and others. It required a total of 50 audit days during the year.

4.5. Development of Information Technologies

In 2014 work was continued to develop and improve the information systems and information technology solutions of SAM, as well as to improve the continuity of their availability and management. The local Agency network was expanded and modernised. SAM participated in the development of the EMA Telematics Strategy and in the preparation of its implementation plan. An audit on the security of IS was carried out, measures were implemented to minimise the identified risk factors and staff member training on IT security issues was conducted. In 2014 the information system for accounting was modernised and improved. The design of SAM website was updated to comply with the requirements for the unified visual identity of State administration institutions. During the year of review the reflection of information regarding prices of medicines on SAM website was improved, ensuring information regarding prices of parallel imported medicines. Improvements were made to the algorithms for selection and processing of information in the SAM IS information system, new integration solutions were introduced. SAM IS migration process was initiated, the first two steps were implemented, the public application was streamlined and the database management system was migrated to a newer version. The LATMED information system was improved by a separate solution to ensure access to the system for external users, as well as a possibility for external users to export LATMED data by a selection process according to different criteria.

Self-service web functionality for employees was introduced in the *Horizon* resource management system ensuring the option for employees to access information in the system through a web browser, for example, calculated fee statements, long-term investments and equipment under their responsibility. The receipt of merchant marketing authorisation applications from the Common European Submission Platform (CESP) was automated. IT infrastructure solutions that are also used by the Ministry of Health and other institutions in the field were introduced: massive disc load distribution and mirror solution, an improved solution for the back-up copy system, modernised virtualisation platform and a diesel generator was set up to minimise risk in case of disruptions in the supply of electricity.

Data exchange within the European Union network

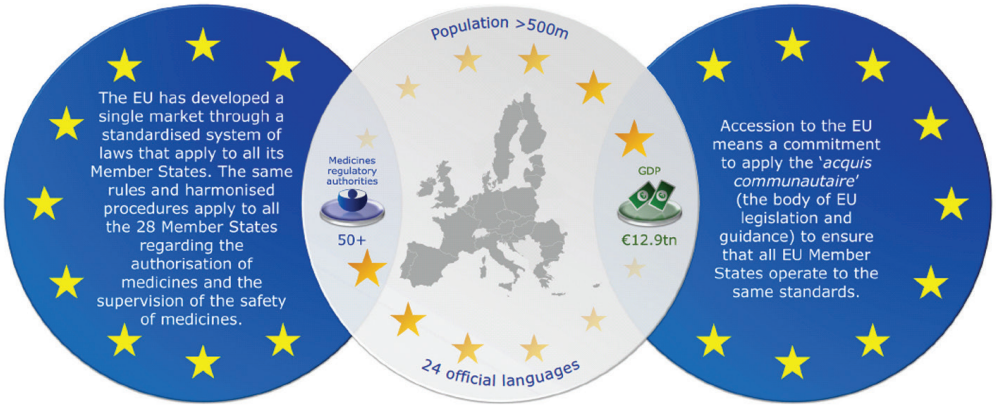
- *Eudralink* (e-mail), *EudraNet* (system) - a coded network for exchange of EMA information.
- *EudraVigilance* - pharmacovigilance information.
- *EV Data Analysis System* (EDVAS) - options for safety data analysis.
- *EudraCT* - clinical trials database, *CITRIX* - VHP system.
- CTS (*Communication and Tracking system*) in the mutual recognition procedure for authorisation of medicines and *MRindex* - databse.
- *Eudra GMP* - GMP and GDP database.
- *EU Telematics Controlled Terms* - telematics terminology database in 26 languages.
- CESP (*Common European Submission Platform*).
- *EUDAMED* (medical devices database).
- RAB (*Rapid Alert Blood*) and RATC (*Rapid Alert Tissue and Cells*).

4.6. International Cooperation

The State Agency of Medicines is a part of the network of national medicines agencies in Europe and the successful performance of the institutional functions and tasks is closely related to the participation in the unified European Medicines Regulatory network - it entails cooperation between the EMA, European Commission and more than 47 regulatory institutions within the European Union and the European Economic Area (EEA). This network of cooperation gives EMA access to a wide range of experts allowing EMA to provide the best possible scientific expertise for regulation of medicines in the EU. Experts participate in the work of EMA as members of working groups and scientific advisory groups, scientific committees, as well as other groups.

In order for SAM colleagues to fully participate in the collective work procedures, the Agency assumes a great responsibility. This cooperation requires SAM human and financial resources. In 2014 SAM employees have been involved in the cooperation with the European Commission and Council working groups, European Commission Directorate General for Health and Food Safety (DG SANTE), WHO, The Uppsala Monitoring Centre (UMC), Euro-

EUROPEAN UNION – KEY FACTS



EU Member States: 28

The European Economic Area (EEA) is formed of the 28 EU Member States plus:

pean Pharmacopoeia Commission, PIC/S, European Directorate for the Quality of Medicines & Healthcare (EDQM), as well as in compliance inspections of clinical trials on behalf of the EMA. In order for the Agency to provide appropriate services to its stakeholders and provide consultations on different issues, cooperation with other institutions, training and exchange of experience are mandatory prerequisites. This year we have actively participated in work-sharing procedures, for example, in the expertise on paediatric data, in the evaluation of periodic safety update reports, in the voluntary harmonisation procedure for clinical trials. To ensure appropriate quality of expertise we invited additional experts with scientific degrees from universities in Latvia.

In 2014 SAM Administration took a more active part in the Heads of Medicines Agencies (HMA) organisation by fully participating also in the work of the HMA Management Group. Working in this group has allowed active participation in the solutions of different issues during preparation for discussions with European or international institutions. Significant is also the fact that the work experience in the Management Group was useful in planning and implementing measures during the Latvian Presidency of the Council of the European Union from 1st January 2015 until 30th June 2015.

For several years SAM has also been involved in the surveillance of medical devices, blood and its components, tissues and cells. SAM is the competent institution with regards to authorisation of medical devices, issuance of authorisation for clinical trials with medical devices and monitoring the safety of medical devices. The responsible SAM specialists regularly participate in the meetings of the representatives from national competent authorities for medical devices in Europe. Participation is ensured in Competent Authorities for Medical Devices (CAMD) meetings, Central Management Committee (CMC) meetings and European Commission Directorate General for Health and Food Safety (DG SANTE) meetings.

To represent the opinion of the Republic of Latvia on issues regarding monitoring of the safety of medicines, in 2012 SAM Administration became a member of the established EMA Pharmacovigilance Risk Assessment Committee (PRAC). This committee deals with issues related to the risk management of medicinal products distributed in the EU, this includes supervising risk management plans and systems for both nationally and centrally authorised medicinal products and evaluating Periodic Safety Update Reports, as well as acting as an advisor on various pharmacovigilance issues.

There are effective cooperation contracts between SAM and the medicines agencies in Estonia and Lithuania in order to promote closer cooperation between the medicines agencies of the Baltic states. A meeting of the representatives from the medicines agencies of the Baltic states took place in September 2014 in Tartu, Estonia. In this meeting the national experts discussed aspects of further cooperation, news and problems in the field, as well as other issues.

To characterise directions of international cooperation of the Agency it has to be mentioned that the memorandum of agreement signed between the SAM and the Food and Drug Administration of the People's Republic of China regarding cooperation in normative regulation of medicines is still in force.

Participants of the Baltic Medicines Agencies Meeting in Tartu, Estonia on 11th of September, 2014

5. PROVIDING INFORMATION TO THE PUBLIC AND COMMUNICATION

In 2014 the State Agency of Medicines provided information to the public and carried out communication activities in accordance with the "Communication Strategy of the State Agency of Medicines for 2014-2016" and the „Operational Strategy of the State Agency of Medicines for 2014-2016". Three operational directions and a set of activities are to be followed in order to achieve the strategic objective of SAM. One of the directions is the information direction: ensure provision of objective, thorough and updated information regarding products and companies, as well as regarding SAM operation to the public and to professionals, as well as cooperation partners in Latvia and in other countries in order to promote public health, carry out disease prevention and to prevent threats to human health.

In 2014 SAM ensured purposeful communication with cooperation partners by providing independent and objective information regarding issues in the competency of SAM to professionals and the general public. Communication was ensured with professional associations, other non-governmental organisations, patient organisations and State institutions.

Publicity in the media

In the year of review 24 different press releases were prepared and distributed to mass media representatives, more than 150 responses were provided to journalist queries. Replies were prepared and provided also to questions from residents of Latvia, as well as to requests for information from the Ministry of Health and its institutions and SAM stakeholders. Three info graphics were prepared in 2014: "What forms the prices of medicines in pharmacies?", "Statistics on medicines consumption in Latvia in 2013" and "20 years of Cito!". Those were distributed to the media and via the SAM informative bulletin "Cito!", published on www.zva.gov.lv and forwarded individually to other interested parties. By following the normative regulation of the field of medicinal products in Europe and in Latvia and by evaluating the information regarding safety of medicines, regular updates were made in the social networks *Facebook*, *Twitter* and *LinkedIn*. As a result of SAM communication activities there were a total of 283 publications in different media in 2014.

Publication topics

Safety of medicines

La.lv: Concerns regarding ibuprofen containing medicines, 25.06.2014.

Delfi.lv: Flu vaccine "Fluad" not related to patient deaths in Italy, 04.12.2014.

Consumption of medicines

Delfi.lv: Turnover of medicines increased by 4 % last year, 11.06.2014.

Radio "SWH+": People in Latvia use more prescription medicines, 29.06.2014.

Clinical trials with medicines

Medicine.lv: New Regulation in the field of clinical trials, 4.06.2014.

Magazine *"Doctus":* Most of the clinical trials in Latvia are conducted in rheumatology, 25.07.2014.

Discarding medicines

Magazine *"Veselība":* What to do with medicines after the expiry date? Can they be thrown out in the trash? 13.10.2014.

Public health

Delfi.lv: "Spice" is not and cannot be a legal product, emphasises the State Agency of Medicines, 25.03.2014.

Events

Magazine *"Materia Medica":* 20 years of the publication "Cito!", August 2014.

Talsi24.lv: Brigita Aišpure receives a special award from the State Agency of Medicines, 03.02.2014.

In addition to the aforementioned, information was regularly updated on SAM website www.zva.gov.lv In the era of information technology the website is not only one of the most cost-effective communication channels, but also allows to provide information directly to the target audience using the Internet.

According to Google Analytics statistical data, in 2014 SAM website was visited 409 297 times. Maintaining the website is an effective way of ensuring the provision of official and updated information to every member of the public regarding SAM operations and latest issues in the field of pharmaceutics.

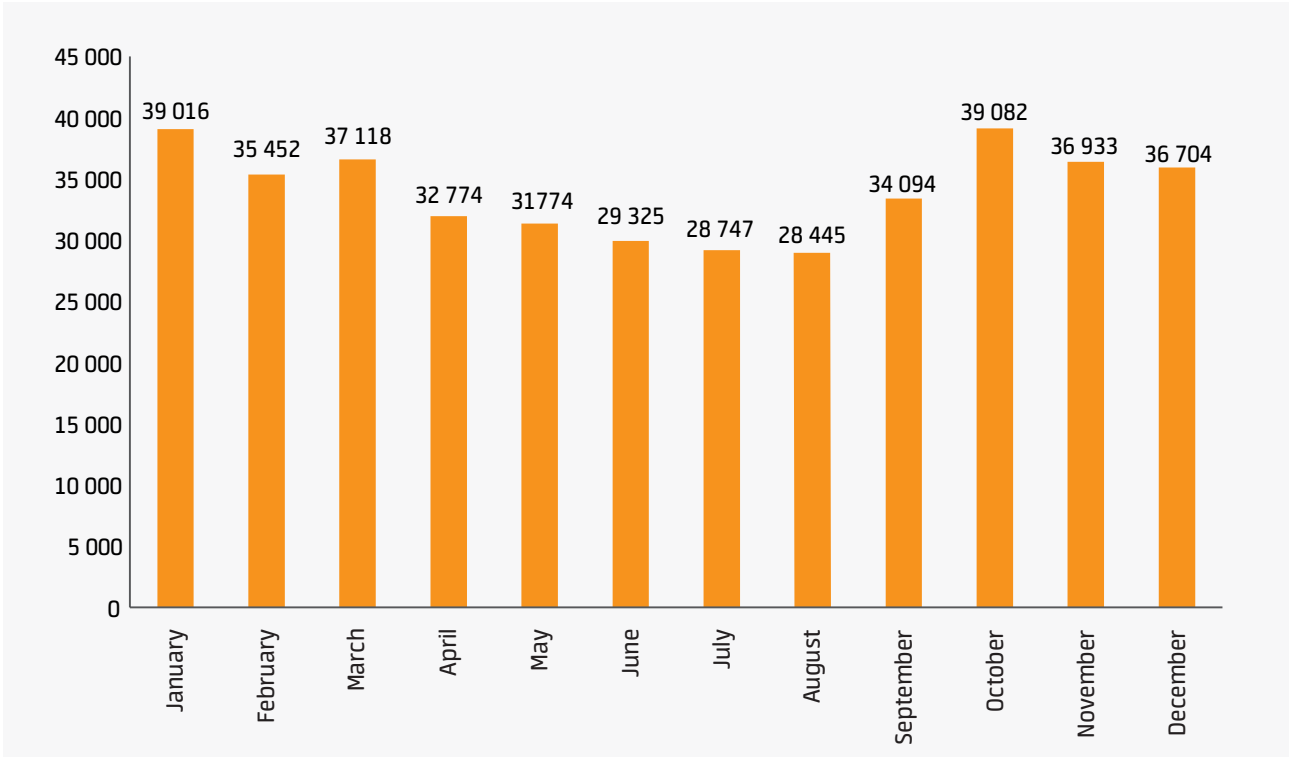
Development of SAM website is planned in 2015 and it will include improvements to the arrangement of information and the design, and ensuring information in separate sections for different SAM target audiences (healthcare professionals, marketing authorisation holders and others).

SAM publications

In order to inform doctors, pharmacists and other healthcare professionals regarding the latest issues in pharmaceutics and SAM operation, as well as regarding safety of medicines, several informative publications were prepared in 2014. Even though doctors, pharmacists and other healthcare professionals can obtain information from different sources such as seminars and conferences, as well as professional publications from different countries, the publications printed by SAM provide updated, objective, verified and focused information to the interested parties who wish to follow the most important developments in pharmaceutics.

The SAM informative bulletin "Cito!" for doctors, pharmacists and other healthcare professionals has already become an integral part of daily operation by providing thorough and updated information regarding the safety of medicines. In the pages of "Cito!" field specialists, including SAM experts, share their experience, publish articles regarding current medical issues, as well as exchange their opinions. Changes in the Medicinal Product Register of the Republic of Latvia are published in each issue of "Cito!", and each issue is also accompanied by an adverse drug reaction report form for healthcare professionals and pharmacists to promote reporting of adverse drug reactions. Four issues of "Cito!"

NUMBER OF VISITORS OF SAM WEBSITE WWW.ZVA.GOV.LV IN 2014



were released in 2014, including a special anniversary issue celebrating the 20 years of "Cito!". Info graphic "20 years of Cito!" was prepared for the special occasion and an exhibit for SAM employees was organised containing 50 issues of "Cito!" from 2003 until the autumn of 2014. The number of recipients of the electronic version of the publication increased by 30% last year reaching a total of 1024.

The Medicinal Product Register of the Republic of Latvia is an official and independent source of information for doctors and pharmacists, containing information regarding medicines authorised in the national, mutual recognition, decentralised and centralised procedures, as well as parallel imported medicines. In addition to the book, an electronic edition of the Medicinal Product Register was prepared in a USB data carrier format containing summaries of product characteristics and package leaflets. A convenient information search form has been developed for this format. No Internet connection is necessary to use this format in the daily work. The summary of product characteristics included in the electronic version of the Medicinal Product Register helps doctors and pharmacists to choose the most appropriate medicines for the patient, as well as to find out or clarify relevant information regarding the correct use of medicines, possible adverse reactions and other information, thus, promoting safe use of medicines.

To provide information regarding trends in the consumption of medicines the statistical report on the consumption of medicines within Latvia was issued for the 12th time, this time including statistical data on medicines consumption from 2009 until 2013. The report included information regarding total turnover of medicines in Euros, number of packages sold, distribution of the turnover according to different consumer groups, dispensing status, turnover of medicines expressed in defined daily doses (DDD) per 1000 inhabitants of Latvia per day (DID). Information was also provided regarding the most sold medicines in Latvia and further information was provided about the market of medicines manufactured in Latvia.

The annual report of the year 2013 was also published last year, summarising information regarding operation of SAM.

Special events and informative seminars

In 2014 two informative seminars were organised for cooperation partners and clients regarding the latest news in the field of marketing authorisations and grouping of variations, clinical trials with medicines and their perspectives in Latvia and other SAM services, including submission of documents to SAM via CESP (Common European Submission Platform). An open door day took place at SAM on 10th October 2014 in order to allow the public to observe the daily work of the Agency. An open lecture on pharmacovigilance issues was given to students of the Master's degree program at the Faculty of Medicine of the University of Latvia on 14th May 2014. A work meeting of representatives from the medicines agencies of the Baltic States took place last year in Tartu, Estonia discussing newest issues and the normative regulation in the pharmaceutical field. In this meeting SAM employees presented and shared their experience on topics such as marketing authorisation, gathering of statistical data on medicines consumption, pharmacovigilance (monitoring of adverse drug reactions), and cooperation of medicines examination laboratories in Latvia, Estonia and Lithuania. The activities of the campaign "Reveal the other side of medicines!" were continued in 2014. The Chief Doctor at the Talsi branch of the Northern Kurzeme Regional Hospital received a special award from SAM for ethical behaviour and significant contribution to reporting of adverse drug reactions, after submitting several reports regarding adverse reactions related to one medicinal product. Information regarding SAM operation was provided in presentation and discussion format in events organised also by other organisations. 2014 was filled with preparations for the events organised by SAM during the Latvian Presidency of the Council of the European Union.

PUBLICATIONS PREPARED BY SAM

Publications	Number of copies
Informative bulletin "Cito!"	10 500
The Medicinal Product Register of the Republic of Latvia	250
Electronic edition of the Medicinal Product Register of the Republic of Latvia containing summaries of products characteristics and package leaflets	100*
SAM Annual Report 2014 (in Latvian and English)	100

* Ensured by the State Agency of Medicines according to the demand.

Activities and special events for employees

Internal communication and employee participation in events organised by other organisations were promoted at the State Agency of Medicines so that employees would be more informed about their work place, more involved in work processes and motivated to bring forward initiatives. In order to promote healthy physical and mental health and to strengthen the collective, a team of SAM employees and their family members participated in the 16th Health Days for healthcare professionals in Latvia organised by the Latvian Red Cross and supported by the Ministry of Health of the Republic of Latvia, Latvian Medical Association, Trade Union of Health and Social Care Employees of Latvia. In 2014 for the first time SAM employees and their family members participated also in the 18th basketball tournament organised by the Pharmacists' Society of Latvia. A blood donation day was organised twice in 2014 in collaboration with the State Blood Donor Centre, and SAM employees together with employees from the nearest companies donated blood in a specialised donor bus and participated in other activities organised for them.

Feedback

SAM communication activities are not based solely on a one-way provision of information, but SAM also gives the opportunity for SAM cooperation partners, clients and employees to express their opinion about the quality of SAM client service and provided services. The received information is used for the improvement of quality of SAM operations.

In 2014 SAM organised three surveys:

1) Survey for stakeholders regarding SAM operation and provided services in order to use the obtained data to improve the quality of client service and provided services.

2) Survey for SAM employees with the purpose of discovering the opinion of employees regarding organisation of work in SAM and cooperation, satisfaction with their own work and with other relevant work aspects, that would allow to determine priorities in working with personnel and make rational and deliberate decisions with respect to staff members in the future.

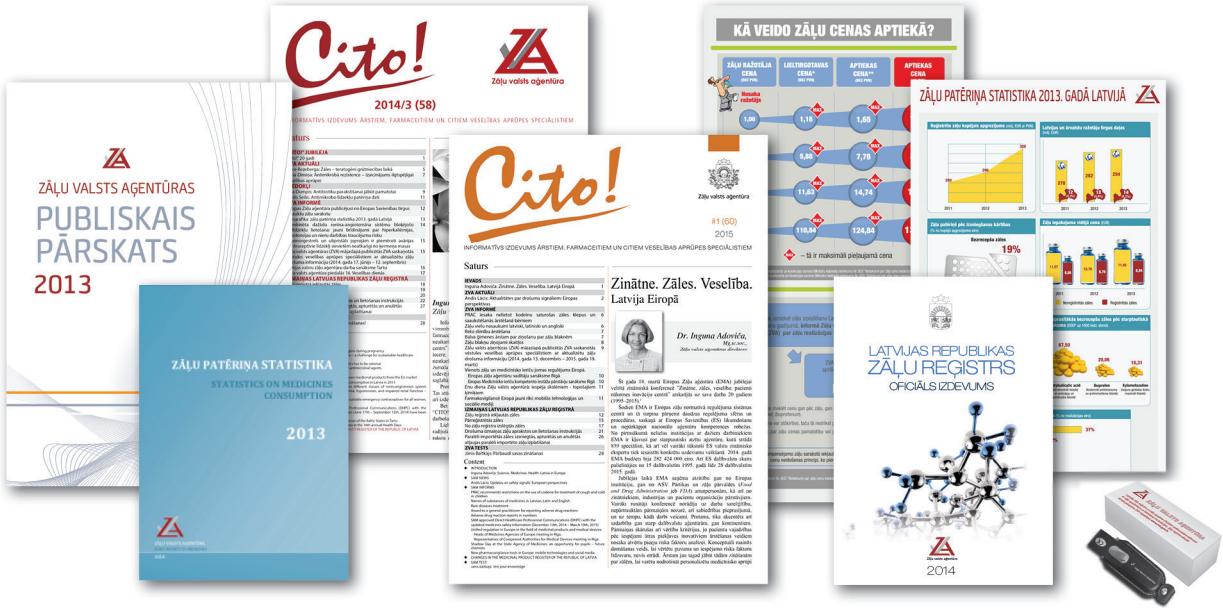
3) Survey for the readers of the informative bulletin "Cito!" to gather their opinions on the usefulness, content, visual design and the most convenient format of this publication.

To enquire the opinion of SAM website visitors, five surveys were conducted in 2014 (the results of these surveys are available on SAM website, in the section "Homepage" > "Survey archive"). Website visitors answered the following questions:

- What do you do, if you think you observe an adverse reaction while using medicines?
- What are biomedicines or biological medicines?
- Can you find medicines easily in the search form of the Medicinal Product Register on SAM website?
- What are falsified medicines?
- Do you think that you use antibiotics correctly?

Surveys were also conducted among participants of SAM organised seminars and open lectures.

USEFUL INFORMATION FOR PHARMACEUTICAL PROFESSIONALS



6. DEVELOPMENTAL PRIORITIES OF THE STATE AGENCY OF MEDICINES IN 2015

The State Agency of Medicines is one of the institutions within the system ensuring public health and it operates to achieve collective tasks in accordance with the necessities of the public. It is done professionally, honestly and in a transparent way and by using international standards and cooperation.

Even though the Agency has many complex tasks, our objective is defined as simply as possible.

The operational objective of the Agency is to implement qualitative and justified services in the evaluation of medicinal products used in healthcare, procurement and storage (utilisation) organisations 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.

SAM has set three priorities that are significant for the public health in the strategic planning period, as well as for the development of SAM and for the improvement of services:

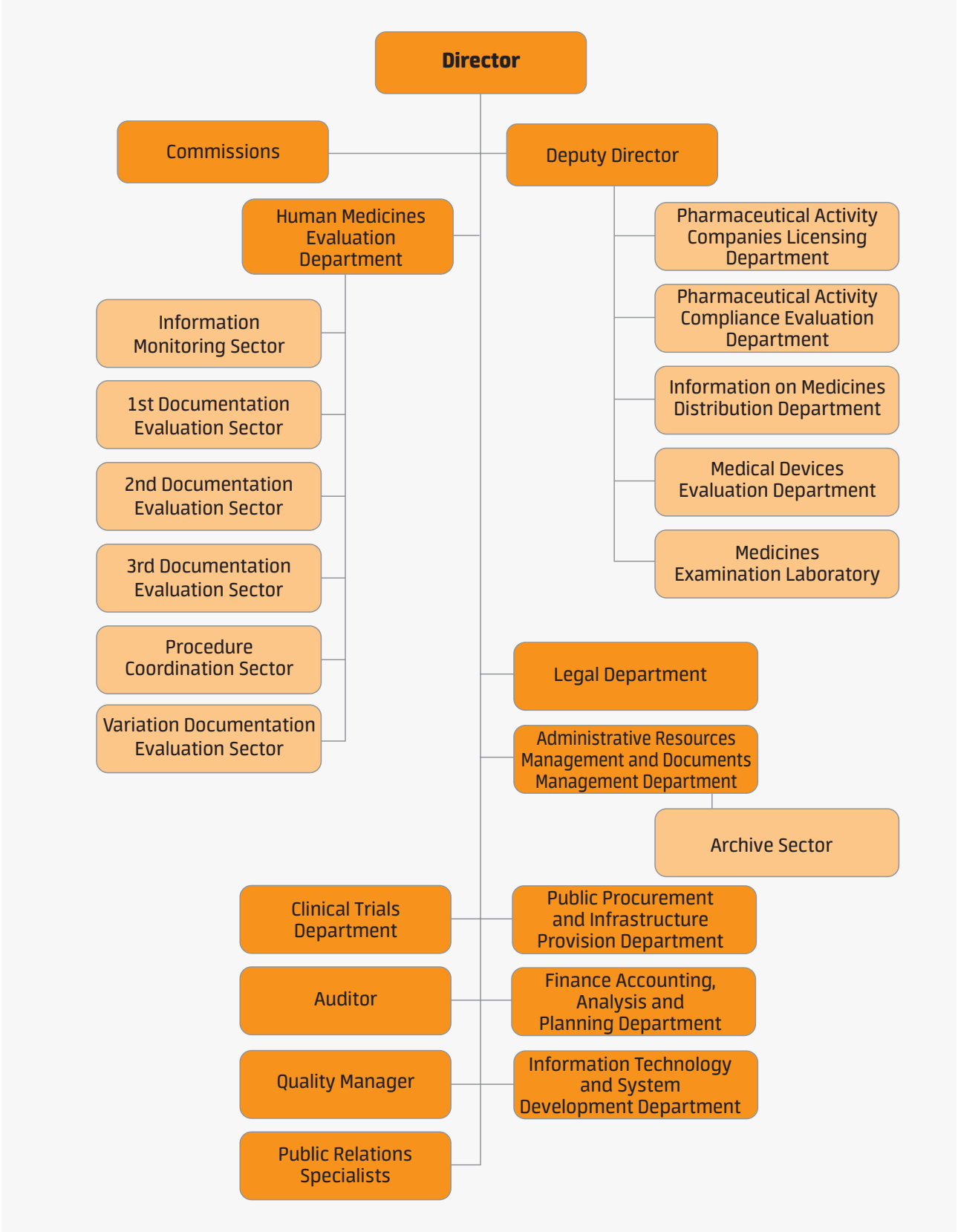
- Promote sustainable development of the national market of medicines.
- Ensure the prerequisites for the safe and rational use of medicines, medical devices, tissues, cells, organs, blood and its components.
- Improve the efficiency of the Agency's operation, also by using the BEMA III experience.

In accordance with the approved strategy for 2014-2016 the following objectives have been set as priorities for 2015:

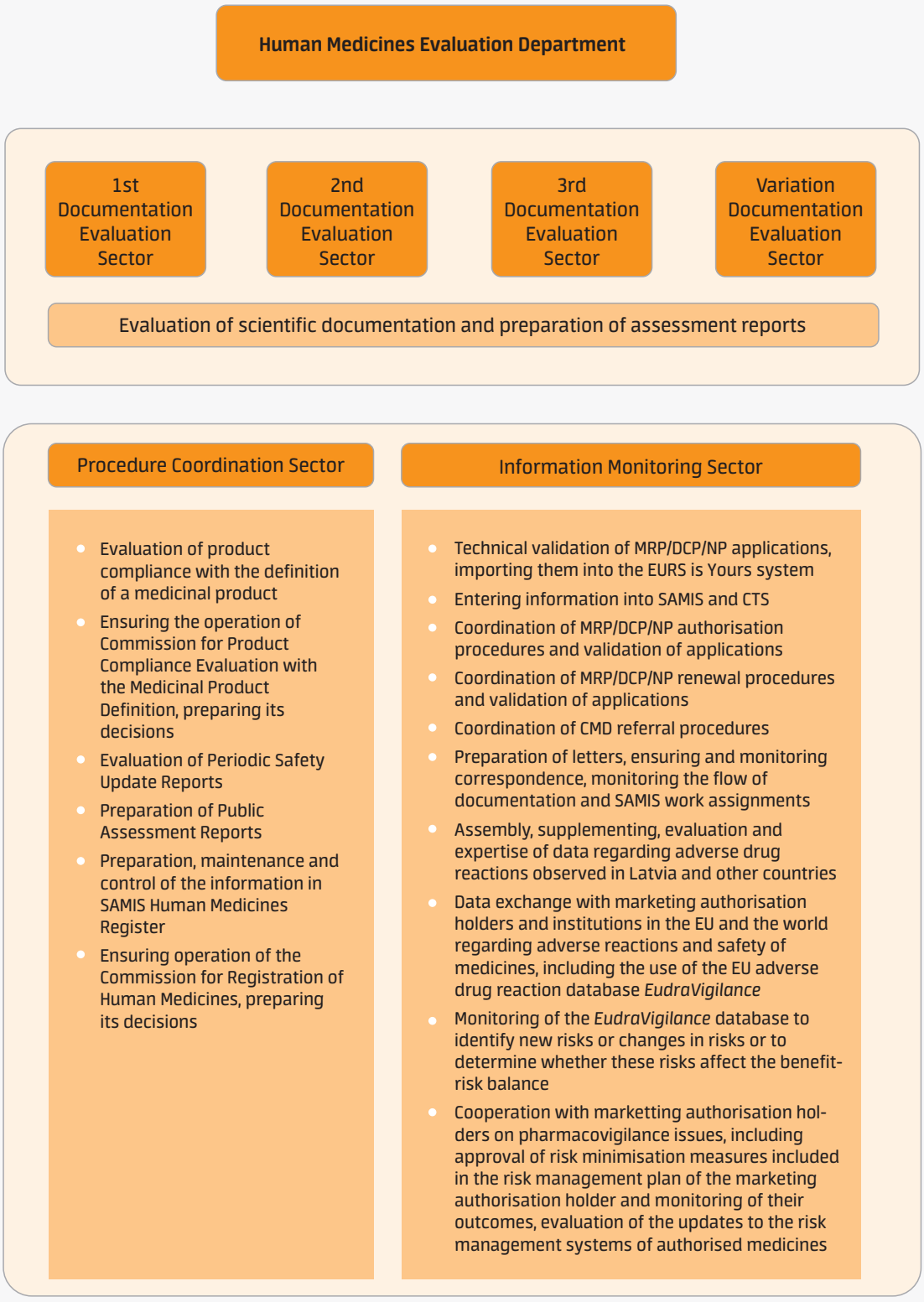
- Operate as a public agency, an institution non-financed from the state budget, foreseeing additional budget grants for the performance of specific functions.
- Increase the number of MRP/DCP procedures assuming the responsibilities of the Reference Member State.
- Participate in centralised authorisation and post-authorisation procedures assuming the responsibilities of a rapporteur/co-rapporteur.
- Promote and develop cooperation with academic and scientific institutions by ensuring involvement of academic forces in complex expertise cases and by offering new skills to pharmaceutical and biomedical research centres to promote innovations.
- Increase expert professionalism and within the range of possibilities - actively participate in EMA scientific committees and working groups, work-sharing programs within the network of European medicines agencies, WHO programs.
- Strengthen the capacity and amount of work of the Medicines Examination Laboratory.
- Introduce e-management; improve the receipt and processing of electronic marketing authorisation documentation (e-CTD, CESP), as well as receipt and sending of electronic documentation whenever possible
- Ensure the events planned in 2015 as part of the Latvian Presidency of the Council of the European Union in accordance with international standards:
- Ensure data exchange with European databases with respect to data regarding medicines, medical devices, clinical trials, manufacturers, distributors and tissue, cell and organ centres (undertake the commitments defined by the *Memorandum of Understanding on the Exchange of information in the context of EU Telematics*).
- Actively participate in e-Health projects and in the IT development projects in the field of health.
- Develop a quality management system and participate in the BEMA III program.
- Update and review SAM internal procedures to increase work efficiency and participation of the public at the time of continuously changing circumstances.

7. ANNEXES

7.1. Annex. SAM Structure



7.2. Annex. Structure of the Human Medicines Evaluation Department



7.3. Annex. Functions of the Structural Units of SAM

Human Medicines Evaluation Department

- Performs marketing authorisation and renewal of medicines in the national, mutual recognition and decentralised procedures, accepts the submitted variations to documentation.
- Carries out expertise on chemical and pharmaceutical, pharmacological and toxicological documentation of medicines, on clinical trials, summaries of product characteristics, package leaflets, labelling and on other documents.
- Collects, updates, evaluates and carries out expertise on data regarding adverse drug reactions observed in Latvia and in foreign countries.
- Carries out data exchange regarding adverse drug reactions and safety of medicines with marketing authorisation holders and institutions in the European Union and in the world, also by using the EU *EudraVigilance* database for adverse drug reactions.
- Monitors data within the *EudraVigilance* database to determine whether there are new risks, the risks have changed or whether these risks have an impact on the benefit-risk balance.
- Cooperates with marketing authorisation holders on pharmacovigilance issues, approves the risk minimisation measures included in the risk management plan of the marketing authorisation holder and monitors their outcomes, as well as evaluates updates of risk management systems for medicines.
- Evaluates the compliance of marketing authorisation holders with good pharmacovigilance practice.
- Prepares information regarding safety of medicines for doctors, pharmacists and the public, participates in the preparation of the SAM bulletin *"Cito!"*. Cooperates with EMA, especially in order to develop pharmacovigilance procedures. Informs competent authorities of other EEA countries, the EMA, as well as the marketing authorisation holder, if new risks have been detected, the current risks have changed or changes in benefits and risks have been detected.

Distribution of Information on Medicines Department

- Carries out expertise on applications and documentation and issues authorisations for:
  - Import and export of psychotropic, narcotic medicines/substances and precursors
  - Use of plants, substances and medicines included in the I, II and III list of narcotic, psychotropic substances and precursors controlled in Latvia for medical and veterinary medical scientific research or training, as well as determining their physical and chemical properties
  - Distribution of unauthorised medicines
  - Import of samples of medicines
  - Distribution of remaining stock of medicines
  - Distribution of and variations to parallel imported medicines in Latvia
- Carries out expertise on applications and documentation and issues special permits (licences) for operation with precursors, issues precursor operator cards.
- Carries out expertise on applications and issues authorisations for purchase of medicines (to ensure own operation).
- Assembles and provides information regarding consumption, prices and availability of medicines, turnover of pharmacies, medicines wholesalers and manufacturing companies.
- Records and controls the legal circulation of narcotic substances, psychotropic substances and precursors controlled in Latvia.

Clinical Trials Department

- Evaluates the applications and related documentation of clinical trials received from local and foreign sponsors, as well as issues authorisations for the initiation of clinical trials in Latvia.
- Supervises and controls the clinical trials carried out in Latvia, as well as evaluates the compliance of clinical trials with the requirements of good clinical practice.
- In relation to applications for marketing authorisation of medicines, carries out good clinical practice inspections at clinical trial centres within the European Economic Area (EEA), as well as in countries outside of EEA.
- Evaluates the applications for non-interventional studies and ensures their authorisation in SAM.

Medicines Examination Laboratory

- Carries out testing of samples of medicines manufactured in the Republic of Latvia and in foreign countries by determining the compliance of samples of medicines with the requirements of normative documentation submitted for marketing authorisation.
- Carries out the selection and testing of purified water samples in pharmacies.
- Prepares volumetric solutions, indicators and reagents upon request from pharmacies.

Medical Devices Evaluation Department

- Performs compliance evaluation and authorisation of medical devices.
- Develops, maintains and updates the LATMED medical devices database that contains information regarding medical devices, their manufacturers, distributors, clinical trials, as well as vigilance system reports.
- Evaluates the compliance of clinical trial documentation with the requirements of normative acts before the initiation of the clinical trial, adopts decisions regarding issuance of authorisations for conduct of clinical trials and monitors the conduct of the trials.
- Performs vigilance for medical devices, ensuring timely circulation of information regarding risks or danger of using medical devices to people receiving healthcare services and users of medical devices that could be exposed to such risks. Supervises corrective safety measures.

Pharmaceutical Activity Compliance Evaluation Department

- Evaluates the compliance of the pharmaceutical activity companies (human medicines manufacturing/ importing companies, including foreign manufacturing companies, medicines wholesalers) in accordance with the legislation and normative acts of the Republic of Latvia, and the requirements of the European Commission.
- Monitors and evaluates the compliance of procurement and storage centres of tissues, cells and organs, blood establishments, hospital blood banks and the State Blood Donor Centre.

Pharmaceutical Activities Company Licensing Department

- Ensures licensing of pharmaceutical activity companies to issue special permits (licences) to companies for pharmaceutical activity.
- Develops and maintains the informative base of licensed pharmaceutical activity companies.
- Evaluates and inspects the compliance of active substance manufacturers and importers with the requirements of good manufacturing practice and issues good manufacturing practice certificates.
- Evaluates and inspects the compliance of distributors of medicines and active substances with the requirements of good distribution practice and issues good distribution practice certificates.
- Registers manufacturers, importers and distributors of active substances.
- Registers persons conducting international transactions with medicines for human use.

Finance Accounting, Analysis and Planning Department

- Conducts account of finances.
- Assembles information regarding economic activities of SAM.
- Prepares and submits reports and declarations.
- Ensures the internal control of accounting processes regarding the application of material, human and financial resources.
- Ensures strategic and short-term financial planning.

Public Procurement and Infrastructure Provision Department

- Organises public procurements.
- Ensures management of material assets and organises activities for work safety.
- Manages the building complex and territory that is in the property of SAM.

Administrative Resources Management and Documents Management Department

- Establishes, implements, controls and develops work processes for planning, selection, involvement, maintenance, evaluation and development of human resources.
- Manages all issues regarding personal files and ensures the documentation of civil service and legal employment relationship in accordance with legislative acts.
- Organises and supervises the record keeping process and the system for management of documentation in the institution.
- Ensures SAM client service by providing information about processes ensuring the functions of the Agency and the appropriate procedure for receiving and issuing of documents.
- Carries out certain functions delegated to it by the SAM administration in accordance with the requirements of the State Administration Structure Law.
- Ensures the operation of SAM library.
- Manages SAM Archive.

Legal Department

- Ensures the compliance of administrative acts prepared by SAM with the requirements of current legislation, including requirements of the European Union legislative acts and rulings of the Court of Justice of the European Union, and also prepares administrative documents regulating SAM operations.
- Lawfully solves legal issues and problems.
- Prepares and evaluates contracts, documentation projects, various opinions.
- Prepares projects for normative acts.
- Represents the interests of SAM in Court institutions.

Information Technology and System Development Department

- Ensures the maintenance of local computer network, servers, software and work stations and a united standardised environment, provides consultations to employees and practical help in dealing with IT issues.
- Ensures connection to the data transmission network for employees and clients.
- Ensures the creation of data backup copies, logical protection of the computer network and data, electronic communication and Internet information service and prevention of damage to the facilities.

Quality Manager

- Organises and carries out the activities necessary for the maintenance of the integrated management system.
- Carries out monitoring and analysis of processes.
- Coordinates SAM participation in BEMA.

Supervisory Auditor

- Prepares internal audit plans.
- Organises and performs pharmacovigilance system audits, internal audits.
- Together with the quality manager organises and carries out the activities necessary for the maintenance of the integrated management system.
- Coordinates the assessment of SAM risks.

Public Relations Specialists

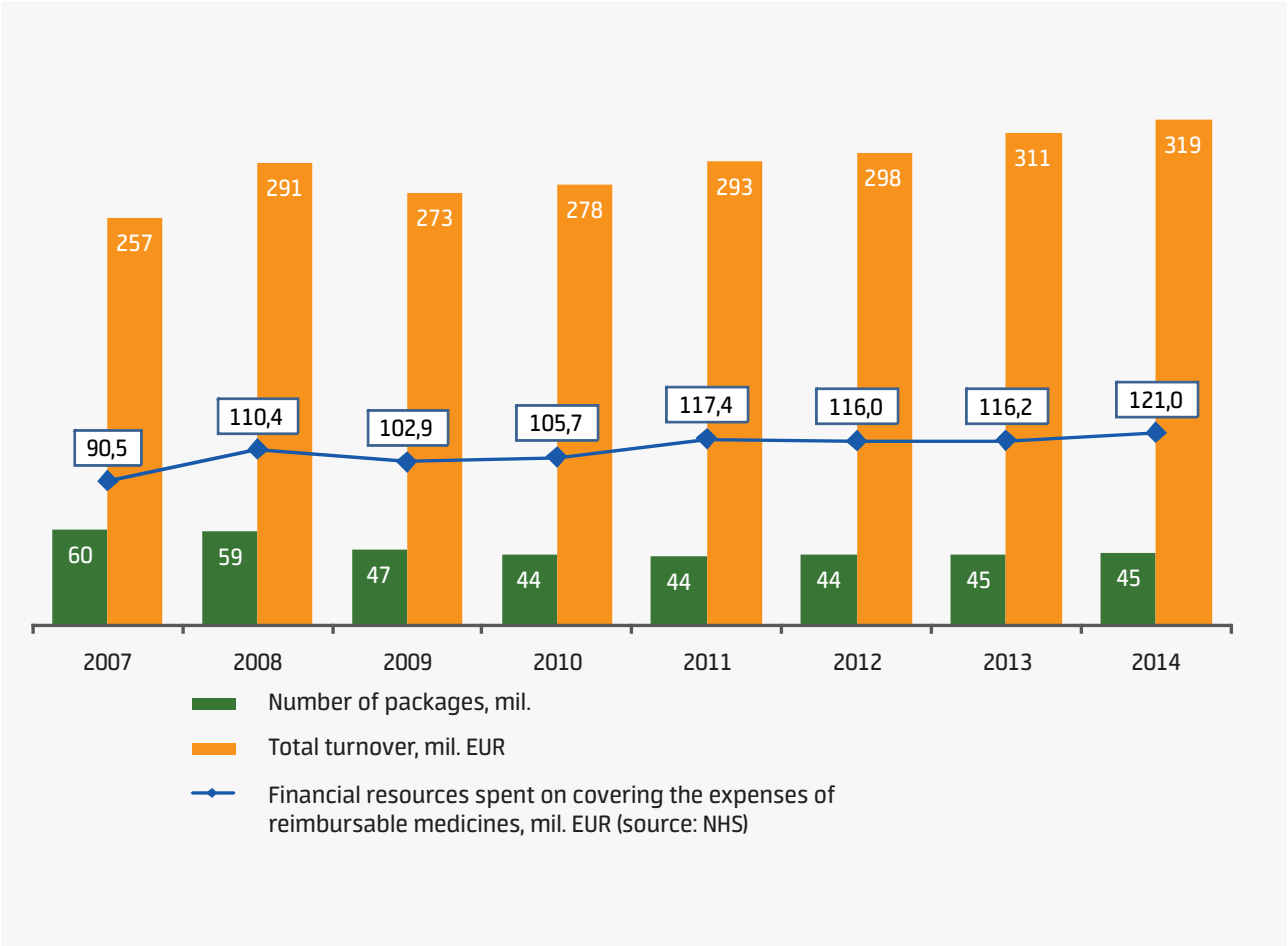
- Inform the public about field politics in the competency of SAM by creating a clear and accurate impression of SAM operations and new developments in the field.
- Represent a SAM administration approved opinion in the mass media.
- Coordinate information updates on the internal and external SAM website.
- Develop the corporative identity of SAM.

7.4. Annex. SAM History

Date	Event
11.09.2014.	Business meeting of the representatives from the medicines agencies of the Baltic states in Tartu, Estonia.
05.09.2014.	20th anniversary edition of SAM informative bulletin "Cito!" for doctors, pharmacists and other health-care professionals.
05.2014.	SAM introduces a project management system, establishes a SAM Development Plan and a SAM Development Commission and initiates the implementation of 10 projects in accordance with the project management methodology.
08.04.2014.	The Adverse Drug Reaction Monitoring Department is reorganised and its functions are transferred to the Human Medicines Evaluation Department.
24-28.02.2014.	BEMA III visit at SAM.
2014	SAM performs new functions related to manufacturing, import and distribution of active substances and starts the registration of persons conducting brokering with medicines.
17.06.2013.	SAM Medicines Examination Laboratory is re-accredited as compliant with the requirements of the ISO 17025 standard; the fixed area of accreditation is expanded into a flexible one.
01.01.2013.	In accordance with the Law on Public Agencies SAM begins operation as a public agency non-financed from the state budget.
21.12.2012.	The SAM integrated management system is certified in accordance with the requirements of the ISO 27001 standard.
19.12.2012.	The SAM integrated management system is certified in accordance with the requirements of the ISO 9001:2008 standard.
22.11.2012.	The Heads of the medicines agencies of the Baltic states sign a contract in Riga regarding cooperation in the field of GMP, GDP, GVP, GCP and testing of medicinal products.
08.11.2012.	SAM receives the Quality Innovation Award 2012 for its interactive map of pharmacies in Latvia developed in 2011 and publicly available on SAM website.
31.07.2012.	The CM Regulation No. 537 "The Statutes of the State Agency of Medicines" is approved and shall come into effect on 1st January 2013 laying down that starting from 1st January 2013 SAM shall operate in accordance with the Public Agency Law and Law on Budget and Financial Management as an institution non-financed from the budget.
23.07.2012.	SAM participates in the opening meeting of the newly established EMA Pharmacovigilance Risk Assessment Committee, Latvia is represented in the Committee by Andis Lācis, the Head of the Residency Section of the Faculty of Continuing Education within Riga Stradins University, and Inguna Adoviča, the Director of SAM.
26.06.2012.	SAM issues a new electronic publication for doctors and pharmacists "Drug Register of the Republic of Latvia" including summaries of product characteristics and package leaflets in DVD format.
13.10.2011.	The medicines agencies of the Baltic states sign an agreement regarding cooperation in the quality control of medicines
09.10.2011.	15 years since the establishment of SAM. To celebrate the 15th anniversary SAM personnel plants a white fir in the Garden of Destiny with an inscription "Pledge to Motherland".
From 26.08.2011 until the end of October	Participation as co-rapporteur in a repeated review by the EMA Committee for Advanced Therapies by authorising newly introduced therapy medicines.
19.07.2011.	A list of active substances is published on SAM website in three languages: Latvian / Latin / English.
16.05.2011.	The first digital map of pharmacies with broad search options is established on SAM website.
02.02.2011.	Contract between the medicines agencies of the Baltic states regarding a unified procedure for labelling medicines.
01.10.2010.	The compliance evaluation and surveillance of procurement and storage organisations of human tissues, cells and organs, blood establishments, hospital blood banks and the State Blood Donor Centre is initiated.
01.10.2010.	The function of compliance evaluation, authorisation and monitoring of safety of medical devices is assumed.
06-08.09.2010.	The European Union Benchmarking (BEMA II) visit at SAM.
09.07.2010.	Memorandum of Agreement with EMA regarding mutual exchange of information and documentation.
25.06.2010.	Memorandum of Agreement with the Food and Drug Administration of the People's Republic of China about cooperation regarding normative regulation of medicines.
01.02.2010.	Establishment of a Client Service Centre.
11.08.2009.	Contract between the medicines agencies of the Baltic states regarding a united packaging of medicines in three languages.
15.07.2009.	The Medicines Examination Laboratory is accredited in accordance with the requirements of the ISO 17025 standard.
19.09.2008.	Recognition from the Riga City Council for original front lawn greenery.
14.01.2008.	Memorandum of Agreement with Lithuania regarding cooperation in the monitoring of medicines.
2008	The first Mutual Recognition Procedure was carried out where Latvia was the Reference Member State.

27.12.2007.	Memorandum of Agreement between national medicines agencies of the EEA member states and the European Medicines Agency about the exchange of information and documents regarding pharmacovigilance.
09. – 12.2007.	The concept for the e-prescription information system is developed.
11.07.2007.	Memorandum of Agreement with Estonia regarding cooperation in monitoring of medicines.
01.02.2007.	State civil service is introduced at SAM.
December 2006	The technological updating and structural modification of the Drug Register is carried out and the State Agency of Medicines Information System SAMIS is developed.
10.11.2006.	A meeting of the medicines agencies of the Baltic states takes place in Riga
01.07.2006.	Due to the introduction of new principles in the quality control of medicines prepared in pharmacies, the Medicines Quality Control Laboratory and its branches in Riga, Daugavpils, Cesis and Liepaja cease their operation.
10.04.2006.	The Pharmaceutical Activities Compliance Evaluation Department is established.
06.-10.02.2006.	The European Union Benchmarking (BEMA I) visit at SAM.
02.01.2006. – 31.12.2010.	The authorisation of veterinary medicines and monitoring their circulation is delegated to SAM.
02.01.2006.	The Pharmaceutical Activities Company Licensing Department is established by reorganising the Legal Department, the function of licensing pharmaceutical activity companies is adopted from it.
02.01.2006.	The Information Department is transformed and the Department of Information on Medicines Distribution and the Information Technology Department are established.
2006	Participation within PIC/S (Pharmaceutical Inspection Cooperation Scheme) is initiated.
2006	The evaluation of employee activities and outcomes is initiated and performed for the first time.
End of 2005	A new function is delegated to SAM - establishment and maintenance of a system for monitoring the prices of medicines.
02.11.2005.	The Cabinet of Ministers of the Republic of Latvia appoints (Order No. 707) Inguna Adoviča as the Director of SAM
25.04.2005.	Jānis Ozoliņš, the Director of SAM, tragically passes away.
2005	An educational publication "Introduction to Pharmacovigilance" is issued.
End of 2004	The Archive building is commissioned.
2004	Access to and unified operation in databases of EU member states is established via the EudraNET network.
01.11.2004.	The non-profit organisation, state JSC "State Medicines Agency" is reorganised as the public agency "State Agency of Medicines" and Jānis Ozoliņš is reappointed as the Director.
01.07.2003.	The Legal Department is established.
2003	The first edition of "Statistics on Medicines Consumption" is published.
2003	The first Benchmarking (BEMA) visit at the Agency.
2002	The Agency is welcomed into the WHO International Drug Monitoring Program as the 66th member state.
2002	The Medicines Examination Laboratory is welcomed into the international network of Official Medicines Control Laboratories (OMCL).
17-18.03.2002.	The 5th European Union meeting of associated drug regulatory authorities takes place in Latvia - within the CADREAC cooperation agreement.
01.10.2002.	The internal audit is introduced and the development of a Quality Management System is initiated.
02.01.2001.	The Adverse Drug Reactions Monitoring Department is established.
From 02.01.2001. until 31.12.2009.	The function of evaluating and approving advertisements of medicines is carried out.
2001	The preparation of an independent informative bulletin "CITO" for doctors and pharmacists is initiated.
2000	International Harmonisation Conference guidelines regarding Good Clinical Practice are published (in Latvian and English).
End of 2000	The second section of the Agency building is commissioned.
1999	The first SAM website is developed.
1999	The first Annual Report is published.
02.03.1998.	The Clinical Trial Inspection Department is established.
1998	The electronic record keeping program "Lotus Notes" is introduced.
1997	The publication of the annual issue "Drug Register of Latvia" is initiated.
05.03.1997.	The first marketing authorisation No. 97-0001 is issued for the medicine "PNU-Imune 23" (Marketing authorisation holder - Cyanamid-Lederle Arzneimittel GMbH).
09.10.1996.	A non-profit organisation - state joint stock company "State Medicines Agency" is established. Jānis Ozoliņš is appointed as the General Director and Chairman of the Board.

7.5. Annex. Total Turnover of Medicines in Latvia



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