State Agency of Medicines of the Republic of Latvia

STATE AGENCY OF MEDICINES
ANNUAL REPORT
2015

State Agency of Medicines of the Republic of Latvia

STATE AGENCY OF MEDICINES

ANNUAL REPORT 2015

CONTENT

FOREWORD

Dear readers,

2015 has been a year filled with challenges for the State Agency of Medicines. Latvia assumed the responsibilities of the presiding member state of the Council of the European Union and organised various events within the collaboration network of pharmaceutical regulatory authorities in Europe. The Latvian presidency was an opportunity to influence processes and priorities on the European Union agenda and to prove that the State Agency of Medicines is an equal partner within the collaboration network of European agencies, as well as to introduce foreign audiences to Latvia and its treasures of culture and history. One of the most significant events under our responsibility was the Heads of Medicines Agencies meeting taking place in Riga on 3–5 February 2015 and attended by 80 delegates from medicines agencies of European countries, from the European Commission (EC) and the European Medicines Agency (EMA). The meeting agenda included several strategic issues such as ensuring the availability of medicines in Europe, the issue of disruptions in the supply of medicines, latest issues in pharmacovigilance or medicines safety surveillance, as well as the preparation of the common HMA and EMA strategy for the following five years. The meeting taking place in Riga was the 79th Heads of Medicines Agencies meeting, meaning that the heads of the medicines agencies of European countries have been collaborating in this format for almost 20 years, thus, promoting the development of a unified regulation within Europe. Overall the State Agency of Medicines organised seven such meetings of experts and managers (see more detailed information in Section 4.6 "International Collaboration" of this report). It should be emphasised that the successful course of all of these events was possible due to the professional conduct of the personnel and the leadership exerted by Inguna Adovica, the previous Director of the State Agency of Medicines.

2015 was also characterised by positive changes in the figures of basic activity of agency. At the end of 2015 the integrated management system of the State Agency of Medicines was recertified as compliant with the requirements of the ISO 9001 and ISO 27001 standards. The recertification audit was successfully concluded by obtaining the new LVS EN ISO 9001:2009 and LVS ISO/IEC 27001:2013 certificates. The certified area of operation verifies the constantly high standards of SAM functions and services within the area of expertise on quality of medicines, expertise on authorisation and post-authorisation documentation of medicines and medical devices, pharmacovigilance and vigilance of medical devices, issuance of special permits (licences), authorisations and marketing authorisations in accordance to the authorisation of the institution, expertise on related documentation, assembly and publication of information according to authorisation. As in the previous years the recertification audit was performed by *Bureau Veritas Latvia*.

With regard to the participation of the State Agency of Medicines in the development of the pharmaceutical policy in Latvia, it has to be noted that in 2015 in collaboration with the Pharmaceutical Department of the Ministry of Health several amendments to normative acts targeted towards the improvement of the availability of medicines were prepared, discussed within the field and approved. In order to implement these amendments minor structural changes were introduced within the State Agency of Medicines to ensure optimal human resources for the performance of the additional tasks.

With the development of the global network and information technologies, more and more often medicines are purchased online. However, medicines are special products, therefore, regulatory authorities have to aspire to ensure maximal consumer protection against illegal traders and illegal products. In order to ensure the safety of purchasing medicines online the European Commission has developed a common logo for authentication of online pharmacies. The State Agency of Medicines was the authority responsible for the introduction and implementation of this project in Latvia. It was successfully introduced in July 2015. There are four pharmacies in Latvia that have received a licence for distribution of non-prescription medicines online and it is the responsibility of these pharmacies to place the "Click here to verify, if this website is operating legally" logo created by the European Commission on their websites as a confirmation of the legality of the website for the visitors.

An important European Union level event was the approval of the new strategic document for the EMA and HMA at the end of 2015. For the first time a unified strategy has been developed for the whole network of regulatory authorities for medicinal products in Europe. This strategy outlines common challenges and lays down common priorities and directions of high-level collaboration with the purpose of reaching the objectives set for the following five years. The strategy document also contains the strategic priorities on the agenda of the European Commission and the European Union related to the public and animal health. The new strategy focuses on areas where collaboration within the network could provide considerable benefits to the public and animal health in the European Union and it has been established basing on the four most important future directions of action, meaning:

- Contribution to the public health;
- Contribution to animal and human health within the context of veterinary medicines;
- Improvement of the operation of the collaboration network;
- Contribution to the global regulatory environment.

In 2016 and further on the State Agency of Medicines will work intensively with the aim to ensure the availability of safe, qualitative and effective medicinal products to the people in Latvia, including also directions such as analysis of disruptions in the chain of supply of medicines and strengthening the role of SAM within the network of European agencies. Another important future direction of operation is strengthening the dialogue with the public, healthcare professionals, pharmacists and manufacturers of medicines and medical devices in Latvia. Finally, issues that are to be dealt with in the near future at the start of 2016 are the development of information technologies, operation in the area of availability of e-services, reduction of the administrative burden and effective operation of the Agency as a whole.

Without doubt the State Agency of Medicines of Latvia is not conceivable outside of the network of pharmaceutical regulatory authorities in Europe. At the moment information technology solutions are actively being developed at the European level to implement the clinical trial regulation adopted in Europe. Intensive work is being done with the objective of establishing a common information technology solution for procedures throughout the life cycle of medicinal products. The year of 2016 will bring new challenges and the State Agency of Medicines is already preparing to meet them.

Director of the State Agency of Medicines,
Svens Henkuzens

ABBREVIATIONS USED IN THIS REPORT

ADR	Adverse drug reaction
BEMA	Benchmarking of European Medicines Agencies
CDPC	Centre for Disease Prevention and Control
CHMP	EMA Committee for Medicinal Products for Human Use
CM	Cabinet of Ministers
CPP	Certificate of Pharmaceutical Product
CRP	Centralised authorisation procedure
DCP	Decentralised authorisation 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	EMA 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"". Since 2nd November 2005 till 2nd November 2015 Inguna Adoviča was the Director of SAM. On 3rd November 2015 Svens Henkuzens has started to fulfil his duties of office as the Director of the SAM.

1.2. FUNCTIONS OF THE STATE AGENCY OF MEDICINES

The 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 (brokers) 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 agencies' 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 2015 was approved on 19th January 2015. The Work Plan lays down specific tasks for each department 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 2015 the following priority tasks were set for the year of review:

- 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 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 the IT development projects in the field of health in Latvia;
- Develop a quality management system and participate in the BEMA audit program;
- Update and review SAM internal procedures to increase work efficiency at the time of continuously changing circumstances.

2. RESULTS OF OPERATION OF THE STATE AGENCY OF MEDICINES

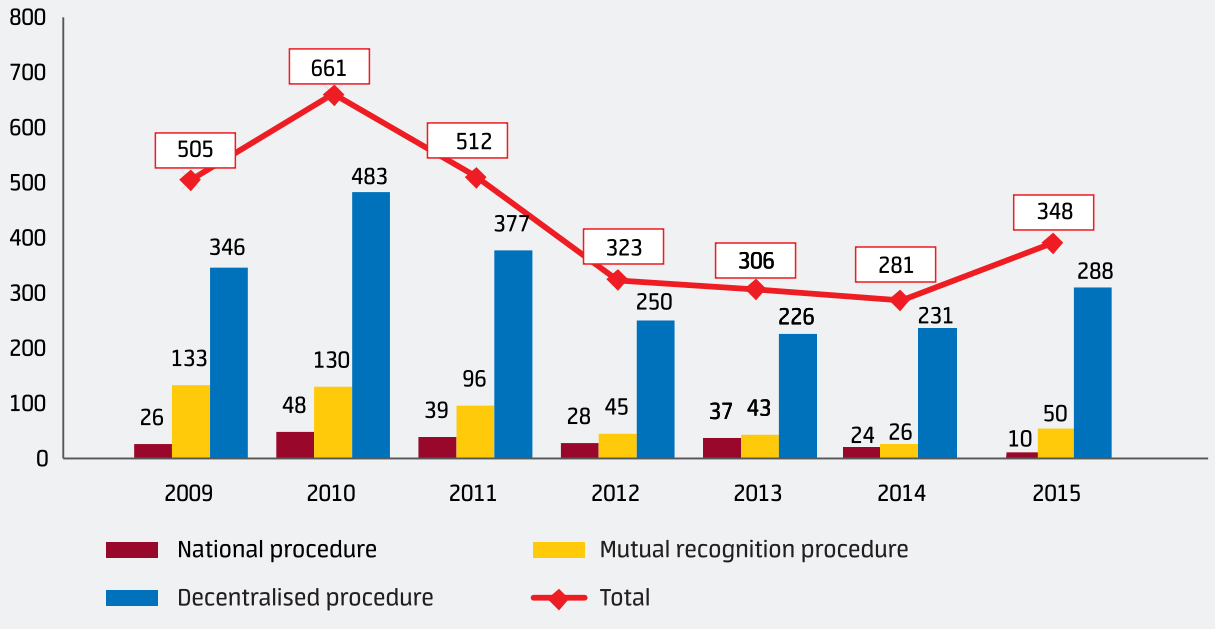
2.1. MARKETING AUTHORISATION OF MEDICINES

On 16th February 2015 the Human Medicines Evaluation Department of the State Agency of Medicines, its main function being authorisation of medicines, was reorganised and a Medicines Marketing Authorisation Department was established consisting of three divisions – Efficacy and Safety Division, Pharmaceutical Information Division and Procedures Coordination Division.

In accordance with the Cabinet of Ministers Regulation No. 376 of 23 June 2006 "Procedure for Registration of Medicinal Products" and other legal acts, in 2015 by evaluating medicinal product documentation with regard to quality, safety and efficacy the State Agency of Medicines conducted expertise more than 2000 times on the general, chemical and pharmaceutical, as well as pre-clinical and clinical sections of the documentation.

In 2015 assessment reports regarding 57 medicinal products were prepared for the SAM Commission on Marketing Authorisation of Human Medicines for the adoption of decision regarding marketing authorisation and renewal of medicines in the national procedure. In 2015 Latvia successfully led one mutual recognition procedure (MRP) and four decentralised procedures (DCP), as well as 5 mutual recognition renewal procedures as a Reference Member State. Also in 2015 Latvia took over four DCP procedures from other member states, thus, becoming the Reference Member State for these procedures. In 2015 Latvia initiated five DCP and two MRP renewal procedures.

MARKETING AUTHORISATION OF MEDICINES

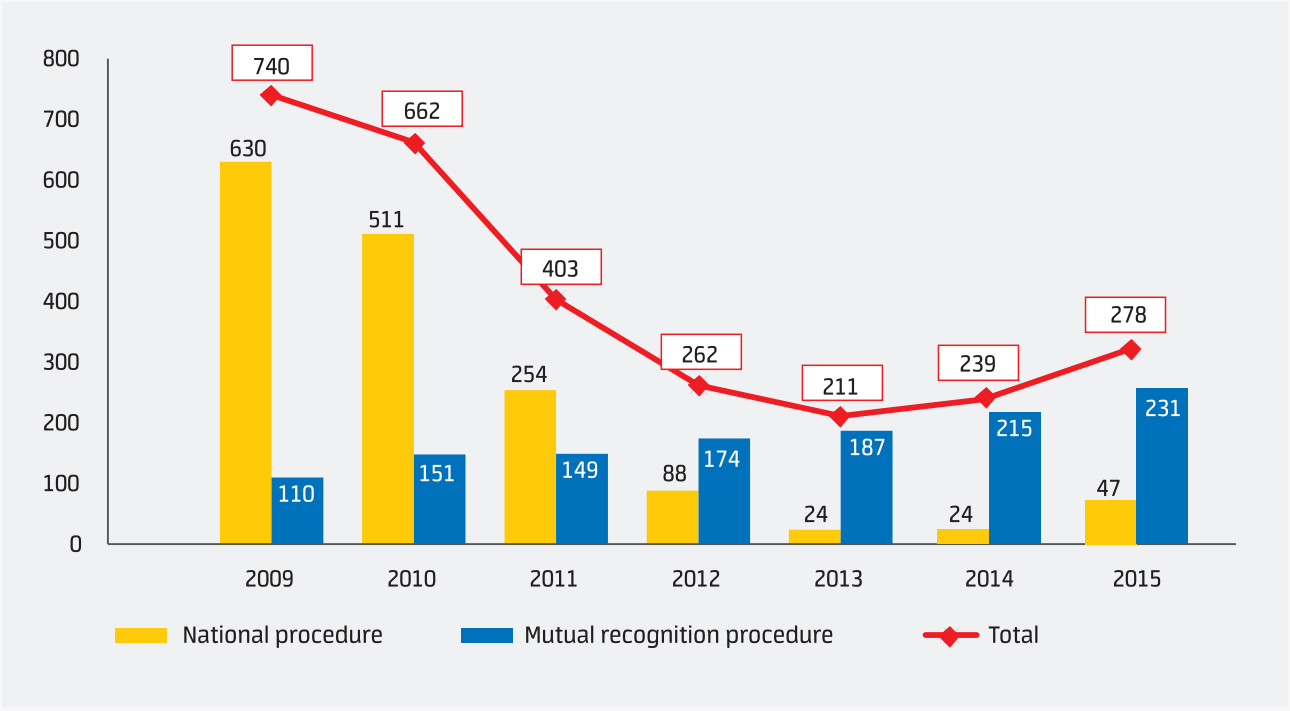


In 2015 the State Agency of Medicines carried out a total of 338 MRP/DCP authorisation procedures and 231 renewal procedures.

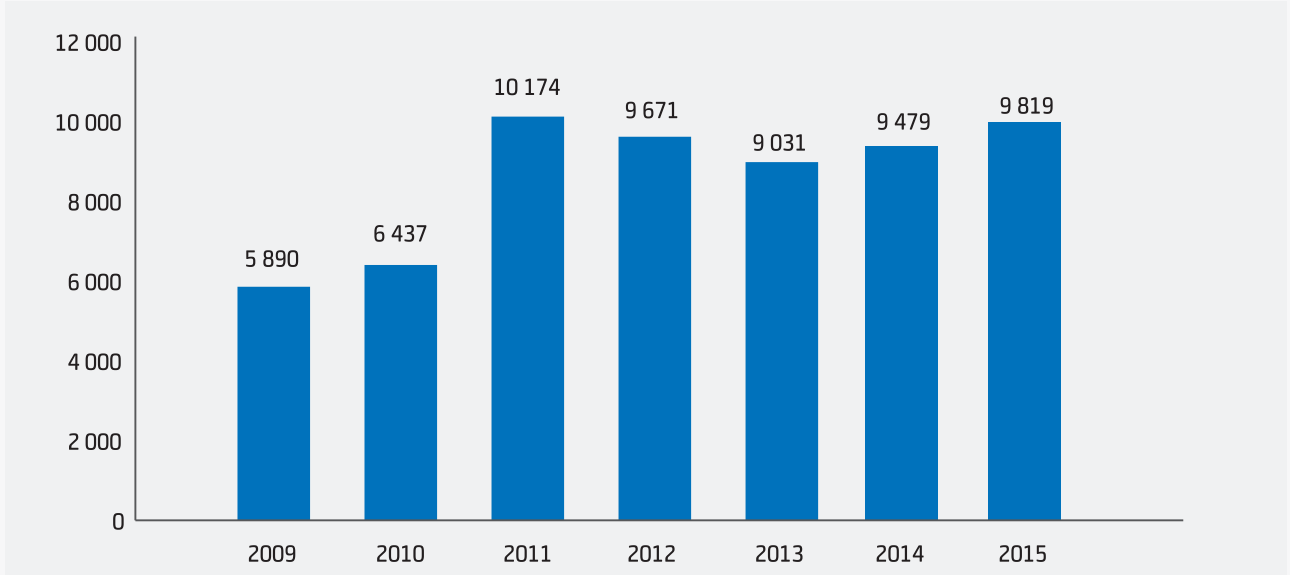
In the year of review SAM expert activity in international procedures was higher than earlier. In 2015 Latvia participated in the EMA Committee for Medicinal Products for Human Use (CHMP) by evaluating four centralised marketing authorisation procedures. In two of those centralised marketing authorisation procedures SAM experts assumed the role of the responsible rapporteur of the medicinal product documentation and the responsible PRAC rapporteur. Evaluation of a type II variation procedure for a centrally authorised medicinal product was also initiated in 2015. Latvia was the leading member state in the single assessment procedures of periodic safety update reports (PSUR) regarding four active substances.

Latvia is represented within the EMA Paediatric

RENEWAL PROCEDURE OF MEDICINES



VARIATIONS TO THE MARKETING AUTHORIZATION PROCEDURE



Committee and participated as a rapporteur in 10 Paediatric Investigation Plan (PIP) procedures and in three procedures as a co-rapporteur, as well as participated in two PIP modification assessment procedures as a rapporteur.

Experts from the Medicines Marketing Authorisation Department together with external experts have actively participated in the work of the Committee on Herbal Medicinal Products. In 2015 the Union monograph on *Polygoni avicularis herba* was successfully evaluated.

9819 variations to the documentation of authorised medicines were submitted and evaluated in 2015.

In the year of review 31 applications were received for the evaluation of compliance with the definition of medicinal product; and SAM issued its opinion regarding the status of these products. 138 periodic safety update reports were evaluated in 2015. 13 public assessment reports for nationally authorised medicines were prepared, coordinated with marketing authorisation holders and published in 2015.

The proportion of prescription and nonprescription medicines included in the Medicinal Product Register of Latvia has remained almost similar from year to year – with approximately 80% prescription medicines and 20% nonprescription medicines. In 2015 the precise proportion was 82% and 18%.

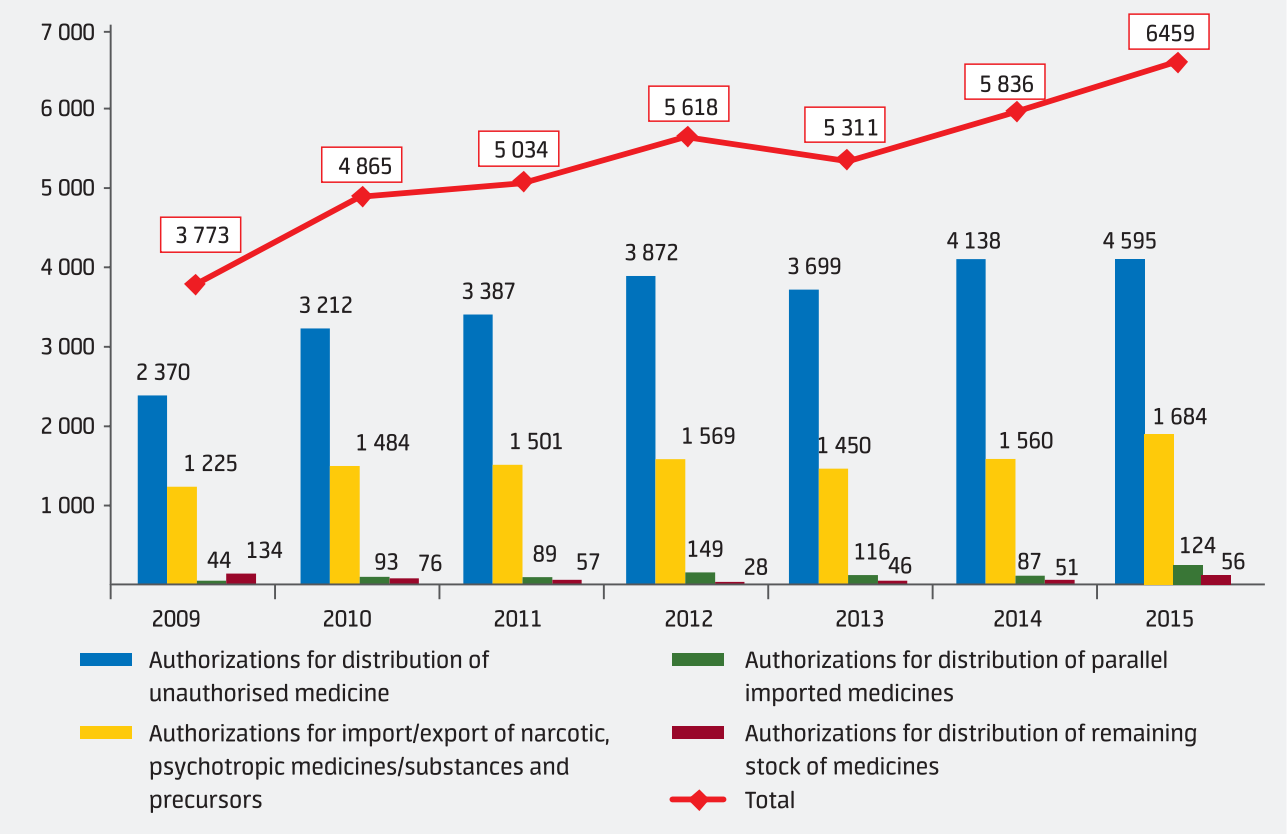
2.2. ISSUANCE OF AUTHORISATIONS FOR DISTRIBUTION OF MEDICINES

In 2015 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 2015 SAM issued 6464 authorisations for import, export and distribution of medicines. This includes 4594 authorisations for distribution of unauthorised medicines,

NUMBER OF AUTHORISATIONS FOR MEDICINES IMPORT, EXPORT AND DISTRIBUTION FROM 2009 UNTIL 2015



124 authorisations for distribution of parallel imported medicines and 56 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 carries 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).

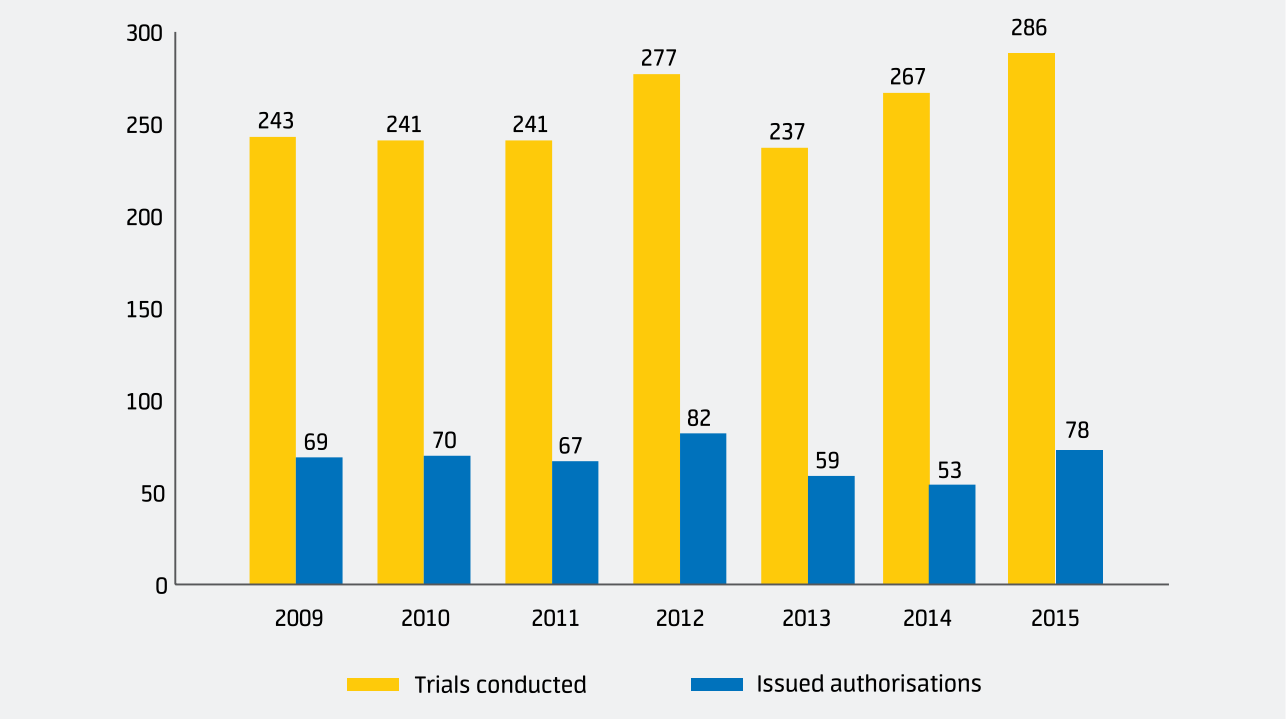
In 2015 five precursor operator authorisation cards were issued to precursor operators and one authorisation was issued for use of plants, substances and medicines included in the I, II and III list of narcotic, psychotropic substances and precursors for medical and veterinary medical scientific research or training, as well as determining their physical and chemical properties. Variations were made to marketing authorisations of 249 parallel imported medicines.

SAM ensures the accountancy 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 gathers and updates the information in the Medicinal Product Register regarding availability and prices of medicines, gathers 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.

NUMBER OF AUTHORISATIONS ISSUED AND CLINICAL TRIALS WITH MEDICINES (2009-2015)



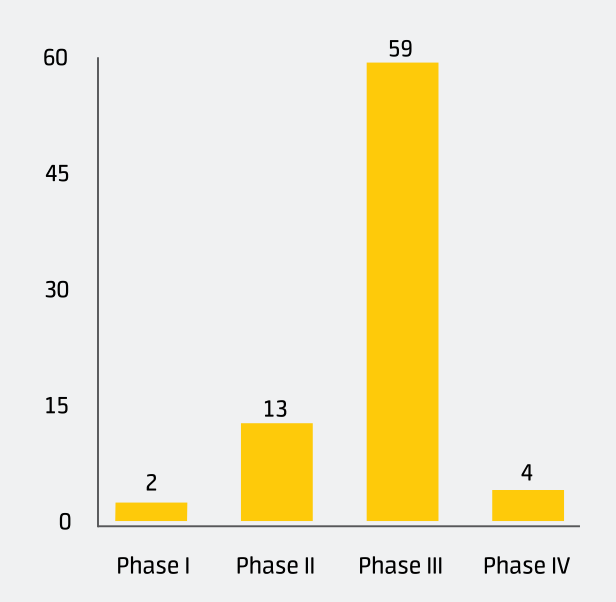
2.3. CLINICAL TRIALS WITH MEDICINES

In accordance with the Cabinet of Ministers Regulation No. 289 of 23 March 2010 "Regulations Regarding the Procedures for Conduct of Clinical Trials and Non-interventional Trials of Medicinal Products, Labelling of Investigational Medicinal Products and the Procedures for Assessment of Conformity of Clinical Trial of Medicinal Products with the Requirements of Good Clinical Practice" and legal acts of the European Union, in 2015 the State Agency of Medicines received 92 clinical trial projects for review, 30 of which were submitted for evaluation within the international harmonisation procedure.

In 2015 the State Agency of Medicines issued authorisations for the conduct of 78 clinical trials with medicines, 18 of which were issued within the international harmonisation procedure, and that is a considerably greater number of authorisations than in 2014 (53 and 12 authorised clinical trials respectively). Three of the authorised clinical trials were approved by applying limiting conditions. In 2015 the State Agency of Medicines granted 219 authorisations for amendments to clinical trials and 5 authorisations for non-interventional studies.

In the year of review two authorisations were issued to clinical trials (in the field of neurology and infectious diseases) with children and adolescents as the intended trial participants.

NUMBER OF CLINICAL TRIALS AUTHORISED IN 2015 ACCORDING TO TRIAL PHASE



NUMBER OF CLINICAL TRIAL AUTHORISED IN 2015 ACCORDING TO MEDICAL SPECIALITY

Speciality	Number of trials
Oncology	15
Pulmonology/Allergology	13
Dermatology	12
Psychiatry/Neurology	10
Gastroenterology	7
Rheumatology	6
Endocrinology	5
Ophthalmology	4
Infectology	3
Cardiology	2
Urology/Nephrology	1

CLINICAL TRIAL CENTRES OF THE CLINICAL TRIALS WITH MEDICINES AUTHORISED IN 2015

Clinical trial centre	Number of trials
P. Stradins Clinical University Hospital	48
Riga Eastern Clinical University Hospital • Clinic "Gailezers" • Latvian Oncology Center • Clinic "Tuberculosis and Lung Disease Centre" • Clinic of Gastroenterology, Hepatology and Nutrition • Chemotherapy and Haematology Clinic • Clinic "Linezers"	41 23 11 2 2 2 1
Daugavpils Regional Hospital	21
Liepaja Regional Hospital	14
LLC „Riga 1st Hospital"	10
Health Centre 4	9
LLC "Union of Balvi un Gulbene Hospitals"	7
LLC "Adoria"	6
JSC "Health Centre Union", medical centre "OLVI"	6
Sarmite Saleniece's medical practice in Rheumatology	5
LLC "Vidzeme Hospital"	5
Other clinical trial centres (122 in total)	1-4 trials at each centre

Out of all the clinical trials authorised in 2015, 28 clinical trials planned to investigate medicinal products obtained with recombinant DNA technology (monoclonal antibodies, hormones), two of them were clinical trials with vaccines and two clinical trials involved somatic cell therapy medicinal products.

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 within the EudraVigilance system by forwarding acknowledgements 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 in accordance with the local and European normative requirements. 76 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 149 annual safety reports prepared by sponsors regarding clinical trials conducted in Latvia. Separate annual safety reports were analysed in depth and the assessment is reflected in an established appropriate format.

Six external experts were involved in the evaluation of documentation of authorised clinical trial projects, conducting expertise in 9 cases.

A total of 286 clinical trials were conducted in Latvia in 2015 and 69 projects were completed during the year.

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 2015: *Amber CRO* (8 projects), *Quintiles* (9 projects), *PSI Company Limited* (7 projects), *Crown CRO Oy* (5 projects) and 21 other contract organisations (1-2 projects each).

A total of 6 inspections of clinical trial compliance with good clinical practice were carried out in 2015. Two inspections were conducted at trial centres in Latvia, but four inspections - in other countries. Both major and minor deficiencies were discovered during the inspections.

In the year of review employees of SAM Clinical Trials Department participated in the development of Regulation regarding clinical trials with medicinal products of the European Parliament and Council, as well as the European Commission and related normative acts and the portal.

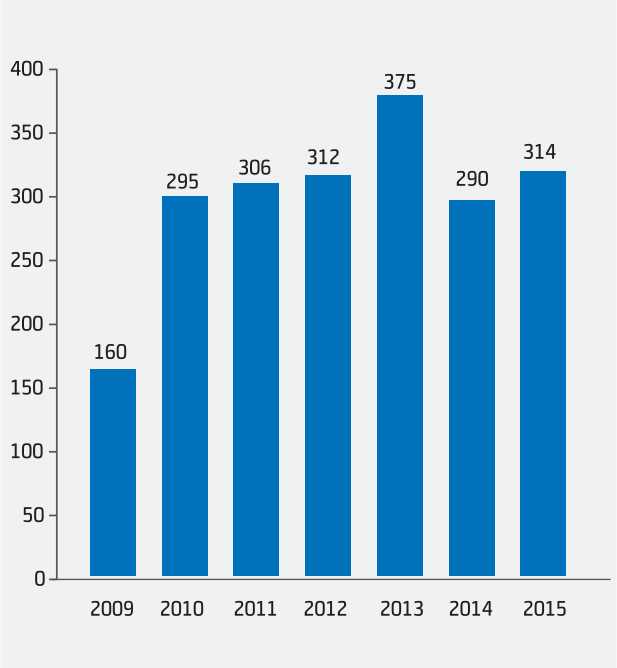
2.4. ADVERSE DRUG REACTION MONITORING AND RISK MINIMISATION

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. Every year SAM analyses the information entered into the database in Latvia and the reporting activity in Latvia.

The adverse drug reaction reporting activity in Latvia slightly increased in 2015. In 2015 the total number of adverse drug reaction cases reported to the State Agency of Medicines was 314.

Doctors and pharmacists submitted 51 reports. The Centre for Disease Prevention and Control (CDPC) submitted 89 reports regarding adverse reactions to vaccines. The reporting activity among marketing

ADVERSE DRUG REACTIONS REPORTS 2009-2015



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

The number of clinical cases reported to the State Agency of Medicines in 2015 increased to 198.

In 2015 SAM carried out 3 Good Pharmacovigilance Practice (GPP) inspections of MAHs.

Operating within the EU single assessment procedure SAM pharmacovigilance experts evaluated periodic safety update reports for medicines for the purposes of the European Community. In 2015 Latvia was a reference member state in the single assessment procedures of periodic safety update reports for 4 active substances.

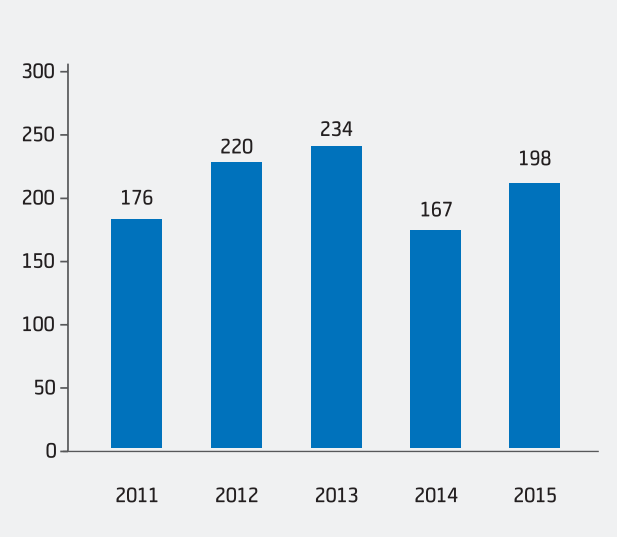
During the year periodic safety update reports were evaluated for 81 nationally authorised medicinal products and their assessments with recommendations regarding the necessary actions were forwarded to the marketing authorisation holders.

Starting from 2014 SAM has taken up the responsibility of signal monitoring for 10 active substances as part of the work-sharing procedure of the European Medicines Agency. Pharmacovigilance experts carried out regular surveillance of the safety information regarding these substances.

In comparison with the previous year, the number of risk management plans (RMPs) submitted for evaluation increased. RMP related documentation was evaluated for a total of 59 MAH applications.

SAM also collaborated with the MAH Qualified

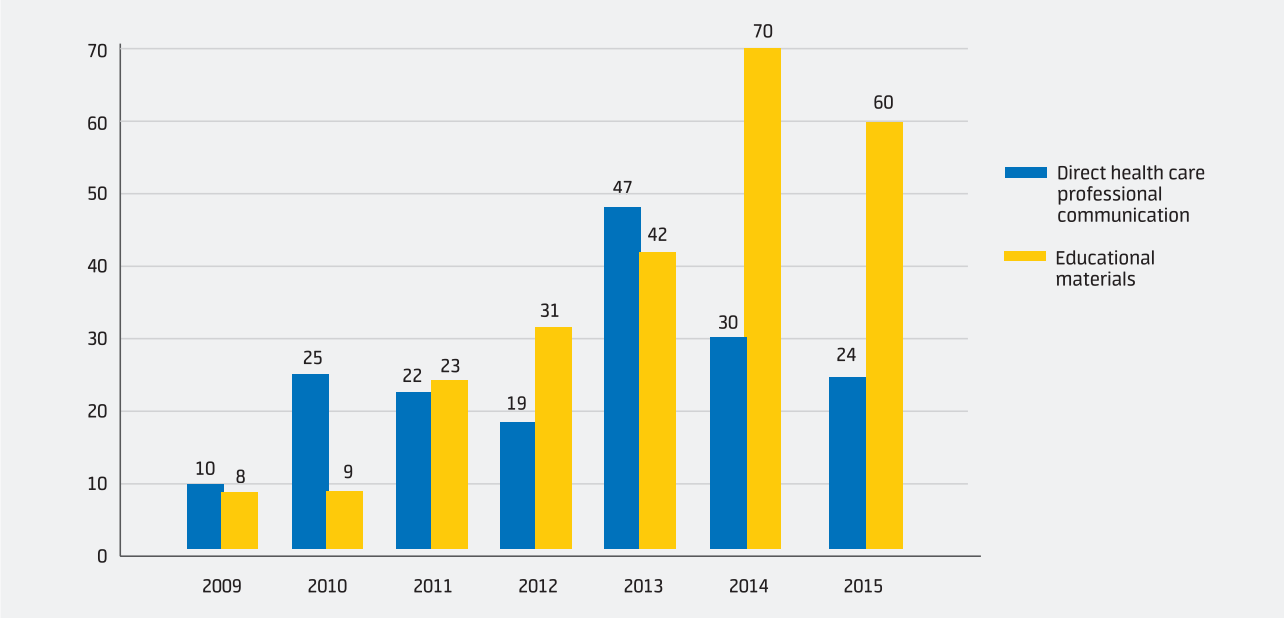
CLINICAL CASES OF ADVERSE EVENTS WITH MEDICINES



Persons Responsible for Pharmacovigilance. This ensures that the MAH established 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 also approves the MAH submitted projects for "Direct Healthcare Professional Communication" letters (DHPCs) and the educational materials (EM) intended for patients with the purpose of risk minimisation. During the year of review expertise was provided for 60 MAH submitted EMs and 24 DHPCs.

SAM regularly ensures the preparation of medicines

APPROVAL OF INFORMATIVE RISK MINIMISATION MEASURES



safety information intended for doctors, patients, the public and marketing authorisation holders and its publication on SAM website and in the informative bulletin "Cito!", as well as prepares reports on medicinal product safety issues brought up by the European medicines agency (EMA).

In 2015 in collaboration with public relations specialists a survey was carried out among general practitioners regarding additional risk minimisation materials for medicines (DHPC, EM), their usefulness and options of receiving them (see more in the Section "Providing Information the Public and Communication").

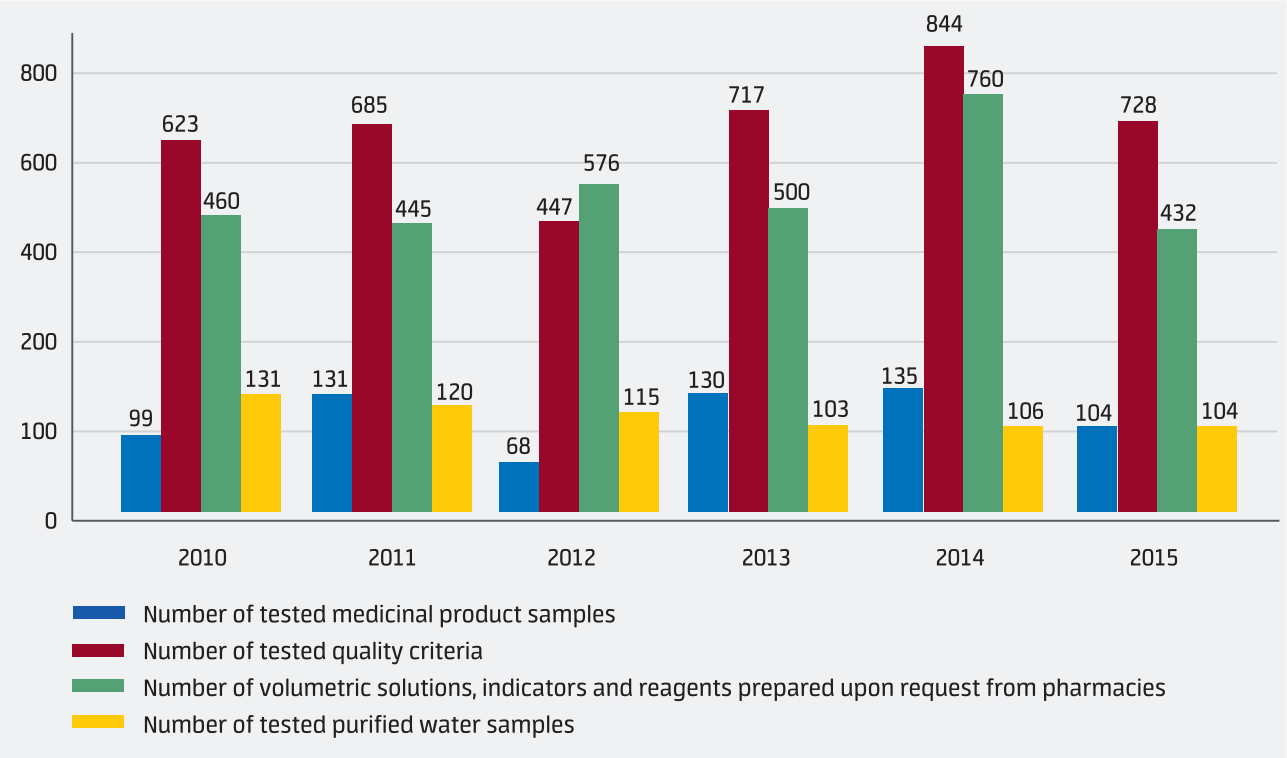
2.5. QUALITY CONTROL OF MEDICINES

In 2015 SAM Laboratory carried out analysis of 104 samples of medicines. In the process of analysis 728 quality criteria were tested. For one sample non-compliance was discovered in the description of the method of testing. 432 volumetric solutions, indicators and reagents were prepared upon request from pharmacies. 104 samples of purified water produced in pharmacies were selected and tested in 2015. Non-compliance with the requirements of the European Pharmacopoeia was discovered in three samples of purified water. Upon request from the Medicines Marketing Authorisation Department expertise was carried out on 16 medicinal products by evaluating the methods for analysis of the active substance and/or the final product and their validation.

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

- A great quantity of the medicinal product on the market;
- Medicinal products for which samples have not been tested in the last 5 years;
- Medicinal products for long-term use;
- Information from the European Union or the Health Inspectorate regarding withdrawal of the medicinal product;
- Outcomes from the Good manufacturing practice (GMP) inspections;
- Changes in the specification and methods of analysis of the final-product quality;
- Medicinal products intended for special patient groups (children);
- Parallel imported medicinal products;

RESULTS OF OPERATION OF THE MEDICINES EXAMINATION LABORATORY



- Recently authorised medicinal products;
- Generic medicinal products.

SAM Laboratory regularly participates in international programs for quality control of medicines and professional standard assessment programs. In 2015 experts from the Laboratory 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 (in accordance with the collaboration agreement between the Baltic States), as well as in the European Market Surveillance Study (MSS) program. In comparison with the previous year in 2015 laboratory experts participated in a higher number of international quality control programs for medicines.

A routine monitoring visit by the Latvian National Accreditation Bureau took place on 10 June 2015. The Laboratory maintained the accreditation regarding compliance with the requirements of the LVS EN ISO/IEC 17025:2005 standard in the following areas:

- Physical and physical-chemical testing of medicines, pharmaceutical active ingredients and excipients (fixed and flexible field);
- Physical testing of purified water (fixed field).

The accreditation of the Laboratory remains in force until 16 June 2018.

The project with the objective of implementing the measures necessary for ensuring the sterility testing in the laboratory was continued in 2015 and it included the construction of class D cleanrooms, purchasing and setting up an isolator and other relevant equipment and carrying out training. Laboratory employees were involved and actively participating in the implementation of the project.

2.6. AUTHORISATION, CLINICAL TRIALS AND SAFETY MONITORING OF MEDICAL DEVICES

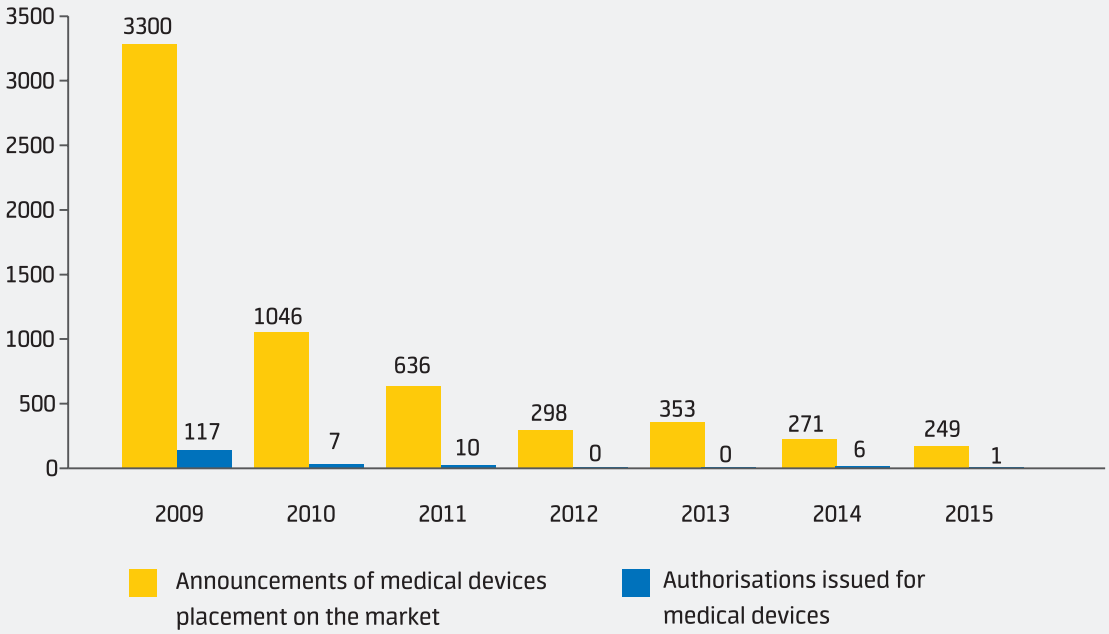
In 2015 eight applications were submitted for authorisation of medical devices in Latvia and 249 notifications were added to the LATMED database regarding placement of medical devices on the market in the Republic of Latvia. 920 primary reports about accidents with medical devices were received within the vigilance (safety surveillance of medical devices) system from competent institutions for medical devices in the EU member states, as well as from manufacturers, distributors and users of medical devices. In 163 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

AUTHORISATION, CLINICAL TRIALS AND SAFETY MONITORING OF MEDICAL DEVICES

Rādītājs	Skaits
Expertise on authorisation documentation of MDs manufactured in the Republic of Latvia	8
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	249
Registration of information provided by MD holders regarding purchase of safety group I and II MDs in the LATMED database	3681
Registration of information provided by MD holders regarding changes in use of safety group I and II MDs in the LATMED database	2221
Acceptance of reports received within the Vigilance system, analysis and processing of information and registration of data in the LATMED database	920
Identification of non-compliant MDs in use in Latvia and implementation of safety measures	163
Expertise of documentation submitted for authorisation of clinical trials with MDs	8
Expertise of documentation submitted for approval of amendments to a clinical trial with MDs	9
Applications for variations to previously issued MD authorisations	1

ANNOUNCEMENTS OF MEDICAL DEVICES PLACEMENT ON THE MARKET AND NUMBER OF AUTHORISATIONS ISSUED FOR MEDICAL DEVICES 2009 – 2015



on documentation for grant of authorisation to eight clinical trials with medical devices (excluding expertise on application documentation for amendments to clinical trial plans (protocols) that have already received authorisation from SAM).

Consultations were regularly provided to the merchants in the field regarding the procedure for authorisation, notification, preparation of documentation and normative acts regulating the field of medical devices. SAM experts participated in European Commission working parties in the fields related to SAM functions, and performed other activities to provide information regarding news in the field of medical devices. SAM experts continued to participate in the meetings of the European Council Working Group on Pharmaceutical Products and Medical Devices by taking part in the evaluation of proposals for regulation of medical devices prepared by the European Commission.

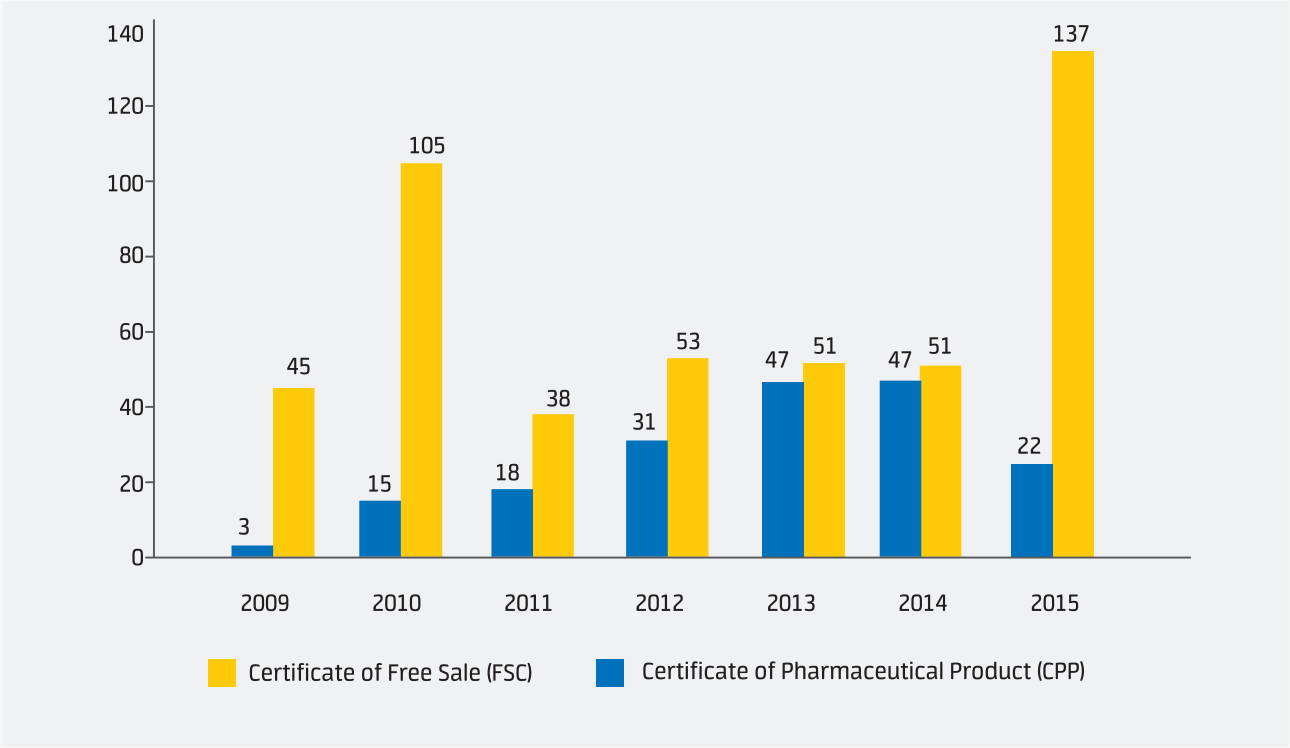
2.7. COMPLIANCE EVALUATION OF PHARMACEUTICAL ACTIVITIES

In 2015 the Pharmaceutical Activities Compliance Evaluation Department conducted 15 inspections in manufacturing/importing companies and one inspection in a contract laboratory that carries out testing for authorised manufacturing companies. In total it required 74 person-days. Three of the inspected medicinal product/active substance manufacturing companies were located in countries outside of the European Economic Area, but five inspections were related to the inspection of manufacturing of active substances. Overall, manufacturing of 20 chemically synthesized and 2 biological active pharmaceutical ingredients was inspected. Department employees in cooperation with the Pharmaceutical Activities Company Licensing Department authorised 7 active substance manufacturers, importers and distributors. 19 medicinal product samples were selected during inspections of manufacturing companies.

In the year of review 13 good manufacturing practice certificates were issued to medicinal product manufacturing/import companies. Upon request from the Latvian medicines manufacturers and wholesalers 137 certificates of pharmaceutical products and 22 certificates of free sale were issued in 2015 in order to promote export of medicines manufactured in Latvia and their marketing authorisation in countries outside of the European Union or European Economic Area.

In 2015 Department experts participated in one inspection (good manufacturing practice of active substance) 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

DYNAMICS OF THE NUMBER OF CERTIFICATES ISSUED TO NATIONAL MANUFACTURERS



experience exchange visit. 37 compliance evaluations of medicines wholesalers, as well as good distribution practice inspections of medicines wholesalers were carried out in 2015 requiring a total of 42 person-days. Two inspections were 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 9 surveillance procedures were performed in 2015. Eight compliance evaluations and three surveillance procedures of tissue/cell procurement and storage centres were conducted. One surveillance procedure was conducted for a transplantation centre, which operates in the field of human organ procurement and transplantation. Compliance evaluation was carried out in three higher education institutions that provide a medical study program and an authorisation was issued for the use of human tissues and cells. Department experts prepared reports to the European Commission regarding serious adverse reactions and adverse events in the field of blood, tissues and cells. Information was also provided for the surveys received from the European Commission Directorate General for Health and Food Safety (DG-SANTE) regarding the current practice in Latvia in relation to the testing of persons donating tissues, cells and blood, as well as for the survey from the European Directorate for the Quality of Medicines and HealthCare (EDQM) regarding fractionation of plasma.

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

In 2015 improvements were made for the SAM website section dedicated to the use of human origin substances (blood, tissues, cells and organs). Biovigilance subsection was established and risk assessment matrices were developed and published in order to facilitate the analysis of adverse events and serious adverse reactions.

2.8. LICENSING OF PHARMACEUTICAL ACTIVITIES 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

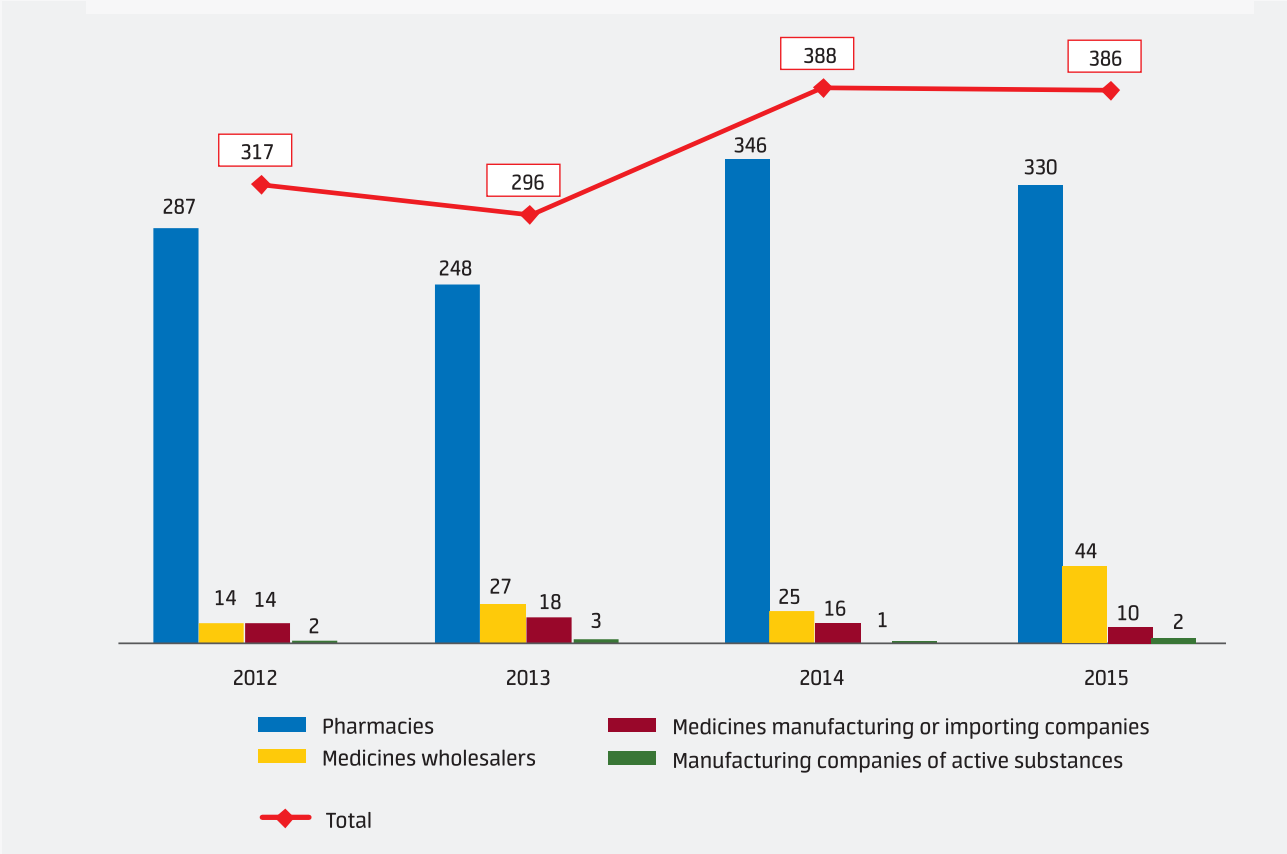
of decisions in SAM regarding issuance, renewal, suspension and annulment of special permits (licences) is laid down in the CM Regulation No. 800 of 19 October 2011 "Procedure for Licensing of Pharmaceutical Activity" (hereinafter – Regulation No. 800).

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 carries out evaluation of plans for premises of general and closed type pharmacies in accordance with the requirements of normative acts, prepares 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 ensures 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 31 July 2012 "Statutes of the State Agency of Medicines", that is, the department evaluates the compliance of pharmaceutical activity companies, evaluates 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, reviews the submitted documents and prepares decisions for authorisation of manufacturers, importers and distributors of active substances.

In 2015 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 cases of establishment and relocation of general type pharmacies, special activity initiation cases (preparation of medicines in the pharmacy or 24-hour operation), and

LICENCES FOR PHARMACEUTICAL ACTIVITY COMPANIES



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 and the Commission operates in accordance with the regulations approved by the Director of the Agency. Organisational preparations and recording of the minutes for Commission meetings are in the competency of the department and 15 Commission meetings were held in 2015.

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 of 2 August 2011 "Criteria for Location of Pharmacies and Pharmacy Branches" (hereinafter – Regulation No. 610) and Regulation No. 800. In 2015 merchants (licence holders) continued to submit applications for new general type pharmacies or pharmacy branches, or relocation of pharmacies. The Agency carried out inspections and approved the new pharmaceutical activity sites in accordance with the criteria for location of pharmacies. The Agency adopted 89 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 (15 requests sent) and also requested regional construction authorities, including the construction board, to provide information regarding the number of residents and the planned initiation of exploitation of the premises of general type pharmacies (8 requests sent). 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. Upon a request from the City Council of Kraslava, SAM evaluated the availability of pharmaceutical care in that specific populated area 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 25 June 2013 "Procedure for Import and Distribution of Active Substances" (hereinafter - Regulation No. 344) laying down the 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 2015 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 EudraGMDP database.

In 2015 SAM received 1441 applications and additional documentation, provided 50 response (information query) letters, carried out compliance evaluation of documentation of 149 general and closed type pharmacies, in cooperation with the Pharmaceutical Activities Compliance Evaluation Department conducted compliance evaluation of 16 medicines wholesalers, 10 medicines manufacturing or import companies and their documentation, prepared 149 opinions regarding pharmacy compliance assessments, 515 decisions regarding issuance, renewal, suspension, annulment of special permits (licences) and extension of case review term. During the year of review 386 special permits (licences) for pharmaceutical activity were renewed and issued to pharmaceutical activity companies (including 330 licences to pharmacies, 44 – to medicines wholesalers, 10 – to medicines manufacturing or import companies, 2 – to companies manufacturing active pharmaceutical ingredients). In 2015 the Agency adopted decisions regarding issuance of special permits (licences) for 4 new general type pharmacies and 9 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

BUDGET AND EXPENSES OF THE STATE AGENCY OF MEDICINES

No.	Financial Resources	Budget implementation in 2013 EUR	Budget implementation in 2014 EUR	2015	
				Budget estimate, EUR	Budget implementation, EUR
1.	Financial resources for covering expenses (total)	3 803 400	5 452 798	4 856 107	5 170 617
1.1.	Income from paid services and other independent income	3 802 586	5 421 136	4 856 107	5 127 338
1.2.	Transfers from the State budget	814	31 662		43 279
2.	Expenses (total)	3 769 903	5 111 696	5 439 452	4 858 019
2.1.	Maintenance expenses (total)	3 593 260	4 422 829	4 447 027	4 064 523
2.1.1.	Regular expenses	2 777 162	3 809 713	4 447 027	4 064 523
2.2.	Transfers of maintenance expenses	816 098	613 116		
2.3.	Expenses for capital investments	176 643	688 867	992 425	793 496
	Financial balance	33 497	341 102	-583 345	312 598
	Financial resources	-33 497	- 341 102	583 345	-312 598
	Increasing (-) or decreasing (+) change in surplus of financial resources from paid services and other independent income	-33 497	-341 102	583 345	-312 598

Zvērinātu revidentu komercsabiedrība SIA "AUDITORFIRMA PADOMS"
Reģ.Nr. 40002056598; LZRA komercsabiedrības licence Nr.68
Juridiskā adrese: Ķekavas nov., Ķekavas pag., Lapenieki, "Bērzavoti k-3" - 24C, LV-2111
Biroja adrese: Mūkusalas iela 33, Rīga, LV-1004
Tālr.: +37167627940, Fakss: +37167627941, Mob. tālr.: +37129239651

A REPORT BY INDEPENDENT AUDITORS

Riga

The date of the document is the time

of the electronic signature on the document **No. 1/2015**

To the State Agency of Medicines

A report on the financial account

We have conducted an audit of the State Agency of Medicines' (hereinafter - Agency) financial report of 2015. The audited financial report of 2015 includes:

1. A report on the financial situation of the Agency on 31st December 2015 - form No. 1 "Balance".
2. A report on the financial results of operation in 2015 - form No. 4-3.
3. A report on the changes in own capital (net assets) in 2015 - form No. 4-1.
4. A report on the flow of financial resources in 2015 - form No. 2-NP.
5. Annexes of the financial report 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 Report", description of the basic principles used for accounting, explanations of reports, including an explanation of the implementation of the budget.

Responsibility of the administration regarding the preparation of the financial report

The administration is responsible for the preparation of this financial report and for 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 Report", as well as for the preparation of a financial report, which does not contain major discrepancies due to fraud or errors.

Responsibility of the auditors

We are responsible for the opinion that we provide on this financial report basing on the audit we have conducted. We conducted the audit in accordance with the International Standards on Auditing. These standards lay down that we shall comply with ethical requirements and we shall plan and conduct the audit in a manner 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 report. The procedures are selected basing 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, the auditors take into account the internal control, that is established to ensure preparation of the financial report and the truthful reflection of the information in that report, in order to determine the appropriate audit procedures for the circumstances, but not to form an opinion regarding the effectiveness of the control.

The audit also includes an assessment of the suitability of the utilised accounting principles and of the justification for the accounting estimates provided by the administration, as well as an assessment of the general account of the financial report.

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

Justification of the opinion with an objection

Until 31st December 2014 an assessment of the degree of completion was not performed for contracts, based on which 100% of advance payments in the amount of 680 102 EUR were received, therefore, it was not possible for us to verify the calculated amount of accumulated income, but basing on our estimations this sum has a significant impact on the income in 2014.

Opinion with an objection

In our opinion, the aforementioned financial report, excluding the impact of the circumstances mentioned in the section "Justification of the opinion with an objection" of this report, provides a truthful and clear overview of the financial situation of the STATE AGENCY OF MEDICINES on 31st December 2015, as well as of the financial results of its operation and flow of financial resources in 2015 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 Report".

Emphasis on circumstances

We bring to the attention that:

a. In the description of the basic principles of accounting and in the explanations of the financial reports there are a lot of duplicate explanations, but the explanations of the changes in balance positions are incomplete.

b. The principles for the accumulation of income and the procedure for their reflection in financial reports has not been adequately explained in the remarks No 2.3 and No. 5.9.1 in the description of the basic principles of accounting and in the explanations of the financial reports. In accordance with the Policy on Accounting (Article 193 and 380[5]) approved by the Ministry of Health (Order No. 191, 18th December 2015) the State Agency of Medicines shall calculate accumulated income basing on the degree of completion of tasks in the year of review. On 31st December 2014 the calculated "accumulated income" was 1 672 252 EUR and, basing on the Article 197 of the Policy on Accounting laying down that "The remainder of debtor claims, debt and advance payments shall be indicated in the balance as a net value", on 31st December 2014 the State Agency of Medicines has decreased the "accumulated income" accounted as part of the debtors in the balance assets and the "received advance payments" in the balance liabilities by 1 422 888 EUR. On 31st December 2015 the "accumulated income" was calculated to be 1 424 225 EUR and by not issuing invoices for tasks completed on 31st December 2015 the Agency has decreased the "accumulated income" in the balance assets and the "income from subsequent periods" in the balance liabilities by that amount. The income in subsequent periods has been acknowledged by decreasing completed advance payments with an incomplete explanation of the principles for the formation and acknowledgement of income during subsequent periods.

Report on completion of other legal and regulatory requirements

We have also examined the report of the administration regarding the year 2015 reflected in the "Administration report" section of the annual report and we have not identified any significant discrepancies between the financial information reflected in this administration report and in the financial report of 2015.

LLC „Auditorfirma Padoms"

Licence No. 68

_____

Vaira Šķibele

Chairman of the board

Sworn auditor

Certificate No. 24

4. GENERAL GOVERNANCE OF THE STATE AGENCY OF MEDICINES

The Operational Strategy of the State Agency of Medicines for 20142016 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 28 April 2015 "Procedure for Preparation and Updating of the Operational Strategy of an Institution and for Evaluation of its Implementation". The strategy is approved by the Ministry of Health Order No. 158 of 5 September 2013 and every year it is updated in accordance with the law on the state budget for that year.

The strategy defines the Agency's:

- Operational authorisation;
- Objective;
- Implemented operational directions and the related services;
- Priorities.

In accordance with the Strategy the objective of the operation of the Agency is to ensure qualitative and reasonable services in the assessment 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 with 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 for implementation of the Strategy, as well as for the development of the Agency and the improvement of its 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 blood 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 Public Procurement and Infrastructure Provision Department. The operational objective of this 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 Public Procurement and Infrastructure Provision Department are as follows:

- Organisation of public procurements;
- Governance 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 maintenance of other rented properties;
- Maintenance of the car park of the Agency and provision of related transportation services;
- Ensuring continuous operation of the infrastruc-

ture of the Agency (electricity, water supply, sewage and heating system, communication network, ventilation system, security and fire safety alarm).

In 2015 SAM announced 16 procurement procedures. There were 30 candidates. Contracts for supply and services were signed for the conducted public procurement procedures. The most important contracts were signed for ensuring infrastructure and primary functions, for example:

- Regular cleaning and maintenance of the facilities and the territory;
- Purchase of testing equipment for the Medicines Examination Laboratory;
- Improvement and maintenance of SAMIS (SAM information system);
- Massive expansion and modernisation of discs.

4.2. LEGAL PROVISION 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 defence of the interests of the Agency in courts, thereby, reiterating the legality of the decisions adopted by SAM within the administrative process, if necessary.

In 2015 the State Agency of Medicines in cooperation with the Ministry of Health developed and submitted its proposals for amendments to more than ten legal acts. In order to improve the surveillance of the distribution of medicines, the requirements for labelling and for manufacturing of medicines, the State Agency of Medicines submitted proposals to the Ministry of Health regarding the following normative acts:

- Cabinet of Ministers Regulation No. 57 of 17 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 26 June 2007 "Procedures Regarding Distribution and Quality Control of Medicinal Products".
- Cabinet of Ministers Regulation No. 803 of 25 October 2005 "Regulations regarding the Principles for the Determination of the Price of Medicinal Products".
- Cabinet of Ministers Regulation No. 436 of 26 June 2007 "Procedure for Import and Export of Medicinal Products".
- Cabinet of Ministers Regulation No. 304 of 18 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 Undertaking".

The State Agency of Medicines in collaboration

Delegates of the EMACOLEX meeting in Riga on 6 May 2015

with the Ministry of Health developed proposals for amendments to the paid service pricelist of the State Agency of Medicines, and as a result on 22 December 2015 the Cabinet of Ministers adopted the regulation No. 785 "Amendments to the Cabinet of Ministers Regulation No. 873 of 17 September 2013 "State Agency of Medicines Publicly Available Paid Service Pricelist"", introducing several changes and favourable conditions for marketing authorisation holders starting from 2016. From now on the State Agency of Medicines may review and adopt decisions on applications regarding waiving of the annual postauthorisation fee for MAHs, if the turnover during the previous calendar year does not exceed 3000 euros. The State Agency of Medicines will also apply a 90% discount to the marketing authorisation fee in the national procedure for expertise on the application and additional documentation for marketing authorisation of generic or biosimilar medicines.

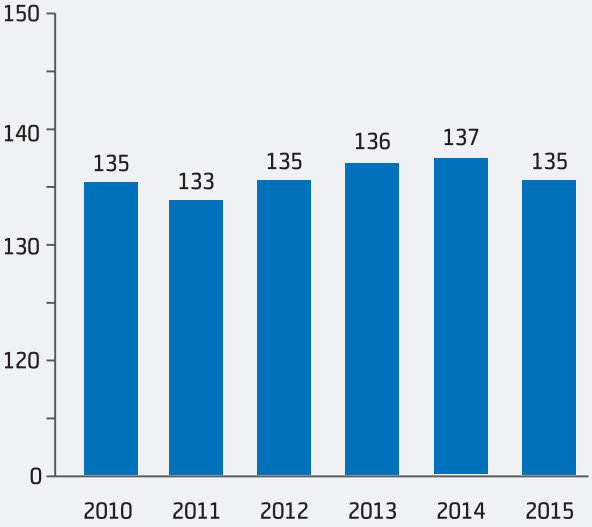
In 2015 SAM adopted 11 938 decisions and two of these decisions (0.017% of the total) were repealed.

In order to ensure the successful participation of the State Agency of Medicines in the Latvian Presidency of the Council of the European Union during the first half of 2015, the Legal Department of the State Agency of Medicines participated in the organisation of the EMACOLEX (European Medicines Agencies Cooperation on Legal and Legislative Issues) meeting on 5-7 May 2015, which was approved by the Ministry of Health Order No. 40 of 19 March 2014 "On the Approval of Working Groups for the Implementation of the Latvian Presidency Regarding Issues in the Competency of the Ministry of Health". The EMACOLEX meeting was organised by taking into account the previous conditions and collaborative practice of the European Medicines Agency, medicines agencies of European countries and competent authorities in the pharmaceutical field, as well as by assessing the priorities, current issues and the traditional format of previous meetings of this working group. The meeting was attended by 55 participants.

4.3. STAFF AND HUMAN RESOURCES MANAGEMENT

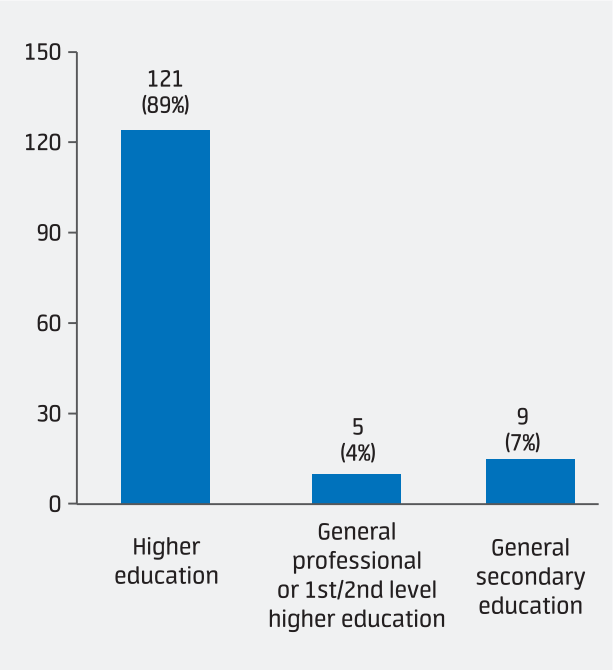
Management of human resources is ensured by the Administrative Resources and Documents Management Department, which resolves issues of human resources management, ensures the work processes for recruitment, selection, assessment and development of personnel, as well as processes the documentation related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

NUMBER OF SAM STAFF MEMBERS FROM 2010 UNTIL 2015



At the end of the 2015 there were 135 civil servants and employees actually working at SAM. In total 142 persons were in a civil service or an employment relationship with SAM in 2015. The image shows the number of employees

STAFF MEMBERS ACCORDING TO LEVEL OF EDUCATION IN 2015

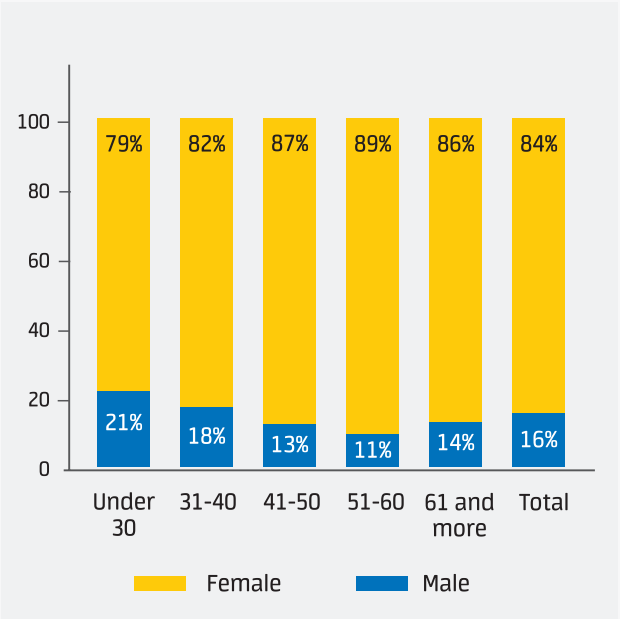


RAISING THE QUALIFICATION OF STAFF MEMBERS 2009–2015

from 2010 until 2015.

During the year of review 11 new employees (4 civil servants and 7 employees) began their employment at the Agency and 22 persons (11 civil servants and 11 employees) terminated their civil service or employment. The average staff turnover was 16% (*staff turnover = number of released staff members in a definite time period/ average number of staff members in the same time period*). The turnover quotient increased by 6% in comparison to the previous year, but it complies with the criteria defined in the State Agency of Medicines' Personnel Management Strategy 20142017.

STAFF MEMBERS ACCORDING TO AGE GROUP AND GENDER IN 2015



Welleducated, 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 image. Overall the education level of SAM staff members is high - 121 (89%) of SAM employees have a higher education, four of these civil servants have a doctoral degree.

One of the basic principles of SAM staff policy is to motivate staff members to raise their qualification. In order to ensure this, based on the training necessities identified in the annual assessment of personnel, in 2015 SAM civil servants and employees (hereinafter – employees) attended 531 training events, including 67 seminars, conferences and forums organised by international organisations. Statistical information regarding events for personnel development are shown in the image.

In 2015 theoretical and practical training on fire safety was ensured and 107 employees were trained; a seminar on the newest issues regarding information security management (implementation of the ISO 27001 requirements) was attended by 130 employees, and 32 employees attended a seminar regarding issues of lobbying, corruption and conflict of interests. Taking into account the knowledge and qualification of Agency experts, based on the contracts signed between the

Agency and European institutions, 27 experts and 2 assistant employees participated in the performance of tasks delegated by European institutions.

4.4. INTEGRATED MANAGEMENT SYSTEM

At the end of 2015 recertification audits were conducted at the Agency resulting in the issuance of certificates certifying the compliance of the management system with the international standards **ISO 9001:2009 and ISO 27001:2013**. The certified areas included the following functions: expertise on marketing authorisation and postauthorisation 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 empowerment of the institution, expertise on related documentation, gathering and publishing of information according to authorisation.

After the surveillance visit by the Latvian National Accreditation Bureau on 10 June 2015, SAM Medicines Examination Laboratory maintained accreditation for compliance with the requirements of the **LVS EN ISO/IEC 17025:2005** standard.

In 2015 an audit of the pharmacovigilance system was conducted in accordance with the requirements of the Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010, and in accordance with good pharmacovigilance practice requirements; the report was sent to the European Commission on 21 September 2015.

The State Agency of Medicines continuously improves the integrated management system by introducing the newest changes in the ISO standard requirements and by involving as many SAM employees in the process as possible.

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 clients, compliance evaluation. The BEMA III report was prepared on 26 October 2014 and the State Agency of Medicines received a positive assessment.

By implementing the strategic audit plan of SAM, internal audits were carried out in various areas during the year of review – personnel and document management, pharmacovigilance, import and export of medicines, Medicines Examination Laboratory procedures and others.

The State Agency of Medicines has defined measures of basic activity that are gathered and analysed in the timeframe defined in the Quality Manual (every quarter, 6 months, year). At the end of 2015 a report by the administration of the State Agency of Medicines was prepared, showing the data for the whole year.

4.5. DEVELOPMENT OF INFORMATION TECHNOLOGIES

In 2015 SAM continued to develop and improve the information system and information technology solutions of SAM, as well as to improve the continuity of their availability and management. In the year of review, the electronic signing functionality in the management system of electronic documents was improved and the development of the system integration solution was initiated.

With Latvia being the presiding country of the Council of the European Union, the SAM website was used for ensuring the publication of information for the participants of SAM organised EU Presidency meetings. During the year of review improvements were also made to the presentation of information of the Medicinal Product Register on the website.

Improvements were made to the algorithms for selection and processing of information in the SAMIS system. The SAMIS migration process to a newer version of the database was successfully completed. In 2015 the classification of the SAMIS list of substances according to several characteristics was completed, thus, ensuring the publication of the updated list of active substances on the website. The SAM IT infrastructure, that used also by the Ministry of Health and institutions in the field, was expanded and improved, and also a two-factor authentication solution was introduced, the infrastructure of the local computer network was expanded and the technology was modernised.

In 2015 an audit of the security of information systems was carried out and measures were taken to minimise the identified risks, staff training was conducted regarding IT security issues and the CERT.LV early warning system

for IT security threats was introduced. Collaboration by exchange of information was continued with different European institutions, competent authorities in other countries by using the unified IT and data exchange solutions, for example, the European clinical trial database *EudraCT*, the secure e-mail and data exchange system *Eudralink*, the pharmacovigilance system *EudraVigilance*, terminology database for telematics EUTCT, the European database for medical devices EUDAMED, the Communication and Tracking System solution for mutual recognition procedures, the Common European Submission Platform (CESP) for marketing authorisation documentation and others.

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 in the pharmaceutical field 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 from European countries participate in the work of EMA as members of working groups and scientific advisory groups, as well as scientific committees.

In order to fully participate in the European collective work procedures, that bring additional responsibilities and tasks for the Latvian agency, qualified human resources, as well as financial resources are necessary. In 2015 SAM employees were 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), European 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 clients and provide consultations on different regulatory issues, cooperation with other institutions, training and exchange of experience are mandatory prerequisites. In 2015 the SAM 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 high quality of expertise the Agency involved additional experts from the academic field – from universities in Latvia.

The very important event of 2015 for the State Agency of Medicines was the Latvian Presidency of the Council of the European Union. Seven different level meetings of regulatory authority working groups in the pharmaceutical field took place in Latvia:

Delegates of the Heads of Medicines Agencies in Riga, on 4-5 February 2015.

- Meeting of the Heads of Medicines Agencies (HMA) – 4-5 February 2015;
- Meeting of the Competent Authorities for Medical Devices (CAMD) – 24 and 25 February 2015;
- Meeting of the Co-ordination group for Mutual Recognition and Decentralised Procedures – human (CMDh) – 6 and 7 May 2015;
- The European Medicines Agencies Cooperation on Legal and Legislative Issues (EMACOLEX) meeting – 6 and 7 May 2015;
- HMA Working Group of Quality Managers – 2 and 3 June 2015;
- HMA Working Group of Communication Professionals (WGCP) – 11 and 12 June 2015;
- HMA Clinical Trials Facilitation Group (CTFG) – 16 and 17 June 2015.

In 2015 SAM director and colleagues 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 ensured a proactive involvement in finding solutions for different issues during preparation for discussions with European or international institutions.

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 regarding authorisation of medical devices, issuance of authorisation for clinical trials with medical devices and monitoring the safety of medical devices. The responsible SAM experts 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 newly established EMA Pharmacovigilance Risk Assessment Committee (PRAC). In 2015 Zane Neikena, the Senior Expert of the Pharmacovigilance Sector of the Efficacy and Safety Division of the SAM Marketing Authorisation Department, became the new Latvian representative in the 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, evaluating Periodic Safety Update Reports, as well as acting as an advisor on various pharmacovigilance issues.

There are cooperation contracts in force 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 on 3 September 2015 in Vilnius, Lithuania. During this meeting the national experts discussed aspects of further cooperation, news and problems in the field, as well as other issues. During this meeting a renewed Agreement on the Common Baltic Packaging Procedure was signed.

5. PROVIDING INFORMATION TO THE PUBLIC AND COMMUNICATION

In 2015 SAM ensured communication with SAM cooperation partners by providing independent and objective information regarding issues in the competency of SAM to professionals and the general public. Communication was performed also with professional associations, other non-governmental organisations, patient organisations and State institutions.

In 2015 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 2014-2016" and the "Operational Strategy of the State Agency of Medicines 2014-2016". Three operational directions are to be followed in order to achieve the objectives laid down in the SAM Strategy. One of the directions is the information direction: ensure provision of objective, thorough and updated information to the public and to professionals, as well as cooperation partners in Latvia and in other countries.

By implementing the introduction of the new common identity within the State administration on 1 January 2015 SAM introduced the new graphic standard – the small, enhanced coat of arms of the Republic of Latvia and the colour orange assigned to the field of health, signifying health, vitality, youth and the sun. Consequently, changes were made to the visual representation of the SAM website www.zva.gov.lv and SAM social network profiles.

PUBLICITY IN MEDIA

In the year of review 52 different press releases were prepared and forwarded to mass media, more than 150 responses were provided to journalist queries. Replies were prepared and provided to questions from residents of Latvia, as well as to requests for information from the Ministry of Health and its institutions and SAM clients – merchants in the pharmaceutical field.

One of the most significant topics that the public had to be informed about in 2015 was the introduction of a common EU logotype on 1 July 2015 for the pharmacies offering residents to purchase medicines online. In order to ensure a more successful communication, SAM participated in the EU wide implementation of the campaign – SAM provided information regarding the common logotype not only in press releases, but also by using video material, banners, a quiz on falsified medicines, images and other materials. The introduction of the common logotype is laid down in the Directive of the European Parliament and of the Council relating to medicinal products for human use regarding the prevention of the entry into the legal supply chain of falsified medicinal products.

To provide information in a more easily perceptible way, five infographics were prepared and distributed in 2015:

- "Know what you use, do not use falsified medicines!"
- "Be careful when using medicines in the sun!"
- "How to store medicines in sunny weather"
- "Trends in the statistics on medicines consumption in 2014"
- "Using medicines together with alcohol is dangerous!"

The infographics were distributed to the media and via the SAM informative bulletin "Cito!", published on

Topic	Examples of publications
Adverse drug reactions and safety of medicines	• *LTV1 program "Ceturtā studija":* Adverse drug reactions. 29.04.2015. • *Medicine.lv:* Storing medicines in sunny weather. 08.06.2015. • *Diena.lv:* Use of medicinal products – a responsible process. 04.10.2015. • *Lvportals.lv:* Using medicines together with alcohol is dangerous. 17.12.2015.
Consumption of medicines	• *Db.lv:* Medicines wholesalers have increased sales. 17.03.2015.
SAM events	• *LR1 News:* European Heads of Medicines Agencies will meet in Riga. 03.02.2015. • *LETA, Diena.lv:* The State Agency of Medicines will be lead by the current Deputy Director Svens Henkuzens.02.11.2015.
Common logotype for online pharmacies in the EU	• *BNS, La.lv*: A common logotype for online pharmacies in the EU from 1 July. 01.07.2015.

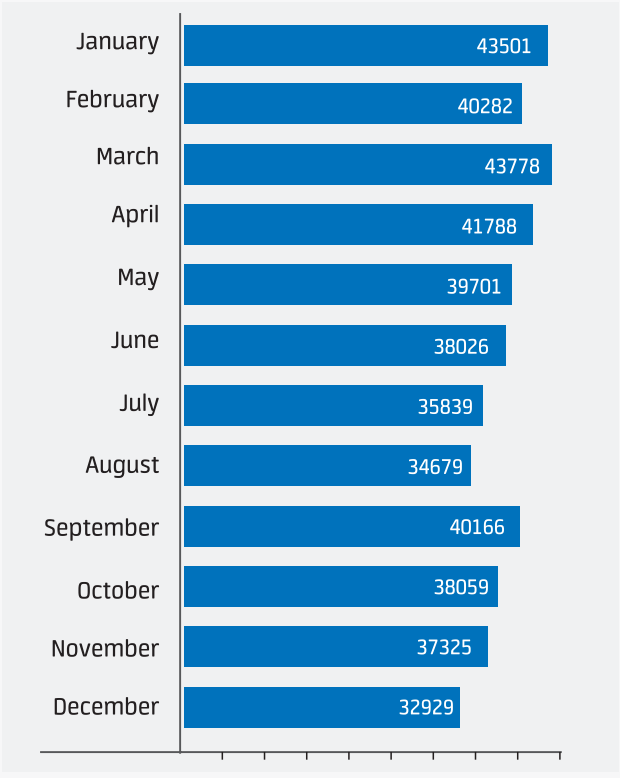
www.zva.gov.lv and forwarded individually to other interested parties. By following the normative regulation of the field of medicinal products in Europe and in Latvia and by evaluating the information regarding safety of medicines, regular updates were made on the social networks *Facebook*, *Twitter* and *LinkedIn*. As a result of SAM media communication activities in 2015 there were a total of 697 publications in different media mentioning SAM.

In addition to the aforementioned, information was regularly updated on SAM website www.zva.gov.lv. In the era of technology, maintenance of 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 2015 SAM website was visited 466 073 times. Maintaining the website is an effective way of ensuring the provision of official and operative information to every member of the public regarding SAM operations and latest issues in the field of pharmaceutics.

Development of SAM website was planned in 2015 and it included improvements to the layout of information, the functionality and the design, and provision of user orientated information in separate sections for different SAM target audiences – healthcare professionals, marketing authorisation holders and patients.

WWW.ZVA.GOV.LV WEBSITE VISITORS IN 2015



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 2015. 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.

SAM PUBLICATIONS

Publications	Number f Copies
Bulletin "Cito!"	6 500
Medicinal Product Register of the Republic of Latvia	250
Electronic version of the Medicinal Product Register of the Republic of Latvia in USB format including summaries of product characteristics and package leaflets	*
SAM Annual Report 2014 (Latvian and English version)	200

* Provided by SAM upon request

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!" were released in 2015.

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 is prepared in a USB data carrier format containing summaries of product characteristics and package leaflets. A convenient information search form has been developed for this format. No Internet connection is necessary to use this format in the daily work. The summaries 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 patients, 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 in 2015 the annual statistical report on the consumption of medicines in Latvia was published. The report includes information regarding total turnover of medicines in euros, number of packages sold, distribution of the turnover according to different consumer groups, dispensing status, turnover of medicines expressed in defined daily doses (DDD) per 1000 inhabitants of Latvia per day (DID). Information was also provided regarding the most sold medicines in Latvia and further information was provided about the market of medicines manufactured in Latvia.

The SAM annual report was also published in 2015, summarising information regarding operation of agency in 2014.

SPECIAL EVENTS AND INFORMATIVE SEMINARS

In 2015 several informative seminars were organised: students visited SAM on the Shadow Day (organised by Junior Achievment - Young Enterprise Latvija) and were introduced with the daily work of senior expert – analyst at the SAM Medicines Examination Laboratory, thus, expanding their understanding of the work and career of a chemist. Students of the bachelor level chemical studies program at the Faculty of Chemistry of the University of Latvia visited SAM and were introduced with the medicinal product sample testing and the main physical, chemical and pharmaceutical-technical methods of analysis.

A meeting of representatives from the medicines agencies of the Baltic States took place last year in Vilnius, Lithuania and the newest issues and the normative regulation in the pharmaceutical field were discussed. At this meeting SAM employees presented and shared their experience on topics such as preparation of the publication on statistical data on medicines consumption in the Baltics, pharmacovigilance (monitoring of adverse drug reactions), issues regarding safety of medicines, risk of falsified medicines and other.

The activities of the campaign "Reveal the other side of medicines!" were continued in 2015. As part of the campaign on 6 February 2015 at the "Annual Awards in Medicine 2014", organised by the Latvian Medical Association and the Ministry of Health, Andris Baumanis, a general practitioner from Riga, received a special award from SAM for responsible and ethical behaviour

by repeatedly reporting adverse reactions related to medicinal products. Information regarding SAM operation was provided in presentation and discussion format in events organised also by other organisations.

EVENTS DURING THE LATVIAN PRESIDENCY OF THE COUNCIL OF THE EUROPEAN UNION

The State Agency of Medicines successfully participated in the Latvian Presidency of the Council of the European Union by organising the working group meetings and other events approved by the Ministry of Health Order No. 20 of 19 March 2014 "On the Approval of Working Groups for the Implementation of the Latvian Presidency of the Council of the European Union Regarding Issues in the Competency of the Ministry of Health". Taking into account the collaborative practice of the European Medicines Agency, other European medicines agencies, and competent authorities within the pharmaceutical field, as well as by assessing the priorities of each working group and the traditional format of the meetings, the State Agency of Medicines organised the following events where communication issues had a very important role:

- Heads of Medicines Agencies (HMA) meeting on 4 and 5 February 2015 and HMA Management Group (MG) meeting on 3 February 2015;
- Competent Authorities of Medicines Devices (CAMD) meeting on 24 and 25 February 2015 and CAMD Executive Group meeting on 23 February 2015;
- Co-ordination group for Mutual recognition and Decentralised procedures – human (CMDh) meeting on 6 and 7 May 2015;
- The European Medicines Agencies, European Commission, European Union member states and European Economic Area Countries Cooperation on Legal and Legislative Issues (EMACOLEX) meeting on 6 and 7 May 2015;
- Meeting of the Working Group of Quality Managers (WGQM) from human and veterinary medicines agencies in the European Economic Area on 2 and 3 June 2015;
- Meeting of Working Group of Communication Professionals (WGCP) from European medicines agencies on 11 and 12 June 2015;
- Meeting of the HMA Clinical Trials Facilitation Group (CTFG) on 16 and 17 June 2015.

All of these events were included in the common event calendar of the Latvian Presidency, event descriptions in Latvian and English were prepared prior to the events and publications were ensured on the website of the

Delegates of the meeting of the HMA Working Group of Communication Professionals (WGCP) on 11 and 12 June 2015 in Riga

Secretariat of the Latvian Presidency of the Council of the European Union https://eu2015.lv/, on SAM website and on the website of the European Heads of Medicines Agencies http://www.hma.eu/. A separate webpage on SAM website www.zva.gov.lv was established for each of the working group meetings with the possibility of registering for the working group and obtaining other information with the purpose of assembling all of the meeting documents (agendas, presentations and other) in one place and to facilitate registration of the delegates. A press release regarding each of the events was prepared in Latvian and English and was published on the website of the Secretariat of the Latvian Presidency of the EU Council www.eu2015.lv and on SAM website www.zva.gov.lv, as well as distributed to the media. A press conference was held after the meeting of the Heads of Medicines Agencies on 5 February 2015. The working group meetings were attended by a total of 344 delegates from national medicines agencies of European countries, European Medicines Agency, European Commission and other institutions.

OTHER EVENTS

Internal communication and employee participation in events organised by other organisations was 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 good physical and mental health and to strengthen the internal communication, a team of SAM employees and their family members participated in the 17th 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 and Trade Union of Health and Social Care Employees of Latvia. In 2015 for the second year in a row SAM employees and their family members participated in the basketball tournament organised by the Pharmacists' Society of Latvia.

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 information received is used for the improvement of the quality of SAM operations. In 2015 SAM organised three surveys:

1) **Annual survey for stakeholders** regarding SAM operation and services in order to use the obtained data to improve the quality of client service;

2) **SAM employee survey** with the purpose of obtaining information regarding staff opinions on organisation of work, job satisfaction and other important aspects of work that could help to identify priorities in working with personnel and make reasonable and considerate

OUR PUBLICATIONS

decisions with respect to employees;

3) **Survey of family physicians** with the purpose of obtaining information about their awareness of additional risk minimisation materials – SAM approved direct healthcare professional communications (DHPC) and educational materials (EM) for risk minimisation, the availability of these materials and their opinion on the usefulness of these materials. This survey was conducted in cooperation with the Latvian Association of Rural Family Physicians and the Latvian Association of Family Physicians. 301 completed surveys were received.

The results of the survey indicated that the respondents (family physicians in Latvia who are members of professional associations) are aware of the additional risk minimisation materials for medicines, receive them, and consider them to be useful. The majority of respondents would like to continue to receive the materials in an electronic format. The cooperation of both of the Latvian associations of family physicians with SAM is important in ensuring the regular distribution of SAM approved DHPCs to members of the associations. Based on the survey, it was concluded that it is necessary to promote the awareness of all healthcare professionals regarding the importance of additional risk minimisation measures in ensuring a positive risk/benefit balance for medicines and the availability of risk minimisation materials has to be improved, and it is necessary to ensure an easily understood message of the materials.

The results of the survey were presented at the meeting of the HMA Working Group of Communication Professionals (WGCP), that took place on 11 and 12 June 2015 in Jurmala during the Latvia Presidency of the EU Council, and on 3 September 2015 at the meeting of representatives from medicines agencies of the Baltic States in Vilnius, Lithuania. The results were also presented to the healthcare professionals in Latvia.

To enquire the opinion of SAM website visitors, five surveys were conducted in 2015 (the results of these surveys are available on SAM website, in the section "Homepage" > "Survey archive"). Website visitors answered the following questions:

- Do you check, if medicines are intended for use in children, before giving them to your child?
- Can you find medicines easily in the search form of the Medicinal Product Register on the SAM website?
- How can a patient report adverse drug reactions?
- Do you use the SAM website section "Check the price of medicines here"?
- Do you consider that you use antibiotics correctly?

6. DEVELOPMENT PRIORITIES OF THE STATE AGENCY OF MEDICINES IN 2016

In 2015 SAM operated in accordance with the three previously defined priorities that are important for the implementation of the institution's Strategy with regard to public health, as well as for the institution's development and for the improvement of quality 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.
- In 2016 special attention will be given to the following aspects:
- Availability of safe, qualitative and effective medicinal/healthcare products;
- Ensuring objective information, communication and cooperation;
- Efficiency of the operation of the State Agency of Medicines.

In order to ensure the planned priorities, by operating within the framework of normative acts, as well as by providing recommendations for their improvement, the State Agency of Medicines will promote the introduction of new medicinal products in the market of medicines in Latvia, the wider their distribution and availability, at the same time contributing to the field of safety of medicinal and healthcare products.

In 2016 the State Agency of Medicines will ensure easily available and qualitative information to cooperation partners, professionals in the field and the public, drawing more attention to the rational use of medicinal products, news in the field and the promotion of good practice principles. SAM will promote reporting of adverse events related to any kind of medicinal products.

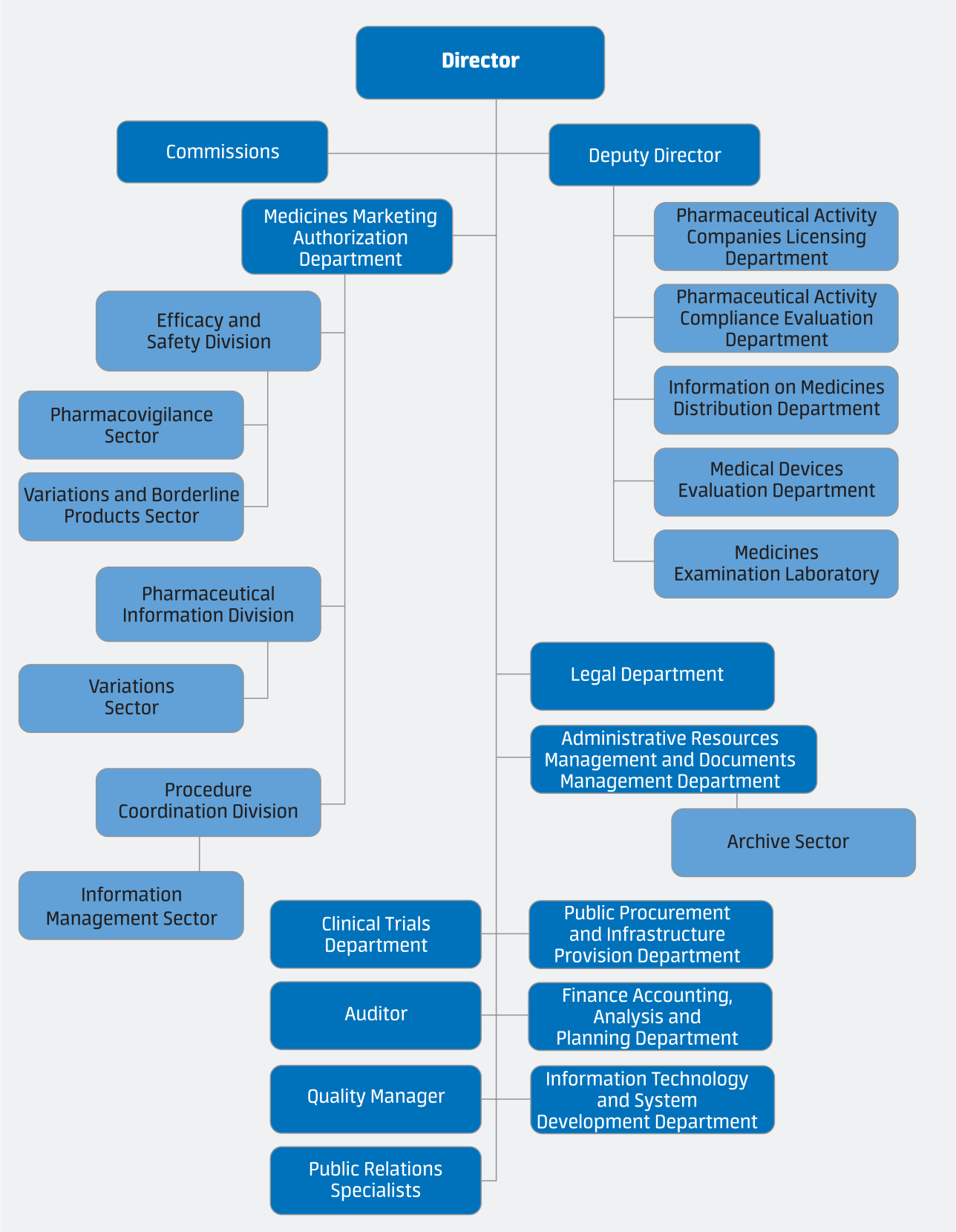
In addition, the State Agency of Medicines will give special attention to the development of human resources and technologies. The basis of any organisation is the professionals working within it and it is necessary to continuously promote their growth, develop their cooperation with field experts and educational institutions. By ensuring this, the State Agency of Medicines will also consider adequate pay, quality of work environment, decreasing the administrative burden, rationality and transparency of processes.

As part of the Benchmarking of the European Medicines Agencies (BEMA) national agencies are assessed and compared with each other in accordance with pre-defined unified operational criteria. The BEMA IV visit in Latvia is set to take place at the end of 2017.

While new strategic priorities in the field of healthcare are being defined on a national level, close cooperation is necessary with the Ministry of Health and other Ministry's subordinated institutions regarding development of normative acts projects and their implementation.

7. ANNEXES

7.1. ANNEX. SAM STRUCTURE



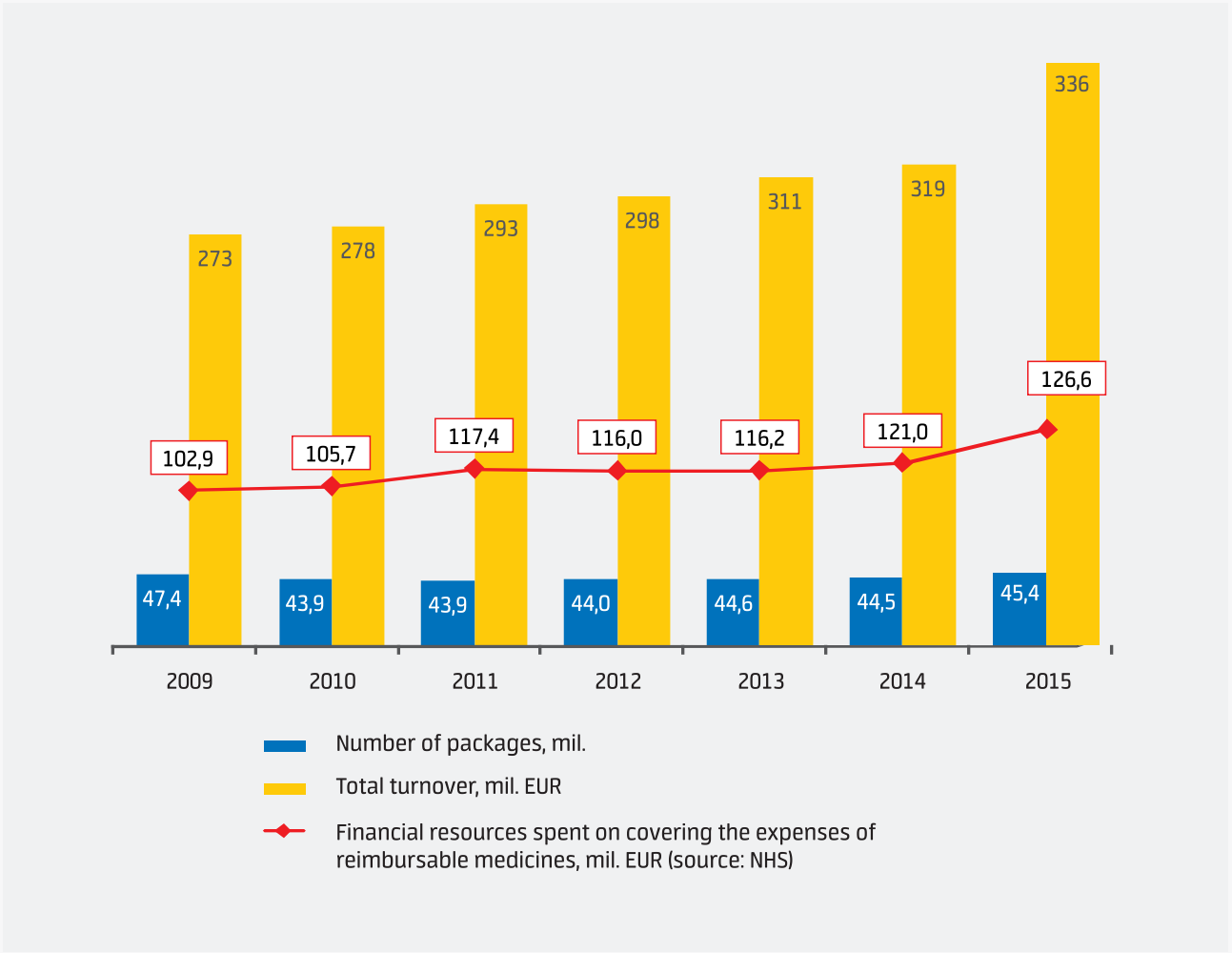
7.2. ANNEX. SAM HISTORY

Date	Event
21.12.2015.	The SAM integrated management system is recertified in accordance with the requirements of the ISO 9001 and 27001 standards
03.11.2015.	Svens Henkuzens becomes the new Director of SAM
03.09.2015.	Meeting of the representatives from the medicines agencies of the Baltic states in Vilnius, Lithuania
16. –17.06.2015.	Meeting of the Heads of Medicines Agencies (HMA) Clinical Trails Facilitation Group (CTFG) in Riga during the Latvian Presidency of the EU Council
11. – 12.06.2015.	Meeting of HMA Working Group of Communication Professionals (WGCP) in Jurmala during the Latvian Presidency of the EU Council
02. – 03.06.2015.	Meeting of HMA Working Group of Quality Managers (WGQM) in Riga during the Latvian Presidency of the EU Council
06. – 07.05.2015.	Meeting of the European Medicines Agencies Cooperation on Legal and Legislative Issues (EMACOLEX) and the Co-ordination group for Mutual recognition and Decentralised procedures – human (CMDh) in Riga during the Latvian Presidency of the EU Council
10.03.2015.	SAM prepares and publishes the supplemented list of names of 5000 substances used in medicines in Latvian, Latin and English
24. – 25.02.2015.	Meeting of the Competent Authorities for Medical Devices (CAMD) in Riga during the Latvian Presidency of the EU Council
16.02.2015.	The Human Medicines Evaluation Department is reorganised and a Medicines Marketing Authorisation Department consisting of three divisions is established – Efficacy and Safety Division, Pharmaceutical Information Division, Procedures Coordination Division
03. – 05.02.2015.	HMA meeting in Riga during the Latvian Presidency of the EU Council
01.01.2015.	SAM introduces a new logotype – the small, enhanced coat of arms of the Republic of Latvia and the orange colour assigned to the field of health
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 healthcare 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.

7.3. ANNEX. TOTAL TURNOVER OF MEDICINES IN LATVIA



Address: Jersikas street 15, Riga, LV-1003
Phone: 67078424
Fax: 67078248
E-mail: info@zva.gov.lv
Homepage: www.zva.gov.lv