STATE AGENCY OF MEDICINES

ANNUAL REPORT

2011

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2011

PREFACE

The year 2011 has been as dynamic for the State Agency of Medicines as all the previous years. This was related to the changes in normative regulations and constantly ensuring rational operations, as well as a more active international cooperation and constantly improving the effectiveness of internal procedures.

According to the statutes the operational objective of the State Agency of Medicines (hereinafter - SAM) is to ensure research of the market of medicines and the availability of effective, safe and qualitative medicines to the residents of Latvia. Because the tasks delegated to us are much broader than that, we have formulated a precise SAM mission statement for ourselves that we use in strategic planning documentation:

Implement local and international pharmaceutical legislation in order to ensure that the products used in health care (medicines, medical devices, blood, cells, tissues and organs), as well as the involved merchants and their activities comply with definite requirements. Provide operative, objective, analytical and independent information to the public, state administration institutions, health care specialists, cooperation partners, as well as international and European Union (hereinafter - EU) institutions.

Agreeably the state administration bureaucratic system in the field of pharmaceutical regulations is very complex, but it is designed, firstly, for the safety of the public health and to regulate business by balancing different interests. In our daily operations we defend both individual rights to receive products and services compliant with European and international standards, as well as the interests of the state. No less important are the interests of merchants that wish to develop their business in Latvia or increase export potential.

A leading theme of the year 2011 has been the safety of medicines. SAM has prepared propositions regarding necessary changes in normative acts to introduce requirements regarding the body of pharmacovigilance normative acts. The significant changes in the normative regulations are set to occur in the first half of 2012.

To relieve the bureaucratic strain and decrease the expenditures of the merchants this year SAM has successfully implemented changes defined by the November 24th 2008 European Commission Regulation (EC) No. 1234/2008 regarding review of variations to the marketing authorisations of human and veterinary medicines and on November 8th appropriate amendments to the regulations regarding SAM publicly available paid services price list were approved regarding review of variations to the requirements of the marketing authorisations of human medicines. During 2011 a total of 10 174 applications for variations to the marketing authorisation documentation were reviewed. Consequently the amendments to the principles of SAM prices regarding variations (the option to group variations and received the applicable discount of 70%) might significantly decrease SAM income distribution in 2012 where merchants would save an equivalent sum.

In accordance with the September 9th 2011 Ministry of Health Order Nr. 190 "Regarding approval of plan of action for centralisation and optimisation of information and communication technology infrastructure and its services" certain tasks have been delegated to SAM to ensure centralisation of data in the field and the possible development of a data centre. SAM has regularly improved and developed information technologies to support SAM primary functions and the possibility for clients to use electronic applications and documents, as well as increase the level of security of State information systems. I would also like to add that within our collaboration with the European Medicines Agency we use several unified European data bases in our daily operations not only as data base users, but also as data providers.

In the year of review the activity of SAM experts in international procedures has been higher than ever. Especially I would like to point out that SAM carried out evaluation of applications in mutual recognition procedures, where Latvia is the Reference Member State in 7 procedures (4 procedures in 2010). We participated in a reevaluation procedure for the European Medicines Agency (hereinafter - EMA) newly founded Therapy Scientific Committee. Within the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (hereinafter - PIC/S) program we participated in 2 collaborative Good Clinical Practice inspections.

After long and emotional discussions the Saeima approved amendments to the Pharmaceutical Law (09.08.2010.) according to which the pharmacies, whose activity licence expires on December 31st 2010 and whose activity does not comply with requirements of Article 36 (regulating ownership rights of pharmacies) of the current Pharmaceutical Law, have the right to extend their licence until December 31st 2011. However, in 2011 the pharmacies had to renew their licences according to the new requirements. In 2011 in relation to the compliance evaluation of pharmaceutical activity companies expertise of 2 202 documents was carried out and 759 special permits for pharmacies were issued, indicating that almost all pharmacies have received new licences.

Since 2011 statistical medicines consumption data from wholesalers is aggregated every month providing the opportunity to carry out a more detailed analysis and sometimes also surveillance.

To develop collaboration between the Baltic States on October 13th the Heads of the Medicines Agencies of Latvia, Lithuania and Estonia signed a collaboration contract in Vilnius regarding unified procedures in monitoring of quality of medicines. This contract will supplement the already existing collaboration activities regarding unified Baltic labelling content, work sharing in labelling approval procedures and joint manufacturer compliance inspections.

I would like to point out that an equally dynamic and complex work has been carried out in all SAM departments.

Regarding broader use of the information in possession of SAM, I would like to draw attention to the SAM developed price verification form for medicines providing an opportunity for anyone to find out information online regarding the maximal permitted

price of medicines in pharmacies (for medicines not included in the list of compensated medicines). By using the price verification form for medicines people can also obtain further information regarding availability of medicines, summary of product characteristics, package leaflets etc.

To improve the availability of medicines to patients and increase the public awareness, we implemented the idea to develop the first digital pharmacy map in Latvia with many search options. The newly developed map of pharmacies improves public knowledge regarding near-by pharmacies and their offered services. The search results also show contact telephone numbers of the chosen pharmacies, so it is easier and quicker to choose a pharmacy for purchasing medicines.

In collaboration with Professor Māris Baltiņš, the Chairman of the Medical Terminology Subcommittee of the Latvian Academy of Sciences, a list of names of active substances in Latvian, Latin and English was developed and it is available on SAM website and it also provides a functional information search option. As we have received a very positive feed-back from our clients, we plan on continuing this work.

SAM operations are fully financed by its income from the paid services it provides. SAM receives full payment for services in advance, but due to the fact that most of the procedures can not be limited to a single year, the surplus of financial means in the SAM bank account at the beginning of the next period of record can not be considered as a surplus of income. The aforementioned contradictions create a misleading impression on the public and our clients regarding the financial situation of the agency. Therefore, the Ministry of Health has begun to review the maintenance of the public agency status that would comply with the status of an institution not financed from the state budget.

At the same time the year of review was related not only to the successful completion of the tasks delegated to us by the state, but also with the 15th anniversary since the establishment of SAM. During the last 15 years the market of medicines in the Republic of Latvia has transformed in its very basics, slowly, but significantly the traditions for choosing medicines, the available sources and ways of obtaining information have changed.

Initially SAM was established to unite all the functions relating to distribution and monitoring of medicines. During this time SAM has become an institution working in the unified European network ensuring marketing authorisation, monitoring, quality control of medicines, as well as licensing and compliance evaluation of pharmaceutical companies and monitoring the marketing authorisation of medical devices.

To celebrate the 15th anniversary the SAM staff planted a white fir in the Garden of Destiny with an inscription “Pledge to Motherland” meaning by that the contribution of each staff member, as well as the collective as a whole to the development of the national market of medicines. Quite possibly 15 years is not a very long time in the history of an institution, but it is clear that SAM has a past, it is in the present and will also have a future.

We are ready for changes and we have new ideas.

I would like to thank all SAM colleagues for their interest and their work in 2011 and I hope that the information included in the annual review will be useful to pharmaceutical specialists, as well as any resident of our country who is interested in the market of medicines in Latvia.

Director of SAM  Inguna Adoviča

ABBREVIATIONS

CPP	CERTIFICATE OF PHARMACEUTICAL PRODUCT
DCP	DECENTRALISED PROCEDURE
EMA	EUROPEAN MEDICINES AGENCY
EU	EUROPEAN UNION
LIC	STATE AGENCY „INFECTOLOGY CENTER OF LATVIA"
MD	MEDICAL DEVICES
CM	CABINET OF MINISTERS
MRP	MUTUAL RECOGNITION PROCEDURE
NP	NATIONAL PROCEDURE
PIC/S	PHARMACEUTICAL INSPECTION CONVENTION AND PHARMACEUTICAL INSPECTION COOPERATION SCHEME
WHO	WORLD HEALTH ORGANISATION
MAH	MARKETING AUTHORISATION HOLDER
VIC	VACCINE INDUCED COMPLICATION
MH	MINISTRY OF HEALTH
ADR	ADVERSE DRUG REACTION
SAM	STATE AGENCY OF MEDICINES
SAMIS	STATE AGENCY OF MEDICINES INFORMATION SYSTEM

CONTENTS

1.GENERAL INFORMATION ON THE STATE AGENCY OF MEDICINES

1.1. Legal status of the State Agency of Medicines

SAM is a State institution under the supervision of the Ministry of Health of the Republic of Latvia that carries out evaluation, marketing authorisation, monitoring, control and regulation of distribution of medicines and medical devices in Latvia.

The operation of SAM is regulated by the State Administration Structure Law, Pharmaceutical Law, Cabinet of Ministers Regulation No. 1006 "Statutes of the State Agency of Medicines" adopted on December 7th 2004 and other normative acts.

1.2. Functions of the State Agency of Medicines

The operational objective of SAM is to implement local and international pharmaceutical legislation in order to ensure that the products (medicines, medical devices, blood, cells, tissues and organs) used in health care, as well as the involved companies and their activities comply with certain requirements, and in addition to provide objective and analytical information for the purposes of state administration, to the public, health care specialists, cooperation partners, as well as international and EU institutions.

Functions of SAM:

- ensure that only effective, safe and qualitative medicinal products are included in the Drug Register by performing expertise on marketing authorisation/renewal and variations documentation;
- ensure inspection of compliance, certification and licensing of companies manufacturing and distributing medicinal products;
- monitor the safety of medicines consumption, control the quality of medicines and ensure risk minimisation measures;
- monitor import, export, transit and distribution of medicines in the state by issuing permits and gathering data on consumption of medicines;
- ensure evaluation of clinical trial projects for medicines, issue authorisation for conduct of clinical trials in Latvia and monitor their compliance;
- ensure evaluation of compliance, registration and monitoring of safety of medicinal devices, issue authorisation for conduct of clinical trials;
- carry out evaluation of compliance of procurement and storage organisations of human tissues, cells and organs, blood establishments and hospital blood banks;
- provide the public and specialists with objective and thorough information regarding medicines, their use and ensure data exchange;
- operate in the European medicines network by participating in work-sharing and complying with the collective standards and procedures, cooperate with other European and international organisations.

1.3. The main objectives of the year of review

In addition to the primary operations of SAM, in 2011 the following priority tasks were set for the year of review:

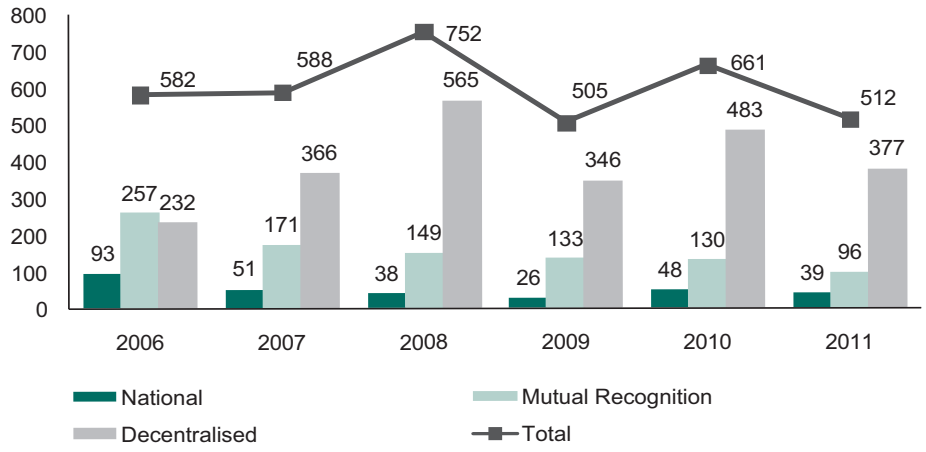
- develop a long-term strategy for the time period 2011-2015;
- increase the number of MRP/DCP procedures where Latvia is the Reference Member State (RMS);
- get involved in the centralised authorisation procedure;
- improve the reception and processing of electronic authorisation documentation (e-CTD);
- ensure data exchange with European databases for data regarding medicinal products, medical devices, clinical trials, manufacturers, distributors and tissue, cell and organ centres (undertake the commitments stated by the Memorandum of Understanding on the Exchange of information in the context of EU Telematics);
- actively participate in e-health projects;
- ensure inspection of compliance of pharmacovigilance systems after they are defined by law;
- actively participate in EMA work, work-sharing programs within the European medicines network, WHO programs;
- ensure and coordinate the development of the list of active substances and excipients in Latvian, involving in the process academic forces and the State Language Center;
- update and review SAM internal procedures to increase work effectiveness;
- ensure the annual SAM publications for clients in a paper and an electronic format;
- continue to develop electronic communication with clients;
- carry out the planned activities to ensure the qualification of the SAM Quality Management System in compliance with the international standard ISO 9001:2008 "Quality Management Systems - Requirements";
- improve inter-institutional cooperation and communication with professional associations of doctors and pharmacists, academic and scientific institutions as well as the public;
- continue to improve the technical possibilities and content of the SAM website and expand the communication possibilities on the public website.

2.RESULTS OF OPERATION OF THE STATE AGENCY OF MEDICINES

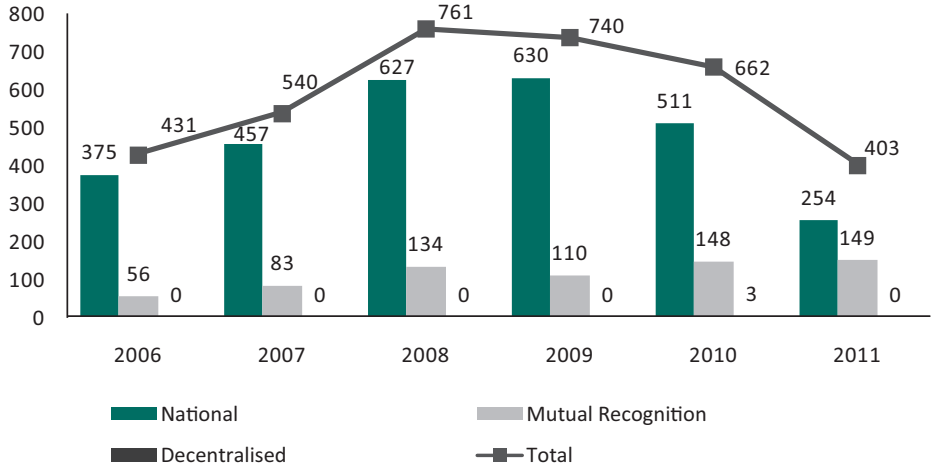
2.1. Authorisation of Medicines

In 2011 by evaluating documentation on quality, safety and effectiveness of medicines SAM has carried out expertise more than 2000 times on general, chemical and pharmaceutical, as well as preclinical and clinical sections of the documentation of medicines. Evaluation reports on 293 medicines have been prepared for the SAM Commission for Registration of Human Medicines for adoption of a decision regarding marketing authorisation and renewal of medicines in the national procedure. In 2011 Latvia has authorised 4 medicines as a Reference Member State in 2 procedures and has renewed 2 medicines in a mutual recognition procedure. In 2011 SAM carried out 512 marketing authorisation procedures and 403 renewal procedures.

Marketing authorisation procedure

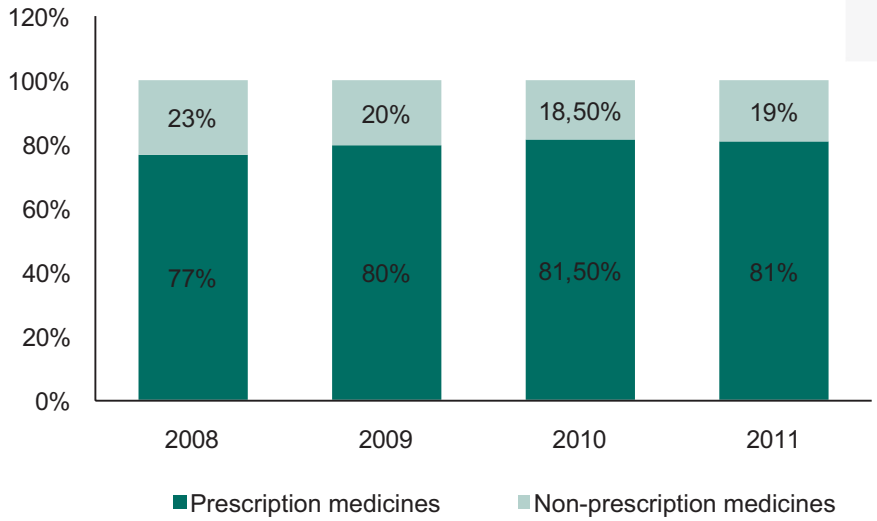


Renewal procedure



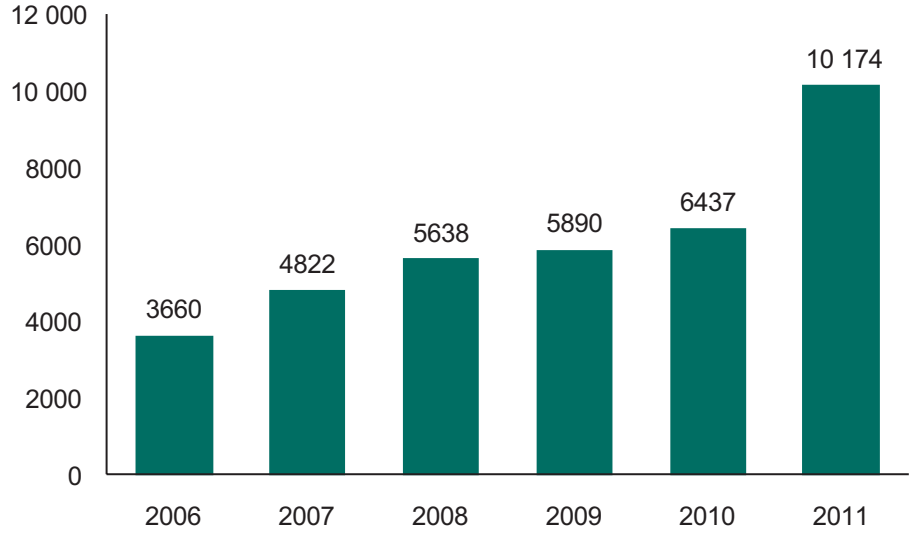
The ratio of prescription and non-prescription medicines in the Drug Register of the Republic of Latvia remains at the usual level.

Ratio of authorised prescription and non-prescription medicines



10 174 variations to the documentation of authorised medicines were submitted and reviewed in 2011. On November 8th 2011 amendments to the Cabinet of Ministers Regulation No. 61 "Regulation on the State Agency of Medicines publicly available paid service pricelist" (adopted on January 17th 2006) came into effect stating a decreased fee for grouped variations, thus, decreasing merchant expenditures.

Variations to the marketing authorisation documentation



In the year of review 33 applications were received for evaluation of product compliance/non-compliance with the definition of a medicinal product where SAM has given an opinion on the product status.

37 Periodic Safety Update Reports were evaluated in 2011 regarding 60 medicines and 77 letters with evaluations and identified deficiencies were written.

In 2011 public evaluation reports were written regarding 12 medicines authorised in the national procedure and regarding 2 medicines authorised in the mutual recognition procedure where Latvia was a Reference Member State.

2.2. Issuing Authorisation for Distribution of Medicines

In 2011 within its competency SAM ensured monitoring of distribution of medicines in Latvia, provided consultations to clients and cooperation partners regarding distribution of medicines and carried out expertise of 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 variations.

In 2011 SAM issued 5045 authorisations for import, export and distribution of medicines, including 3387 authorisations for distribution of unauthorised medicines, 89 authorisations for distribution of parallel imported medicines and 57 authorisations for distribution of remaining stock of medicines after the withdrawal of the medicine from the Drug Register of the Republic of Latvia. 54 variations were made to the authorisations for distribution of parallel imported medicines.

Dynamics of the number of authorisations issued for import, export and distribution of medicines (in the period 2007-2011)

Type of authorisation	2007	2008	2009	2010	2011
Distribution of unauthorised medicines	718	1910	2370	3212	3387
Distribution of parallel imported medicines	29	19	44	93	89
Import/export of narcotic, psychotropic medicines/substances and precursors	1330	1348	1225	1484	1501
Distribution of remaining stock of medicines	-	57	134	76	57
Total	2077	3242	3785	4873	5045

In addition to the aforementioned functions SAM carries out expertise of applications:

- regarding issuance of special permits (licences) for operation with precursors and issuance of precursor operator cards;
- regarding 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;
- regarding purchase of medicines (to ensure operation).

10 authorisation cards were issued to precursor operators and 8 authorisations were issued for use of plants, substances and medicines included in the I, II and III list of narcotic, psychotropic substances and precursors for medical and veterinary medical scientific research or training, as well as determining their physical and chemical properties.

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

SAM regularly processed and supplements the information in the Drug Register regarding availability and prices of medicines, gathers and processes data regarding the turnover of pharmacies, wholesalers and manufacturing companies. Since January 2011 every month SAM processes statistical information regarding consumption of medicines submitted by wholesalers and once a year prepares the publication "Statistics of Medicines Consumption" that is available in a compact disc format and is also 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 changes in normative regulations regarding distribution of medicines. Following amendments to legislation SAM prepares explanatory materials and educational seminars to health care specialists and merchants, as well as provides routine consultations to clients.

2.3. Clinical trials

In 2011 SAM received 69 applications for clinical trail projects for medicines. In compliance with the current European guidelines regarding the voluntary harmonisation procedure for reviewing multinational clinical trials, 8 applications for the international harmonisation procedure for clinical trials were submitted to SAM. SAM employees participated in the evaluation of clinical trial documentation and coordinated their opinions with experts in the field of quality, preclinical and clinical trials of investigational medicines from other competent institutions in the EU. This procedure was carried out respecting a strict time schedule that allowed for an effective and thorough evaluation of the main clinical trial documentation - clinical trial protocol, investigator's brochure and the case file for the quality of investigational medicines.

After evaluating benefits and risks SAM employees decided on the approval of clinical trials in 24 department meetings. One clinical trial project was withdrawn because the applicant could not meet the requirements set by SAM to ensure safety of patients. In 2011 SAM issued a total of 67 authorisations for initiation of clinical trials in Latvia.

11 clinical trial projects involving children were reviewed in 2011 and 9 were approved. Paediatric clinical trials were authorised in several medical specialities - pulmonology, endocrinology, rheumatology, urology and abdominal surgery. Among the authorised trials, 20 clinical trials included biological medicinal products, including products that had been obtained with the help of recombinant DNA technology (for example, monoclonal antibodies, interferons, growth factor inhibitors) and were intended for treatment of oncological, rheumatic, neural and other types of diseases.

218 authorisations were issued for significant changes in clinical trial protocols or other documentation related to the clinical trial.

Information regarding applications for clinical trials, the time of their authorisation, the dates of approval of applications for significant changes, opinions of ethical committees, completion of trials, as well as inspections of good clinical practice was regularly entered into the European clinical trial database Eudra CT. Due to the publication of the European Clinical Trials Register and the EMA requirements, a SAM employee ensured that complete information regarding clinical trials with medicines in Latvia was entered into the Eudra CT.

SAM ensured electronic data exchange in the EudraVigilance system by forwarding acknowledgements of receipt of safety reports relating to the clinical trials conducted in Latvia to clinical trial sponsors that had submitted safety reports in the Clinical Trial Module of the EudraVigilance data base according to European and local normative requirements. The 72 reports that were received in the year of review regarding significant adverse drug reactions observed at trial sites in Latvia were analysed and included in a register developed by SAM. In total SAM received, reviewed and recorded 107 safety reports in the year of review regarding clinical trials conducted in Latvia.

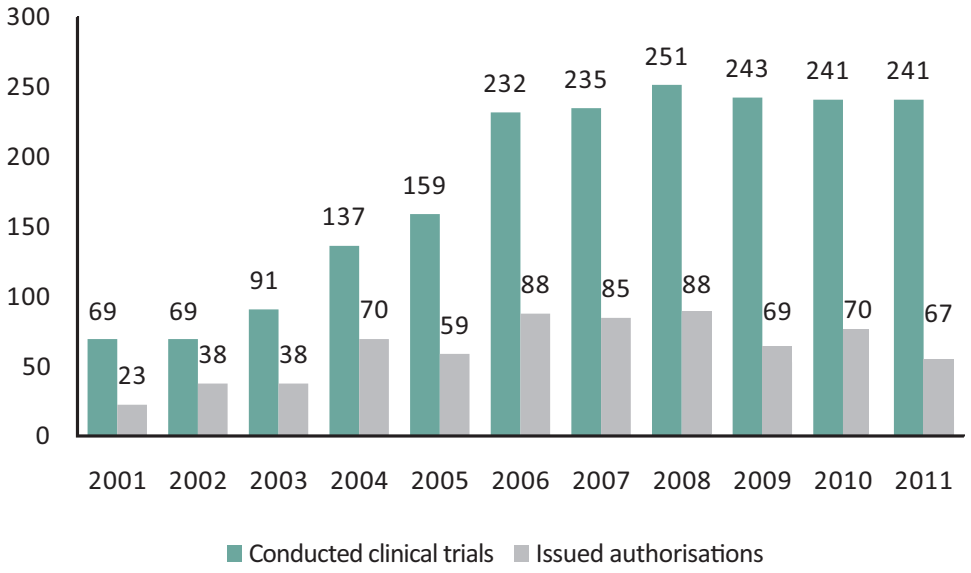
22 external experts were involved in the evaluation of documentation of authorised projects. Altogether expertise was carried out on 62 projects in 2011. 4 experts were involved for the first time.

Altogether 241 clinical trials were conducted in Latvia in 2011. 49 projects were completed.

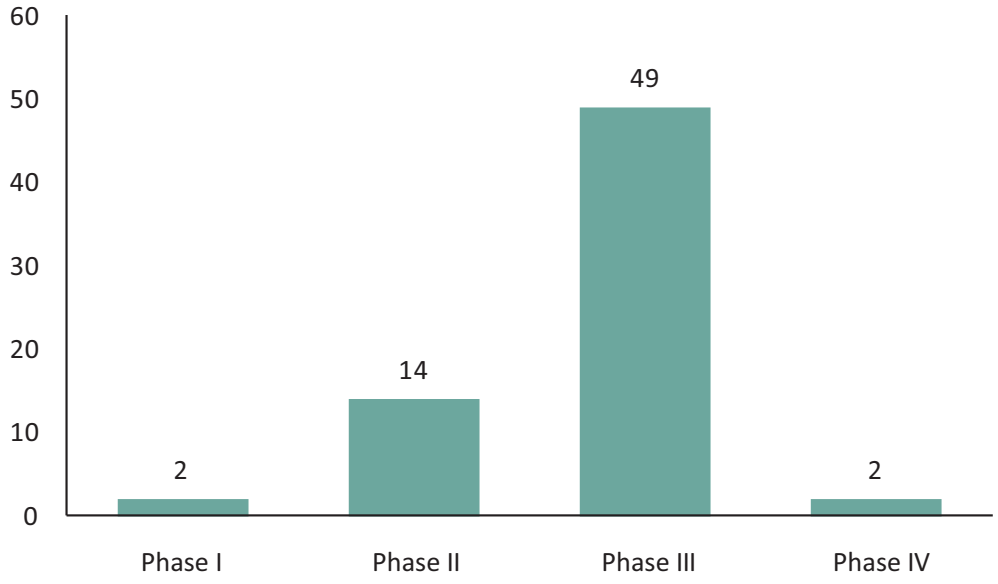
The authorised clinical trial projects were sponsored by a total of 38 foreign pharmaceutical companies. In accordance with the power of attorney from the

sponsors, the following contract research organisations participated in the organisation and ensured the quality of conduct of clinical trials in Latvia: Quintiles (11 projects), ICON (7 projects), Crown CRO (5 projects), Amber CRO (4 projects), Parexel International (4 projects), Dokumeds (3 projects), Ergomed Sp.z o.o. (3 projects), Covance Inc (3 projects) and 9 other contract organisations (1-2 projects each).

Number of issued authorisations and conducted clinical trials



Distribution of the number of clinical trials authorised in 2011 according to phase



Distribution of authorised clinical trials in 2011 according to medical speciality

Medical speciality	Number of clinical trials
Oncology	11
Neurology	8
Pulmonology	7
Dermatology	7
Endocrinology	6
Psychiatry	6
Rheumatology	5
Surgery	5
Cardiology	4
Hematology	3
Urology/nephrology	3
Ophthalmology	2

Clinical trial centres that started participating in the clinical trials authorised in 2011

Clinical trial centre	Number of clinical trials
P. Stradins Clinical University Hospital	29
Riga Eastern Clinical University Hospital	22
● Clinical hospital „Gaiļezers”	10
● Latvian Oncology Center	10
● Clinic „Linezers”	2
Daugavpils Regional Hospital	21
Children Clinical University Hospital	9
MedaD	7
“Health Center 4”	7
State Limited Responsibility Company „Maritime Hospital”	7
Northern Kurzeme Regional Hospital	6
Clinical Centre for Sexually Transmitted and Skin Disease	6
Hospital „Ģintermuiža”	6
Latvian Maritime Medicine Centre	6
Vidzeme Hospital	5
Liepāja Regional Hospital	5
Strenči Psychoneurological Hospital	5
Riga Regional Hospital, Sigulda Hospital	5
Daugavpils Psychoneurological Hospital	5
Other clinical trial centers (66 in total)	1-4 at each centre

SAM authorised non-intervention studies

6 inspections of clinical trial compliance of with good clinical practice were carried out at trail centres during the conduct of the trials. In 2011 a highly qualified SAM employee participated in inspections within the European good clinical practice inspector experience exchange program at 2 trial centres (in Greece and in Latvia) and also carried out inspections of 2 Latvian medicines manufacturers together with 2 other good manufacturing practice inspectors. During the inspections major and other deficiencies were discovered.

In the year of review SAM received and evaluated 5 applications for non-intervention studies, 3 of these are recorded in the list of SAM authorised non-intervention studies available on SAM website.

2.4. Adverse Drug Reaction Monitoring and Risk Minimisation

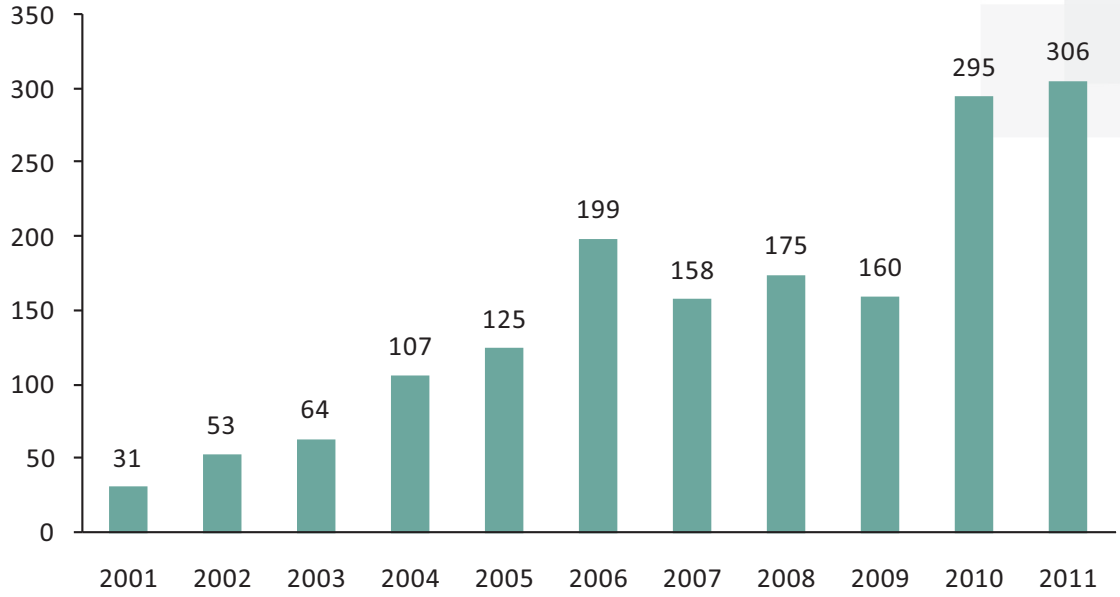
In 2011 SAM received 306 reports of observed adverse drug reactions (ADR). The number of reports during the last few years is stable, mostly due to the well organised exchange of vaccine induced complication (hereinafter - VIC) data with the state agency "Infectology Centre of Latvia" (hereinafter - LIC). However, the reporting activity of doctors and pharmacists has not increased. Expertise was carried out on all received reports and according to requirements they were forwarded to the EU ADR database EudraVigilance, as well as to the World Health Organisation (WHO) database Vigibase.

SAM carries out evaluation of the pharmacovigilance systems developed by marketing authorisation holders (hereinafter - MAH) that are required within the marketing authorisation process. In the period of review 593 pharmacovigilance systems were evaluated. The nature of this process is also related to the pharmacovigilance inspections planned in the future.

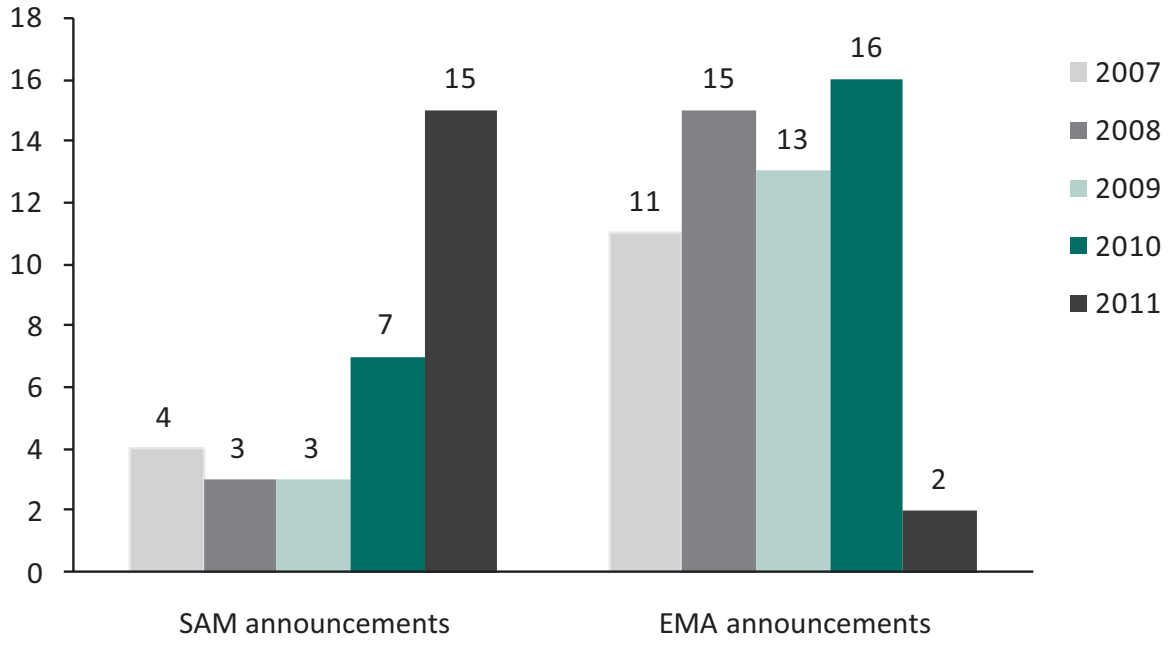
As a part of the EU Periodic Safety Update Reports Work-sharing in 2011 one PSUR evaluation was carried out for the European Community regarding an active substance of an original preparation.

According to the new EU normative acts in pharmacovigilance the harmonisation of safety information in medicines authorisation documentation will have a clarified legal base, therefore, the activities in previous years ensuring Latvian translations of the standard formulation of medicines safety information to the marketing authorisation holders are not being developed at the moment.

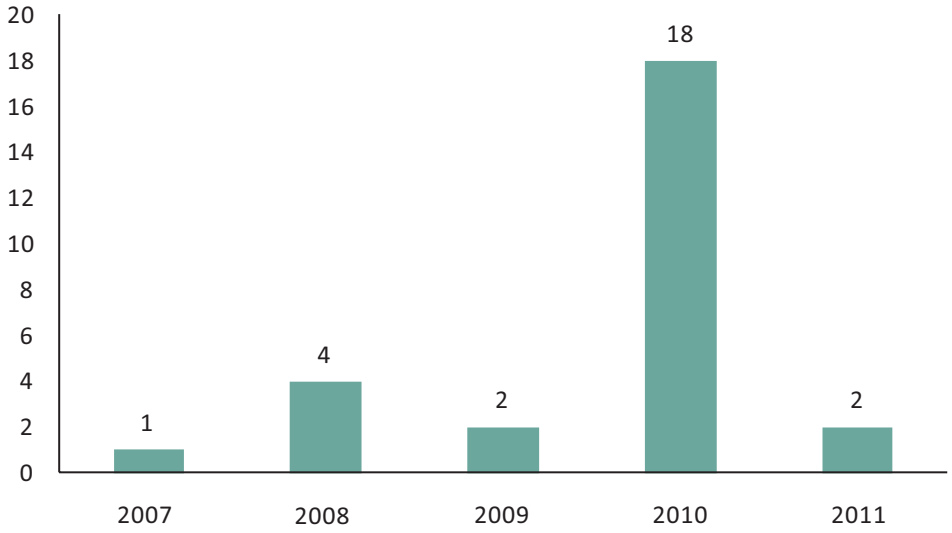
Adverse Drug Reaction reports



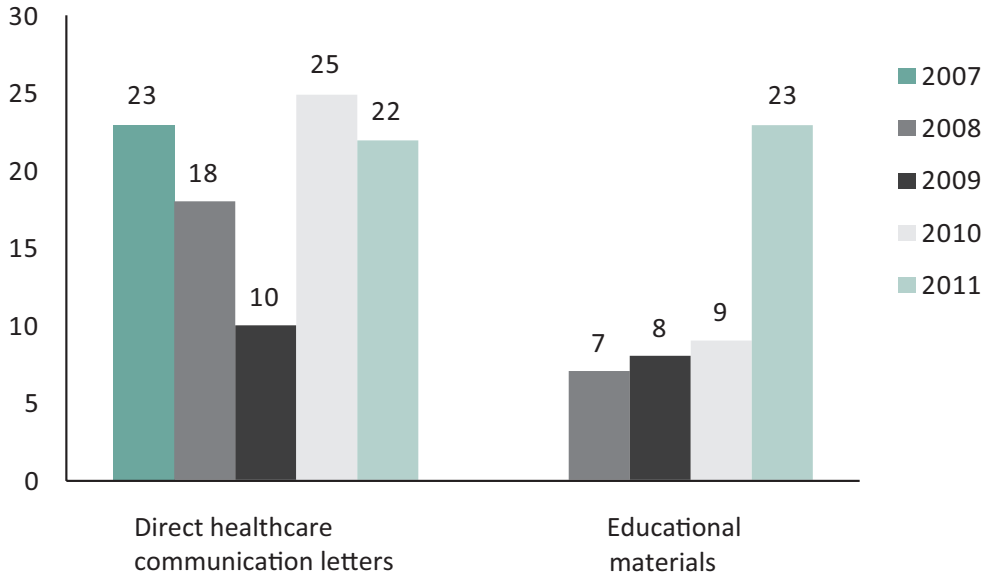
Informative materials regarding safety of medicines on SAM website



Harmonisation of safety information in marketing authorisation documentation



Coordination of informative risk minimisation measures



An ADR Monitoring Advisory Board operates within SAM and its activity is coordinated by the ADR Monitoring Department. 6 Board meetings were conducted during the period of review.

SAM cooperates with qualified persons for pharmacovigilance for MAH to ensure data exchange regarding ADRs observed in Latvia and ensure communication with health care specialists, patients and the public regarding the safe use of medicines. In the period of review expertise was carried out on 23 educational materials for risk minimisation and 22 "Direct healthcare Communication Letters" submitted by MAH to SAM were approved.

Information regarding safety of medicines intended for physicians, patients and the public is constantly published on SAM website. 15 SAM and 2 EMA announcements were prepared for publishing. Issues regarding safety of medicines and risk minimisation are updated in the SAM informative bulletin "Cito!".

Due to the new EU normative acts coming into effect in 2012 that will regulate pharmacovigilance more precisely, SAM has actively worked on the development of a project for a new Cabinet of Ministers Regulation in the year of review.

2.5. Quality Control of Medicines

In 2011 SAM laboratory carried out analysis of 131 samples of medicines. In the process of analysis 685 quality indicators were examined. It was discovered that the quality of 2 samples did not comply with the requirements of normative documentation according to the following indicators: pH (1 sample) un deviations from the mean mass (1 sample). 445 volumetric solutions were prepared upon the request from pharmacies.

Starting with January 1st 2008 according to the Cabinet of Ministers Regulation No. 304 "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 laboratory carries out sample selection and quality control of purified water obtained in pharmacies according to the requirements of the European Pharmacopoeia. 120 samples of purified water were selected and tested in 2011. Noncompliance with the requirements of the European Pharmacopoeia was discovered in 7 samples of purified water.

On July 15th 2009 the Latvian National Accreditation Bureau accredited the State Agency of Medicines according to the requirements of the LVS EN ISO/IEC 17025:2005 standard in the following fields: physical and physicochemical testing of medicines, veterinary medicines and active substances; physical testing of purified water. The accreditation has been issued until July 14th 2013. On May 5th 2011 an inspection visit by the Latvian National Accreditation Bureau took place. The laboratory maintained its accreditation for the requirements of the LVS EN ISO/IEC 17025:2005 standard in the current field of accreditation.

Results of operation of Medicines Examination Laboratory

Year	Number of employees	Number of analysed medicines samples	Number of examined quality indicators of medicines	Number of volumetric solutions, indicators and reagents prepared upon the request from pharmacies	Number of examined purified water samples	Participation in quality control programs for centrally authorised products (CAP)	Participation in European Market Surveillance Studies (MSS)	Participation in international professional level inspection programs
2006	9	436	2 984	-	-	1	1	4
2007	9	222	905	1 004	-	1	-	5
2008	8,5	111	550	557	158	1	2	5
2009	8 (until 30.06.09.) 7 (from 01.07.09.)	115	611	361	131	1	-	5
2010	6	99	623	460	131	1	1	5
2011	6	131	685	445	120	1	2	3

2.6. Evaluation of Compliance and Authorisation of Medical Devices, Surveillance of Safety and Clinical Trials of Medical Devices

In 2011 ten medical devices were authorised in Latvia and 636 notifications were added to the LATMED database regarding placement of medical devices on the market in the Republic of Latvia. 636 reports of accidents with medical devices were received within the vigilance system from responsible institutions, as well as from manufacturers and distributors of medical devices. In 146 cases action was taken to apply safety measures in Latvia.

In the year of review expertise was carried out on documentation for grant of authorisation to 8 clinical trials with medical devices (excluding expertise on application documentation for amendments to protocols of clinical trials that have already been granted authorisation by SAM).

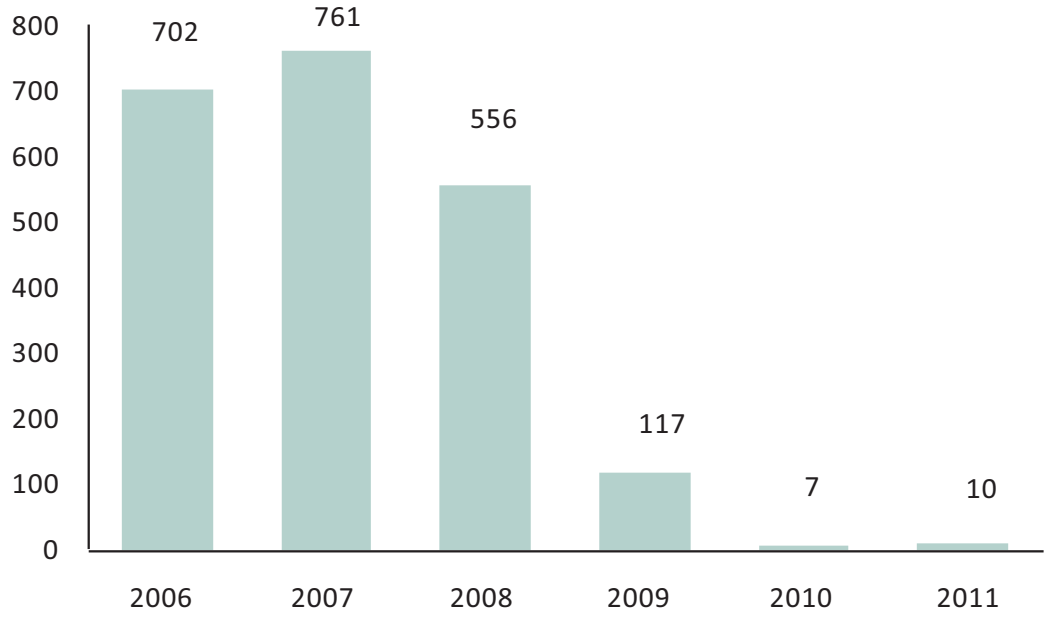
Consultations have been regularly provided to clients regarding procedures for authorisation, announcement of medical devices, as well as preparation of documentation and normative acts regulating this field.

SAM specialists participate in seminars and provide information regarding news in the field of medical devices.

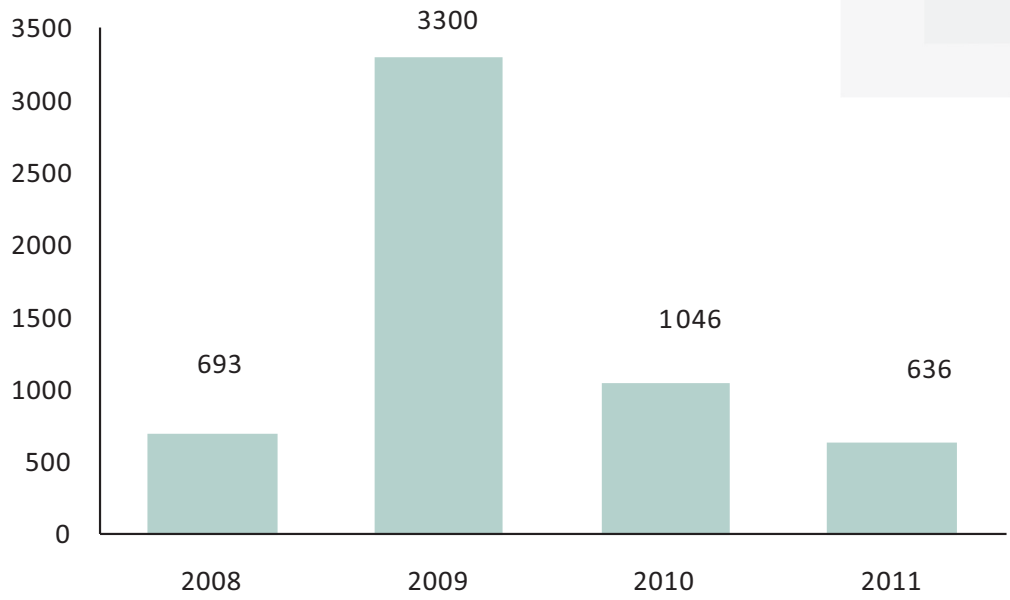
Evaluation of compliance, authorisation, surveillance of safety and clinical trials of medical devices (MD) in 2011

Criteria	Number
Expertise of authorisation documentation of MD manufactured in the Republic of Latvia	27
Expertise of authorisation documentation of MD without CE marking	0
Expertise of documentation for issue of authorisation to specially supplied MD	2
Registration of information submitted within the notification procedure into the LATMED database	636
Registration of information provided by MD holders regarding purchase of safety group I and II MD into the LATMED database	3089 (including www – 1271)
Registration of information provided by MD holders regarding changes in use of safety group I and II MD into the LATMED database	1994 (including 461 that have been removed from records)
Acceptance of reports received within the Vigilance system, registration, analysis and processing of information and registration of data into the LATMED database	636
Identification of non-compliant MD in exploitation in Latvia and implementation of safety measures	146
Expertise of documentation submitted for authorisation of clinical trials with MD	8
Expertise of documentation submitted for approval of variations to a clinical trial with MD	8
Applications for variations to previously issued MD authorisations	1

Number of authorisation certificates issued for medical devices in the Republic of Latvia



Number of notifications regarding placement of medical devices on the market in the Republic of Latvia (including medical devices for in vitro diagnostics)



2.7. Evaluation of Compliance of Pharmaceutical Activity

In 2011 there were 18 inspections carried out on manufacturing/importing companies and 1 contract evaluation conducted (regarding renewal of marketing authorisation). In total this required 39 person-days. One of the inspected manufacturing companies was located outside of the European Economic Area, but 3 inspections were carried out on the manufacturing of active substances upon the request from the manufacturers themselves. In total the manufacturing of 11 pharmaceutically active compounds was inspected.

In 2011 three inspections (1 in Latvia, Lithuania and Estonia each) were conducted together with PIC/S inspectors during experience exchange visits.

14 product (medicines) samples were selected in the inspections of manufacturing companies. During the year of review 21 Good Manufacturing Practice certificates were issued to manufacturing/importing companies.

In 2011 there were 35 evaluations carried out on compliance of wholesalers of medicines and veterinary medicines, as well as inspections of good distribution practice of wholesalers. Altogether this required 38 person-days.

Upon the request of medicines manufacturers and wholesalers in Latvia 38 product certificates and 20 free trade certificates were issued in 2011 to promote export of medicines manufactured in Latvia and their authorisation in countries outside the EU/ European Economic Area.

In 2011 compliance evaluation and monitoring procedures were carried out on 25 human blood establishments and hospital blood banks. Compliance evaluations of 3 procurement and storage organisations of tissues/cells were conducted. Inspections carried out in 2011 required a total of 105 person-days.

In 2011 PIC/S initiated a repeated SAM review procedure with the purpose of verifying that the normative acts and authorisation system for medicines manufacturers, as well as the procedures for conduct of inspections in Latvia comply with the unified organisation standards. The review will be completed in 2012.

SAM employees represent SAM in the EMA GMP inspector working group, in PIC/S activities, as well as

working groups organised by the European Commission Directorate General for Health and Consumers (DG SANCO) regarding safety of human blood and its components, tissues, cells and organs.

2.8. Licensing of Pharmaceutical Activity Companies

On October 27th 2011 the Cabinet of Ministers Regulation No. 800 (adopted on October 19th 2011) "Procedure for Licensing Pharmaceutical Activity" (hereinafter - Regulation No. 800) came into effect defining the procedure how SAM reviews documentation and adopts decisions regarding issuance, renewal, suspension or withdrawal of special authorisations (licences).

On August 9th and October 20th 2010 amendments to the Pharmaceutical Law were approved and came into effect on January 1st 2011. These amendments define radical changes in the pharmacy ownership rights, in the possibilities for opening a new closed type pharmacy branch within day time clinics, there are no restrictions for opening branches of a general type of pharmacy, changes were defined in the operation of medicines wholesalers and manufacturing/importing companies regarding manufacturing and distribution of veterinary medicines in manufacturing and distribution companies of medicines for human use etc.

In accordance with Article 141 of the Transitional Regulations of the Pharmaceutical Law general type pharmacies whose licence expired until December 31st 2011 had the rights to reorganise their operation during 2011 in accordance with Article 36 of the Pharmaceutical Law. As general type pharmacies wished to continue their operation after this term, owners of the general type pharmacies took corresponding actions in accordance with Article 36 of the Pharmaceutical Law and submitted to SAM applications for renewal of terminated licences for an indefinite time period or for a time period of 5 years. SAM carried out renewal of licences of general type pharmacies for an indefinite time period or for a period of 5 years.

On August 12th 2011 the Cabinet of Ministers Regulation No. 610 (adopted on August 2nd 2011) "Criteria for Location of Pharmacies and Pharmacy Branches" (hereinafter - Regulation No. 610) came into effect. In accordance with Regulation No. 610 and No. 800 a new procedure was defined for opening or changing the location of a new general type pharmacy or pharmacy branch, a new method for measuring the 500 (five hundred) meter distance between an existing pharmacy and the new or relocated pharmacy was defined. Regulation No. 610 indicated that upon carrying out evaluation of the availability of pharmaceutical care 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 functional 24 hour pharmacy or other pharmacies are located farther than 3 kilometres away. SAM carried out evaluation of such applications indicating the possibilities for opening a general type pharmacy to the local authorities that organise the appropriate competitions regarding opening of general type pharmacies. SAM approved addresses for opening new general type pharmacies or pharmacy branches, for relocation of pharmacies or pharmacy branches by adopting appropriate decisions and publishing information regarding adopted decisions on SAM website www.zva.gov.lv.

SAM is responsible for carrying out evaluation of the documentation submitted to SAM by pharmaceutical activity companies (medicines wholesalers, manufacturing or importing companies, manufacturing companies of pharmaceutically active compounds, pharmacies) to receive special authorisations (licences). SAM carried out evaluation of the interior planning of pharmacies in accordance with the requirements of normative acts; prepared opinions regarding compliance evaluation of pharmacies, prepared decision projects regarding issuance, renewal, suspension or withdrawal of special authorisations (licences). In accordance with amendments to normative acts starting from October 27th 2011 it is no longer necessary to indicate the special activity stipulation (distribution of compensated medicines) in the licences of general type pharmacies.

SAM responsibilities include processing documentation regarding compliance evaluation and licensing of pharmaceutical activity companies, storage of information submitted by licensed pharmacies, medicines wholesalers and manufacturing companies, preparation of special authorisations (licences) for pharmaceutical and veterinary pharmaceutical activity, regular data updates on SAM website www.zva.gov.lv regarding issued special authorisations (licences) for pharmaceutical activity after the adoption of SAM decisions, organising and protocoling meetings of the SAM Pharmaceutical and Veterinary Pharmaceutical Activities Licensing Commission (hereinafter - Commission).

Issues regarding licensing were reviewed before adopting a SAM decision regarding issuance, renewal, suspension or withdrawal of special authorisation (licence) in the Commission, that is a SAM developed structural unit. Commission decisions have the nature of a recommendation. The Commission operates in accordance with the regulations approved by the Director of SAM.

The department ensured completion of the function delegated by the Pharmaceutical Law, Article 10, Paragraph 12 and 16 and Article 3.2 of the December 7th 2004 Cabinet of Ministers Regulation No. 1006 "Statutes of the State Agency of Medicines", meaning that the department evaluated the compliance of pharmaceutical and veterinary pharmaceutical activity companies, reviewed the compliance of the qualification and professional experience of the responsible official at medicines manufacturing companies and wholesalers with the requirements of normative acts regarding manufacturing and distribution of medicines.

In the year of review 2199 applications and supplementary documentation were received, 247 letters of response were forwarded, compliance evaluation was carried out in 163 pharmaceutical activity companies, 154 opinions regarding pharmacy compliance evaluations were prepared, 808 decisions were prepared regarding issuance, renewal, suspension and withdrawal of special authorisations (permits), approval of pharmaceutical activity location and extension of case review term, 801 special authorisations (licences) for pharmaceutical activity were renewed and issued - 759 to pharmacies, 24 to medicines wholesalers, 15 to medicines manufacturing or importing companies, 3 to companies manufacturing pharmaceutically active compounds.

Licences issued to pharmaceutical activity companies

Category	2007	2008	2009	2010	2011
Pharmacies	428	535	322	831	759
Medicines and veterinary medicines wholesalers	34	25	29	44	24
Medicines manufacturing and importing companies	28	12	9	14	15
Medicines manufacturing companies that manufacture pharmaceutically active compounds	0	0	0	2	3
Total	490	572	360	891	801

3. BUDGET AND EXPENSES OF THE STATE AGENCY OF MEDICINES

SAM obtains 100% of the financial resources necessary for carrying out the delegated functions and ensuring operations from provision of paid services.

SAM income and expenses

No.	Financial Resources	Budget in 2010 (actual data)	Year of review (2011)	
			Statutory	Actual data
1.	Financial resources for covering expenses (total)	4 293 025	3 784 189	4 404 968
1.1.	Income from paid services and other independent income	4 293 025	3 784 189	4 404 968
2.	Expenses (total)	5 698 794	4 034 289	4 109 366
2.1.	Maintenance expenses (total)	5 474 215	3 606 889	3 860 909
2.1.1.	Regular expenses	2 011 825	3 606 889	2 093 851
2.2.	Expenses for capital investment	224 579	427 400	248 457

4. GENERAL ADMINISTRATION OF THE STATE AGENCY OF MEDICINES

4.1. Ensuring Public Procurement and Economic Activities

In 2011 SAM announced 18 procurement procedures. There were 31 candidates. Contracts for supply and services were signed for the announced and performed public procurement procedures. The most significant procurement procedures were:

- improving the energy efficiency of the SAM administrative building - 1st round of heat insulation of the facade;
- development of a cluster solution for the current SAM visualisation system;
- implementation of changes and maintenance of the SAM information system.

4.2. Cooperation with State Administration Institutions in the Development of Normative Acts

The year of 2011 was highlighted by the development of several significant and completely new projects for the Cabinet of Ministers (CM) Regulations. To ensure the incorporation of the December 15th 2010 European Parliament and Council Directive No. 2011/83/EK on the Community code regarding medicines for human use into the national normative acts it was necessary to develop a project for a Cabinet of Ministers Regulation that would define the procedure for pharmacovigilance. Therefore, SAM developed a project for the CM Regulation "Pharmacovigilance Regulations" with an annotation and also prepared recommendations for amendments to the Pharmaceutical Law in relation to the introduction of the new pharmacovigilance terminology and a project for amendments to CM Regulations - SAM recommendations for amendments to the May 9th 2006 CM Regulation No. 376 "Procedures for the Registration of Medicinal Products" and recommendations for amendments to the January 17th 2006 CM Regulation No. 57 "Regulations Regarding Procedures for the Labelling of Medicinal Products and the Requirements to be set for Package Leaflets of Medicinal Products".

Following the introduction of the July 7th 2010 European Parliament and Council Directive 2010/45/ES regarding quality and safety standards of human organs for transplantation, SAM developed a project for Cabinet of Ministers Regulation "Procedure for Donating, Procuring, Testing, Processing, Preserving, Storing and Distributing Human Tissues and Cells" to ensure the incorporation of the directive in the national normative acts.

To improve the SAM provided services to its clients and decrease the administrative strain, several SAM recommendations were submitted to the Ministry of Health for amendments in Cabinet of Ministers Regulations, for example, June 26th 2007 CM Regulation No. 416 "Procedures Regarding Distribution and Quality Control of Medicinal Products", recommendations for amendments in the Procedure for Licensing of Pharmaceutical Activity, January 17th 2006 CM Regulation No. 61 "Regulations Regarding The State Agency of Medicines Publicly Available Paid Service Pricelist" etc. SAM also participated in the review and analysis of many projects for normative

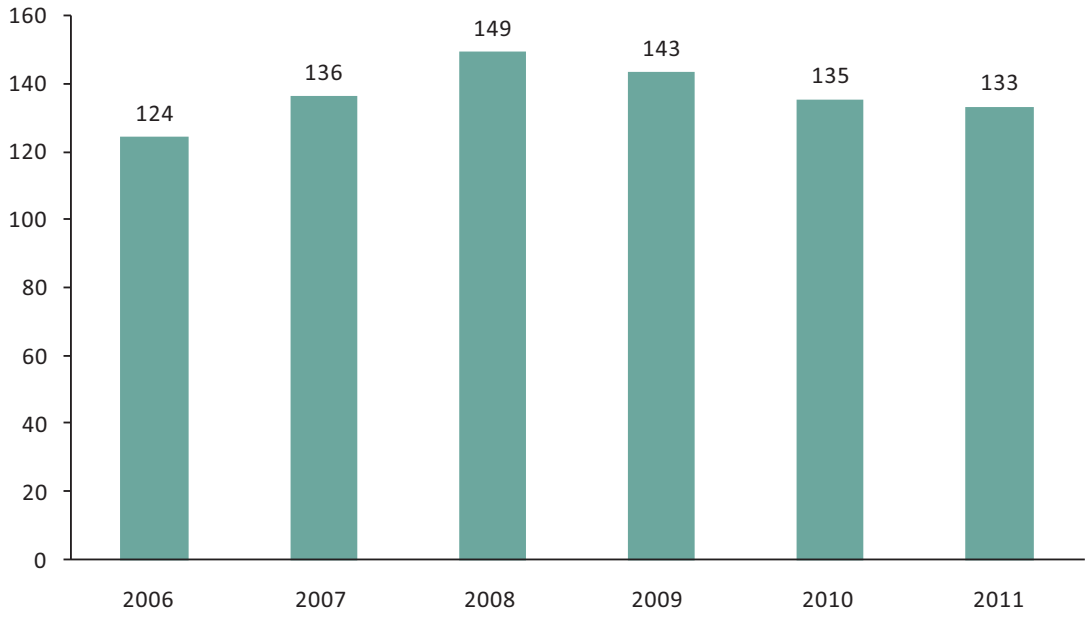
acts, for example, the project for amendments in the August 2nd 2005 CM Regulation No. 581 "Procedures for Registration, Conformity Assessment, Distribution, Operation and Technical Supervision of Medical Devices" was supplemented with SAM recommendations, a SAM opinion was provided regarding the project for amendments to the October 31st 2006 CM Regulation No 899. "Procedures for the Reimbursement of Expenditures for the Acquisition of Medicinal Products and Medical Devices Intended for Out-patient Medical Treatment".

In 2011 SAM representatives participated in regular meetings at the Ministry of Health to discuss the aforementioned projects for Cabinet of Ministers Regulations and amendments. Other institutions under the supervision of the Ministry of Health, pharmaceutical merchants and non-governmental organisations also participated.

4.3. Staff and Human Resources Management

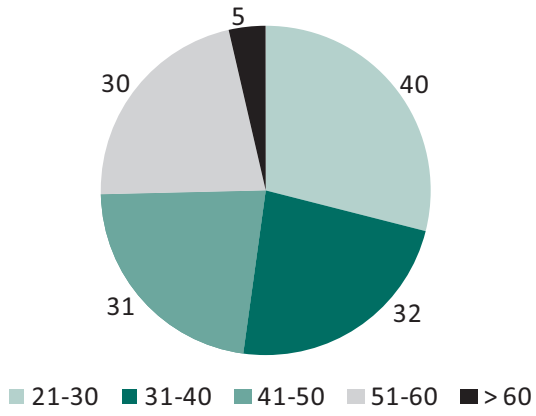
At the end of the 2011 there were 133 civil servants and employees actually working at SAM. In total there were 138 staff members in civil service or employment relationship with SAM in 2011: 68 civil servants and 70 employees. The number of staff members from 2006 until 2011 can be seen in the image below.

Dynamics of the number of staff members according to year

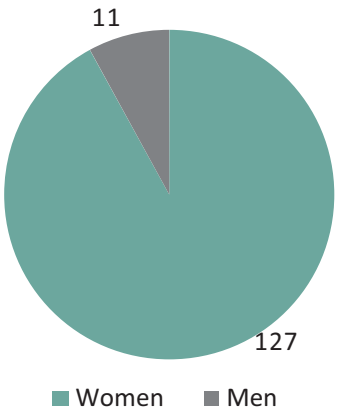


In 2011 20 staff members terminated, but 13 staff members began their civil service or employment at SAM. The staff turnover quotient in 2011 was 14% (staff turnover = number of released staff members in a definite time period/ average number of staff members in the same time period).

Distribution of staff members according to age group

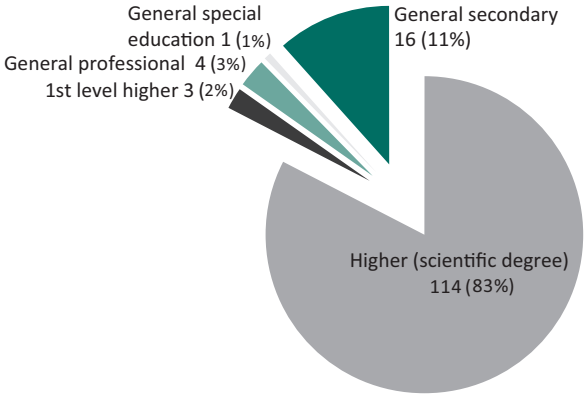


Distribution of staff members according to sex



Well-educated, competent and highly qualified specialists are necessary to successfully ensure the functions assigned to SAM. The education level of SAM staff members is high - 85 % of SAM staff members have higher education, of these 5 civil servants have a doctorate degree and 1 civil servant has a habilitation degree.

Distribution of staff members according to education



One of the basic principles of SAM staff politics is to motivate staff members to raise their qualifications and level of education. In 2011 to raise their qualification SAM staff members have attended 52 training sessions and seminars organised by international organisations. A great deal of attention was devoted to training at SAM: 21 staff members participated in the seminar regarding prevention of corruption, 18 experts participated in training for quality experts and 13 staff members participated in training for internal auditors. To ensure a unified understanding among the state administration officials regarding EU issues, 25 SAM staff members participated in the Ministry of Health organised seminar regarding coordination of EU issues. The table below shows raising of qualification among staff members in comparison with the previous years.

Raising qualification of staff members

Category	2007	2008	2009	2010	2011
Courses for raising qualification	123	125	269	107	162
Training, seminars, conferences coordinated by international organisations	51	62	52	64	52
English language courses	25	12	5	1	0

4.4. Quality Management

In 2011 SAM adopted a decision to introduce the international standard ISO 27001 that defines requirements for the information safety management system. The ISO 27001 standard is oriented towards identification and prevention of information risks and is based on risk management principles. This allows to develop an integrated management system by merging the requirements of both ISO 27001 and ISO 9001 standards.

In 2011 effort has been put into updating and optimising the documentation of the quality management system, paying special attention to ensure the compliance of the documentation with the requirements of the normative acts and the ISO 9001:2008 standard.

4.5. Development of Information Technologies

In 2011 work was continued to improve support processes for SAM information technologies (IT) by introducing or partially reconstructing information systems of State significance and information systems under the supervision of SAM: SAMIS, Medical Device Register LATMED, portal for receiving electronic documentation, SAMIS data export to EU central register

of medicines EudraPharm. Also the range of public e-services on SAM website www.zva.gov.lv has been supplemented with a prices of medicines verification form and a map of pharmacies.

To continue to improve the high performance of SAM information systems, as well as their availability to SAM clients, a series of improvements have been made to the virtualisation of technical platforms. By optimising the available technical resources the number of physical units has been decreased and that has provided a reduction in costs for maintenance of electrical energy and technical resources.

In the context of longterm cost reduction SAM has begun to combine the information technology resources available to SAM and to the Ministry of Health, thus, even further decreasing the number of physical and logical units employed in the field of health.

4.6. Cooperation with International Organisations

SAM is a part of the European Medicines Regulatory Network and the successful realisation of the institutional functions and tasks is closely related to the participation in the unified European medicines network - it entails cooperation between the EMA, European Commission and more than 40 medicines regulatory institutions within the European Union and the European Economic Area (EEA). This network of cooperation gives EMA access to a great number of experts allowing EMA to provide the best possible scientific expertise for regulation of medicines in the EU. Experts participate in the work of EMA as members of working groups un scientific advisory groups, scientific committees, as well as other groups.

This puts a great responsibility upon SAM to ensure that our colleagues can fully participate in the collective work procedures. It should also be mentioned that the cooperation requires human and financial resources from SAM. SAM staff members are also involved in cooperation with the European Commission and its Council work groups, European Commission Directorate General for Health and Consumers (DG SANCO), the World Health Organisation, The Uppsala monitoring centre (UMC), European Pharmacopoeia Commission, PIC/S, European Directorate for the Quality of Medicines & Healthcare (EDQM).

Since 2010 SAM has also been involved in the monitoring of medical devices, blood and its components, tissue and cells. SAM is also the competent institution with regards to authorisation of medical devices, issuance of authorisation for clinical trials with medical devices and monitoring the safety of medical devices. The responsible SAM specialists regularly participate in the meetings of the representatives from national competent authorities for medical devices in Europe. Participation is also ensured in Competent Authorities for Medical Devices (CAMD) meetings, Central Management Committee (CMC) meetings and European Commission Directorate General for Health and Consumers (DG SANCO) meetings.

There are effective cooperation contracts between SAM and EMA and the State Agency of Medicines in Estonia and Lithuania. On October 13th 2011 the Heads of the Medicines Agencies of Latvia, Lithuania and Estonia signed a cooperation contract for a unified procedure for the monitoring of safety of medicines. It entails that starting from next year the quality of the selected samples of nationally authorised medicines will be verified in one of the specialised laboratories in the Baltic States. On June 25th 2010 a memorandum of agreement was signed between the State Agency of Medicines of the Republic of Latvia and the Food and Drug Administration of the People's Republic of China regarding cooperation in normative regulation of medicines.

5. COMMUNICATION WITH STAKEHOLDERS (PUBLIC, HEALTH CARE SPECIALISTS, MERCHANTS)

In 2011 significant work has been invested in the development and maintenance of external communication. Communication with SAM cooperation partners has been purposefully increased by providing independent and objective information regarding issues within SAM competency to the professional target audience, as well as the general public.

In the year of review 36 press releases were prepared and forwarded to the mass media representatives, replies were prepared to more than 98 requests for information, a seminar was organised for SAM clients (regarding newest issues in the procedure for marketing authorisation of medicines), information was updated on SAM website and in the Latvia State portal www.latvija.lv (information on SAM public services). In total proactive communication includes more than 612 news in different types of mass media.

SAM publications according to topic

Topic of publication	Number of publications
Safety of medicines	183
The market, consumption and price of medicines	125
Price of medicines verification form	57
Digital map of pharmacies	35
SAM operations and budget	28
Availability of medicines	31
Number of pharmacies,authorisation of pharmacies	19
Clinical trials	18
Normative acts	14
System of compensated medicines	13
Marketing authorisation of medicines	12
Other	77

In 2011 SAM prepared several informative publications in order to inform doctors, pharmacists and other health care specialists about newest issues in pharmaceutics and in SAM operations, as well as about the safety of medicines. Although doctors, pharmacists and other health care specialists can obtain information from various sources like seminars and conferences and professional publications from different countries, SAM provides updated, objective, verified and concentrated information for those who wish to follow the most important developments in the field of pharmaceutics.

The SAM informative bulletin "Cito!" has already become an integral part of daily operations by providing information regarding safety of medicines, serious adverse drug reactions and what doctors and pharmacists should know in case of theses adverse reactions.

The LR Drug Register is an official and updated source of information regarding medicines included in the LR Drug Register and it contains information regarding medicines authorised in national, mutual recognition and decentralised procedures and parallel imported medicines. In addition to the book, an electronic version of the Drug Register in a CD format was also prepared and it provides an easy and practical information search option.

To provide information regarding trends in medicines consumption according to consumer groups, SAM prepared an informative publication "Statistics of Medicines Consumption" (an electronic publication in a CD format). The source of data resources are the data provided by medicines wholesalers and manufacturers that has been categorised according to various criteria (sales amount to hospitals, pharmacies, other health care institutions and medicines wholesalers). Every year the distribution of medicines consumption according to the procedure for issuance of medicines is published. The electronic version also contains a comparison of actual consumption of medicines from 2005 until 2010 (according to DDD - defined daily dose per 1000 residents of Latvia per day)

Publications prepared by SAM

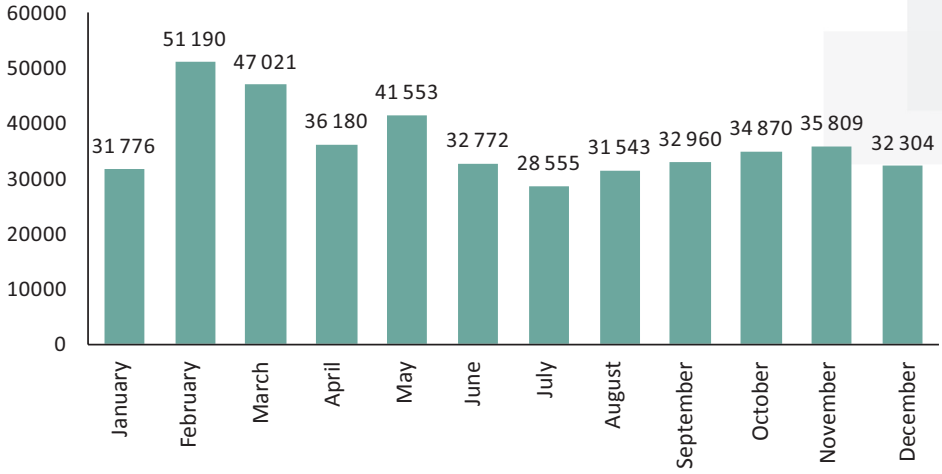
Publication	Number of copies
Informative bulletin "Cito!" (including "Cito!" anniversary edition)	4X300 copies
LR Drug Register and the electronic version in a CD format	450 copies
Electronic version of the Statistics of Medicines Consumption in a CD format	80 copies
SAM Annual Review (in Latvian and English)	100 copies

Along with cooperation with the mass media and informative publications, SAM also ensures regular updates to the information on SAM website www.zva.gov.lv. Undoubtedly in the age of technology the maintenance of the website is not only one of the most cost-effective channels for communication, but it also allows to provide information directly to the target audience using the internet.

Maintaining the website is an effective way of ensuring the provision of official and operative information to every member of the public (also to SAM clients) regarding SAM operations and newest issues in the field of pharmaceutics. According to Google Analysis statistical data in 2011 SAM website has been visited 436 533 times and sections of the website have been browsed a total of 2 031 672 times. The results indicate that the average number of first time visitors of the SAM website per month is approximately 8200.

At the same time it should be said that intensive work on the development of SAM website is planned for 2012 by improving the arrangement of information and the design, thus, ensuring that information is clear and easily perceptible not only to health care professionals, but also to any resident of Latvia.

Website visitors in 2011



To enquire the opinion of the website visitors, 4 surveys were carried out in 2011 and replies from 2109 respondents were received. Website visitors answered the following questions:

- „Do you always read the package leaflet included in the packaging of medicines and available on SAM website before you start using the medicines?"
- "Can the information contained in the SAM developed map of pharmacies be easily found?"
- "Where, in your opinion, the patient should received information about prices of medicines?"
- "Are you satisfied with the level of pharmaceutical care that clients receive in pharmacies?"

SAM external communication activities are not based solely on a one-way provision of information, but SAM also provides the opportunity for SAM cooperation partners to express their opinion about the quality of SAM client service and provided services. The received information is used for the improvement of SAM operations quality. In 2011 SAM organised 3 surveys:

- a survey for pharmacy managers regarding discounts for prices of medicines and applicable increase in price in order to evaluate the project for normative act prepared by the Ministry of Health and the risk created by it on the further operation of pharmacies;
- a survey for clients regarding SAM operations and provided services in order to improve the quality of client service and provided services according to the gathered data;
- a survey for SAM staff members with the purpose of discovering the opinion of staff members regarding work aspects that are important to them and that would allow to determine priorities in working with personnel and make rational and deliberative decisions with respect to staff members.

Useful information for pharmaceutical professionals!

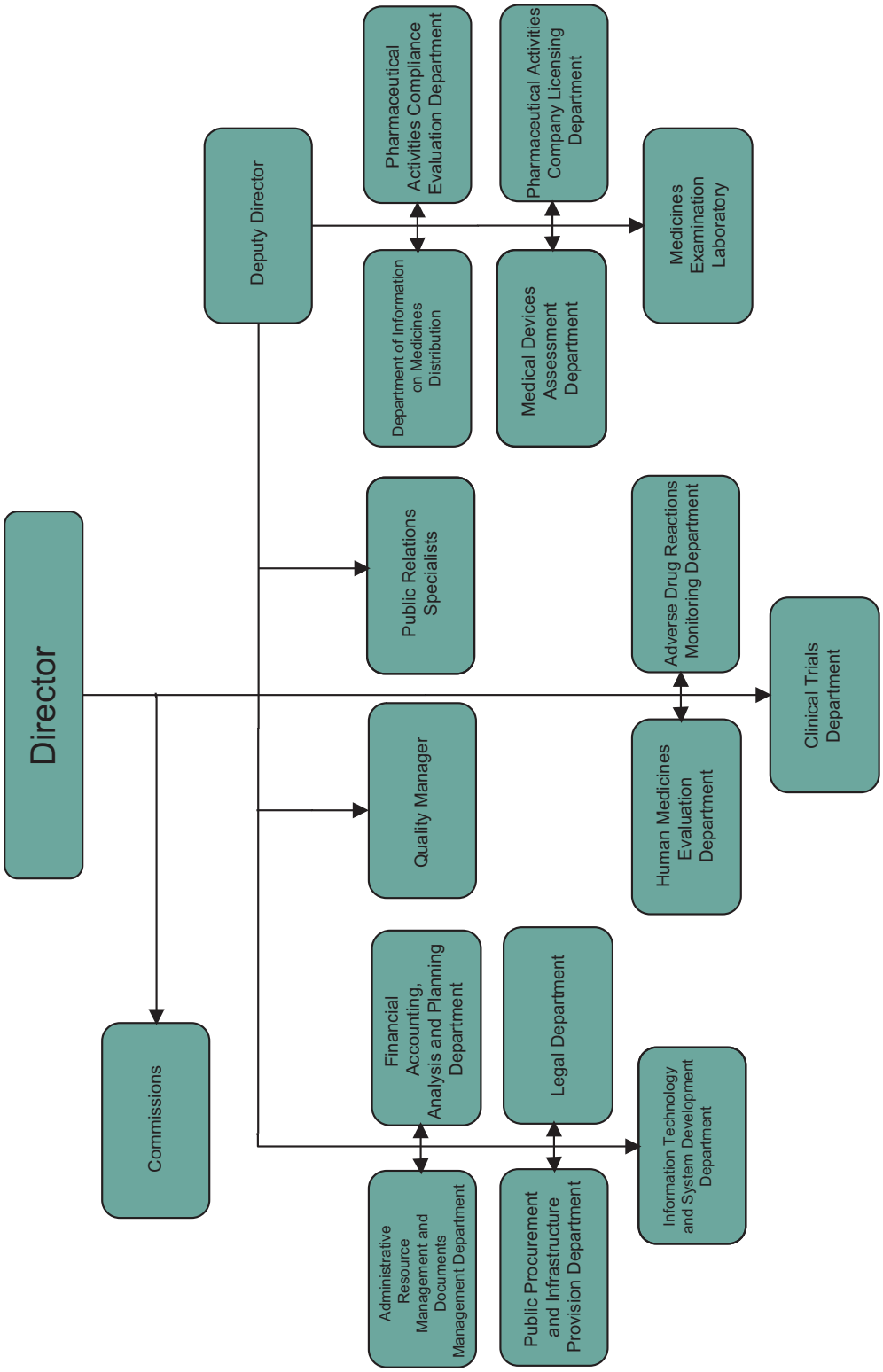
6. DEVELOPMENTAL PRIORITIES OF THE STATE AGENCY OF MEDICINES FOR 2012

The operational plan for the SAM for the year 2012 was approved on February 1st 2012. Taking into account the functions and tasks assigned to the SAM the operational plan assigns specific tasks for each structural unit and the institution as a whole. In addition to the main operations of SAM the following objectives have been set as priorities for 2012:

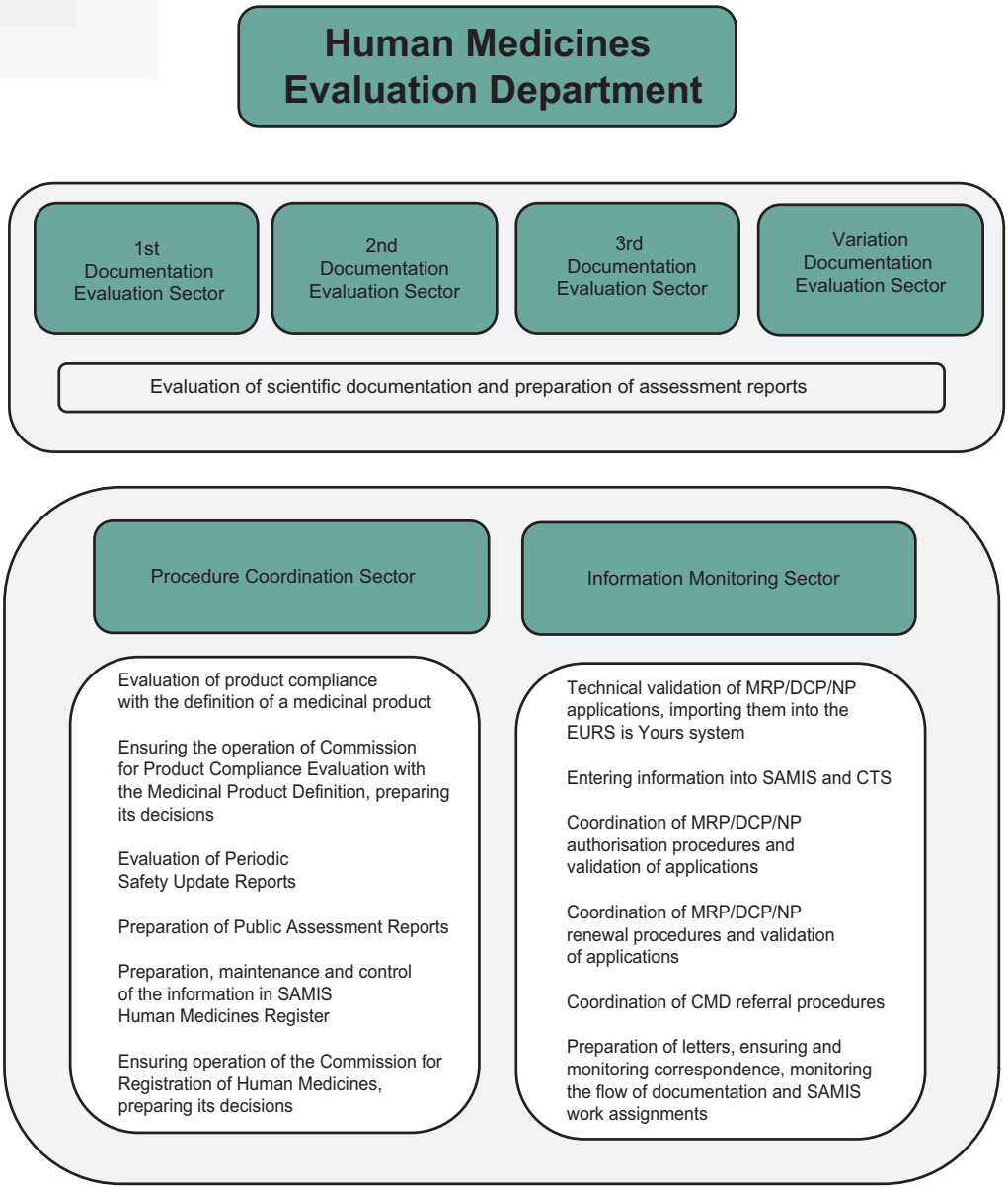
- resolve the issue regarding the possible SAM status change (an institution not financed from the state budget) that would allow a rational management of procedures and finances;
- increase the number of MRP/DCP procedures where Latvia is the Responsible Member State
- get involved in the centralised authorisation procedure assuming the responsibilities of the co-rapporteur;
- promote and develop cooperation with academic and scientific institutions by ensuring involvement of academic forces in case of a complex expertise and by offering new skills to pharmaceutical and biomedical research centres to promote innovations;
- ensure the requirements of the new Pharmacovigilance normative act, including inspections of pharmacovigilance system compliance after they are defined in the normative acts;
- actively participate in e-health projects and ensure possibilities for centralisation of data in this field;
- improve receiving and processing of electronic authorisation documentation in the sector of medicines for human use (e-CTD);
- ensure data exchange with European databases with respect to data regarding medicines, medical devices, clinical trials, manufacturers, distributors and tissue, cell and organ centres (undertake the commitments defined by the Memorandum of Understanding on the Exchange of information in the context of EU Telematics);
- within the limits of available resources actively participate in the work of EMEA and work-sharing programs within the European Medicines Regulatory Network and also in WHO programs;
- ensure and coordinate the development of the list of active substances and excipients in Latvian, involving academic forces and representatives of the State Language Center in the process;
- promote the development of the quality management system un prepare for the ISO certification;
- update and review SAM internal procedures to increase work effectiveness;
- promote a more active and broader two-way communication with SAM cooperation partners (doctors, pharmacists, clients, mass media representatives and other stakeholders, as well as the public as a whole), thus, creating a positive understanding of SAM operations and pharmaceutics as a whole;
- continue the development of means of electronic communication with clients.

ANNEXES

Annex 1
Structure of the State Agency of Medicines



Annex 2
Structure of the Human Medicines Evaluation Department



Annex 3
Functions of the State Agency of Medicines structural units

HUMAN MEDICINES EVALUATION DEPARTMENT

- Performs marketing authorisation and renewal of medicines in the national, mutual recognition and decentralised procedures and accepts the submitted variations to documentation.
- Carries out expertise on pharmaceutical, pharmacological and toxicological documentation, clinical trials, Summary of Product Characteristics, Package Leaflet, labelling and other documents.

DEPARTMENT OF INFORMATION ON MEDICINES DISTRIBUTION

- Carries out expertise on applications and documentation and issues authorisation for:
  - import and export of psychotropic, narcotic medicines/substances and precursors;
  - using 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;
  - distribution of unauthorised medicines;
  - import of samples of medicines;
  - distribution of remaining stock of medicines;
  - distribution of and variation to parallel imported medicines in Latvia.
- Carries out expertise on applications and documentation and issues special authorisations (licences) for working with precursors, issues precursor operator cards.
- Carries out expertise on applications and issues authorisations for purchase of medicines (to ensure operation).
- Assembles and provides information regarding consumption, prices and availability of medicines, turnover of medicines wholesalers and manufacturing companies.
- Records and controls the legal circulation of narcotic substances, psychotropic substances and precursors controlled in Latvia.

CLINICAL TRIALS DEPARTMENT

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

ADVERSE DRUG REACTIONS MONITORING DEPARTMENT

- Collects, updates, evaluates and carries out expertise of data on adverse drug reactions observed in Latvia and in foreign countries.
- Carries out data exchange regarding safety of medicines with marketing authorisation holders and institutions in the European Union and in the world, as well as with the EudraVigilance data base for adverse drug reactions.
- Cooperates with marketing authorisation holders regarding pharmacovigilance issues. That includes approval of the educational materials and letters to doctors and pharmacists prepared by MAH regarding risk minimisation of medicines and evaluation of detailed descriptions of the MAH pharmacovigilance systems within the national marketing authorisation procedure.

- Prepares medicines safety information for communication with physicians, pharmacists and the society.
- Participates in the preparation of the SAM bulletin "Cito!".
- Cooperates with EMA, especially in order to promote pharmacovigilance procedures and prepare for the implementation of the newly prepared EU pharmacovigilance normative acts in July 2012.

MEDICINES EXAMINATION LABORATORY

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

MEDICAL DEVICES ASSESSMENT DEPARTMENT

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

PHARMACEUTICAL ACTIVITIES COMPLIANCE EVALUATION DEPARTMENT

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

PHARMACEUTICAL ACTIVITIES COMPANY LICENSING DEPARTMENT

- Ensures licensing of pharmaceutical activity companies to issue special authorisations (licences) to companies for pharmaceutical activity.
- Devises and maintains informative base of licensed pharmaceutical activity companies.

FINANCIAL ACCOUNTING, ANALYSIS AND PLANNING DEPARTMENT

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

PUBLIC PROCUREMENT AND INFRASTRUCTURE PROVISION DEPARTMENT

- Organises public procurements.
- Ensures management of material assets and organises activities for work protection.

LEGAL DEPARTMENT

- Ensures the compliance of administrative acts devised by SAM with the requirements of current legislation, including European Community regulations and the requirements of current rulings of the Court of the European Community, as well as devises administrative documents regulating SAM operations.
- Legally solves juridical issues and problems.
- Prepares and evaluates contracts, documentation projects, various opinions.
- Devises projects for normative acts.
- Represents the interests of SAM in Court institutions.

ADMINISTRATIVE RESOURCES MANAGEMENT AND DOCUMENTS MANAGEMENT DEPARTMENT

- Carries out planning, selection and account of the personnel.
- Organises the establishment of legal employment relationship with employees and the appointment of civil servants, the termination of legal employment relationships with SAM and the release of civil servants from their duty, the transfer of employees and civil servants to other staff positions.
- Organises and supervises the record keeping process and the system for management of documentation in the institution.
- Ensures SAM client service by providing information about processes ensuring the functions of the agency and the appropriate procedure for receiving and issuing of documents.
- Carries out certain functions delegated to it by the SAM administration in accordance with the requirements of the State Administration Structure Law.
- Ensures the operation of the SAM library.
- Manages the SAM Archive.

INFORMATION TECHNOLOGY AND SYSTEM DEVELOPMENT DEPARTMENT

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

QUALITY MANAGER

- Organises the introduction, maintenance and improvement of the Quality Management System.
- Carries out monitoring and analysis of processes.

PUBLIC RELATIONS SPECIALIST

- Informs the public about field politics in the competency of SAM by creating a clear and accurate impression about SAM operations and actual processes.
- Presents a SAM administration approved opinion in the mass media.
- Coordinates information updates on the internal and external SAM website.
- Promotes SAM corporative identity.

Annex 4
The State Agency of Medicines in dates

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
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)
1997	The publication of the annual issue "Drug Register of Latvia" is initiated.
1998	The electronic record keeping program "Lotus Notes" is introduced.
02.03.1998.	Clinical Trial Inspection Department is established.
1999	The first annual review is published.
1999	The first agency website is developed.
End of 2000	The second section of SAM building is commissioned.
2000	International Harmonisation Conference guidelines regarding Good Clinical Practice are published (in Latvian and English)
2001	The development of an independent informative publication "CITO" for doctors and pharmacists is initiated.
From 02.01.2001. until 31.12.2009.	The function of evaluating and approving advertisements of medicines is carried out.
02.01.2001.	Adverse Drug Reactions Monitoring Department is established.
01.10.2002.	Internal audit is introduced and the development of a Quality Management System is initiated.
17. - 18.03.2002.	The 5th EU meeting of associated drug regulatory authorities takes place in Latvia - within the CADREAC cooperation agreement.
2002	The Medicines Examination Laboratory is welcomed into the international network of Official Medicines Control Laboratories (OMCL).
2002	SAM is welcomed into the WHO International Drug Monitoring Program as the 66th member state.
2003	The first Benchmarking visit (BEMA) in SAM.
2003	The first "Statistics of Medicines Consumption" is published.
01.07.2003.	Legal Department is established.
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.
2004	Access to and unified operation in databases of EU member states is established via the EudraNET network.
End of 2004	The Archive building is commissioned.
2005	An educational issue "Introduction to Pharmacovigilance" is published.
End of 2005	A new function is delegated to SAM - to develop and maintain a system for the monitoring of prices of medicines.
2006	For the first time the evaluation of staff member operations and results is initiated and completed.
2006	Participation within PIC/S is initiated.
02.01.2006.	The Information Department is transformed and the Department of Information on Medicines Distribution and the Information Technology Department are established.
02.01.2006.	The Pharmaceutical Activities Company Licensing Department is established by reorganising the Legal Department and adopting from it the function of licensing pharmaceutical activity companies.
02.01.2006. – 31.12.2010.	The authorisation and monitoring the circulation of veterinary medicines is delegated to SAM.
10.04.2006.	The pharmaceutical Activities Compliance Evaluation Department is established.
06.-10.02.2006.	The EU Benchmarking (BEMA I) takes place.
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.

10.11.2006.	A meeting of SAM of the Baltic states takes place in Riga.
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.
01.02.2007.	Civil service is introduced at SAM.
11.07.2007.	Memorandum of agreement with Estonia regarding cooperation in monitoring of medicines.
09. – 12.2007.	The concept for the e-prescription information system is developed.
27.12.2007.	Memorandum of agreement between national medicines agencies of the EEA member states and the EMA about the exchange of information and documents regarding pharmacovigilance.
2008	The first Mutual Recognition Procedure was carried out where Latvia was the Reference Member State.
14.01.2008.	Memorandum of agreement with Lithuania regarding cooperation in monitoring of medicines.
19.09.2008.	Recognition from the Riga City Council for original front lawn greenery.
11.08.2009.	Contract between the Baltic State Agencies of Medicines regarding a united packaging of medicines in three languages.
01.02.2010.	Establishment of a Client Service Centre.
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.
09.07.2010.	Memorandum of agreement with EMA regarding exchange of information and documentation.
06.-08.09.2010.	The EU Benchmarking (BEMA II) takes place.
01.10.2010.	The function of compliance evaluation, authorisation and monitoring of safety of medical devices is adopted.
01.10.2010.	The compliance evaluation and monitoring of procurement and storage organisations of human tissues, cells and organs, blood establishment, hospital blood banks and the State Blood Donor Centre is initiated.
02.02.2011.	Contract between the Baltic State Agencies of Medicines regarding a unified procedure for labelling medicines.
16.05.2011.	The first digital map of pharmacies with broad search options is developed on SAM website.
19.07.2011.	The list of active substances is published on SAM website in three languages: Latvian / Latin / English
From 26.08.2011. Until end of October	Participation as co-rapporteur in the repeated review of the EMA Committee for Advanced Therapy by authorising the newly introduced therapeutic 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".
13.10.2011.	The State Agencies of Medicines of the Baltic States sign an agreement regarding cooperation in quality control of medicines.
06.-08.09.2010.	The EU Benchmarking (BEMA II) takes place.
01.10.2010.	The function of compliance evaluation, authorisation and monitoring of safety of medical devices is adopted.
01.10.2010.	The compliance evaluation and monitoring of procurement and storage organisations of human tissues, cells and organs, blood establishment, hospital blood banks and the State Blood Donor Centre is initiated.
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