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Operational Strategy of the State Agency of Medicines 2017-2019

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Contents

Abbreviations and terminology

CM	Cabinet of Ministers
DCP	Decentralised Procedure
EDQM	European Directorate for the Quality of Medicines and Healthcare
EEA	European Economic Area
EMA	European Medicines Agency
EU	European Union
GDP	Good distribution practice [medicines]
GMP	Good manufacturing practice
HMA	Heads of Medicine Agencies
ICMRA	International Coalition of Medicines Regulatory Authorities
INCB	International Narcotics Control Board
ICT	Information and communication technologies
IS	Information systems
LV	Republic of Latvia
MH	Ministry of Health
MRP	Mutual Recognition Procedure
NGO	Non-governmental organisation
PIC/S	Pharmaceutical Inspection Co-operation Scheme
SoHO	Substances of human origin
WHO	World Health Organization
Agency	State Agency of Medicines

1. Introduction

The Operational Strategy of the State Agency of Medicines (hereinafter – Agency) 2017-2019 is a document for the mid-term policy plan. The purpose of this document is to lay down the strategic operational directions and objectives for the period of 2017-2019 creating the framework within which the Agency shall plan and organise its operation, taking into account the amount of financial resources available and the time period included in the strategy.

The Agency prepares the strategy in accordance with the national priorities[1] and objectives set to ensure public health, as well as international priorities reflected in the strategy of the network of European medicines agencies and its action plan for 2016-2020.

1.1. Authorisation, mission and vision of Agency operation

According to the Cabinet of Ministers Regulation No. 537 of 31 July 2012 "Statutes of the State Agency of Medicines", the Agency is a state institution subordinate to the Minister of Health. Minister of Health implements oversight through the Ministry of Health.

Functions of the Agency

Through provision of services to private persons, state and municipal institutions and foreign institutions, the Agency carries out the functions and tasks laid down in the Pharmaceutical Law, Law on Medical Treatment, Law "On the Protection of the Body of Deceased Human Beings and the Use of Human Tissues and Organs in Medicine", Law "On Procedures for the Legal Trade of Narcotic and Psychotropic Substances and Medicinal Products", Law "On Precursors" and other normative acts.

The Cabinet of Ministers of the Republic of Latvia has incorporated the **Agency's mission** in its **operational objective**:

To ensure qualitative un justified services in the evaluation of medicinal products used in healthcare, procurement and utilisation centres of human blood, tissues, cells and organs, as well as pharmaceutical activity companies in accordance with the state and public interests in the field of healthcare.

Vision

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

[1] Conceptual report "Regarding Reform of the Healthcare System",
Ground principles of public health 2014-2020
National Development Plan of Latvia 2014-2020
Strategy for Sustainable Development of Latvia until 2030
WHO European Strategy "Health 2020"

1.2. Impact assessment of the Operational Strategy of the Agency for 2014-2016

In alignment with the policy implemented by the MH, the Agency as a subordinate institution had set the following 3 strategic priorities in 2014-2016[2] within the delegated functions to ensure its operational objective:

- Promote sustainable development of the national market of medicines
- Ensure prerequisites for the safe and rational use of medicines, medical devices, tissues, cells, organs, blood and blood components
- Improve efficacy of Agency operation, using the BEMA III benchmarking experience

In order to ensure results in the period of review for the laid down in above stated strategic priorities and implementation of the requirements of EU legal acts and normative acts in Latvia, the results of Agency's operational tasks were planned in 3 directions: *product, merchant and information*.

In order to ensure the relevant planned results in the period of review, the strategy was revised and specified according to the state budget in 2015 and 2016.
An overview of the results achieved in each operational direction is provided below.

In the product direction the following were set forth:

Objectives

- ✓ Ensure and promote marketing authorisation and renewal procedures for medicines and medical devices with the help of consultative support and discussions on specific problems
- ✓ Continuously increase the number of mutual recognition and decentralised authorisation procedures where the Agency assumes the position of a reference member state
- ✓ Promote utilisation of fee waivers – apply and establish fee waivers for products that are necessary for public health, but have low consumption and turnover
- ✓ Regularly, as well as following requests from merchants provide updated information regarding consumption data of medicinal products
- ✓ Prepare reports on national consumption of medicinal products

Goal

Medicines and medical devices intended for human use and utilised in public healthcare are authorised, qualitative, effective and safe.

Results achieved

In the period of review, in relation to marketing authorisation:

a) 27 742 applications for variations to marketing authorisation documentation were evaluated
b) 2023 applications for summaries of product characteristics, package leaflets and package labelling for centrally authorised medicinal products were evaluated and a linguistic check was performed
c) 92 applications regarding product compliance or non-compliance with the definition of a medicinal product were reviewed and opinion was provided
d) 2132 applications for marketing authorisation and renewal of medicinal products were evaluated
e) 731 renewal procedures were conducted
f) Marketing authorisation procedures were conducted and 901 medicinal products were included in the Medicinal Product Register of Latvia
g) 940 medicinal products were withdrawn from the Medicinal Product Register of Latvia

[2] Taking into account the *Road map to 2015. The European Medicines Agency's contribution to science, medicines and health*. / 26.01.2011 version /. and *A Strategy for the Heads of Medicines Agencies, 2011-15* /25.10.2010 version /.

h) At the end of 2016 there were 4314 medicinal products in the Medicinal Product Register of Latvia

Agency experts are highly qualified and esteemed among the professionals in the field and this opinion is reinforced by regular invitations for Latvia to assume the position of a reference member state and take the lead in compliance evaluations and quality assessments in marketing authorisation and renewal procedures both within MRP and DCP. In the period of review, Agency experts assumed the leading position in 24 DCP, 6 MRP authorisation procedures and 9 MRP renewal procedures.

A decrease (-20% per year) in the applications for registration of medical devices manufactured in Latvia was observed within the strategic period. The main reasons include the small size of local market for medical devices and low activity of manufacturers in development of new products, as well as complex regulatory normative acts and planned changes in the EU normative acts with regard to requirements for medical devices.

In the field of pharmacovigilance, changes[3] were implemented in Agency processes related to evaluation of adverse drug reaction reports. The number of pharmacovigilance reports submitted in Latvia increased by 14% in the period of review. In the 2017-2019 strategic period the Agency plans on continuing intensive educational activities for patients and healthcare professionals regarding observation and reporting of adverse drug reactions.

In collaboration with the Ministry of Health, amendments to the paid public service pricelist of the Agency were prepared, including the following remissions for marketing authorisation holders coming into force in 2016:

- If the turnover of a medicinal product does not exceed 3000 EUR in the previous calendar year, the Agency may review applications and adopt decisions on waiving the annual post-marketing authorisation fee for marketing authorisation holders
- A 90% discount for the marketing authorisation fee in the national procedure for expertise on application and additional documentation for generic medicinal products or biosimilar medicinal products

During the strategic period, 6515 accident reports were received within the EU vigilance system for medical devices, 3085 of these were primary reports. The Agency received majority of reports (2476 or ~20% increase in comparison to 2015) and primary reports (1063 or ~5% increase in comparison to 2015) in 2016.

One of the reasons for the rapid increase in the number of reports is the increase in the activity of medical device users in Latvia resulting in productive collaboration between the Agency and manufacturers, and distributors of medical devices, ensuring timely exchange of information following receipt of accident reports.

As a result, following receipt of a report within the vigilance system, the appropriate actions and safety measures were implemented in compliance with the normative acts:

	2014	**2015**	**2016**	**Total**
Following receipt of reports regarding accidents outside of LV	169	147	172	**488**
Following receipt of reports regarding accidents in LV	23	30	61	**114**
Total	**192**	**177**	**233**	**602**

[3] In accordance with the amendments to the Cabinet of Ministers Regulation No. 47 on 22 January 2013 "Procedure for Pharmacovigilance", taking into account the Directive 2012/26/EU of the European Parliament and of the Council of 25 October 2012 amending Directive 2001/83/EC as regards pharmacovigilance.

The doubling of safety measures implemented in 2016 (following reports of accidents in Latvia) may be considered as an indicator of increasing understanding among medical device holders in Latvia of the importance of the vigilance system, responsibility and participation, and their role in ensuring public health.

For the merchant direction the following were set forth**:**

Objectives

- ✓ Ensure the quality of existing services and develop new services in accordance with the foreseeable changes in legislation
- ✓ Minimisation of the administrative burden and client-oriented service
- ✓ Continuously raise professionality of experts and all Agency personnel
- ✓ Establish creative collaboration with external experts from scientific institutions
- ✓ Maintain the integrated management system in accordance with ISO 9001:2008, ISO/IEC 17025:2005, ISO/IEC 27001:2005;
- ✓ Ensure implementation of the new normative acts regarding pharmacovigilance
- ✓ Strengthen evidence-based methodology in decision-making procedures
- ✓ Promote the export capacity of national merchants
- ✓ Continue to develop and improve the partnership with merchants, marketing authorisation holders, distributors, representatives of doctor organisations and non-governmental organisations with regard to minimisation of health risks

Goal

Compliance certification of merchants involved in manufacturing or distribution of specific medicines and products with the relevant requirements.

Results achieved

As part of licencing of pharmaceutical activity[4]:

- 4079 documents submitted by licence holders were evaluated in accordance with the requirements of normative acts
- 1159 special permits (licences) for pharmaceutical activity were issued
- Persons conducting pharmaceutical activity, as well as services and products offered by merchants with regard to materials of human origin (blood, tissues, cells and organs) comply with the established quality and safety requirements, and during the period of review no critical deficiencies were identified that could not be corrected promptly, and, thus, there were no significant threats to public interests and health

Overall, the merchant activity within the field of pharmaceutical activity can be assessed as high, slightly surpassing the initial estimations.

The export capacity of Latvian manufacturers was promoted, including the following:

- 45 Good Manufacturing Practice certificates and 34 Good Distribution Practice certificates were issued certifying compliance of Latvian merchant manufacturing sites with the common requirements in the EU.
- The 13 Good Manufacturing Practice certificates issued for active pharmaceutical ingredients covered a wider range of active pharmaceutical ingredients (36 active substances in total).
- Upon request from merchants, 473 pharmaceutical product certificates, 83 abbreviated pharmaceutical product certificates and other certifications were issued, as required for registration of medicines manufactured in Latvia in new export markets.

[4] By implementing the performance of functions laid down in the Pharmaceutical Law, Section 10, Article 12 and Article 16 with regard to issuance of special permits (licences) for pharmaceutical activity to medicines wholesalers, medicinal product manufacturing and distribution companies, general type pharmacies and closed type pharmacies.

The number of compliance certificates issued in the period of review continues to increase every year and promotes the export capacity of Latvian manufacturers to third countries.
Amendments to the regulations regulating the procedure for manufacturing and control of medicines were approved in active collaboration with representatives from the industry, Section of Industrial Pharmacists of the Pharmacists' Society of Latvia, Latvian Generic Medicines Association, Association of International Research-based Pharmaceutical Manufacturers, Latvian Society of Free Pharmacists, Association of Pharmacy Owners and other organisations.

The administrative burden for merchants and the Agency aldo has been decreased, for example:

a) Transition to unlimited certificates in compliance evaluation of blood cabinets with the purpose of decreasing hurdles in the availability of urgent medical care. In the long-term, unlimited certificates will allow to apply a risk-based approach in supervision of blood cabinets. Thus, resources may be focused on blood cabinets and blood establishments requiring additional support in quality improvements.
b) In order to ensure packaging of medicines, pharmacies do not have to receive a licence for medicines manufacturing.
c) Receipt of individually issued permits for import of unauthorised medicines was simplified and receipt in electronic format was ensured.
d) Application of risk-evaluation principles in planning of monitoring inspections was initiated.
e) Where possible, the compliance monitoring inspection of merchant activity is merged with compliance evaluation of changes in normative acts and merchant activity.
f) A new action model was introduced in the Good Manufacturing Practice compliance evaluation of manufacturing sites of merchants manufacturing active substances – it covers all of the substances manufactured at the specific site, and the compliance certificate is issued for 5 years, not 3 years as previously.
g) Electronic communication with Agency clients was facilitated.

For the information direction the following were set forth:

Objectives

- ✓ Actively participate in EMA expertise according to work tasks, in work-sharing within the European network of national medicines agencies, in EDQM and WHO programs.
- ✓ Continuously improve exchange of information in procedures where the Agency will be a concerned agency in mutual recognition and decentralised procedures.
- ✓ Ensure information exchange with national and international databases in pharmacovigilance and other vigilances.
- ✓ Continuously provide information regarding products and merchants, potential risks and their minimisation measures, rational use of healthcare products.
- ✓ Regularly collect and distribute information regarding consumption of medicines.
- ✓ Ensure the opportunity for patients to report adverse drug reactions, develop online submission of reports.
- ✓ Continue the development of electronic communication with clients and the public.

Goal

Stakeholders were provided with objective, thorough and updated information regarding healthcare products, as well as Agency operations aimed towards improvement of public health, disease prevention and prevention of threats to human health.

Results achieved:
On Agency's website, merchants operating with materials of human origin (blood, tissues, cells, organs) have been provided with access to risk assessments, recommendations and updated information regarding new potential threats (Zika virus, etc.) issued by the European Centre for Disease Prevention and Control.
Exchange of information with EMA and national competent authorities of other EEA member states was ensured in areas of merchant compliance evaluation (medicines, human tissues, cells and organs, clinical trials).

Electronic submission of vigilance reports was ensured for:

a) Observed adverse drug reactions (healthcare professionals, pharmacists, patients)
b) Accidents with medical devices (users, owners of medical devices)
c) Serious adverse reactions (medical treatment institutions – blood cabinets, centres for utilisation of tissues, cells and organs for transplantation)
d) Adverse events (medical treatment institutions – blood cabinets, blood establishments, tissue centres)

An increase in the number of received electronic vigilance reports: from 52% in 2014 to 81% in 2016. Measures were taken to ensure that information mentioned in normative acts would be regularly available to the public and merchants, as well as concerned institutions (for example, Health Inspectorate, Society of Pharmacists of Latvia, Food and Veterinary Service). On Agency's website, updated information is available regarding licenced pharmaceutical activity companies, and maintenance and updating of the map of pharmacies in Latvia is ensured.

The risk to public health was minimised and, in accordance with the common EU principles, an additional safety measure was implemented for control of pharmacies distributing non-prescription medicines online – a common logo with the aim of preventing falsified medicines from entering the legal supply chain of medicines[5]. The logo allows identification of pharmacies that have received a permit from the Agency to ensure marketing of non-prescription medicines using internet websites legally registered by a licenced merchant.

To ensure access to important information regarding use of medicines, the following materials were published on Agency website:

a) Educational materials for doctors and pharmacists prepared by medicines manufacturers for risk minimisation
b) Announcements from the EMA Pharmacovigilance Risk Assessment Committee and Committee for Medicinal Products for Human Use related to the safety of medicines
c) Package leaflets and summaries of product characteristics of medicines included in the Medicinal Product Register of Latvia
d) Announcements regarding withdrawal of medicines and vaccines from the distribution network

The information included in the Medicinal Product Register and the Register of Medical Devices has been created and maintained as a collection of reliable, neutral, justified and verified information regarding medicinal products and their safety.

In 2015, as part of the Latvian Presidency of the EU Council, the Agency organised seven different level meetings of EU regulatory working groups in the pharmaceutical field, including the 79th HMA

[5] Compliance with the Directive 2011/62/EU of the European Parliament and of the Council amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products

meeting attended by 80 delegates from national medicines agencies of European countries, European Commission and EMA. The agenda of the HMA meeting included important issues within EEA regarding availability of medicines, disruptions in the supply of medicines, news in the field of pharmacovigilance or medicinal product safety surveillance, as well as preparation of the common HMA and EMA operational strategy for 2015-2020.

Summary

In order to ensure the prerequisites for availability and rational use of safe medicines, tissues, cells, organs, blood and their components, the Agency:

a) Actively participatesd in EMA work-sharing procedures for evaluation of medicines, for example, expertise on paediatric data, assessment of periodic safety update reports, voluntary harmonisation procedure for clinical trials
b) Collaborated with experts from the academic filed in Latvia on issues related to advanced expertise on medicines
c) Ensured expert participation in various forums, including:
    - Training intended for national competent authorities on compliance evaluation of active substance manufacturing sites, specialised manufacturing sites, innovative therapies, in the field of manufacturing of radiopharmaceutical medicines, biovigilance and assisted reproductive technologies
    - EU Health Program Common Action VISTART as a collaboration partner
    - Active substance Good Manufacturing Practice inspection of manufacturing company in an EU member state as part of experience exchange in pharmaceutical inspection cooperation scheme.

In the period of review, the Agency participated and was assessed based on the common criteria in the BEMA III benchmarking program, and was compared to other EEA medicines agencies. BEMA assessors verified that the Agency operates in accordance with the common criteria and principles.

Significant contribution has been made to decrease the administrative burden in order to ensure efficacy of Agency operation with the purpose of ensuring electronic receipt of merchant applications and issuance of decisions.

Also substantial improvements have been made to the Agency’s information system for collection of information regarding marketing authorisation and distribution of medicines, as well as information related to the field of medical devices.

1.3. Operational directions and strategic priorities of the Agency for 2017-2019

In order to continue improvements and ensure long-term availability of qualitative services for the public health in Latvia, the following operational directions and priorities of the Agency are planned for the period of 2017-2019:

- **Service direction** – with the purpose of ensuring qualitative performance of the functions delegated to the Agency by promoting availability of effective, safe and qualitative medicines and other products used in healthcare on the market in Latvia
- **Collaboration and information direction** – with the purpose of promoting effective interaction between the Agency and its stakeholders with regard to services and collaboration
- **Sustainable Agency development direction** – with the purpose of continuous development of the Agency as a centre for transfer of knowledge by implementing responsible management of knowledge and improving the learning process within the organisation in order to ensure high quality of the delegated functions and services in the long-term.

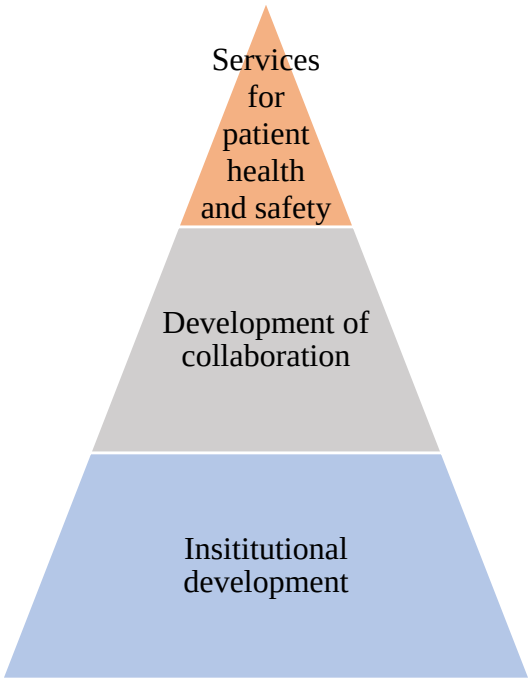

Figure 1.
Visualisation of operational directions of the Agency

Operational priorities of the Agency for the period of 2017-2019 are as follows:

1) Promote availability of appropriately evaluated medicines, including minimisation of short-term and long-term disruptions in availability of medicines as much as possible
2) Ensure further application of risk assessment principles to compliance evaluation in the field of pharmaceuticals, procurement and storage centres of human blood, tissues, cells and organs, as well as clinical trials, and ensure a more comprehensible use of Agency's capacity in the field of compliance evaluation
3) Contribute to the public understanding of use of safe and rational medicines and promote awareness of healthcare professionals regarding the role of monitoring in ensuring quality, safety and effectiveness
4) Improve the use of ICT solutions in support and main processes, as well as ensure safety of the environment for exchange of information as part of receiving services. This priority is to be implemented in compliance with the common developmental priorities of the Ministry of Health in the field of ICT
5) Continuously improve the knowledge and professionality of experts and Agency personnel

2. Description of operational directions

2.1. Service direction

Name of operational direction: Service direction**.**

Description of current situation

The first strategic operational direction is related to the functions within the competency of the Agency and is directly applicable to the services provided to merchants in order for the public to receive safe, effective and qualitative healthcare products and ensure health.[6]

Within the strategy, the outcomes of this operational direction are mainly aimed towards availability of appropriately evaluated medicines in Latvia and pharmaceutical compliance evaluation.

I. Availability problems on the market can be divided into long-term issues or lack of supply of medicines on the market in Latvia following marketing authorisation and short-term issues or disruptions in the supply of medicines. Marketing authorisation holders are not obligated to authorise medicines in Latvia or release medicines on the market following marketing authorisation. Availability of approximately 40% of the authorised medicines is not ensured for patients in Latvia[7]. Furthermore, there are no alternative medicines available on the market in Latvia to more than half of the centrally authorised medicines according to the Anatomical Therapeutic Chemical (ATC) codes. Short-term disruptions in the supply of medicines are increasingly affecting all EU member states[8]. It is also recognised on an EEA level that the causes of disruption in supply of medicines are complex and they cannot be solved in isolation on a national level. Disruptions in supply of medicines cannot be completely avoided, but when they are identified it is important to act immediately in order to identify alternative products, waive labelling requirements, issue permits for parallel import or unauthorised medicines. Preventive actions are possible also in the long-term – promotion of harmonised labelling requirements in the northern regions of Europe or promoting inclusion of necessary medicines in the Medicinal Product Register of Latvia in collaboration with other competent authorities.

   In addition, affordability of medicines is also a significant contributing factor to the availability of medicines. It is a very important issue for patients and the public as a whole, because over the recent years the expenses for retail sales of medicines have substantially increased in Latvia[9], and the rise in cost of medicines plays an important role in this. Even though the Agency cannot set the price for medicines sold in Latvia by marketing authorisation holders, the Agency shall pay particular attention to the potential impact of regulatory changes in the pharmaceutical field on the affordability of medicines to patients in the long-term.

II. The Agency has extensive competency to perform compliance evaluation of pharmaceutical activity with the common EU standards, including:
   - Compliance of medicinal product and active substance manufacturing with standards of Good Manufacturing Practice
   - Compliance of medicinal product wholesalers with standards of Good Distribution Practice
   - Compliance of marketing authorisation holders with standards of Good Pharmacovigilance Practice
   - Compliance of clinical trial sponsors/investigators with standards of Good Clinical Practice

[6] Healthcare products (medicinal products and medical devices), human tissues and cells, blood and blood components

[7] Agency data regarding medicines placed on the market by marketing authorisation holders following marketing authorisation

[8] EU Medicines Agencies Network Strategy to 2020; European Heads of Medicines Agencies website

[9] OECD, Key Findings of the 2017 Analytical Report on Sustainable Access to Innovative Therapies.

- Quality control of medicinal products

In the presence of limited resources, it is important to utilize the resources available efficiently. Efficient use of resources means focusing compliance evaluation activities on the areas where the risk of non-compliance is high. The Agency has carried out risk-based planning of its activities as much as possible, but work needs to be continued in order to ensure that the risk assessment models applied are harmonised, validated and reviewed, if necessary.

III. During the strategic period, preparations are made for the implementation of the requirements of the regulation regarding medical devices amending Directive 2001/83/EC, Regulation (EC) No.179/2002 and Regulation (EC) No.1223/2009 and the Regulation of the European Parliament and of the Council regarding in vitro diagnostic medical devices, within the competency of the Agency and for the preparation of the appropriate normative acts on a national level. These regulations include centralisation of registration of national medical device manufacturers and medical devices, as well as introduce new normative requirements and obligations for national competent authorities such as the Agency.

IV. According to the public health risk assessment approach, the Agency also maintains compliance evaluation and compliance monitoring of merchants conducting activities with tissues, cells, organs, blood and blood components of human origin. During the three-year cycle of the strategic period, changes are planned in the EU legal acts with the purpose of increasing the quality of blood components intended for transfusion and safety of the preparation process by laying down new requirements for the operation of blood establishments (i.e., the State Blood Donor Centre and other blood establishments) and new obligations for the competent authorities (Agency) in compliance evaluation and monitoring of such establishments. In addition, in 2017 new amendments came into force to the regulations laying down the procedure for utilisation of tissues and cells, relating to the introduction of a common EU coding system, as well as a procedure for evaluation of tissue and cell import.

Objective of the operational direction: ensure qualitative implementation of Agency functions by promoting conditions for the availability of safe, qualitative and effective medicinal products on the market in Latvia.

Operational results

Result	Parameter	Numerical value of parameter			
		2016	**2017**	**2018**	**2019**
1. Promoted availability of appropriately evaluated medicinal products to the public in Latvia.	Proportion of therapeutic areas (according to ATC level 5[10]) where at least one authorised medicinal product is available	68%	69%	70%	71%
	Proportion of Agency queries answered within the set time for MRP/DCP procedures, where Latvia is a reference member state (%)	100%	98%	98%	100%
	Proportion of compliance with the 30-day timeline of the national phase in MRP/DCP procedures (%)	70%	80%	90%	90%

Operational results (cont.)

[10] In the ATC classification system, medicinal products are categorised in 5 different levels depending on their effect on organs or organ systems, their therapeutic, pharmacological and chemical properties and active substances.

Result	Parameter	Numerical value of parameter			
		2016	2017	2018	2019
2. Minimised risks to availability of medicines and impact of supply disruptions on ensuring medical treatment process.	Cases of supply disruptions of medicines with no alternative available, where the time for review of application for "authorisation for distribution of medicines not authorised in Latvia" is 1 working day	78%	80%	85%	90%
	Cases of disruptions in the availability of medicines with no analogue products available for these particular medicines, where the time for review of application for "authorisations for distribution of medicines in Latvia with a packaging intended for another country" is 1 working day	75	85	90	95
3. Fully utilised Agency capacity in compliance evaluation.	Number of medicinal product quality parameters tested (from pharmacies, wholesalers and manufacturing sites)	830	650[11]	650[11]	650[11]
	Proportion of compliance evaluations areas[12], where a risk-assessment approach was applied to compliance evaluation	61%	68%	81%	94%

Tasks for implementation of operational direction

1. Provide proposals for improvement of normative acts, as well as develop other options for promoting timely availability of appropriately evaluated medicines in segments where availability of medicines does not meet the needs of public health.
2. Implement actions related to minimisation of public health risks created by disruptions in the supply of medicines, as well as lack of release of authorised and necessary medicines on the market in Latvia by marketing authorisation holders.
3. Contribute to the preparation of normative acts and policy documents on a national and international level, particularly relating to the impact of regulatory framework on the long-term affordability of qualitative, safe and effective healthcare products and effective use of Agency resources.
4. Improve the compliance evaluation process in the pharmaceutical and healthcare field within the competency of the Agency by gathering information and applying a risk-based compliance evaluation as much as possible.

Participate in the implementation of new EU regulations, paying particular attention to resource-related issues.
The planned activities, timelines and structural units responsible for performance of tasks have been included in the strategic work plan of the Agency.

Authorities concerned
Ministry of Health, Health Inspectorate

[11] The number of parameters depends on the number of medicinal product samples, pharmaceutical form and other characteristics of medicines actually withdrawn from the market by the Health Inspectorate. There is no plan to decrease the number of tested samples of medicinal products.
[12] Compliance monitoring of Good Clinical Practice, Good Manufacturing Practice, Good Distribution Practice, Good Pharmacovigilance Practice, as well as procurement, storage and utilisation centres for human tissues, cells and organs.

2.2. Collaboration and information direction.

Name of operational direction: Collaboration and information direction.

Description of current situation

This direction is related to the Agency's task to collaborate with professional organisations of doctors and pharmacists, the industry and non-governmental organisations, foreign and international institutions, as well as to ensure mutual exchange of information in the areas of Agency operation.

I. The average consumption of non-prescription medicinal products in Latvia is higher than in neighbour countries – Lithuania and Estonia.[13]. In addition, the amount of money that patients pay for choosing medicines that are not the reference products included in the list of reimbursable medicinal products is increasing every year[14]. Taking into account the concerns about public health, the Agency will pay particular attention to rational use of medicines, i.e., prescription of medicines appropriate to the medical needs of the individual patient, minimising patient and public costs for medicines and use of medicinal products in compliance with the prescribed treatment course. Thus, one of the Agency's priorities during the strategic period is education of the public, contributing to the understanding of safe and rational use of healthcare products and promoting awareness of healthcare professionals regarding the role of monitoring in ensuring quality, safety and effectiveness of medicinal products.

II. In the strategic period, substantial changes are planned to the normative acts in Latvia related to the safety, compliance evaluation and monitoring of clinical trials, medical devices, as well as preparation of blood components, and it is foreseen that the new regulation will correct the previous flaws in normative acts and will improve the system for public health and safety in the long-term. Stakeholders will be provided with the necessary guidelines and clarifications regarding implementation of the regulation in Latvia to ensure understanding of the implementation of these regulations, thus, giving assurance that Latvia is an appropriate location for development of medicinal products and medical devices.

III. The legal framework for monitoring of medicines is mostly unified across Europe. It includes common procedures for monitoring of the life-cycle of medicines, the results of these procedures are mutually recognised throughout EU. The Agency needs to utilise the advantages provided by membership in European organisations and participation in procedures, allowing experts to maintain a high level of professionality. In order to facilitate implementation of harmonised requirements in Latvia, Agency experts:
   - collaborate with experts from medicines agencies in other countries, industry representatives and stakeholders in relation to agency services;
   - collaborate with medicines agencies in other eu member states in the field of work-sharing for evaluation procedures and providing scientific expertise;
   - actively participate in international organisations: edqm, incb, icmra, pic/s and others;
   - perform audits and inspections of companies and organisations in the field of pharmaceutics in EU member states and third countries;
   - expand and develop scientific cooperation possibilities with the academic sector in latvia in order to promote synergy between the experience of the regulator and the knowledge of the scientific sector;
   - inform and consult representatives of the scientific sector (inventors of innovative products) regarding requirements for manufacturing of medical devices and preparation of documentation to ensure compliance with the requirements of normative acts in EU.

[13] State Agency of Medicines, Baltic Statistics on Medicines 2013-2015

[14] Source, National Health Service.

Objective of the operational direction: promote effective interaction between the Agency and stakeholders with regard to services and collaboration**.**					
Operation results					
Result	**Parameter**	**Numerical values of parameters**			
		2016	**2017**	**2018**	**2019**
1. Contribution to public understanding of safe and rational use of healthcare products and promoting healthcare professional awareness of the role of monitoring in ensuring the quality, safety and effectiveness of medicines and medical devices.	Total number of adverse drug reaction reports	341	358	375	394
	Number of adverse drug reaction reports received from healthcare professionals / patients	56 / 12	60 / 20	63 /25	65 / 30
	Number of primary reports regarding accidents with medical devices in Latvia	61	64	67	70
	Institutions that submitted annual biovigilance reports until 1st of May of the following year (%)	30%	40%	60%	80%
	Number of informational activities for healthcare professionals[15]	11	12	13	13
	Number of public information activities[16]	120	126	132	138
	Number of implemented informational activities for representatives of the industry, in addition to consultation	2	4	5	6
2. Improved Agency collaboration with the industry, particularly on issues regarding application of EU and national regulations.	Published informative materials[17]	11	12	13	14
	Participation in procedures coordinated by EMA scientific committees (number)	30	32	33	35
3. Improved use of Agency potential in national and international collaboration, ensuring coordinated and unified regulatory action.	Participation in procedures and actions of international organisations[18] (number)	55	32	33	35

[15] Seminars, participation in conferences, information in the media
[16] News www.zva.gov.lv, press releases, etc.
[17] Publication "Cito!", summary publication of the State Agency of Medicines, statistics on consumption, public report, infographics, etc.
[18] EDQM, PIC/S, Vistart, JAP

Tasks for implementation of operational direction

1. Implement educational activities (seminars, conferences, consultations, printed information and information on Agency's website, etc.) and collaboration with the industry[19] according to the particular target audience, paying special attention to issues promoting safe and rational use of healthcare products, changes in legal acts, new or improved methods and tools in monitoring safety of medicines.
2. Expand the Agency's proactive participation in formal EMA work-sharing procedures, as well as informal work-sharing initiatives, proactively contribute in international forums.
3. Develop international collaboration with scientific workers in the field of development of medical devices, paying particular attention to mutual exchange of information and knowledge.

The planned activities, timelines and structural units responsible for performance of tasks have been included in the strategic work plan of the Agency.

2.3. Sustainable Agency development direction.

Name of operational direction: Sustainable Agency development direction.

Description of current situation

The third operational direction of the Agency is a collection of measures required for effective and qualitative implementation of the Agency's authority, functions and application of the abovementioned strategy as a whole. The results and tasks included in this direction continue the development of internal processes initiated during the previous strategic period with the aim of ensuring effective management of resources.

I. The employee turnover of the Agency has been maintained at a level that does not compromise continuity of work (10-15% turnover in the previous seven years). The overall satisfaction of employees has also been unwaveringly high (86-88%).

   As the Agency provides services to merchants in industries characterised by rapid technological developments[20], only appropriately educated and competent experts, who continuously expand their knowledge and follow the latest scientific developments, are able to provide high quality services to merchants in the fields of pharmaceutics and healthcare. For highly qualified professionals to choose to work at the Agency, it is very important to ensure that the Agency is an attractive workplace for current and potential experts.

   In order to keep up with the scientific and professional growth of representatives of the industry, during the strategic period the Agency will take active measures to motivate the personnel, support initiatives and promote professional growth in the regulatory field, as well as to ensure:

   - succession in the processes of agency's main operation
   - timely identification of the competencies required for experts
   - allocation of adequate resources for training
   - education according to the trends of developments in the quality, safety and effectiveness of healthcare products, tissues, cells, organs, blood and blood components
   - possibilities to expand and gain professional competencies and knowledge in the appropriate Latvian and foreign institutions.

[19] State institutions, professional organisations, non-governmental organisations.

[20] Manufacturing of medicinal products and medical devices, utilisation of human blood, tissues, cells and organs

II. *Strategy for sustainable development of Latvia until 2030* emphasises productivity of work as an important priority on a national level and has defined E-management as one of the three priority action directions in the long-term with the aim of ensuring availability of services by utilising more effective management opportunities provided by new information technologies.

III. Qualitative organisation of work is one of the most important elements in ensuring the operational results of the Agency. In order to promote this, the Agency purposefully increases the efficacy of the process for circulation of documents and takes action to decrease the administrative burden by:
- initiating issuance of decisions in electronic format;
- developing receipt of documents and information online;
- ensuring automatic inclusion of client data in IS;
- strengthening the capacity of the main operational functions[21];
- making adjustments in the internal processes and technical solutions to prepare for the implementation of e-addresses in Latvia.

At the same time, above mentioned activities are also important to Agency clients who assess the quality of the services provided by the Agency in the annual client survey.

In the strategic period, the Agency is planning to actively participate in the EU telematics program that ensures a more efficient and transparent operation of the network of national European medicines agencies by unifying and centralising systems and databases with the purpose of collecting information from the industries and regulators of the member states in order to support evaluation of risks and benefits of medicines and provide high quality information to the public. In the strategic period, the Agency plans on continuing work on implementation of the relevant solutions and IS, data integration, ensuring availability within the set terms in the areas of clinical trials, good manufacturing practice, vigilance, marketing authorisation documentations, etc.

Objective of the operational direction: continue the development of the Agency ensuring effective management of resources and improving processes.

Operational results

Results	**Parameters**	**Numerical values of parameters**			
		2016.	**2017.**	**2018.**	**2019.**
1. Agency is an attractive place of work for educated, competent and highly qualified specialists, based on sustainable development of human resources.	Employee participation in training, courses (number of employees) / Participation in conferences and seminars organised by international organisations (number of employees).	374 / 65	450 / 60	400 / 60	400 / 60
	Employee satisfaction with the work environment and work at the Agency in the annual survey (%)	86,5%	≥ 88%	≥ 89%	≥ 90%
	Average turnover of personnel (%)	10%	≤ 10%	≤ 9%	≤ 9%
	Proportion of job positions classified for ensuring main operational functions (%)	55%	58%	60%	62%

[21] In accordance with the requirements of the Electronic Documents Law and the CM Regulation No. 473 of 28.07.2005. "Procedures for the Preparation, Drawing Up, Storage and Circulation of Electronic Documents in State and Local Government Institutions, and the Procedures by which Electronic Documents are Circulated between State and Local Government Institutions, or Between These Institutions and Natural Persons and Legal Persons"

Operational results (cont.)					
Results	**Parameters**	**Numerical values of parameters**			
		2016.	**2017.**	**2018.**	**2019.**
2. Maintained and improved quality management system	Proportion of corrective actions identified in the internal audit that have been implemented within the set terms (%)	35%	60%	70%	75%
	Number of changes in processes that have resulted in facilitation of effective management of resources (number)	42	50	55	60
	Proportion of clients that have given a positive assessment of the quality of services provided by the Agency (%)	98%	90%	90%	90%
3. Effective use of ICT with the purpose of increasing efficacy, decreasing the administrative burden and ensuring a safe ICT environment	Proportion of documents received electronically (%).	n/a	55%	60%	65%
	Proportion of documents sent electronically (%)	n/a	65%	75%	85%
	Number of structured documents received in online platforms	47	50	80	100
	Number of implemented ICT changes directly increasing efficacy of work	120	100	100	100
	Number of critical vulnerabilities identified in external security audits	<3	<3	< 2	≤1

Tasks for implementation of operational direction

1. Continue improving the competency of employees, paying particular attention to scenarios for future development of healthcare products. As part of this task, it is necessary to fully utilise the EU training centre established by EMA, the Health program in Common actions and opportunities offered by the PIC/S.
2. Apply and improve opportunities for non-material motivation of employees as much as possible.
3. Implement measures ensuring thorough use of the competence of external experts in areas where the Agency does not have the required specific knowledge.
4. Plan and implement ICT projects and changes with the aim of improving process efficacy, including promotion of the development of e-services.
5. Implement activities within the EU Telematics project according to the terms set by EMA.
6. Maintain and improve the integrated management system in accordance with the specific standards.
7. Voluntarily implement the elements of standard guidelines for environmental management, effective utilisation of resources (including financial resources).

The planned activities, timelines and structural units responsible for performance of tasks have been included in the strategic work plan of the Agency.

3. Description of resources

Human resources and work organization

The administrative capacity of the Agency is composed of the financial, human, material, technical and other resources at its disposal that are effectively managed in order to ensure the performance of functions delegated to the Agency. Personnel is one of the main resources and the Agency consciously creates a state administration environment where civil servants and employees (hereinafter – employees) are motivated to work and ensure qualitative and effective achievement of the Agency's objectives.

The operation of the Agency is led by the Director of the Agency. The Director is appointed and relieved of duties by the Minister for Health in accordance with the procedure laid down by the State Civil Service Law. The Director approves the list of Agency positions which included 149 positions in 2017, see the structure in Annex 1.

55% of the positions are classified for performance of main operational functions in order to ensure the performance of tasks delegated by normative acts, 45% of positions are classified for performance of administrative and support functions (management, legal support, administration of human resources, accounting, support personnel for employees ensuring main operation, ICT, etc.). In the strategic period, the number of employees involved in provision of support functions may be reviewed, if the transition to circulation of documents and use of documents in electronic format, as well as merging the electronic document management systems with (accounting and human) resource management systems will be ensured within the institutions under the Ministry of Health.

Educated, competent and highly qualified specialists are required for the successful performance of functions delegated to the Agency. The level of education of Agency employees is high – in 2016, 89% of employees had obtained higher education, four employees had received a doctorate. The process of personnel selection is organised in a manner to allow employment or acceptance in civil service of the most appropriate candidate via the selection procedure as a result of fair competition without discrimination of gender, nationality, religion or other beliefs differing one person from another. The main task of the selection procedure – identify the most appropriate candidate, based on their education, competencies, skills and professional experience. The turnover of Agency personnel is low (10-15%). One of the most significant problems is professional experts ending their employment at the Agency and beginning to work for pharmaceutical companies in Latvia. Taking into account the aforementioned, one of the aims of the strategic period is to promote a succession and mentorship program to ensure the development and continuity of competencies and knowledge critically important to the institution, as well as to promote the interest of employees to continue their career path within the sector of Ministry of Health.

One of the ground principles of personnel management at the Agency is motivating employees to raise their professional qualifications. In order to implement it, further education and raising of qualification is ensured with the resources available according to the educational requirements identified in the annual personnel evaluation process. A significant role in professional development is played by participation in the work of national medicines agencies of the European countries, EU institutions, committees and working groups, as well as participation in international seminars and experience exchange.

Once a year the opinion of employees regarding work conditions and environment is collected via the employee survey. To increase the motivation of personnel, as well as raise the level of satisfaction, a flexible work schedule was introduced in 2016, and to continue the development of progressive personnel management methods, there are plans to develop opportunities for working remotely.

Public relations

In accordance with the statutes of the Agency, the Public Relations Department ensures planning and implementation of external and internal communication of the institution. External communication activities include provision of information to the public and establishing dialogue with collaboration partners (stakeholders) using traditional communication tools and channels (establishing media relations, including the social media environment, content management of the website www.zva.gov.lv, preparation of informative publications).

The Public Relations Department of the Agency prepares and ensures publication of the Medicinal Product Register of Latvia, annual public report, "Cito!" publication for doctors, pharmacists and healthcare specialists, collections of statistical data, as well as creates infographics and other data visualisations.

Internal communication activities include measures related to promoting motivation and sense of belonging to the organisation of Agency employees, and studies of employee satisfaction. The Public Relations Department is also responsible for the Agency's library that gives access to professional literature, periodicals and databases. To promote professional growth of employees, the library contains more than 5000 units of professional literature in Latvian, Russian, English and German, the most historic item of bibliography being the "Pharmacopea Helvetica" published in 1907 in German.

The Department consists of the Head of Department, two public relations specialists and one librarian. Maintenance and administration of the website www.zva.gov.lv requires the involvement of the personnel (website administrator) from the Information Technologies and System Development Department.

Provision of infrastructure

Management of the real estate of the Agency is ensured by the Public Procurement and Infrastructure Provision Department, and it oversees 6500 m^2 of land where the Agency's administrative and archive building (with the total area of the premises being 3144 m^2), as well as auxiliary buildings are located. 24-hour physical and electronic security, as well as fire safety alarms are ensured for all the premises and territory. In addition, archive premises, with an area of 1060 m^2, are rented for storage of additional Agency documentation and management of these premises is ensured.

In case of disruptions in the electrical supply of the city, the continuity of Agency operation is ensured by an alternative, autonomous supply of electrical energy by a diesel generator. The Agency cares for effective use of resources and ensures responsible management of the individual boiler-house (ensures heating and hot water supply to the buildings) at its disposal, and ensures disposal and recycling of waste, including hazardous waste.

Compliance with the requirements of work safety, fire safety and civil protection is ensured, including annual personnel training in these areas.

Information communication technologies

In order to ensure performance of the Agency's functions and tasks, folowing information systems are used:

for main operational processes	IS for support processes
Agency's Information System – ZVAIS	Accounting – Horizon
Register of Medical Devices – LATMED	Record-keeping – ELDIS
	Personnel administration – PVS

The ICT infrastructure is managed centrally, is regularly updated, ensures information system security in accordance with the ISO 27001:2013 standard, as well as ensures employee work environment that is appropriate for performance of their direct responsibilities.

Financial resources

Code	Parameter/code name	2016[22] (EUR)	2017 (EUR)	2018 (EUR)	2019. (EUR)
21300; 21400; 21100; 21200; 18000; 19000; 21700	**RESOURCES FOR COVERING EXPENSES (INCOME) – TOTAL**	**4 892 390**	**4 856 107**	**4 856 107**	**4 856 107**
21400	**Other income of budget institutions for paid services provided by budget institutions not classified in group 21.3.0.0 and other own income**	**4 892 390**	**4 856 107**	**4 856 107**	**4 856 107**
18000	**State budget transfers**				
1000–9000	**EXPENSES – TOTAL**	**6 170 476**	**5 459 986**	**5 472 421**	**4 867 975**
1000–4000; 6000–7000	**Maintenance expenses**	**5 762 004**	**5 071 566**	**5 114 298**	**4 548 284**
1000–2000	**Regular expenses**	**4 119 177**	**5 071 566**	**5 114 298**	**4 548 284**
1000	Payment	2 754 566	3 140 951	3 351 866	2 965 645
1100	Remuneration	2 135 037	2 435 559[23]	2 583 545[23]	2 280 043[23]
2000	Goods and services	1 364 611	1 930 615	1 762 432	1 582 639
5000; 9000	**Capital expenses**	**408 472**	**388 420**	**358 123**	**319 691**
5000	**Establishment of main capital**	**408 472**	**388 420**	**358 123**	**319 691**
7000	**Maintenance expense transfers**	**1 642 827**	**0**	**0**	**0**
7800	Maintenance expense transfers to public persons partially financed from the state budget and institutions not financed from the state budget	1 642 827	0	0	0
7810	Maintenance expense transfers to the state budget from public persons partially financed from the state budget and institutions not financed from the state budget	1 642 827	0	0	0
[18000–21700]–[1000–9000]	**Financial balance**	**-1 278 086**	**-603 879**	**-616 314**	**-11 868**
F21 01 00 00	**Financial resources**	1 278 086	603 879	616 314	11 868
F21 01 00 00 1	Increase (-) or decrease (+) in the remaining financial resources from paid services or other own income	1 278 086	603 879	616 314	11 868

[22] Actual expenses for 2016

[23] In accordance with the Order of the Cabinet of Ministers, starting from 2018 remuneration shall not be reflected in the approved Agency budget

3.1. SWOT analysis

Strengths	Weaknesses
Clearly defined objectives and tasks for main operation	Ensuring continuity of Agency operation during a crisis
Unique competence of human resources	Processes that are human resource-consuming, uniform and monotonous (at some departments)
Collaboration network of national medicines agencies of European countries	Unpredictable work-load for experts
Appropriate and developed infrastructure for the work environment	Slow digitalisation of document circulation
Continuity of main operational activities is ensured	Demographics and turnover of personnel
Functional flexibility and operative solutions for problem situations	Succession of professional knowledge
Management of corruption prevention	Limited knowledge in separate specific areas of the industry
Personnel evaluation system	Limited opportunities for personnel growth
Social guarantees are ensured	Remuneration is not competitive with the private sector of the industry
Institution not financed from the state budget	Management of discrepant results
Integrated management system – implemented, maintained, certified in accordance with the requirements of ISO standards, thus, there is an organised process system that is continuously improved and streamlined *(Management system. Testing laboratory. Information security management system.).*	Succession of knowledge of the personnel in separate business processes

Opportunities	Threats
Introduction of new services: - Within existing resources; - Within the e-health project.	Deficiencies in the normative regulation, frequent changes in separate sections and expansion of requirements
Improved collaboration with: - National competent authorities of the member states of the European Economic Area - EU institutions - Competent state administration institutions in Latvia - NGOs and patient organisation in Latvia	Unsystematic and repetitive data queries from state administration institutions
Improved communication with merchants: - Process transparency - Streamlining of the information included in ZVAIS	Deficiencies in the information submitted by merchants, lack of knowledge regarding the relevant normative regulations
Concordance of operational objectives with the strategic tasks in the industry (MH, HMA, EMA)	Limited human resources: - Unavailability of appropriate education in Latvia - Limited knowledge of separate specific areas related to the industry
Proposals for amendments to normative acts related to improvement of the main operational tasks of the Agency	Timelines for complex processes of main operation laid down by normative acts
Implementation of educational activities to promote public awareness within the EU structural funds	Impact of normative regulation and merchant activity on the income part of the budget
Regular client consulting	Dynamics of change in political priorities and their impact
Measures for minimisation of administrative burden	High level of remuneration in the private sector of the industry
Streamlined and environmentally-friendly management of resources	Risk to reputation. Potential for corruption and conflict of interests
Expanded network of external experts	Unpredictable work-load
Development of tools for ensuring succession of personnel knowledge and experience	
Development of a system for non-material stimulation of personnel	
Improved efficiency of the Integrated Management System: - Implementation and maintenance of the requirements of the ISO 9001:2015 standard (Management system) - Implementation of requirements of the relevant ISO standards in several business processes (risk management, ensuring continuity of operation, environmental management)	

Annexes

Annex 1. Schematic structure of the State Agency of Medicines