ANNUAL REPORT **2017**

STATE INSTITUTE FOR DRUG CONTROL

SÚKL

International cooperation / Expert opinions / Surveillance / Legal regulations / Projects / Economy / Education / Security Management

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Surveillance of the risks associated with the use of medicinal product / **Legal regulations**

Regulatory standards harmonisation / **Clinical trials**

Standardisation activities / **Issue of antimicrobial resistence**

Cooperation with EU / Solution of the occurence of the occurence of counterfeit medicinal products

Rules for the safety features appearing on the packaging of medicinal products for human use

Controls of the compliance with the Act on prices / **Marketing authorisation of medicinal products**

378 nationally submitted applications for authorisation / notification of a clinical trial

CONTENT

1 INTRODUCTION

In 2017, the State Institute for Drug Control (hereinafter referred to as the "Institute") continued its intensive cooperation with the Ministry of Health of the Czech Republic (hereinafter referred to as "MoH"). This cooperation concerned, in particular, the implementation of tasks within the scope of cooperation with the EU, namely in the sphere of pharmaceuticals and medical devices, and also in the preparation and subsequent legislative process of adoption of new legal regulations, highly relevant for the scope of the Institute´s operation. The legislative process of adoption of amended Act No 378/2007 Coll., on Pharmaceuticals, as amended, and its implementing regulations, was completed. The amendment was published in the collection of Acts under no. 66/2017 Coll. The Institute, moreover, cooperated with the MoH in the preparation of Decree No 415/2017 Coll., implementing some provisions of the Act on Pharmaceuticals regarding electronic prescriptions. In addition to activities associated with these major tasks, the Institute also paid due attention to cooperation in the drafting of other legal regulations governing other areas of relevance for its operation. The Institute continued to explain the statutory requirements for individual areas of its expert activities via published guidelines. In these guidelines, the Institute also informed the public about guidance published by the European Commission and the European Medicines Agency (hereinafter referred to as "EMA").

International cooperation continues to be one of the major priorities for the Institute. Cooperation was carried out within the scope of more than 70 workgroups and committees in the bodies of the EU Council, European Commission, and EMA, the World Health Organisation (hereinafter referred to as "WHO"), Council of Europe and its European Directorate for the Quality of Medicines and Health Care (hereinafter referred to as "EDQM") or the Organisation for Economic Cooperation and Development (hereinafter referred to as "OECD"). Constant priorities of the Institute include also representation in EMA scientific committees which address issues associated with medicinal product safety on the EU market or the approval of new pharmaceuticals.

In total, 590 applications were submitted for expert assessment in the sphere of regulatory issues. The total of 252 applications concerned marketing authorisation renewal and, furthermore, 261 applications for marketing authorisation revocation were settled.

In 2017, the Institute received 378 applications for clinical trial authorisation/notification, which was approximately the same number as in the previous year. Most of the applications concerned phase III studies; international multicentric randomised, placebo- or active- controlled clinical trials conducted by foreign sponsors. An increase was seen in the sphere of DSUR (Development Safety Update Report) assessment and SUSAR control; 410 DSURs were submitted.

The Laboratory Control Section completed 855 sample analyses. The number of samples rated as non-compliant decreased. These concerned primarily pharmacy samples and samples queried by doctors and patients. In the previous years. A major increase in the number of instigations regarding the occurrence of counterfeit medicinal products in the legal distribution chain or product theft was experienced. In 2017, the Quality Defects Department addressed 45 such cases in total, of which 14 were cases of theft of medicinal products from the legal distribution chain.

In the course of 2017, the Price and Reimbursement Regulations Branch commenced 133 in-depth revisions (1 685 SÚKL codes), within which it was assessed whether the established maximum prices do not exceed the limitations set forth by the Act on Public Health Insurance. In cases where it was identified that the established maximum price exceeded these limitations, the maximum price of the medicinal product was reduced.

Savings in public health insurance funds were generated particularly through abbreviated revisions initiated usually upon request of health insurance companies. The total savings generated by the abbreviated revisions in 2017 is estimated at 1 111 111 005 CZK.

Furthermore, the Institute, as a supervisory authority, conducts inspections of manufacturers, importers, distributors, medical device dispensaries, servicing organisations, and vendors, as well as assessments of proper placement of medical devices onto the market.

In 2017, the Department of the State Agency for Medical Cannabis (OSALK) was involved in the safeguarding of processes and activities aimed at ensuring availability of the medical cannabis active substance from a Czech grower for Czech patients. In compliance with the Institute's power set forth by law, the Department arranged for the opening of a tender for another supply of medical cannabis grown in the Czech Republic for 2017–2021. On the basis of a successfully implemented public contract for the supply of medical cannabis, a framework contract with the supplier was concluded and the supplier was granted a licence for growing in compliance with the Act on Dependency-Producing Substances.

With a view to the requirements for mandatory electronic prescription and the establishment of a Central E-Prescription Repository, legislatively based in the Act on Pharmaceuticals, the process of modernisation of the entire system started as early as in 2015, and in 2016, a public contract on the development, delivery, and implementation of the ePrescription information system (hereinafter referred to as "IS ePrescription") and provision of service support for the system was announced and concluded. In 2017, the contract for work was being performed. Since August 2017, the performance of a service contract on the provision of service support for this system for the period of 4 years commenced. The implementation of the IS ePrescription project followed the valid schedule and the project was completed in December 2017. In the course of project implementation, 11 workshops and webinars for the suppliers of medical, hospital and pharmacy software were organised. A new website, www.epreskripce.cz, was put in production operation. In the course of 2017, moreover, at least 130 events took place where the ePrescription was presented; these included seminars for doctors or pharmacists, conferences and congresses, or articles and presentations in the media.

As part of its obligation to inform professionals and the general public, the Institute administered websites www.sukl.cz, www.olecich.cz, www.nebezpecneleky.cz. It also administered the website of the ARTHIQS project www.arthiqs.eu and the OSALK website www.sakl.cz.

2 THE INSTITUTE´S ORGANISATIONAL STRUCTURE

In 2016, the Institute´s systemisation was approved, within the scope of which organisational changes aimed at optimising the headcount and increasing the effectiveness of work, particularly in the Medical Device Branch, were implemented as of 1 January 2017. In this branch, the existing departments were restructured and the Medical Device Registration and Notification Section and Department for the Drawing of Expert Opinions and OTC Sale Certificates were established. Furthermore, the Department of Legal and Legislative Activities was brought back under the Director´s Office.

In association with further approved systemisation, the Data Support Department under the Information Technology section was dissolved and a new Data Analysis Department under the Surveillance Branch was established as of 1 June 2017.

The organisational structure effective as of 31 December 2017 is provided below.

DIRECTOR

SURVEILLANCE BRANCH
- Advertising Regulation Dept.
- Quality Defects Dept.
- Legal Support and Enforcement Dept.
- Data Analysis Dept.
- **Inspection Section**
  - GMP Dept.
  - Clinical Practice Dept.
  - Surveillance over Biological Material Dept.
- **Pharmacy and Distribution Section**
  - OKL 31210-31280
  - GDP Dept.
- **Laboratory Control Section**
  - Analytical Chemistry Dept.
  - Biological Methods Dept.
  - Pharmacopoeia and Pharmaceuticals Standardisation Dept.

MEDICAL DEVICE BRANCH
- MD Registry Coordinator
- MD Clinical Trials Dept.
- Control Dept.
- Medical Device Branch Legal Support Dept.
- Vigilance Dept.
- **Marketing Authorisations and Notifications Section**
  - MD Notifications Dept.
  - Issuance of Expert Opinions and Free Sale Certificates Dept.
  - Notification of Persons Dept.

SERVICE ACTIVITIES BRANCH
- Public Tender Dept.
- **Operations Section**
  - Purchasing, Transport and Building Operation Dept.
  - Documentary Service Dept.
- **Economic Section**
  - Accounting Dept.
  - Budget and Assets Dept.
- **Information Technology Section**
  - IT Security Manager
  - IT Operation Dept.
  - IT Application Support Dept.
  - ePrescription Dept.
  - Business Analysis Dept.

Deputy Director

Director´s Office
- EU Affairs Manager
- Legal and Legislative Service Dept.
- International Relations Dept.
- Press and Information Dept.

Internal Audit and Control

Information Quality and Security Management

State Agency for Medical Cannabis

Human Resources and Education Dept.

CAU and REG Coordinator

PRICE AND REIMBURSEMENT REGULATION BRANCH
- Medicinal Product Evaluation Dept.
- Dept. Dealing with Selected Types of Administrative Procedures
- Administrative Procedure Coordination Dept.
- **Analytical and Management Support Section**
  - Validation and Administrative Support Dept.
  - Complex Data and Analysis Preparation Dept.

MARKETING AUTHORISATION BRANCH
- Preclinical and Clinical Documentation Dept.
- Pharmacovigilance Dept.
- Marketing Authorisation Legal Support Dept.
- **Pharmaceutical Documentation Assessment Section**
  - Chemical and Herbal Product PDA Dept.
  - Biological Product & Clinical Trial PDA Dept.
  - Variation and Parallel Import PDA Dept.
  - Clinical Trial PDA Dept.
- **Clinical Trials on Pharmaceuticals and Non-Authorised Medicinal Products Section**
  - Ethics Committee Coordination Dept.
  - Dept. of Clinical Trials on Pharmaceuticals Coordination and Administrative Dept.
- **Administrative and Procedural Support Section**
  - European Assessment Implementation Dept.
  - MA Branch Validation Dept.
  - National Applications Dept.
  - MRP Applications Dept.
- **Coordination and Regulation Section**
  - MA Procedure Coordination Dept.
  - National Regulation Dept.

3 INVOLVEMENT IN THE NETWORK OF NATIONAL, EU, AND OTHER INTERNATIONAL INSTITUTIONS

3.1 Cooperation with the Ministry of Health and Other State Institutions in the Czech Republic

In 2017, the Institute intensively cooperated with the MoH, particularly in the implementation of tasks within the scope of cooperation with the EU in the sphere of pharmaceuticals and medical devices, as well as in the preparation and subsequent legislative process of adoption of new legal regulations with significant impact upon the scope of the Institute´s operation.

In 2017, the legislative process of adopting amendment to Act No 378/2007 Coll., on Pharmaceuticals, as amended, and its implementing regulations was under way. This amendment was adopted as part of the adaptation of Regulation No 536/2014, on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC. The amendment included also provisions allowing to adopt measures preventing the export of medicinal products intended for patients in the Czech Republic in case such export would result in unavailability of such medicinal product for Czech patients. These changes required both amendment to the Act on Pharmaceuticals and amendment to its implementing regulations. The legislative process concerning the draft amendment to the Act on Pharmaceuticals was completed and the amendment was published in the Collection of Acts under no. 66/2017 Coll.

In the course of 2017, also works on the adaptation of Commission Regulation (EU) No 2016/161 supplementing Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use, continued. Although this is a rather complex amendment by regulation, the adaptation will require an amendment to the Act on Pharmaceuticals.

At present, this draft amendment to the Act on Pharmaceuticals is within the legislative process at the MoH and further steps are to follow. In the course of 2017, the Institute also closely cooperated with the MoH in the legislative process regarding the transposition of Commission Directive (EU) 2015/566 of 8 April 2015 implementing Directive 2004/23/EC as regards the procedures for verifying the equivalent standards of quality and safety of imported tissues and cells. The transposition was completed by an amendment to Act No 296/2008 Coll., on the Safeguarding of Quality and Safety of Human Tissues and Cells Intended for Use in Man and on Amendment to Related Acts, as amended, published in the Collection of Acts under no. 136/2017 Coll., and amendment of implementing regulation implemented by Decree No 167/2017 Coll.

Furthermore, in 2017, the Institute cooperated with the MoH in the preparation of transposition of Directive 2016/1214, amending Directive 2005/62/EC as regards quality system standards and specifications for blood establishments. The transposition of this Directive will require another amendment to the Act on Pharmaceuticals and amendment to Decree No. 143/2008 Coll. At the end of 2017, the draft amendment was presented to the Chamber of Deputies of the Parliament for discussion.

The Institute cooperated with the MoH also in the preparation of Decree No 415/2017 Coll., implementing some provisions of the Act on Pharmaceuticals regarding electronic prescriptions.

In the sphere of medical devices, in 2017, the Institute and the MoH commenced cooperation in the legislative process of adapting Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC, and Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU. The adoption of two new regulations governing the sphere of medical devices will require changes to the relevant legal regulations, particularly to Act No 268/2014 Coll., on Medical Devices and Amendment to Act No. 634/2004 Coll., on Administrative Fees, as amended, and to Act No 22/1997 Coll., on Technical Requirements for Products and Amendment to Some Acts, as amended.

In addition to the activities associated with these major tasks, the Institute also cooperated in the preparation of legal regulations governing areas also relevant for its operation.

The statutory requirements governing individual areas of expert activities were further explained by the Institute in the guidance published thereby. The Institute was informing the public about the guidance published by the European Commission and by EMA.

As in the previous years, cooperation with the MoH in drafting of opinions of the Czech Republic on first questions raised by the European Court of Justice regarding the sphere of powers of the Institute continued also last year.

The Institute continued its cooperation with the Institute for State Control of Veterinary Biologicals and Medicines in Brno. In the sphere of market surveillance, the Institute´s partners were particularly the Czech Agriculture and Food Inspection Authority and the Customs Administration of the Czech Republic and communication with the Czech Trade Inspection also took place.

Cooperation with the Czech Office for Standards, Metrology, and Testing was carried out in the area of standardisation within the Medical Device Technical Standardisation Commission TNK 81 and inspectors from the Medical Device Branch participated in two inspections with the Czech notified persons to which they were invited due to their

specialisation in market surveillance, medical device vigilance, and clinical investigations of medical devices.

The Institute continues its cooperation in addressing the issue of antimicrobial resistance (hereinafter referred to as "AMR") by connecting its Advisory Body for Anti-infectives with the Central Coordination Group for the National Antibiotic Programme of the Czech Government and the Advisory Board for Antimicrobials of the Ministry of Agriculture of the Czech Republic. Compared to previous year, the Institute intensified its involvement in the preparation of a new action plan of the National Antibiotic Programme, where it became one of the co-guarantors for the plan´s two priorities and continued to update the List of Essential Anti-infectives (SEAI) as an integral part of the Action Plan. For the purposes of the Central Coordination Group for the National Antibiotic Programme and the Sub-commission for Antibiotic Policy of the Czech Medical Association of J. E. Purkyně, it also set up a system of regular hand-over of information on the consumption of antibiotics (on deliveries to pharmacies and other healthcare facilities) together with an overview thereof for individual quarters. Since 2008, the Institute has been involved also in the preparation of their basic assessment through the ECDC methodology.

In order to safeguard SEAI items, the Institute was actively involved in the activities of a newly established platform managed by the MoH. In this area, the Institute strives to enhance the Sub-commission for Antibiotic Policy of the Czech Medical Association of J. E. Purkyně with its experts in the anticipated reconstruction of the group.

3.2 Cooperation with EU Institutions and Other Foreign Partners

The Institute is actively involved in international cooperation within more than 70 working groups and committees. These represent, in particular, bodies of the EU Council, European Commission, and EMA, as well as the working bodies of WHO, the Council of Europe and its EDQM, or OECD. Constant priorities of the Institute include namely representation in EMA scientific committees which address e.g. issues associated with medicinal product safety on the EU market or the approval of new pharmaceuticals. Last but not least, the Institute is also actively involved in informal groups that bring together experts from various countries specialised in the area of regulation of pharmaceuticals and medical devices, pricing and medical technology assessment, or the regulation of human tissues and cells. The main of these informal groups is the network of the Heads of Medicines Agencies (hereinafter referred to as "HMA") based on voluntary membership, in whose activities the Institute also regularly participates not only via the membership of the Institute's director, but also through direct involvement in the team for executive support of the steering group of the entire network and the development of regulatory strategy, including implementation thereof. It is a member of HMA working groups and management structures and it is involved in the coordination of priorities of a joint HMA/EMA strategy working plan for several years. In total, 404 business trips abroad took place in 2017, of which 164 were paid for by the Institute and 240 were fully or partially reimbursed by the organising institutions (European Commission, EU Council, EMA, etc.).

The Institute´s international activities on the EU level include also involvement in the process of adoption of new European legislation and discussion of non-legislative proposals in the EU Council falling under the Institute´s responsibility. In 2017, the Institute actively participated in the debate on amendment to Regulation (EC) No 726/2004, laying down Community procedures for the authorisation and supervision of medicinal products, and conclusions of the Council on raising voluntary cooperation among health care systems on the initiate of Member States.

The Institute´s global level of international cooperation was enhanced by intensifying working relationships with partners from the People´s Republic of China, which resulted in practical fulfilment of the signed memorandums of cooperation with the regulatory authority in Tianjin and a memorandum with the nation-wide China Food and Drug Administration. Concurrently, the Institute continued to develop contacts with the representatives of regulatory authorities of Shanghai, aimed at signing a similar memorandum in the next period.

Relevant strategic information is transferred from international negotiations also onto the national level through membership in advisory boards of the Czech Government or the MoH. One of the key issues addressed on the global international level is also the area of antimicrobial resistance. The issue of AMR also became one of the 11 key priorities of the HMA action plan for several years, approved in 2016, where the Institute plans to become more actively involved through its membership in the respective working group should it be extended by the area of products for human use. The implementation of plans to address AMR will be verified in 2017-18 by the European Commission in all EU Member States. This was also one of the reasons why the Institute was actively represented at the AMR "One Health" healthcare summit in Sweden. The Institute presented the issue of its contribution to cooperation in addressing AMR at the Budapest 16 + 1 healthcare summit and at the regulatory summit for third countries organised by CFDA and MOFCOM in China. The Institute is going to continue to support the solution for public health protection from this global threat through its participation in the activities of internal as well as external advisory bodies also in the coming years.

3.3 Projects

In the sphere of international projects, in 2017, the Institute was involved in two Joint Actions within the scope of the second programme of Community action in the field of health (2008-2013) co-funded by the European Commission and the EU Member States.

One of them focused upon the area of pharmacovigilance (Strengthening Collaborations for Operating Pharmacovigilance in Europe, SCOPE) was successfully concluded in 2017. In the SCOPE project, the Institute acted as an associated partner and in Work Package 4 it cooperated in the development of procedures for adverse drug reaction reporting. In the course of the project, a number of guidelines, working instructions, educational modules, and other materials were created to enhance the pharmacovigilance systems of the Member States. Detailed information on the project outputs has been published at www.scopejointaction.eu.

The other Joint Action concerned the area of assisted reproduction and haematopoietic cell transplantations (Assisted Reproductive Technologies and Haematopoietic Stem Cells Improvements for Quality and Safety throughout Europe, ARTHIQS). Co-funding by Member States is provided in the form of hours worked by their experts, who fulfil the tasks established in expert parts, so called Work Packages. The ARTHIQS project started on 1 May 2014 and it will end in May 2018. the Institute has been actively involved in both of its expert parts and, furthermore, continues to act as one of the five main partners – so called Work Package Leaders, safeguarding specifically communication with the public and submission of information about the outputs from the project. Within the scope of the ARTHIQS project, the Institute has established and operates the www.arthiqs.eu website and caters for the printing and distribution of information materials. It also organised a two-day workshop for the representatives of competent authorities of the EU Member States, where to-date outputs were presented and issues of assisted reproduction regulation discussed.

The Institute has been, moreover, a very active member of the EMA/HMA steering group for regulatory standard harmonisation in the EU and the EU-NTC European training centre. This way it has been involved in the preparation of the educational strategy for the entire medicines regulatory network of the European Union and of the EEA and in the development of cooperation with other stakeholders in this area, particularly with the academia. For more information, please refer to http://euntc.eudra.org.

In 2017, the Institute hosted three international educational events within the scope of the EMA-HMA joint initiative, so called EU Network Training Centre (EU-NTC). First of them was an April Preclinical Assessors Meeting (PAM). The workshop of preclinical assessors takes place on a regular basis, under the auspices of the members of the Safety Working Party (SWP), which is one of EMA´s standing scientific groups providing recommendations in matters associated with preclinical safety aspects to the Committee for Medicinal Products for Human Use (CHMP). This event was followed by a meeting of other 30 preclinical experts from all over the world organised in cooperation with the European Federation of Pharmaceutical Industries and Associations (EFPIA).

Other two educational events were organised in October 2017 in association with the adoption of new European legislation in the field of clinical trials and focused on exchange of experience and harmonisation of approach of clinical trial assessors in the area of quality and safety. Assessors from 27 European countries, besides the EU e.g. from Switzerland, Norway or Iceland, attended the training.

4 REGULATORY ACTIVITIES OF THE INSTITUTE

4.1 Record System

In 2017, the electronic record system of the Institute, incl. its regional workplaces, registered 145 986 delivered documents and 84 288 dispatched documents (Tab. 1, 2). The remarkable increase both in the number of received and dispatched documents was due to processing in the sphere of electronic prescriptions and medical devices. The priority for official document delivery are data mailboxes.

Tab. 1 **Registration of documents in 2015–2017**

	2015	2016	2017
Received documents	73 925	74 504	145 986
Dispatched documents	50 016	60 168	84 288

Tab. 2 **Overview of communication channels in 2016**

	Mail room	E-mail messages	Data messages	Electronic notice board	Total
Received documents	94 614	41 359	10 013	-	145 986

	Dispatch room	E-mail messages	Data messages	Electronic notice board	Total
Dispatched documents	43 274	1 546	36 468	3 000	84 288

MARKETING AUTHORISATION BRANCH

Prior to their placement on the market in the Czech Republic, proprietary medicinal products are subject to marketing authorisation. Within the scope of the marketing authorisation procedure, the Marketing Authorisation Branch assesses dossiers, in which the future marketing authorisation holder evidences the safety, efficacy and quality of the product. Indications, contraindications, product posology, classification for dispensing, as well as the package leaflet for patients and proposed labelling are assessed. Upon the issuance of the marketing authorisation, the marketing authorisation holder is informed about the approved Summary of the Product Characteristics, which serves doctors and healthcare professionals as a key source of information about the medicinal product.

The Institute issues opinions on applications for specific therapeutic programmes for the MoH. Specific therapeutic programmes allow for the use, distribution, and dispensing of non-authorised medicinal products for human use, if certain conditions are met.

The Department of Clinical Trials assesses applications for authorisation/notification of clinical trials, applications for hospital exemptions, surveys the conduct of clinical trials, and issues opinions on applications for specific therapeutic programmes for the MoH. Specific therapeutic programmes allow for the use, distribution, and dispensing of non-authorised medicinal products for human use, if certain conditions are met. The Institute issues opinions for project assessment and where clinical trials not regulated by the Institute are concerned, it keeps records on the use of non-authorised medicinal products.

The Department of Pharmacovigilance is involved in surveillance over the risks associated with the administration of medicinal products. This surveillance includes, in particular, the collection and evaluation of information from reports on suspected adverse reactions filed by healthcare professionals and patients and from non-interventional post-authorisation safety studies.

4.2 Marketing Authorisation of Medicinal Products

Applications for New Marketing Authorisation

In 2017, following successful validation, 590 applications in total were forwarded for expert assessment. Most of them were applications for MRP/DCP marketing authorisations. In the area of DCP/MRP marketing authorisations, the number of procedures with the Czech Republic as the Reference Member State is essential. In 2017, the number of submitted applications for DCP/MRP marketing authorisation with the Czech Republic as the Reference Member State grew from 87 applications in 2016 to 97 applications. The number of submitted applications for national marketing authorisations grew from 51 applications in 2016 to 64 applications in 2017 (Tab. 3).

Renewals of Marketing Authorisations

In 2017, following successful validation, 252 applications in total were forwarded for expert assessment. Most of them were applications for MRP/DCP marketing authorisation renewals; the number of applications for MRP/DCP as well as national marketing authorisation renewals decreased.

Variations to Marketing Authorisations

In 2017, the number of received applications for variations to national marketing authorisations slightly decreased, but the number of received applications for variations to MRP/DCP marketing authorisations grew.

The number of filed applications for variations to MRP/DCP marketing authorisations with the Czech Republic as the Reference Member State increased from 364 applications in 2016 to 436 applications in 2017. The number of filed applications for variations to MRP/DCP marketing authorisations with the Czech Republic as the Concerned Member State increased from 3 875 applications in 2016 to 3 993 applications in 2017. Concurrently, the number of submitted applications for transfers of MRP/DCP as well as national marketing authorisations increased from the total number of 246 applications in 2016 to 313 applications in 2017.

Parallel Import

In 2017, the number of submitted applications for parallel import authorisation was the same as in 2016; 46 parallel imports were authorised.

Revocation of Marketing Authorisation

In 2017, 261 applications for revocation of marketing authorisation were decided.

Tab. 3 **Marketing authorisation (MA) applications**

Process of marketing authorisation of medicinal products	Submitted in 2017	Decided in total in 2017	Pending as of 31 December 2017
New MAs	622	591	779
of which national	64	33	57
of which MRP-RMS	1	0	23
of which DCP-CMS	96	86	80
of which CMS (MRP and DCP)	461	472	619
MA renewals	235	425	560
of which national	19	133	139
of which RMS	31	62	32
of which CMS	185	230	389
National variations to MA	2 487	2 424	424
of which MA transfers	134	129	12
of which PI and labelling	268	205	43
of which bulk NAT variations	2 085	2 090	369
MRP-RMS variations	462	419	108
of which MA transfers	26	20	1
of which PI and labelling	16	10	6
of which bulk MRP-RMS variations	420	389	101
MRP-CMS variations	4 146	3 939	1 271
of which MA transfers	153	163	2
of which PI and labelling	165	133	53
of which bulk MRP-CMS variations	3 827	3 643	1 216
MA revocations	279	261	14
Parallel import	40	46	9
Variation to parallel import	58	49	21
Parallel import renewals	5	6	4
Parallel import revocations	2	2	0

The Table does not reflect the numbers of pending applications from the previous period.

Explanatory notes for the Table: RMS – Reference Member State CMS – Concerned Member State MRP – Mutual Recognition Procedure DCP – Decentralised Procedure.

Expiry/Non-expiry of Marketing Authorisations

As illustrated by tab. 4, in 2017, the Institute conducted 77 administrative procedures regarding the granting of exemptions from the Sunset Clause.

In the course of 2017, the Sunset Clause as referred to by Section 34a of the Act on Pharmaceuticals was applied to 112 marketing authorisation numbers and the marketing authorisation of these medicinal products expired.

Tab. 4 **Procedures regarding applications for exemption from the "Sunset Clause" conducted in 2017**

Administrative procedures for granting of an exemption from the Sunset Clause	**77**
of which initiated based on filed applications	**72**
of which ex officio initiated administrative procedures	**5**
granted	52
declined	15
suspended as undue	10
suspended as unjustified	0
suspended for failure to supplement	0
withdrawal of application	0

Note: The table does not reflect the numbers of pending applications from the previous period.

Consultations and Seminars in the Area of Marketing Authorisation of Medicinal Products

In 2017, the Institute gave 18 oral consultations and issued 16 written opinions on process-regulation and expert requests for consultations.

In June 2017, the Institute held 2 full-day seminars for companies regarding news in the area of marketing authorisation of medicinal products.

4.3 Cooperation with the European Medicines Agency and CHMP

In 2016, within the scope of cooperation with EMA and the Committee for Medicinal Products for Human Use (hereinafter referred to as "CHMP"), the Institute was involved in the assessment of centralised marketing authorisations as follows:

- Seven times as the Rapporteur/Co-Rapporteur;
- Twice as the "Peer Reviewer";
- Once assessed type I and II variations to centralised marketing authorisations.

Furthermore, the Institute provided comments on other centralised procedures. It regularly and actively participated in discussions held during CHMP meetings.

4.4 Clinical Trials

Compared to the previous year 2016, the total number of applications for authorisation/notification of a clinical trial submitted in 2017 remained the same. Most applications were those for phase III studies; international, multicentric, randomised, blinded, placebo or active substance controlled clinical trials conducted by foreign sponsors (Tabs. 5 and 6).

In 2017, the number of submitted applications for phase I clinical trials increased. Of the total number of 378 nationally submitted applications for authorisation/notification of a clinical trial, 26 clinical trials were submitted by non-commercial entities (academic research); 36 applications concerned orphan drugs (medicinal products for rare diseases); 42 clinical trials included also children or studied medicinal products directly intended for the paediatric population (paediatric trials), which was 8 more than in 2016. Ten clinical trials in total involved advanced therapy products (1 gene therapy, 6 somatic cell therapies, and 3 tissue engineering trials). Ten applications were of the FIH (First-in-Human) type. In the course of the assessment process, 29 applications for authorisation/notification of a clinical trial were withdrawn, which was the same number as in 2016. No application was declined.

Tab. 5 **Clinical trials (CT)**

	Pending from the previous period	No. of applications received in 2017	No. of decisions issued in 2017	Of which declined	Of which withdrawn
Applications for CT authorisation	0	106	106	0	5
Notifications of CTs	0	272	284	0	24
Notifications of amendments to CTs	0	2 890	2 975	0	0

Tab. 6 **Numbers of applications in 2017 by clinical trial phase**

	No. of applications received in 2017	No. of applications assessed in 2017
Phase I	31	28
Phase II	102	107
Phase III	199	206
Phase IV	16	21
Bioequivalence studies	30	28

In 2017, the Institute continued its assessment of DSURs (Development Safety Update Reports) and checks of SUSARs. In 2017, 535 DSURs were submitted, which was 125 more than in 2016. In 2017, the project for DSUR assessment and drafting of Assessment Reports, with the participation of other Member States, continued. The Assessment Safety Report Worksharing (ASRW) operation has been coordinated by the Czech Republic. In 2017, 11 Member States were involved and 78 Assessment Reports were drafted, which was 29 more than in 2016. The Czech Republic drafted 14 ARs. DSUR assessment and Assessment Report drafting is to continue also in 2018. This results in the setting of rules and development of a functional model for future Assessment Reports, to reflect the requirements of the clinical trial regulation, once the processing of Assessment Reports for DSURs is mandatory. The Institute participated in 11 TCs and 1 meeting in EMA.

In the autumn of 2017, the Institute organised 2 two-day international meetings: a meeting for safety data assessors – EU-NTC Course: Clinical Trials Regulation: Assessment of Safety Reports, and for pharmaceutical documentation assessors – EU-NTC course: Clinical Trials Regulation: Quality Assessment (IMPD).

The Institute continues its involvement in the Voluntary Harmonisation Procedure (VHP), which is a voluntary harmonisation process of joint assessment of clinical trial dossiers managed by the EMA Clinical Trial Facilitation Group (CTFG). Within the scope of the VHP, 191 applications for clinical trial authorisation/notification were submitted in the EU, of which the Czech Republic was asked to participate in 84 applications and it accepted participation in 83 VHPs (one was declined, as pursuant to the conditions set forth by the Act on Pharmaceuticals, it was not possible to conduct the CT in the Czech Republic), which was two more than in 2016. In respect of 32 VHPs, the Czech Republic asked to act as the Reference Member State, in 24 VHPs, the Czech Republic conducted the assessment process as the Reference Member State. In 2017, 510 major amendments were submitted within the scope of VHPs, of which 229 were in the Czech Republic, and in 47 cases, the Czech Republic conducted the assessment procedure as the RMS.

In 2017, a large proportion of the Institute´s activities were the preparatory works for the adoption of regulation No 536/2014 on clinical trials. A working group composed of the employees of the Institute and representatives of ethics committees held 5 joint working meetings to commence the VHP-plus project, i.e. involvement of multicentric ethics committees in the VHPs. Members of ethics committees were trained in VHPs, cooperation in the field of standard procedures was being prepared and activities coordinated. The Institute´s representatives in the working group were preparing source materials for the set-up of a new system of ethics committees and they prepared source materials for repeated discussions with the MoH. Preparatory meetings for the creation of a database of clinical trials within the Institute´s project and preparation of documentation for a tender to be announced continued. We have continued our active involvement in the EMA working group for the creation of a portal and a new EU database of clinical trials. The Institute participated in 9 meetings in EMA and 5 teleconferences. In 2017, the EU portal was twice tested, the employees of the Institute took part in both testing runs. The preparations for the adaptation of the regulation are to continue intensively also in 2018.

The Institute continues its active involvement in international expert groups. Within the scope of the CTFG (Clinical Trials Facilitation Group), it participated in 8 meetings (7 in EMA and 1 in the form of connecting to the meeting); and 2 teleconferences on product safety. The working group addressed current issues regarding the adaptation of Regulation No 536/2014 and new protocol designs and approach to Basket Trials, Matrix Trials, Umbrella Trials, Q&A on RSI (Reference Safety Information), etc. in the EU. Six times the Institute took part in the meeting of an ad hoc group for the adaptation of Regulation No 536/2014 in Brussels.

In the area of ethics committees, in 2017, the Institute actively participated in 2 seminars of the Ethics Committee Forum; it organised 5 working meetings with the representatives of multicentric ethics committees, all of them joint with the working group for the adaptation of regulation No 536/2014; and it summoned one meeting with the representatives of regulated entities and interest groups (AIFP, ČAFF, professional societies, ethics committees, contract organisations, Ethics Committee Forum, representatives of the Czech Association of Patients).

The Institute held 3 seminars for sponsors, contract organisations and monitors in total, of which one was a two-day seminar on good clinical practice, where the representatives gave 9 external domestic presentations, 3 for doctors, 2 for patient organisations, 3 for ethics committee members, and 1 for qualified persons; and one foreign presentation at the DIA conference on the status of adaptation of the Clinical Trials Regulation in the Czech Republic.

Specific therapeutic programmes: 48 applications for the issuance of an opinion on proposed specific therapeutic programmes were submitted. An opinion was issued for 45 applications; 34 pending ones were brought forward to 2018.

Non-authorised medicinal products: In 2017, 6 600 reports on the use of non-authorised medicinal products were received, which

was 1 412 more than in 2016. The Institute continues to control the prescribing of non-authorised medicinal products and reporting by doctors.

In 2017, the Institute gave 18 consultations and issued 4 written opinions on issues regarding the activities of the Clinical Trials Department and 36 opinions on the distinction of grant projects between clinical trials subjected or not subjected to clinical trial

4.5 Pharmacovigilance

In 2017, 3 804 primary reports of suspected adverse drug reactions (hereinafter referred to as "ADR") from the territory of the Czech Republic were received (Chart 1), of which 1 777 were reports from marketing authorisation holders (pharmaceutical companies) and 2 027 reports sent directly to the Institute by healthcare professionals and patients (712 were reports from patients). Each individual report received by the Institute is processed, individually assessed, and entered into the database of adverse drug reactions from the Czech Republic (hereinafter referred to as "CDNÚ") and, concurrently, sent to the European EudraVigilance database as well as to the global WHO database. Records in ADR databases are regularly checked and evaluated using statistical as well as qualitative methods in order to allow for the identification of new pharmacovigilance signals. In addition to comprehensive ongoing evaluation of all adverse drug reactions reported in the Czech Republic, pharmacovigilance assessors are responsible for the evaluation of signals pertaining to 63 active substances on the European level. In 2017, the Department of Pharmacovigilance (PV) assessed 533 monthly adverse reaction excerpts from the EudraVigilance database regarding substances for which the Czech Republic is the pharmacovigilance signal rapporteur for the EU.

With regard to the fact that in EMA, the EudraVigilance ADR database was undergoing changes, all Member States had to ensure compatible national ADR reporting databases. For this reason, the Institute held a project "Implementation of a New Central database of Adverse Drug Reactions (CDNÚ)" and in 2017, its essential part was implemented. The development of the database took place in close cooperation between the selected vendor (Orsia spol. s r.o.) and data managers from the PV department with IT support. In addition to the application proper, its connection to the newly developed web form for adverse drug reaction reporting, to the new gateway and data outputs for the Institute´s BI were being prepared. The application was delivered by the vendor in early June 2017, and it had been preceded by user testing of the processing and verification of access to reports and by training of all users. The application functionality testing in respect of sending to and receiving of reports from the EudraVigilance database in EMA took place in July and August 2017 – the connection to the Institute´s new gateway Axway Activator version 5.12, sending and receiving of reports in the R2 and R3 formats, and set-up of report receipt via so called report rerouting from EMA were tested. Finetuning and error elimination took place in the following months. A control migration of all data from the old database was done twice and PV´s comments on the correctness of migration were incorporated. An exact plan of the transfer from the existing R2 ADR database to a new, R3 database connected to the new gateway was prepared and communicated on the Institute´s website to EV partners. On 7 November 2017, the old CDNÚ application was disconnected from the originally used gateway, the application was closed and moved to the new application. On 22 November 2017, this application was (in line with other EV partners) connected to the gateway and the exchange of electronic reports with EMA commenced in compliance with the new rules applicable within the EU. Thereafter, problems arising in association with the live operation were addressed, and the preparation of the web form continued – user testing in the Institute as well as outside the Institute took place. Requirements for BI outputs from data were specified; the control of output accuracy has been continuing also in 2018. The project of Implementation of the Central Database of Adverse Drug Reactions was completed in December 2017 and works on the new web form and BI continue.

The department of Pharmacovigilance keeps increasing its involvement in international pharmacovigilance procedures. In the sphere of Periodic Safety Update Reports (PSURs) for individual products, in 2017, the Institute assessed 13 PSUSAs (PSUR Single Assessment for a specific substance) from the position of so called PSUSA-lead Member State. As the PRAC rapporteur (the lead pharmacovigilance assessor) for blinatomumab, a substance authorised in the EU in 2015, the Institute completed assessment of marketing authorisation renewal, 2 post-authorisation safety study protocol assessments, 4 assessments of variations to marketing authorisation, and 2 PSUSA assessments for the EU in the course of 2017, i.e. an assessment of nine procedures concerning this substance in total. In 2017, we also became the PRAC rapporteur for centrally authorised substance mexiletin, for which we assessed the pharmacovigilance part of the marketing authorisation dossier.

The Institute took actively part in 11 meetings of the EMA Pharmacovigilance Committee (PRAC) and 10 teleconference meetings of the PRAC Committee. The Institute was appointed the PRAC rapporteur in the pan European review of risks and benefits of fluoroquinolone antibiotics (EU referral pursuant to Article 31). This evaluation is conducted in several rounds and continues onto 2018. The Institute has been also actively involved in the European Pharmacovigilance Inspectors Working Group (PhV IWG), EudraVigilance Expert Working Group (EV EWG) and the PhV Business Team.

The conclusions of the CHMP and of the EMA Pharmacovigilance Committee (PRAC) were being transposed to the Czech clinical practice in cooperation with other units of the Marketing Authorisation

Branch on an ongoing basis. In 30 cases, the Institute published information intended for healthcare professionals or for the general public regarding the safety of medicinal products on its website. In cooperation with marketing authorisation holders, it published 157 educational materials and 28 letters for healthcare professionals, focused upon enhanced safety of use.

Assessors from the Department of Pharmacovigilance were involved in the assessment of marketing authorisation dossiers where they reviewed their pharmacovigilance sections; in 2017, they drafted 840 reports on pharmacovigilance documentation in total.

The Institute published 4 issues of the Information Bulletin "Adverse Reactions to Medicines", which provided current information on suspected adverse drug reactions reported from the Czech Republic in the course of the previous year, other pharmacovigilance news, as well as the regular column called "You reported to us" where specific cases of adverse drug reactions reported from the Czech Republic were published.

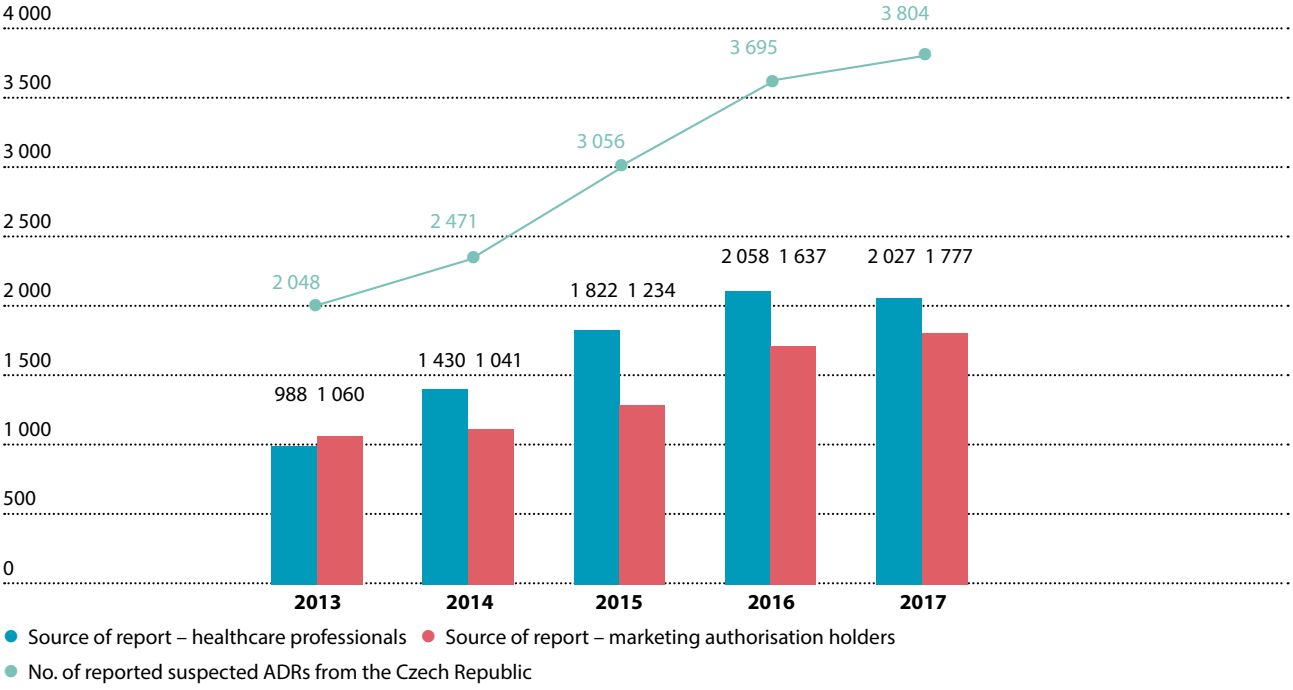
Fifty-five notifications (commencement or termination) of post-marketing safety studies were processed.

In the course of 2017, the Pharmacovigilance Department conducted the total of 11 inspections of the pharmacovigilance system of marketing authorisation holders, of which 3 were from the EMA programme.

The Pharmacovigilance department communicates with the public and answers questions from healthcare professionals, the general public, as well as pharmaceutical companies. In 2017, it answered more than 530 questions in writing or by phone.

Within the scope of the educational project to increase the reporting of suspected adverse drug reactions, the Pharmacovigilance Department assessors gave 10 presentations at expert congresses or workshops through which they informed doctors or pharmacists on the safety of medicinal products and the importance of suspected adverse drug reaction reporting. The Department also conducted tuition in pharmacovigilance at the 2nd School of Medicine of Charles University for 4th-year medical students. On an ongoing basis, training in pharmacovigilance as part of pre-attestation preparation in the field of clinical pharmacy takes place; in the course of 2017, the Department gave 3 such training courses. Furthermore, the Institute has been involved in the education of pharmaceutical companies in good pharmacovigilance practice. In 2017, the Pharmacovigilance Department organised 2 one-day workshops for these companies regarding news in pharmacovigilance from the previous year, and, in addition thereto, 2 two-day seminars in the basics of pharmacovigilance.

Chart 1 **Number of reported suspected adverse drug reactions from the Czech Republic and the source of the reports**



SURVEILLANCE BRANCH

The Laboratory Control Section conducts analyses of pharmaceuticals required by the law (e.g. from random inspections of pharmaceuticals on the market, batch release), upon request of other units of the Institute or state administration bodies and within the scope of international cooperation. The laboratories are integrated into the international General Network of Official Medicines Control Laboratories. The laboratories do not perform analyses upon request for any commercial entities (except for batch release pursuant to the Act on Pharmaceuticals). The Pharmacopoeial Department is involved in the publishing of the Czech Pharmacopoeia and the preparation of the European Pharmacopoeia.

The Pharmacy and Distribution Section ensures surveillance over compliance with legislative requirements in the area of wholesale distribution of pharmaceuticals, with focus upon the principles of good distribution practice and the issuance of authorisations for wholesale distribution activities, including the administration of a register of brokers of medicinal products, and, furthermore, performs surveillance over the area of dispensing, sale, and preparation of medicinal products. The inspected entities are wholesale distributors, pharmacies, vendors of selected medicinal products, and specialised workplaces of healthcare facilities. The inspection of handling of medicinal products applies also to any other healthcare facilities. The inspections are performed by individual regional units of the Institute according to their territorial competence.

The Inspection Section ensures supervisory activities in the area of manufacture of pharmaceuticals, good clinical and laboratory practices, issuing of binding opinions on the import and export of medicinal products, including cooperation with customs authorities. It also oversees donation, procurement, testing, processing, storing, and distribution of human tissues and cells aimed at safeguarding their quality and safety. This activity includes the issuance of authorisations to engage in the activities of a tissue centre, donation centre or a diagnostic laboratory, the conduct of inspections, monitoring of serious adverse events and reactions or suspicion of the above, and, in cases of doubt, issuance of decisions as to whether tissues and cells which are regulated by the applicable law are concerned.

The Quality Defects Department addresses quality defects of pharmaceuticals and excipients available on the market in the Czech Republic.

The Department of Legal Support and Enforcement is involved in the identification and penalisation of infringements of law as well as law enforcement in cases where illegal status has been detected, i.e. unauthorised handling of pharmaceuticals. Within the scope of enforcement, the Institute cooperates with other institutions in the Czech Republic as well as abroad (particularly with the Police of the Czech Republic, Czech Customs Administration, Czech Agriculture and Food Inspection Authority, and control authorities of EU Member States).

The exercise of surveillance over compliance with the Act on the Regulation of Advertising in the sphere of advertising for medicinal products for human use (HMPs) and sponsorship in this area (with the exception of radio and television broadcasting) is performed by the Department of Advertising Regulation. It conducts investigations into complaints of inappropriate advertising for HMPs, provides expert opinions on advertising materials and on advertising regulation issues.

4.6 Laboratory Control

Laboratory control is conducted by the Laboratory Control Section both within the scope of requirements defined by the Act on Pharmaceuticals, i.e. it controls the quality of pharmaceuticals placed on the market pursuant to predefined projects and releases batches of defined medicinal products, and on the basis of internally submitted requirements (requirements of other units of the Institute). This includes, in particular, addressing of quality defects of medicinal products, analyses of pharmacy samples, suspected counterfeit and illegal pharmaceuticals, adverse reactions, etc. Since 1995, the Laboratory Department of the Laboratory Control Section has been an active member of the international OMCL (Official Medicines Control Laboratories) network under the European Directorate for the Quality of Medicines (EDQM). The employees of both laboratory departments attend annual OMCL meetings and are members of working groups.

The section has established a quality management system pursuant to the ČSN EN ISO/IEC 17025 standard. In 2017, a regular verification of the established quality system by a group of EDQM auditors took place. International recognition of the quality management system is a precondition for participation in international studies of control of centrally authorised medicinal products organised by EMA/EDQM, recognition of the results of MRP/DCP product analyses, and international recognition of batch release certificates for selected medicinal products (OCABR) within the EU.

The results of sample analyses conducted in 2017 by both laboratory departments of the Laboratory Control Section are summarised in Table 7.

Tab. 7 **Supervision over the quality of pharmaceuticals on the market by means of laboratory analyses according to predefined projects (projects concluded in 2017**)

Project name	Number of analysed products	Number of analysed samples	Number of compliant samples	Number of non-compliant samples	Number of comments on MA dossier
2/2015 – Counterfeit products*	83	83	0	0	1
5/2015 – OTC products in the form of gels	12	24	22	2	0
3/2016 – Pharmacy samples *	62	202	173	29	0
1a/2015 – Meloxicam	11	21	21	0	0
1b/2015 – Montelucastum	11	21	21	0	0
1c/2015 – Escitalopram	18	64	64	0	0
1d/2015 – Cetirizin	15	31	31	0	0
1e/2015 – Dr. MAX medicinal products	3	6	6	0	0
7/2015 – Control of Braille on the labelling	58	76	76	0	0
8/2015 – Corticosteroids	31	62	62	0	2
3BIO/2015 – Verification of microbiological quality of medicinal products for nasal administration	20	20	20	0	0
1BIO/2016 – Control of flu vaccines for the 2016/17 season	2	6	6	0	0
2BIO/2016 – Verification of microbiological quality of lozenges for sore throat	12	22	22	0	0
Total (ex 2/2015 and 3/2016)	**265**	**353**	**351**	**5**	**5**

** Samples from these products included in 2016.*

Projects are prepared on the basis of a "risk-based" analysis. The criterion is, in particular, high consumption of the controlled products, less common pharmaceutical forms or routes of administration, target patient group, or frequent complaints filed by patients or medical and pharmaceutical professionals. Drafts of these projects and reports on completed projects are approved by the Institute's Quality Team. In 2018, works on the following projects is under way: Control of vasodilators, Control of medicinal products containing telmisartan, loratadine, betaxolol and salicylic acid. The following projects have been approved: Control of medicinal products containing diclofenac; projects of the Department of Biological Methods (Control of flu vaccines for the 2017/2018 season, Verification of microbiological quality of herbal teas, Verification of microbiological quality of live medicinal products, Control of MMR vaccines). A project concerning the conduct of the LAL test in tissue glues is approaching conclusion. Pharmaceutical samples, Braille on the labelling of medicinal products continue to be controlled and analyses of identified counterfeit products carried out.

Tab. 8 **Batch release for defined medicinal products**

Type of product	Number of reported medicinal products	Number of reported batches	Released on the basis of certificate	Number of laboratory -verified samples	Total number of released batches*	Not released
Blood derivatives	61	956	945	11	956	0
Vaccines	34	349	349	0	349	0
Other	1	1	0	1	0	1

** Some batches were released repeatedly.*

Tab. 9 **Laboratory control of pharmaceuticals and excipients requested by other units of the Institute, other state administration organisations or EDQM**

	Number of samples	Of which compliant	Of which non-compliant
Suspected quality defect of a pharmaceutical	46	38	7
Suspected counterfeit, illegal samples*	60	0	0
Pharmacy samples	224	204	20
International studies within OMCL*	7	0	0
Internal quality control of purified water	138	135	3
Verification of quality of a reference substance for Ph. Eur.	1	1	0
Other analyses**	14	14	0
Total	**490**	**392**	**30**

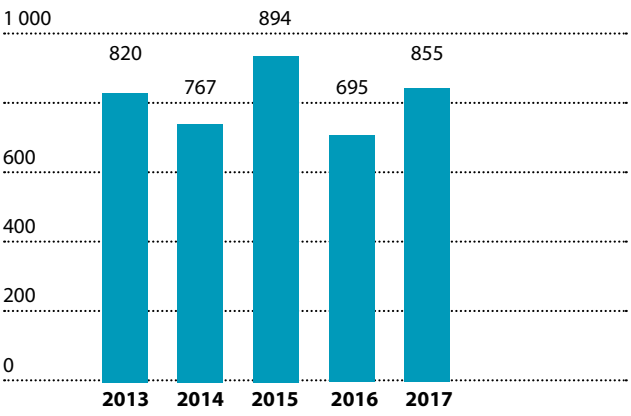
* *Sample compliance cannot be evaluated.*

** *E.g. requested microbiological controls, other requested analyses, etc.*

The tables above indicate that in the Laboratory Control Section, 855 sample analyses were completed. Compared to 2016, the number of samples rated as non-compliant (ex. counterfeit products and samples from international studies) decreased and amounted to 3.9% (6.3% in 2016; 5.3% in 2015; 4.8% in 2014; 3.5% in 2013). Quality defects were confirmed particularly for pharmacy samples (incl. adjusting defects) and samples queried by doctors and patients. The reduced percentage of non-compliant samples has been caused primarily by a larger number of controls of proprietary medicinal products the quality of which is good (only two non-compliant samples out of 347).

Within the scope of the statutory task of batch release, all of the reported batches were released onto the market in time, i.e. within timelines stipulated by the law.

Chart 2 **Number of sample analyses in 2013–2017**



International Cooperation within the Area of Laboratory Control

In addition to other cooperation within the OMCL EDQM network, the Section participates in joint studies on the control of the quality of marketed pharmaceuticals (this concerns, in particular, analyses of MRP or DPC authorised medicinal products conducted upon request of other members of the OMCL network), comparative studies, verification of the quality of reference substances for the European Pharmacopoeia, and in the laboratory verification of the quality of centrally authorised medicinal products (joint EMA and EDQM activity – CAP programme).

In 2017, the Laboratory Control Section participated in collaborative international studies listed in Table 10.

Tab. 10 **Involvement in international studies**

Study	Study title	Rating
PTS 168	Liquid Chromatography	Good
PTS 169	UV-VIS Spectrophotometry	Good
PTS 173	Prekallikrein Activator in Human Albumin	Out of specification - nonconformity
PTS 177	Liquid Chromatography	Good
PTS 178	Dissolution	Good
CAP 17/36	Javlor	Good
CRS	Calcium Folinate	Good

Legend to abbreviations:

PTS – EDQM Proficiency Testing Study. Quality control of the work of the laboratory; EDQM provides the samples, reference substances and method. Once the results are sent back to EDQM, they are statistically processed and the laboratory obtains the rating of the study.

CAP – Analysis of a Centrally Authorised Product as part of the joint EMA and EDQM programme.

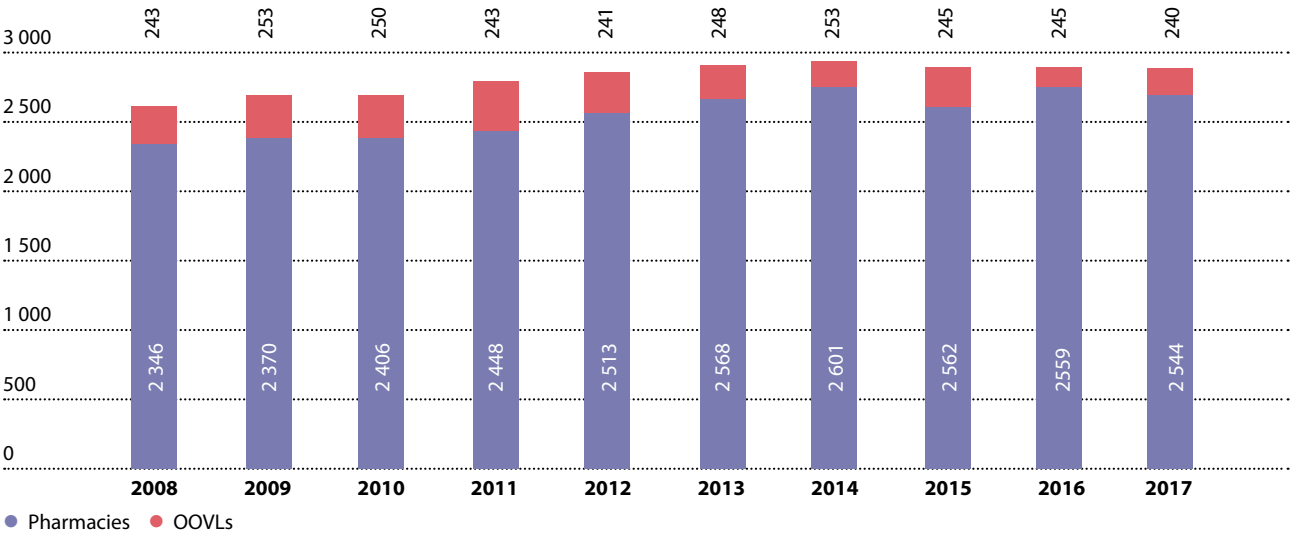
CRS – Verification of the quality of the reference substance for EDQM/Chemical Reference Substance.

4.7 Surveillance in the Area of Preparation, Dispensing, Sale, and Distribution of Pharmaceuticals

The principal activities of the Pharmacy and Distribution Section include supervision in the area of medicinal product handling conducted by the Institute in pharmacies, at vendors of selected medicinal products, in healthcare facilities (including their specialised departments), and wholesale distributors of pharmaceuticals. The Pharmacy and Distribution Section is also entrusted with the performance of price inspections of medicinal products and foods for special medical purposes, inspections of the conditions of dispensing of prescription-only medicinal products in compliance with the Act on Public Health Insurance, and inspections of handling of dependency-producing substances and precursors, including products containing the aforementioned, in pharmacies. The Pharmacy and Distribution Section also keeps and regularly updates publicly accessible databases of the specified regulated entities with the exception of healthcare facilities.

In late 2017, the Institute kept a record on a total of 2 544 pharmacies, of which 4 fell within the scope of powers of the Ministry of Defence of the Czech Republic; moreover, the Institute kept a record on 240 detached pharmaceuticals and medical device dispensing units (hereinafter referred to as "OOVL"), 406 medical device dispensaries, 2 368 vendors of selected medicinal products, 44 nuclear medicine departments of healthcare facilities, and 451 wholesale distributors of medicinal products. The stagnation in the total number of pharmacies continued; compared to 2016, the total number of pharmacies decreased by 15 entities and the number of OOVLs remained the same (Chart 3).

Chart 3 **Number of pharmacies and OOVLs in the last 10 years (as of the last day of each concerned year)**



In 2017, the inspectors of the Pharmacy and Distribution Section conducted 876 inspections in pharmaceutical care facilities – pharmacies in total, of which 40 were hospital pharmacies of inpatient care providers. Of the total number of inspected pharmacies, 38 inspections were targeted inspections, carried out on the basis of reports.

Separate inspections aimed at handling of dependency-producing substances and precursors were carried out in 452 pharmacies.

Price control focusing upon compliance with the Act on Prices and rules of price regulation was conducted in 110 pharmacies, of which 4 inspections were targeted, and at 14 wholesale distributors´.

On the basis of facts identified during the conducted inspections, in total, 258 final decisions to impose a fine for breach of obligations stipulated by the Act on Pharmaceuticals in the total amount of 12 433 000 CZK were adopted (this includes also finalised administrative proceedings based upon inspections conducted in the previous period). The preparation of medicinal products was suspended for a pharmacy in 5 cases, all of them due to non-verified weights used in the preparation of medicinal products.

The main reasons for the issuance of a decision imposing a fine included non-compliance with the rules of good pharmacy practice in the preparation and control of medicinal products, particularly the use of active substances and excipients after their shelf-life expiry or without a document evidencing their quality and insufficient records of the preparation and control; furthermore, dispensing of medicinal products without medical prescription or on invalid prescription; dispensing by unauthorised staff; serious shortcomings in the record-keeping of the number of pieces received, dispensed and stored;

storage and dispensing of medicinal products which should have been withdrawn from the market based on a decision of the marketing authorisation holder; failure to comply with the conditions governing the storage of medicinal products; transfers of medicinal products between pharmacies; and illegal export of medicinal products abroad.

Within the scope of inspections of the handling of dependency-producing substances in pharmacies, in 2017, identification of major breaches of the Act on Dependency-Producing Substances resulted in the total of 31 final decisions on fine imposition to pharmacy operators amounting to 647 000 CZK in total; and 11 final decisions on fine imposition for breaches of the Act on Precursors amounting to the total of 115 000 CZK.

The main reasons for the issue of the decision on fine imposition included serious breaches of the Act on Dependency-Producing Substances in terms of record-keeping and documentation of dependency-producing substances and products, incl. relevant documents; failure to submit the annual report on the stock and movement of dependency-producing substances and products within the statutory timeline; or incorrect or incomplete data in the annual report. In respect of handling of precursors, it was failure to meet the notification duty in case of changes to data in a special licence; failure to keep documents and records of the activities with precursors and inadequate method of their storage.

Inspections focusing on compliance with price regulation rules in pharmacies identified a breach of price regulations in 65 cases. Pharmaceutical care providers were issued 25 final decisions on fine imposition pursuant to the Act on Prices amounting to 625 000 CZK in total for price offences regarding failure to comply with the binding procedure for pricing of magistral formulas and proprietary medicinal products treated prior to dispensing; failure to maintain or store evidentiary price records; failure to observe officially fixed maximum prices during sales; and disregard for the conditions and procedures for their application.

A breach of the ban on offering and provision of advantageous sale in respect of reimbursed medicinal products dispensing was identified in 5 cases. This concerned the offer to obtain loyalty points and the possibility to use them in association with the dispensing of prescription-only medicinal products covered by the public health insurance. On the basis of the inspection findings, 6 final decisions on fine imposition were issued pursuant to the Act on Public Health Insurance, with the fines amounting to the total of 90 000 CZK (this includes also finalised administrative procedures based on inspections conducted in the previous period).

Furthermore, un 2017, 300 inspections of the handling of medicinal products in healthcare facilities were conducted. The inspections were carried out in 32 inpatient departments of healthcare service providers and in 268 separate outpatient offices of general practitioners and medical specialists, and in other healthcare facilities. On the basis of reports received by the Institute in connection with the operation of healthcare facilities, where health care is provided, a total of 20 targeted inspections took place. A total of 19 final decisions on fine imposition in the total amount of 1 110 000 CZK were taken for the identified violations of the Act on Pharmaceuticals (this includes also finalised administrative procedures based on inspections conducted in the previous period).

The major reasons for the issue of the decision on fine imposition included, in particular, handling of medicinal products contrary to the summary of the product characteristics; failure to meet the medicinal product storage conditions; failure to keep records on the handling of medicinal products; and other serious breaches of the obligations governing the handling of medicinal products set forth by an implementing regulation.

Inspections of vendors of selected medicinal products in 2017 involved 111 outlets in total; 9 final decisions on fine imposition in the total amount of 55 000 CZK for breach of the obligations implied by the Act on Pharmaceuticals were taken.

In other healthcare facilities authorised to prepare medicinal products (Nuclear Medicine Departments – ONM, and workplaces preparing autogenous vaccines for human use – HAV), a total of 18 inspections were carried out; the findings from the inspections did not result in the need for the imposition of any penalty.

Summary results from inspections completed in 2017 are provided in Table 11.

Tab. 11 **Inspection surveillance over pharmacies, nuclear medicine departments, healthcare facilities, and vendors of selected medicinal products in 2017**

			Classification of defects						Penalties		
Inspected entity	**Type of inspection**	**Number**	**1**	**%**	**2**	**%**	**3**	**%**	**A**	**B**	**C**
Pharmacies	Regular inspections	876	477	54,4	253	28,9	146	16,7	5	-	258
	Price inspections	110	Not rated by classification of defects						-	-	25
	Inspections of dependency-producing substances and precursors	452	299	66,2	115	25,4	38	8,4	-	-	42
Nuclear medicine departments		16	12	75,0	3	18,8	1	6,2	-	-	-
Workplaces preparing autogenous vaccines for human use		2	-	-	2	100,0	-	-	-	-	-
Healthcare facilities		300	195	65,0	72	24,0	30	10,0	-	-	19
Vendors of selected medicinal products		111	84	75,7	16	14,4	10	9,0	-	-	9

Note: Three inspections of healthcare facilities and 1 inspection of a vendor of selected medicinal products were not rated.

Classification of defects
1 – None or minor defects identified
2 – Major or repeated defects
3 – Critical defect or serious breach of law

Penalisation
A –Suspended preparation
B – Suspended operation
C – Fine imposed (final decision)

In 2017, inspectors from the Pharmacy and Distribution Section took a total of 250 samples of medicinal products during inspections in pharmacies, of which 93 were pharmaceutical products intended for the preparation of extemporaneous products in the pharmacy. Out of 157 pharmacy samples (medicinal products prepared in pharmacies), 7 in total were out-of-specification, the defects being out-of-specification content of active substances, total weight of the sample, and inadequate galenic processing (tendency towards disintegration and weight uniformity). In respect of the total of 19 samples intended for dispensing, defects in their labelling were identified.

Comparison of occurrence of monitored defects in out-of-specification pharmacy samples in the last years is provided in Table 12.

Tab. 12 **Occurrence of monitored types of defects in% (of the total number of non-compliant samples)**

Type of defect	**2015**	**2016**	**2017**
Out-of-specification content of active substance	42,9	25,0	57,1
Out-of-specification total weight	42,9	50	14,3
Out-of-specification purified water Microbiological compliance	-	-	-
Out-of-specification galenic processing	-	25,0	28,6
Out-of-specification microbiological compliance	14,2	-	-
Active substance and excipient identity confusion	-	-	-

Other activities of the Pharmacy and Distribution Section include issuance of binding opinions on the technical and material equipment of pharmacies and dispensaries of medical devices. In 2017, a total of 296 applications for issuance of an opinion were received from pharmacy operators and 288 positive binding opinions were issued. In the case of dispensaries of medical devices, a total of 18 operators applied for a binding opinion and 15 positive binding opinions were issued.

In 103 cases, the issuance of the binding opinion was associated with an inspection in the pharmacy (on-the-spot check of technical and material equipment) and in 6 cases with an inspection of OOVLs (Table 13). Furthermore, in this context, 10 initial inspections of medical device dispensaries and 227 consultations on the technical equipment of existing pharmacies or the construction of new pharmacies and issues related to Decree No. 84/2008 Coll. and other regulations implementing the Act on Pharmaceuticals or Act on Dependency-Producing Substances and Act on Precursors took place. Table 13 also provides data on newly established and defunct pharmacies/OOVLs.

Tab. 13 **Other activities of the Pharmacy and Distribution Section**

Initial pharmacy inspections	**Establishment of a new pharmacy/OOVL**	**Defunct pharmacies/OOVLs**
103	68/10	83/15
Initial OOVL inspections	**Initial medical device dispensary inspections**	**Consultations**
6	10	227

Distribution of Medicinal Products

In 2017, the number of distributors increased by 11 entities to the total of 451 medicinal products distribution authorisation holders. Of the total number of approved distributors, 157 entities were both a pharmacy operator and a distribution authorisation holder.

In 2017, 42 new distribution authorisations and 142 decisions on variations to distribution authorisations were issued, and 31 authorisations were revoked upon request of their holders. In 2 cases, the distribution authorisation expired in compliance with Section 76, paragraph 4 of the Act on Pharmaceuticals. In respect of one entity, the authorisation was revoked by the decision of the Institute pursuant to Section 76, paragraph 3 of the Act on Pharmaceuticals.

The total of 20 entities applied for entry into, variation, or deletion from the Registry of Brokers of Human Medicinal Products in 2017. As of 31 December 2017, the Registry included the total of 33 entities.

Table 14 provides an overview of received applications and issued decisions in respect of distribution authorisation, variations thereto or revocation thereof, and the registration of brokers of medicinal products.

Tab. 14 **Distribution and intermediation of pharmaceuticals in 2017**

	Received applications	Authorisations issued/register entries made
Application for distribution authorisation	44	42
Application for variation to distribution authorisation	149	142
Application for revocation of distribution authorisation	34	31
Application for entry in the Registry/variation to entry in the Registry/deletion from the Registry	20	18

The table does not include the numbers of pending applications from the previous period.

In 2017, the total of 355 inspections of distributors and 4 inspections of brokers took place, of which 15 were targeted inspections carried out on the basis of internal and external reports. In total, 27 reports were received and investigated; in 2 cases, an administrative procedure regarding fine imposition was initiated on the basis thereof.

The inspection activities focused upon compliance with the requirements set forth by the Act on Pharmaceuticals, the Decree on the Manufacture and Distribution of Pharmaceuticals, EU guidance on good distribution practice and associated guidelines of the Institute.

Of the total number of 268 rated inspections of distributors (follow-up and targeted inspections), 73.1% were rated with grade 1 (good), 20.2% with grade 2 (satisfactory), and 6.7% with grade 3 (not satisfactory).

Following the completed inspections, the total of 200 post-inspection good distribution practice certificates were issued, of which 49 certificates were of limited validity (one year in 10 cases; 2 years in 38 cases; in one certificate, the inspection findings resulted in limited scope of the distributor´s certified activities. All of the issued certificates, as well as distribution authorisations and variations thereto, have been regularly entered into the EudraGMDP European Database.

The Department of Good Distribution Practice was also involved in 4 investigations of suspected quality defect of a medicinal product and possible presence of a counterfeit product in the distribution chain, and, with the authorisation of the Strasbourg EDQM inspectorate and the Institute´s Laboratory Control Section performed sampling of authorised medicinal products in the distribution chain for the purposes of their laboratory control. Within the scope of consultation activities, it gave the total of 17 consultations regarding the application of good distribution practice principles and on an ongoing basis has been providing opinions and source materials upon request from other bodies and organisations, including those from abroad (the Czech MoH, revenue authorities, courts of justice, the Czech Police, MHRA or EMA).

In 2017, 14 price inspections of distributors focusing upon control of compliance with the Act on Prices and rules of price regulations governing medicinal products were conducted. A breach of price regulations was identified in 2 cases and they consisted of failure to comply with the officially established maximum price of medicinal products, or non-observation of the conditions and procedures for its application. Three fines amounting to the total of 20 000 CZK were finally imposed for the price offences in 2017.

On the basis of facts identified during the completed inspections, distributors were imposed the total of 33 final decisions on fine for breach of obligations set forth by the Act on Pharmaceuticals and its implementing regulations amounting to 4 532 000 CZK in total (incl. also finalised administrative procedures based on inspections conducted in the previous period).

The main reasons for the proposed fine imposition included non-observance of the obligation to provide the Institute with complete and correct data about distributed medicinal products; failure to

comply with the rules of good distribution practice; distribution of medicinal products purchased from the position of a pharmacy operator; failure to safeguard the services of a qualified person; inadequately effective quality assurance system, incl. determination of procedures and measures for risk management; and serious shortcomings in the keeping of regulatory and record documentation of the distributor.

In 2 cases, the validity of the distribution authorisation was suspended and declarations of non-conformity with the rules of good distribution practice issued due to serious breaches of the obligations implied by the Act on Pharmaceuticals and conditions of good distribution practice; these were entered in the EudraGMDP database.

The results of distributor inspections in 2017 are provided in Table 15.

Tab. 15 **Inspection surveillance over distributors**

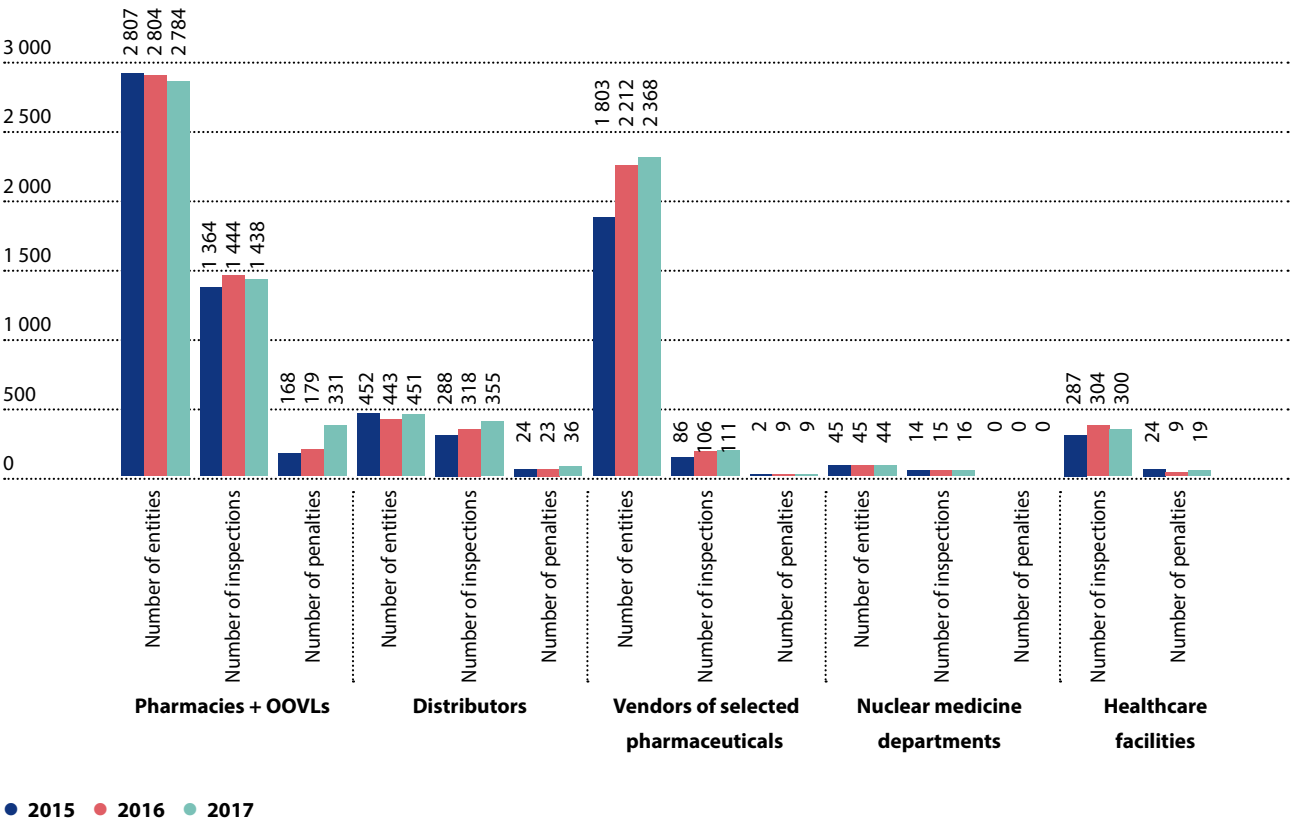
	Number of inspections				Inspection rating			Measures	
Total	Initial	Follow-up	Targeted	Variation	1	2	3	NCR	Proposed fine
355	44	253	15	43	196	54	18	2	47

Inspection Rating

On the basis of the identified shortcomings and their severity the inspection is rated and according to the achieved point score, the overall level of compliance with the principles of good distribution practice is expressed by the following rating: 1 – Good / 2 – Satisfactory / 3 – Not satisfactory.

Comparison of the number of regulated entities, conducted inspections and imposed penalties for the last 3 years is illustrated by Chart 4.

Chart 4 **Information on surveillance activities in 2015–2017**



4.8 Surveillance in the Area of Manufacture of Pharmaceuticals, Human Tissues and Cells, Good Laboratory and Clinical Practice

The Inspection Section ensures surveillance activities in the sphere of manufacture of pharmaceuticals (including the manufacture of transfusion products and starting materials for further manufacture of pharmaceuticals – hereinafter referred to as "TP"), good clinical practice and good laboratory practice, issuance of binding opinions on the import and export of medicinal products, incl. cooperation with the customs authorities. Furthermore, the Section carries out surveillance over the donation, procurement, examination, processing, storage, and distribution of human tissues and cells (hereinafter referred to as "HTC") aimed at the assurance of their quality and safety. This activity involves also the issuance of authorisations to engage in the operation of a tissue centre, donation centre, HTC distributor or diagnostic laboratory, the conduct of inspections, monitoring of actual or suspected serious adverse events and reactions, and, where doubts arise, decision-making as to whether tissues and cells subjected to regulation by a particular act are concerned. Furthermore, it caters for the activities in the sphere of haemovigilance, monitoring of serious adverse reactions experienced by transfusion product donors or recipients, and serious adverse events associated with blood donation, examination, processing, storage, and distribution of transfusion products or starting materials for further production or with transfusion product dispensing. The Section, moreover, receives and assesses reports from the European rapid alert systems for blood (hereinafter referred to as "RAB") and for HTC (hereinafter referred to as "RATC").

Manufacture of Pharmaceuticals

The updated lists of supervised operators in the sphere of manufacture and research of pharmaceuticals are provided on the Institute´s website.

In the sphere of manufacturers (incl. blood centres) the total of 95 applications for manufacturing authorisation or variations thereto were received (Tab. 16). The number of cases brought forward from one year to another corresponds to the intervals for application processing. The number of decisions issued for variation to manufacturing authorisation was 5% more than in 2016.

Human Tissues and Cells

This is an area regulated by the Institute pursuant to Act No 296/2008 Coll., on Human Tissues and Cells.

In 2017, 55 applications for operating authorisation and applications for variations to operating authorisations were received. The number of submitted applications was 5% more than in 2016 (Chart 5).

Tab. 16 **Activities associated with applications in the sphere of manufacture of pharmaceuticals and in the sphere of human tissues and cells**

Application type		**2015**		**2016**		**2017**	
		Received applications	**Issued decisions**	**Received applications**	**Issued decisions**	**Received applications**	**Issued decisions**
Application for manufacturing authorisation	Manufacturer of medicinal products	1	0	3	2	4	4
	Control laboratory	2	3	2	1	1	1
	Blood centre	0	0	1	0	2	3
Application for variation to manufacturing authorisation	Manufacturer of medicinal products	63	61	55	55	56	53
	Control laboratory	4	3	5	4	2	3
	Blood centre	29	36	23	26	27	26
Application for revocation of manufacturing authorisation	Manufacturer of medicinal products	2	2	2	3	0	1
	Control laboratory	4	2	0	2	2	2
	Blood centre	5	5	0	0	1	1
Application for operating authorisation	Tissue centre	4	4	1	1	3	2
	Distribution of tissues and cells	0	0	0	0	1	0
	Diagnostic laboratory	0	0	0	0	0	0
Application for variation to operation	Tissue centre	28	26	41	37	40	39
	Donation centre	0	0	0	0	1	1
	Diagnostic laboratory	10	9	8	8	4	6
Application for revocation of operation	Tissue centre	1	1	2	2	1	1
	Donation centre	0	0	0	0	0	0
	Diagnostic laboratory	0	0	0	0	2	2
Total		**154**	**158**	**143**	**141**	**150**	**148**

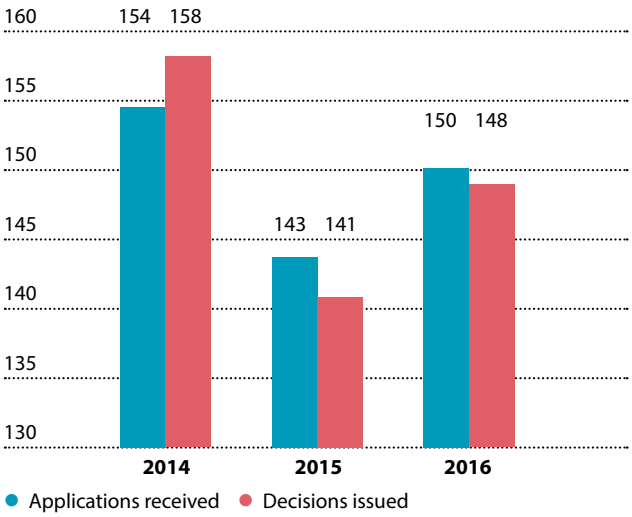
In 2017, the Institute carried out 292 inspections in total, of which 84 inspections were associated with the regulated area of tissues and cells. A comparison of the number of inspections and breaches of the Act on Pharmaceuticals, or of the Act on Human Tissues and Cells, where applicable, in 2014 to 2017 is provided in Table 18 and Charts 6 and 7.

An initial inspection was carried out in connection with an application for operating authorisation under Section 63, paragraph 4 of Act No. 378/2007 Coll. Follow-up inspections were carried out at the sites of manufacturers of medicinal products and active substances, in control laboratories or blood centres at intervals established by Decree No. 229/2008 Coll. and, for blood centres, pursuant to Decree No. 143/2008 Coll. or in abbreviated intervals on the basis of previous inspection rating which, in addition to the evaluation of the standard of good manufacturing practice (GMP) proper, contains also manufacture risk assessment and other criteria rating. Inspections related to a variation are carried out only if the conditions under which the activities were authorised have changed. Targeted inspections are conducted in order to review a certain section of activities (e.g. an inspection associated with a quality defect of a medicinal product).

Of the total number of 104 inspections at manufacturers of medicinal products and active substances, and in control laboratories, a breach of the Act on Pharmaceuticals was identified in 9 cases. The standard of GMP in blood centres was rated mostly as good; no breach of law was identified. The plan of follow-up inspections was complied with for all regulated entities and the inspection interval established by the Decree was observed.

Inspections in tissue centres, donation centres or diagnostic laboratories are conducted pursuant to Decree No. 422/2008 Coll., on detailed requirements for the safeguarding of the quality and safety of human tissues and cells intended for human use.

Chart 5 **Numbers of received and concluded applications**



Tab. 17 **Inspections conducted in 2017 and their outcomes**

	Number of inspections						Inspection rating		
	Total	**Initial**	**Follow-up**	**Targeted**	**Variation**	**Compliant**[1)]	**Non -compliant**	**Breach of law**	**Fine/ Order**
Manufacturers of medicinal products	**57**	5	43	1	8	48	0	8	2
Manufacturers of active substances	**20**	1	14	0	5	15	0	1	0
Control laboratories	**22**	1	18	1	2	19	0	0	0
Active substance importers	**5**	0	5	0	0	5	0	0	0
Blood centres	**57**	2	50	0	5	52	0	0	0
Blood banks	**22**	0	22	0	0	22	0	0	0
GCP inspections – Ethics Committees	**0**	0	0	0	0	0	0	0	0
GCP inspections – others	**25**	0	2	23	0	2	0	7	0
TC, DC, DL inspections	**84**	13	55	11	5	68	0	0	2

Explanatory notes: GCP – Good Clinical Practice; TC – tissue centre; DC – donation centre; DL – diagnostic laboratory; 1) – rated only in case of initial and follow-up inspections.

Tab. 18 **Inspections conducted in 2014–2017**

	2014		2015		2016		2017	
	No. of inspections	**Breaches of law**	**No. of inspections**	**Breaches of law**	**No. of inspections**	**Breaches of law**	**No. of inspections**	**Breaches of law**
Manufacturers of medicinal products	71	1	52	0	71	3	57	8
Manufacturers of active substances	27	0	15	0	18	2	20	1
Control laboratories	11	0	23	0	9	0	22	0
Active substance importers	-	-	-	-	4	0	5	0
Blood centres	46	0	47	0	47	0	57	0
Blood banks	11	0	17	0	22	0	22	0
GCP inspections + Ethics Committees	21	0	15	0	16	7	25	0
Tissue centres, donation centres, diagnostic laboratories	107	0	171	0	104	1	84	0
Total	**294**	**1**	**340**	**0**	**295**	**13**	**292**	**0**

Chart 6 **Number of manufacturers of medicinal products, active substances and control laboratories and an overview of conducted inspections**

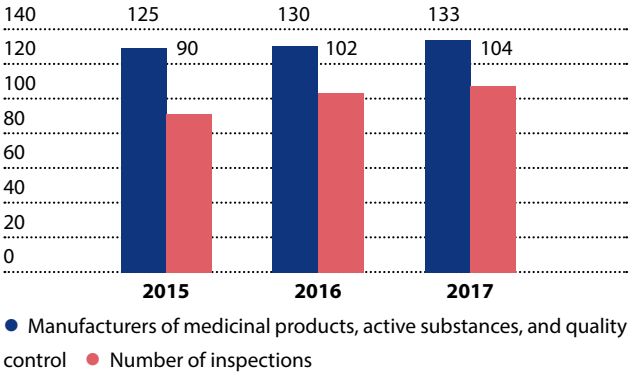
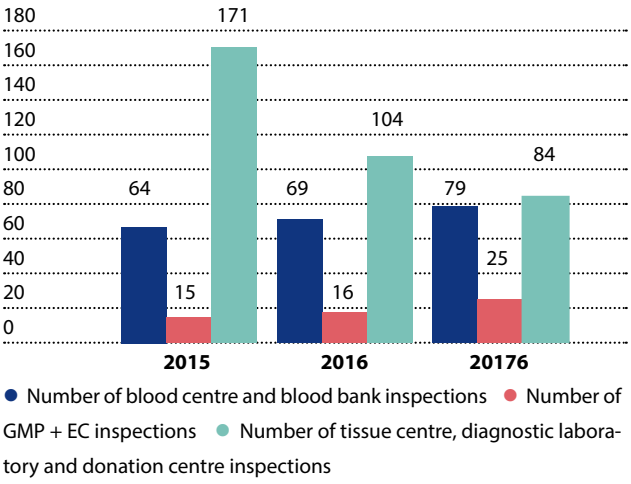


Chart 7 **Overview of inspections in the sphere of blood centres, GCP and HTC conducted in 2014–2017**



Haemovigilance

In 2017, 32 reports of suspected serious adverse reactions (hereinafter referred to as "SAR") experienced by donors of blood or blood components or recipients of transfusion products from 16 regulated entities (blood centres or blood banks) were received. Of this, 5 cases of SARs concerned donors of blood or blood components, 18 cases of SARs involved a post-transfusion reaction in TP recipients, 8 cases did not constitute a SAR, and 1 case has not been concluded to date. In 4 cases of SARs experienced by TP recipients serious consequences were suffered, in 1 case mild consequences were suffered, in 2 cases the TP recipient died without association with the transfusion, in case of the other SARs, full recovery followed. Furthermore, 34 reports of suspected serious adverse event (hereinafter referred to as "SAE") associated with blood drawing, examination, processing, storage, and distribution of TPs or starting materials for further production or the dispensing of TPs were received from 8 regulated entities. Of this number, 7 cases concerned dispensing of a product with an additionally identified defect; 4 cases a human error; 2 cases fall within the category of Others; and 19 cases did not concern a SAE; and 2 events have not been concluded to date. Each report which the Institute received was processed, evaluated, and entered in the database of SARs and SAEs and, concurrently, processed to be incorporated in the Annual SAE and SAR Report for the Czech Republic for the European Commission. Educational activities to raise the awareness of regulated entities regarding the importance of suspected SAR and SAE reporting continue to be carried out. In cooperation with the Transfusion Medicine Society, a document containing recommendations on how to evaluate and report adverse reactions was prepared (available from the Institute's website). Within the scope of its involvement in the European RAB system, the Institute in 2017 received 18 reports from 5 countries. Sixteen cases involved an epidemiological situation (12x associated with the occurrence of the West Nile virus; twice with the occurrence of malaria; and twice with the occurrence of the chikungunya disease) and 2 cases constituted a warning regarding the quality and safety of medical devices used by TP manufacturers.

Good Laboratory Practice (GLP)

In 2016, a total of 9 holders of Good Laboratory Practice Certificates issued by the Institute were listed, with prevailing scope of activities in toxicological studies; these are included in the National GLP Programme. In the same year, 5 follow-up inspections were completed.

Good Clinical Practice (GCP)

In the course of 2017, the total of 25 inspections of good clinical practice were conducted, of which 21 concerned a targeted inspection of a trial site (a GCP inspection at the investigator´s); 2 cases concerned an inspection to verify corrective and preventive action; one case concerned a systemic inspection, and one case concerned a systemic inspection based upon an application for a GCP certificate issuance.

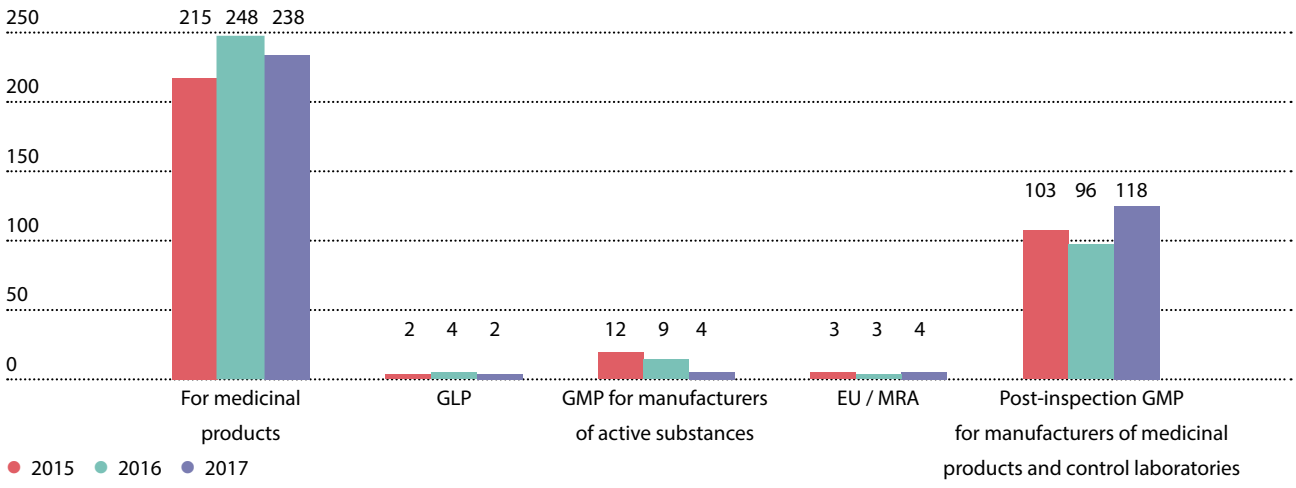
Actions and Penalties

In 2017, a breach of the Act on Pharmaceuticals was identified in 9 cases. Pursuant to the Act on Human Tissues and Cells, 2 penalties were imposed.

Certification

In total, 365 various certificates were issued. Post-inspection good manufacturing practice certificates are subsequently entered in the EudraGMP database kept by EMA. All of the certificates for medicinal products were issued within the prescribed 30-day timeline, and all good manufacturing practice certificates within the 90-day timeline.

Chart 8 **Issued certificates**



Assessment of GMP Compliance within the Scope of Marketing Authorisation Activities

A total of 1 190 cases were received (a 7.5% decrease compared to 2016), all of them were processed within the timelines.

Foreign Inspections

In 2017, 4 good manufacturing practice inspections at foreign entities in Turkey and in India were performed. On behalf of EMA, the GCP Department, in cooperation with inspectors from another EU Member State, completed 3 international inspections, and furthermore, one international observed inspection within the PIC/S-JVP programme took place.

Tab. 19 **Foreign inspections**

	2015	2016	2017
Number of inspections	7	3	8
Certificate issuance	3	3	3
Issued non-compliance	0	1	0

4.9 Quality Defects of Pharmaceuticals

Between 2009 and 2013, there was a rapid increase in the number of reports in the area of quality defects of pharmaceuticals. A relatively significant increase in the number of reports compared to 2014 and 2015 can be seen also in 2016 and 2017. To date, the number of received reports in 2017 was the highest from the establishment of the Quality Defects Department (Tab. 20 and Chart 9 refer).

In 2017, the reports concerned not only authorised medicinal products and magistral formulas, but also starting materials for the preparation of medicinal products in pharmacies as well as non-authorised and investigational medicinal products. Through the Rapid Alert System of the EU, MRA, and PIC/S countries, the Institute received and evaluated the total of 76 reports on quality defects of pharmaceuticals.

Compared to previous years, in 2015, 2016 as well as in 2017, the Institute saw a marked increase in the number of reports regarding the occurrence of counterfeit medicinal products in the legal distribution chain or their theft (Chart 9 refers). In 2017, the Quality Defects Department addressed 45 such cases in total, of which 14 cases concerned theft of medicinal products from the legal distribution chain.

Mutual exchange of information with the Slovak State Institute for Drug Control (ŠÚKL) in Bratislava has continued and the Quality Defects Department collaborated with ŠÚKL in Bratislava on several occasions in 2017.

Reports received from abroad also included reports on noncompliance of the manufacturing site of a medicinal product or an active substance with the Good Manufacturing Practice principles. The Quality Defects Department received a total of 54 such reports in 2017.

Within the scope of addressing quality defects, effective actions have been taken to reduce the impact of the quality defects of pharmaceuticals upon patient health. With reference to the new power of the Institute, since 1 April 2017,pursuant to Section 13, paragraph 2(n) and Section 23, paragraph 2(b) of amended Act No 378/2007 Coll., on Pharmaceuticals and on Amendments to Some Related Acts (Act on Pharmaceuticals), as amended, the total of 20 administrative procedures regarding the possibility to distribute, dispense, place on the market, or use in the provision of healthcare services pharmaceuticals with a quality defect not constituting a jeopardy to the life or health of people were commenced. Table 21 gives an overview of actions adopted as part of addressing the quality defects in individual medicinal products (related to the Institute codes) in 2017. In all cases, the actions in respect of the market, however, were implemented by the marketing authorisation holders or operators themselves, with the Institute solely monitoring or adjusting those measures.

The Quality Defects Department, moreover, monitored recalls of medicinal products due to reasons related to marketing authorisation (such as a shortened shelf-life, changed method of dispensing, etc.). For these reasons, in 2017, 21 medicinal products (in SÚKL codes) were recalled in total.

Tab. 20 **Number of reports received in 2017**

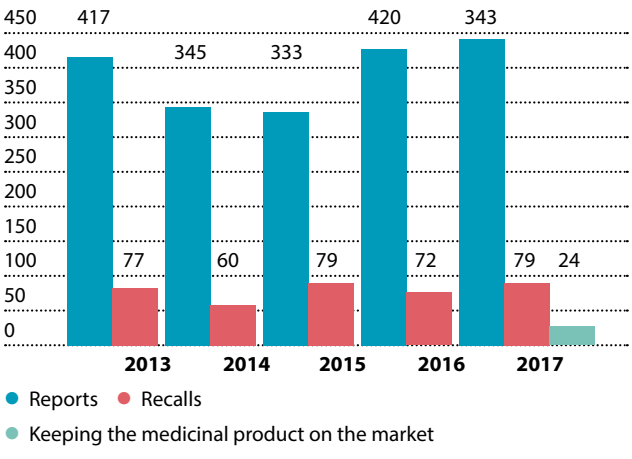
Quality Defects					
Reports received in total	417	345	333	420	443
Reports from the Czech Republic	210	181	181	243	277
Reports from abroad	207	164	152	177	166
Resulted in recall*	77	60	79	72	79
Administrative procedure (newly from 04/2017)	-	-	-	-	20
Issued RWs	1	6	16	18	19
Issued RAs	3	6	11	17	22

*RW – Rapid Warning, RA – Rapid Alert *in SÚKL codes*

Tab. 21 **Actions taken in 2017 (in SÚKL codes)**

Actions taken	**Number**
Recalls from distributor level	0
Recalls from healthcare facility level	71
Recalls from patient level	8
Suspended distribution, dispensing and therapeutic use	8
Released distribution, dispensing, and therapeutic use	3
Permitted distribution, dispensing, marketing, and use in the provision of healthcare services through an administrative procedure	24

Chart 9 **Number of reports and recalls of medicinal products in 2013–2017**



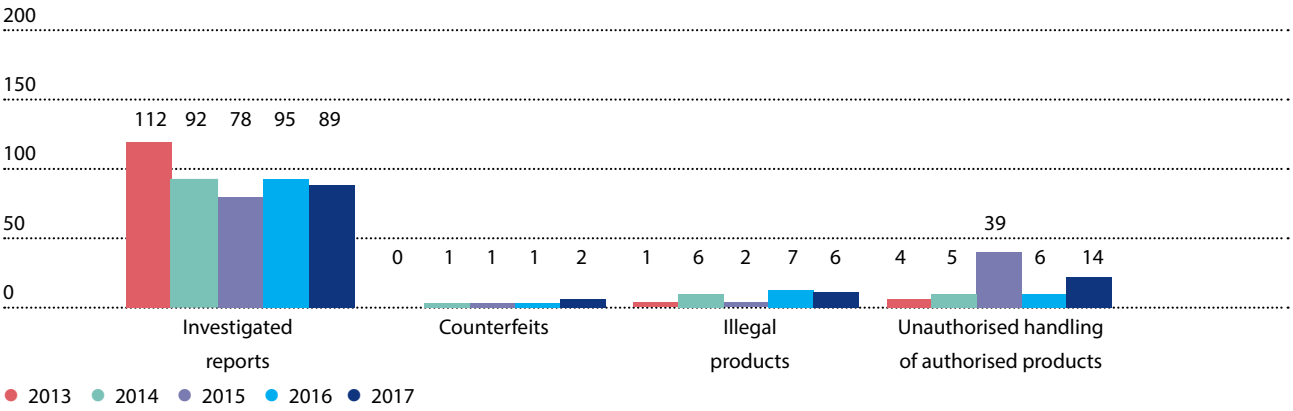
As in previous years, the Institute focused upon surveillance over compliance with the obligation of marketing authorisation holders stipulated under the provisions of Section 33, paragraph 2 of Act No. 378/2007 Coll., on Pharmaceuticals and on Amendments to Some Related Acts (Act on Pharmaceuticals), as amended. The Institute addressed 11 such reports in total, of which 2 were forwarded for the issuance of an order for breach of the aforementioned obligation. Compared to previous years, the number of reports has been dropping, as marketing authorisation holders have adapted to the fulfilment of this obligation during the past years.

4.10 Enforcement

In 2017, active surveillance in the area of illegal handling of medicinal products focused, in particular, upon the identification, investigation, and penalisation of cases of distribution and sales by unauthorised persons and upon monitoring of the internet environment, where illegal sale of medicinal products is being carried out.

In the sphere of enforcement, the Institute closely cooperates with the Czech Customs Administration, Czech Police, Czech Trade Inspection, and the Czech Agriculture and Food Inspection Authority (CAFIA). Cooperation has been extended also to foreign partners, not only in the exchange of information, but also in the investigation of specific cases with potentially international impact.

Chart 10 **Control activities in for the period of 2013–2017**



In 2017, a total of 89 reports (either the Institute's own or received reports) were investigated. In 2017, the Institute much focused upon the monitoring and detection of illegal offers of medicinal products in the internet environment and checked 722 websites and executed 21 control purchases, in which 5 cases of handling of unauthorised medicinal products, 14 cases of unauthorised handling of authorised medicinal products, and 2 cases of counterfeit medicinal products were identified.

In 2017, the Institute prepared a total of 143 opinions for the customs authorities for the purposes of release/non-release of medicinal products imported from third countries. These concerned medicinal products that were authorised neither in the Czech Republic, nor in any other EU Member State, were not properly labelled and their import was not performed in compliance with the applicable legislation.

Graf 22 **Results of investigated cases**

Cases concluded by:	**2013**	**2014**	**2015**	**2016**	**2017**
Administrative procedure with proposed penalty imposition	1	5	2	6	4
Reports of crime	3	4	2	2	8
Cases forwarded to other authorities (CAFIA, etc.)	3	1	1	1	1

4.11 Surveillance in the Area of Regulation of Advertising for Medicinal Products

In 2017, the Institute investigated a total of 151 reports of suspected breaches of Act No. 40/1995 Coll., on Advertising Regulation, as amended (hereinafter referred to as the "Act on Advertising Regulation"). Compared to 2016, the Institute received 1 more new report in 2017 (132 reports). In 2017, 17 administrative procedures were completed which resulted in the imposition of 20 fines in the aggregate amount of 4 255 000 CZK.

The subject of investigation into advertising was printed advertising matter (50%), websites (30%), sponsorship (3%), and promotional samples (17%).

Advertising for prescription-only medicines accounted for 49% of the investigated cases, advertising for over-the-counter medicines represented 51% of cases. Pharmaceutical companies or their legal representatives filed 9% of reports on suspected breaches of law, 6% of reports were filed anonymously, 6% were lodged by private individuals, 1% by state administration bodies, and 78% by the employees of the Institute.

Tab. 23 **Overview of investigated reports of suspected breaches of the Act on Advertising Regulation**

	Reports brought forward from 2016	Newly received reports in 2017	Total
Number of reports	19	132	151
Investigation completed	19	126	145
Forwarded for commencement of administrative procedure	1	5	6
Completed administrative procedures	0	1	1
No. of finally imposed fines	0	1	1

Chart 11 **Overview of investigated reports of suspected breaches of the Act on Advertising Regulation for the period of 2013–2017 (in %)**

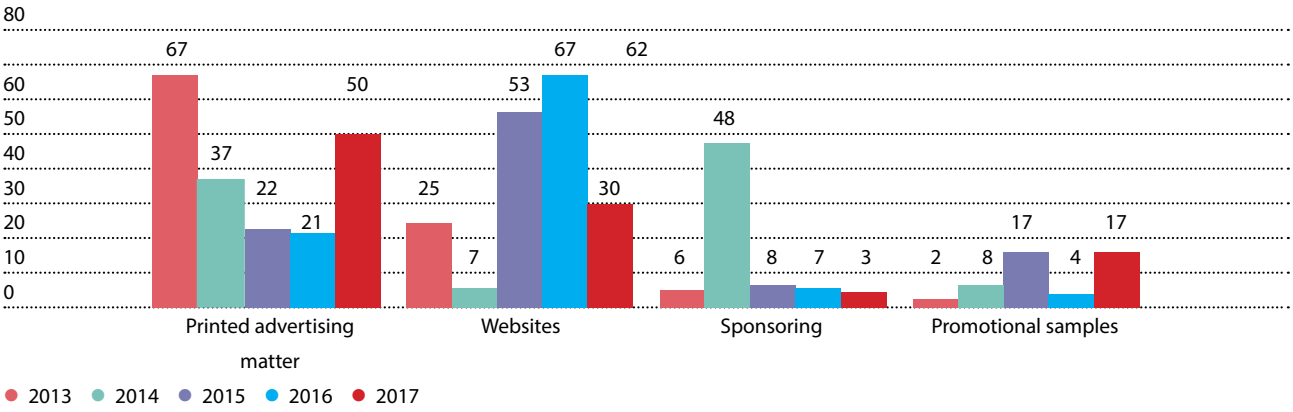
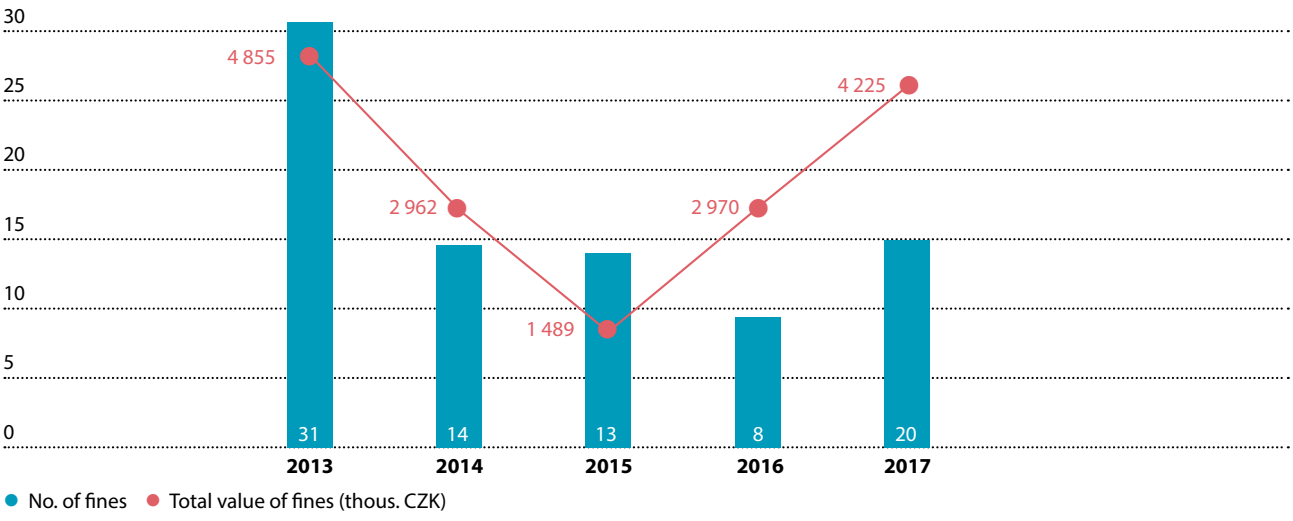


Chart 12 **Overview of fines imposed for breaches of the Act on Advertising Regulation in the period of 2013–2017**



Upon request, the Institute issued/provided 38 expert opinions/ consultations on the issue of proposed advertising for medicinal products for human use.

The inspectors of the Department of Surveillance over Advertising conducted 25 inspections of compliance with the Act on Advertising Regulation and the Act on Pharmaceuticals.

Surveillance in the Area of Decision-making about the Nature of the Product

In 2017, the Institute commenced investigation into 71 cases of various products, most often dietary supplements and cosmetic products, for suspected classification as a medicinal product. In 14 cases, an administrative procedure regarding the nature of the product was initiated ex officio or upon request. In 2017, the Institute reclassified 8 products in total to the group of medicinal products.

4.12 Standardisation and Pharmacopoeial Activities

New Czech Pharmacopoeia (hereinafter referred to as CP 2017), which was being amended by the employees of the Pharmacopoeia and Pharmaceuticals Standardisation Department in cooperation with the Grada publishing house in the first half of 2017, was, as opposed to expectations, published in four volumes binding as of 1 December 2017.

In the European Part, this edition contains translations of the texts of the 9th edition of the European Pharmacopoeia (hereinafter referred to as the Ph. Eur.), which includes the total of 2 329 monographs and 358 general texts, of which 19 are new and revised general texts and 866 new and revised active substance, excipient or medicinal product monographs.

The employees of the Pharmacopoeia and Pharmaceuticals Standardisation Department, moreover, prepared the manuscript of the European part of the Czech Pharmacopoeia 2017 – Supplement 2018 (hereinafter referred to as "CP 2017 – Suppl. 2018"), which contains the translations of texts of five supplements (9.1 to 9.5) of the 9th edition of Ph. Eur.

In total, this concerns 418 texts, of which the general part contains 49 general texts (4 new, 45 revised), 9 revised general articles concerning pharmaceuticals forms, and six revised general articles, incl. article Producta fermentationis (1468), which was implemented by the AP-CPH (18)1 resolution as of 1 April 2018 by being made binding through a rapid procedure. Concurrently, its text was published on the Institute's website. The special part contains texts regarding vaccines for human use (6 revised monographs) and for veterinary use (also six revised monographs), radiopharmaceuticals (14 monographs, of which 4 are new ones), herbal drugs (55 monographs, of which 14 are new ones), mostly from the area of Traditional Chinese Medicine, homeopathic products (14 monographs, of which 4 are new ones), and surgical suture fibres (4 revised monographs). The number of texts of special revised or amended chemical monographs on active substances and/or excipients amounts to 255; 20 monographs are new.

Tab. 24 **Number of texts in the European Part of CP 2017 – Suppl. 2018**

European Part	General part	Special part	Total
New	4	42	46
Revised	60	312	372
Total	64	354	418

In coordination with the Pharmacopoeia and Pharmaceuticals Standardisation Department, also other experts of the Institute contributed to the preparation of CP 2017 - Suppl. 2018.

Cooperation with the European Pharmacopoeia Commission (hereinafter referred to as "EPC") in the preparation of other Ph. Eur. Supplements and in the preparation of their Czech translations and inclusion in the database of standard terms of pharmaceuticals forms, methods of administration, and packaging continued.

The employees of the Pharmacopoeia and Pharmaceuticals Standardisation Department informed about the binding nature of individual Ph. Eur. editions in the Institute's information media.

An external workshop on the changes and news in CP 2017 was organised, and it also recalled the 20th anniversary of harmonisation between the Czech and European Pharmacopoeia.

The employees of the Department regularly attended the EPC meetings and meetings of secretariats of national pharmacopoeial commissions.

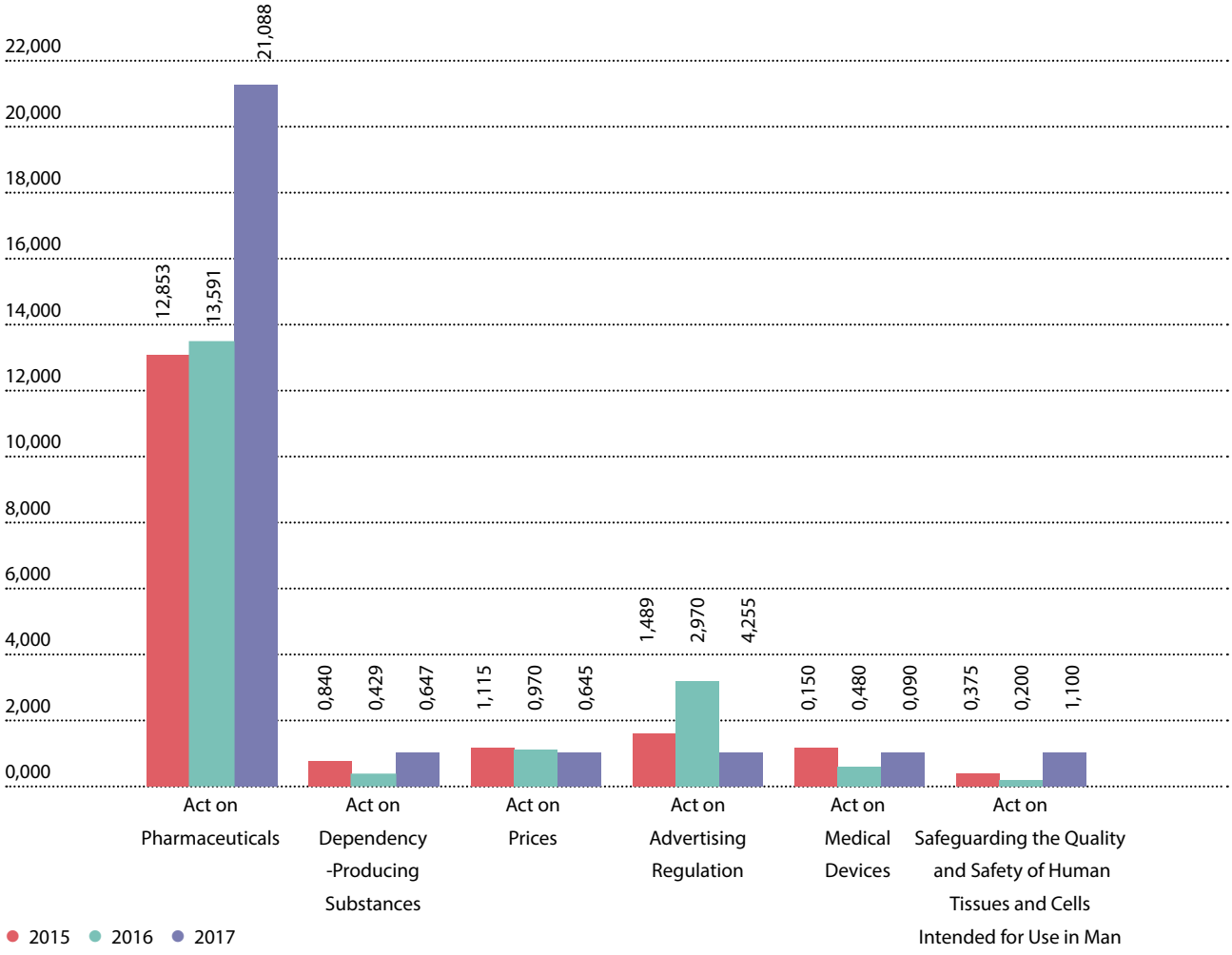
Standardisation

In the sphere of standardisation, tables providing an overview of published, announced or revoked Czech technical standards for medical devices were regularly, on a monthly basis, published on the Institute´s website. In 2017, a representative from the Vigilance Department was actively involved in the work of the TNK 81 Technical Standardisation Commission for Medical Devices..

4.13 Imposed Penalties

Based on its ex-officio findings and breaches of legislative requirements identified in the course of inspections in the area of medicinal products and human tissues and cells, or in the surveillance of advertising and based on reports, the Institute initiates administrative procedures on administrative offences within which penalties referred to in the applicable laws are imposed according to the severity of the identified breach. Since August 2011, the Institute has been availing also of the option to impose penalties on the basis of so called administrative order, under the Administrative Code. The Institute observed this practice also in 2017. Since January 2015, the Institute has been imposing also penalties for committing an administrative offence referred to by the Act on Public Health Insurance regarding the provision of unauthorised bonuses in the dispensing of prescription-only medicinal products. In 2017, the Institute continued also the imposition of penalties in the form of so called summary fines for committed administrative offences governed by several laws within the powers of the Institute in the sphere of medicinal products. As of 1 July 2017, the Institute has been applying Act No 250/2016 Coll., on Liability for Offences and Procedures Pertaining Thereto, in its practice of administrative penalisation.

Chart 13 **Imposed penalties which became final in 2015–2017 (in mil. CZK)**



- *Act No. 378/2007 Coll., on Pharmaceuticals and on Amendment to Some Related Acts.*
- *Act No. 167/1998 Coll., on Dependency-Producing Substances and on Amendment to Some Other Acts.*
- *Act No. 526/1990 Coll., on Prices.*
- *Act No. 40/1995 Coll. on Advertising Regulation and on Amendment to Act No 468/2004 Coll., on the Operation of Radio and Television Broadcasting, as amended.*
- *Act No. 268/2014 Coll., on Medical Devices and on Amendment to Act No 634/2004 Coll., on Administrative Fees, as amended.*
- *Act No. 296/2008 Coll., on Safeguarding the Quality and Safety of Human Tissues and Cells Intended for Use in Man and on Amendment to Related Acts.*

PRICE AND REIMBURSEMENT REGULATION BRANCH

In compliance with the provisions of the Act on Public Health Insurance, the Price and Reimbursement Regulation Branch decides on maximum prices and reimbursement of medicinal products and foods for special medical purposes. For proprietary medicinal products, this is done in administrative procedures that fully comply with the transparent procedures set forth by the European legislation. Administrative procedures are conducted in cases specified by law ex officio (mainly so called in-depth and abbreviated revisions) or upon request of persons authorised by law (marketing authorisation holders in the case of authorised medicinal products; importers or domestic manufacturers of medicinal products if the medicinal product imported or produced thereby is used in the territory of the Czech Republic within a specific therapeutic programme or other persons applying for a specific therapeutic programme; importers or domestic manufacturers of foods for special medical purposes; health insurance companies). A request for the initiation of an administrative procedure ex officio may be submitted by any person.

4.14 Determination of Prices and Reimbursements

In the course of 2017, the Branch continued in the initiation of in-depth reimbursement revisions in accordance with the schedule. For 2017, the initiation of 145 in-depth revisions was scheduled, of which 133 administrative procedures (1 685 SÚKL codes) were actually commenced. The difference in the number of scheduled and initiated administrative procedures reflects process and organisational & technical facts at the time of in-depth revision initiation (pending previous in-depth revision, termination of marketing authorisation or cancellation of reimbursement of medicinal products containing a particular active substance, etc.) – Table 25 refers.

Maximum Ex-factory Prices

A major legislative change in the area of price regulation was brought by the Price Regulation of the Ministry of Health of the Czech Republic 1/2013/FAR on the regulation of prices of medicinal products and foods for special medical purposes (hereinafter referred to as the "Price Regulation") and the Price Decision of the Ministry of Health of the Czech Republic 1/13-FAR laying down a list of ATC groups that are not subject to price regulation by setting a maximum price in the specified pharmaceutical form (hereinafter referred to as the "Price Decision"); both regulations amended the method of price regulation with effect from 1 January 2013 and remained unchanged in 2017.

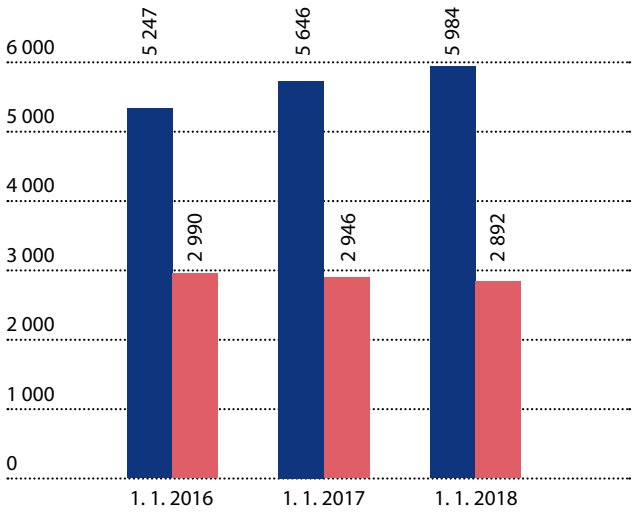
In 2017, 94 administrative procedures regarding the maximum ex-factory price change were commenced (compared to 92 administrative procedures in 2016); applications filed by health insurance companies slightly prevailed (52 applications filed by health insurance companies and 42 applications filed by marketing authorisation holders).

With a view to the stability of the price regulation, the share of medicinal products regulated by the profit margin only remained almost unchanged compared to 2016. A slight increase in the number of medicinal products regulated by maximum price and profit margin was caused less by the entry of new medicinal products and more by the extension of presentations of existing medicinal products and the entry of products of competing manufacturers in the reimbursement system (Chart 13).

Tab. 25 **Overview of administrative procedures in 2017**

Applications for determination of maximum ex-factory price	**No. of SÚKL codes**
Initiated	14
Decided	9
Appeal procedure pending	0
Became final	8
Applications for maximum ex-factory price change	
Initiated	173
Decided	131
Appeal procedure pending	9
Became final	121
Applications for maximum ex-factory price reduction – abbreviated procedures	
Initiated	0
Decided	0
Appeal procedure pending	0
Became final	0
Applications for maximum ex-factory price cancellation	
Initiated	8
Decided	8
Appeal procedure pending	8
Became final	8

Chart 14 **Structure of reimbursed products by the type of price regulation (no. of codes of medicinal products/foods for special medical purposes)**



- Regulation through maximum price and profit margin.
- Regulation through profit margin only.

With a view to the structure of medicinal products (tab. 26), it may be stated that the numbers of medicinal products in the below listed zones by maximum price mostly increased and did so continuously in the course of the entire year. The most pronounced increase was seen in the above 300 CZK to 1 000 CZK zone. A mild decrease in the number of medicinal products occurred only in the first four zones (up to 200 CZK).

Tab. 26 **Overview of the number of codes of medicinal products/foods for special medical purposes in the maximum price zones as per the List of Prices and Reimbursements (SCAU) by month**

Price regulation zone	**01**	**02**	**03**	**04**	**05**	**06**	**07**	**08**	**09**	**10**	**11**	**12**
Up to 20 CZK inclusive	20	20	20	19	19	19	19	19	18	18	18	18
Over 20 CZK – 50 CZK inclusive	370	369	362	361	356	354	357	361	359	358	357	355
Over 50 CZK – 100 CZK inclusive	701	705	699	695	689	690	695	703	694	685	684	689
Over 100 CZK – 200 CZK inclusive	905	897	909	901	893	891	900	902	896	886	891	892
Over 200 CZK – 300 CZK inclusive	501	502	505	507	509	515	518	523	518	515	514	525
Over 300 CZK – 500 CZK inclusive	540	543	547	554	553	559	571	579	585	591	593	599
Over 500 CZK – 1 000 CZK inclusive	698	705	708	722	729	739	755	763	766	774	780	791
Over 1 000 CZK – 2 000 CZK inclusive	648	652	652	656	658	664	669	683	683	681	682	684
Over 2 000 CZK – 3 000 CZK inclusive	245	247	250	252	251	257	257	258	258	259	261	267
Over 3 000 CZK – 5 000 CZK inclusive	317	319	319	320	323	322	324	327	332	335	337	346
Over 5 000 CZK – 10 000 CZK inclusive	258	259	258	261	262	262	268	274	273	273	275	280
Over 10 000 CZK – 20 000 CZK inclusive	199	202	202	203	202	204	205	204	208	210	211	218
Over 20 000 CZK – 30 000 CZK inclusive	80	78	82	84	85	88	89	89	89	90	91	92
Over 30 000 CZK – 50 000 CZK inclusive	66	66	66	66	67	66	68	68	69	70	71	71
Over 50 000 CZK – 100 000 CZK inclusive	54	54	56	57	58	61	61	60	62	63	62	65
Over 100 000 CZK	44	42	42	41	41	39	39	39	39	39	42	45
Number of codes	**5 646**	**5 660**	**5 677**	**5 699**	**5 695**	**5 730**	**5 795**	**5 852**	**5 849**	**5 847**	**5 869**	**5 937**

Development of Average End-User Prices

In 2017, there was no change to the profit margins or to the VAT, which for medicinal products was 10% in 2017. In respect of medicinal products regulated by the determined maximum price (maximum price determined by an administrative procedure and profit margin as per the Price Regulation), the average end-user price increased by 5.5%. The average price increase was not caused by the growth of unit prices of medicinal products compared to the previous period, but was influenced particularly by an increase in the deliveries of relatively expensive medicinal products (expensive care increase). In respect of medicinal products regulated by notified price and profit margin (as per the Price Regulation and the Price Decision), the average end-user price dropped by 0.7%. The situation in ex-factory price levels (ex. profit margin and VAT) focusing upon a more detailed comparison of the latest quarters is provided below.

Chart 15 **Prices of pharmaceuticals regulated by maximum price – comparison of average prices in Q4 2016 and Q4 2017 by price zones (%)**

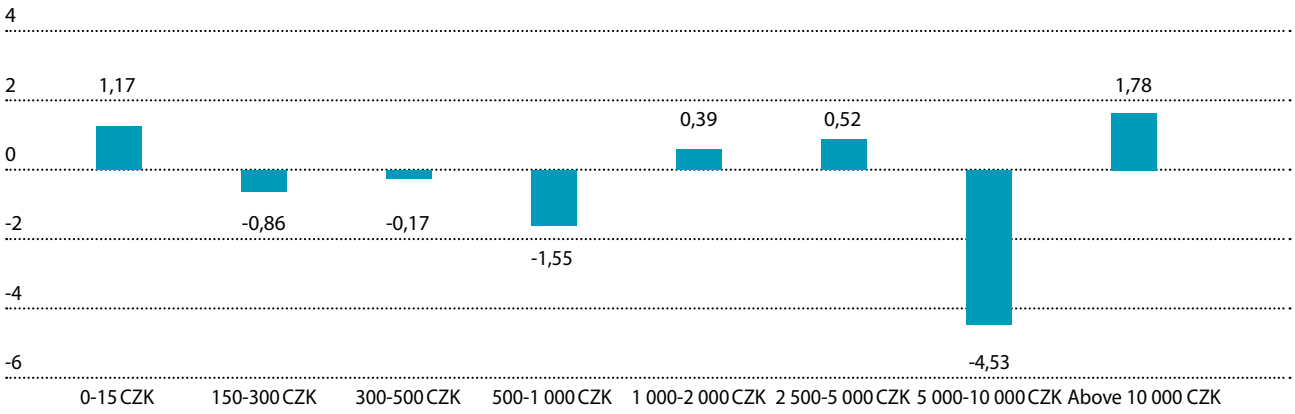
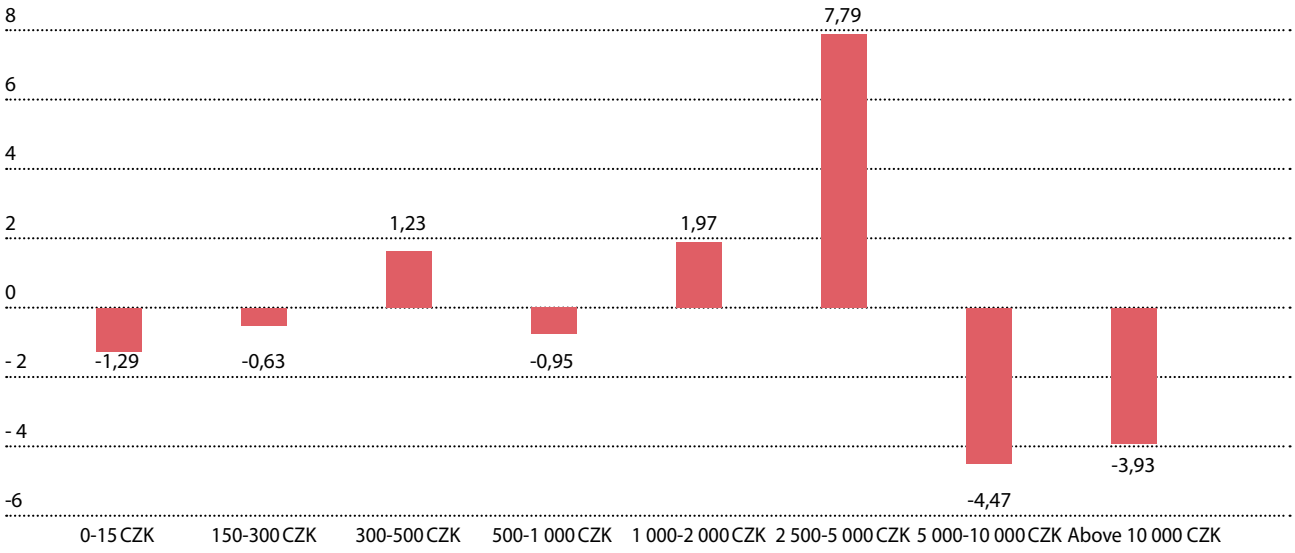


Chart 16 **Prices of pharmaceuticals regulated by profit margin – comparison of average prices in Q4 2016 and Q4 2017 by price zones (%)**



Overview of the Most Often Distributed Medicinal Products for Which Maximum Price Was Changed

On the basis of the periodical distributor reports on executed supplies of medicinal products, an overview of ten most often distributed medicinal products was compiled, along with an overview of ten products with the highest financial volume by the ex-factory price, for which the maximum ex-factory price was changed.

In 2017, the maximum prices both increased and decreased in the group of the most distributed medicinal products in respect of which the maximum price was changed. Nevertheless, where the price increased, this happened in the case of medicinal products which may be classified as relatively cheap ones. Excessive price increase was performed in compliance with the public interest with a view to maintaining availability of the product on the market (e.g. SOLU-MEDROL). In the case of relatively expensive medicinal products (SYMBICORT, TOUJEO), the price, on the contrary, was decreased (tab. 27).

Tab. 27 **Ten most often distributed medicinal products by number of packages reported in compliance with DIS-13 for which the maximum price was changed**

Code	ATC	Name	Name supplement	No. of packages	Original maximum price (CZK)	New maximum price (CZK)	Change of maximum price in %
0215978	A12CC30	MAGNOSOLV	365MG POR GRA SOL SCC 30	750 979	103,93	107,57	+ 3,5
0009709	H02AB04	SOLU-MEDROL	40MG/ML INJ PSO LQF 40MG+1ML	496 774	32,84	76,56	+ 133,1
0076064	B03BB01	ACIDUM FOLICUM LÉČIVA LÉČIVA	10MG TBL OBD 30	484 782	62,97	74,83	+ 18,8
0001940	N05BA04	OXAZEPAM LÉČIVA	10MG TBL NOB 20	477 787	23,82	31,06	+ 30,4
0014821	M01AX25	CONDROSULF	800MG TBL FLM 30	460 001	255,42	258,42	+ 1,2
0083318	C01AA05	DIGOXIN 0,125 LÉČIVA	0,125MG TBL NOB 30	445 659	20,81	28,35	+ 36,2
0017189	A12BA01	KALIUM CHLORATUM BIOMEDICA	500MG TBL ENT 100	371 494	36,42	65,62	+ 80,2
0180087	R03AK07	SYMBICORT TURBUHALER 200 MIKROGRAMŮ / 6 MIKROGRAMŮ / INHALACE	160MCG/4,5MCG INH PLV 1X120DÁV	363 356	780,95	647,25	-17,12
0199466	N05AD03	BURONIL	25MG TBL FLM 50	305 195	81,44	100,28	+ 23,1

Medicinal products with the highest financial volume are distributed across a broad range of price zones. For all of the aforementioned medicinal products, however, the maximum price was reduced (tab. 28)

Tab. 28 **Ten most often distributed medicinal products by financial volume in end-user prices reported in compliance with DIS-13 for which the maximum price was changed**

Code	ATC	Name	Name supplement	Financial volume in end-user price	Original maximum price (CZK)	New maximum price (CZK)	Change of maximum price in %
0185368	L01XC03	HERCEPTIN	600MG INJ SOL 1	668 440 948	39 260,69	37 574,31	-4,3
0194345	L04AB02	REMSIMA	100MG INF PLV CSL 1	409 927 948	8 099,32	7 704,13	-4,9
0180087	R03AK07	SYMBICORT TURBUHALER 200 MIKROGRAMŮ / 6 MIKROGRAMŮ / INHALACE	160MCG/4,5MCG INH PLV 1X120DÁ	389 359 640	780,95	647,25	-17,1
0210402	A10AE04	TOUJEO	300U/ML INJ SOL 3X1,5ML	351 443 461	1 039,47	914,57	-12,0
0028028	L01XE01	GLIVEC	400MG TBL FLM 30	297 301 450	53 221,71	48 204,09	-9,4
0194769	N07XX09	TECFIDERA	240MG CPS ETD 56	270 390 062	27 329,38	23 880,28	-12,6
0029740	A10BD08	EUCREAS	50MG/1000MG TBL FLM 60 I	250 186 301	897,88	709,97	-20,9
0184377	R03AK08	COMBAIR	100MCG/6MCG /DÁV INH SOL PSS 180DÁV	221 249 537	1 012,91	940,00	-7,2
0168451	A10BH05	TRAJENTA	5MG TBL FLM 90X1	203 126 675	2 903,15	2 689,55	-7,4
0027192	L01XE04	SUTENT	50MG CPS DUR 30	189 598 571	113 482,44	107 642,21	-5,1

Amounts and Conditions of Reimbursements from Health Insurance

Since the end of 2011, parties to procedure have had the option to submit an application in a new type of administrative procedure to determine the maximum price and the amounts and conditions of reimbursement of a similar product which ensures that the maximum price and the amount and conditions of reimbursement are determined within 30 days of submission of the application if all statutory conditions are met. This type of administrative procedure is much availed of, particularly for generic products.

The determination, change or cancellation of the amounts and conditions of reimbursement can be also requested by the parties to procedure defined by the Act on Public Health Insurance. In the event of such procedure, the applicant is fully in charge of its application and may deal with it in accordance with legal regulations (tab. 29).

Tab. 29 **Overview of administrative procedures in 2017**

Applications for determination or change of the amount and conditions of reimbursement	**No. of SÚKL codes**
Initiated	865
Decided	759
Appeal procedure pending	19
Became final	722
Applications for determination or change of maximum prices and the amount and conditions of reimbursement	
Initiated	193
Decided	96
Appeal procedure pending	3
Became final	57
Applications for reimbursement cancellation	
Initiated	61
Decided	43
Appeal procedure pending	0
Became final	41
Applications for maximum price and reimbursement cancellation	
Initiated	46
Decided	35
Appeal procedure pending	0
Became final	35
Procedures initiated ex officio	
Initiated	1 853
Decided	498
Appeal procedure pending	64
Became final	420
Procedures on similar products	
Initiated	430
Decided	415
Appeal procedure pending	0
Became final	380

In 2017, 21 applications for determination of reimbursement for highly innovative products were filed.

Pursuant to the provisions of Section 39l of the Act on Public Health Insurance, the Institute is required, among other things, to assess the amount of the basic reimbursement, the consistency of the amounts of reimbursements for all principally therapeutically interchangeable medicinal products with the basic reimbursement, the uniformity and effectiveness of the determined conditions of reimbursement, and compliance of the determined amounts and conditions of reimbursement with this Act, specifically meeting the expected results and reasons for pharmacotherapy, the effectiveness of the establishment of reference groups, the amount of basic reimbursement, conditions of reimbursement, assessment of the clinical & cost effectiveness and comparison with the original goals of pharmacotherapy. This process takes place within so-called in-depth revision of the reimbursement system. The Institute initiates also other types of administrative procedures ex officio, such as abbreviated revisions or individual administrative procedures to change or cancel the amounts and conditions of reimbursement.

In 2017, savings of public health insurance funds were generated particularly from abbreviated revisions initiated usually upon request of health insurance companies. The total savings arising from abbreviated revisions completed in 2017 is estimated at 1 111 111 005 CZK.

Tab. 30 **Overview of final decisions on the revision of reimbursements and the impact on public health insurance funds**

Effective date	**No. of SÚKL codes**	**No of administrative procedures**	**Impact on health insurance funds**
01/2017	361	17	215 707 672 CZK
02/2017	336	25	315 741 411 CZK
03/2017	790	23	354 584 894 CZK
04/2017	214	23	85 671 028 CZK
05/2017	196	21	177 436 257 CZK
06/2017	570	26	334 644 361 CZK
07/2017	48	9	-18 155 353 CZK
08/2017	411	19	214 866 488 CZK
09/2017	77	13	165 061 868 CZK
10/2017	28	8	-1 901 961 CZK
11/2017	215	25	83 054 339 CZK
12/2017	212	21	136 249 894 CZK

Note: Positive figures represent savings from health insurance, negative figures an increased impact upon the budget.

Tab. 31 **Overview of the number of codes of medicinal products/foods for special medical purposes in reimbursement price zones according to the List of Prices and Reimbursements (SCAU) by month**

Price zones	01	02	03	04	05	06	07	08	09	10	11	12
Up to 20 CZK inclusive	178	178	177	177	200	193	192	202	203	200	197	197
More than 20 CZK – 50 CZK inclusive	824	815	845	843	892	891	895	889	884	872	862	860
Over 50 CZK – 100 CZK inclusive	1 255	1 235	1 237	1 233	1 223	1 166	1 170	1 213	1 211	1 204	1 207	1 208
Over 100 CZK – 200 CZK inclusive	1 481	1 478	1 429	1 420	1 360	1 403	1 416	1 422	1 416	1 404	1 403	1 414
Over 200 CZK – 300 CZK inclusive	681	681	696	714	717	741	743	725	726	727	739	745
Over 300 CZK – 500 CZK inclusive	703	705	711	711	716	731	743	728	726	723	747	762
Over 500 CZK – 1 000 CZK inclusive	1 066	1 058	1 063	1 081	1 051	1 068	1 093	1 107	1 101	1 104	1 086	1 103
Over 1 000 CZK – 2 000 CZK inclusive	913	919	911	912	913	911	919	927	917	923	926	942
Over 2 000 CZK – 3 000 CZK inclusive	304	312	314	325	328	330	327	334	331	326	330	333
Over 3 000 CZK – 5 000 CZK inclusive	337	334	333	324	324	333	326	330	333	337	332	342
Over 5 000 CZK – 10 000 CZK inclusive	343	346	345	346	348	345	366	367	359	361	365	371
Over 10 000 CZK – 20 000 CZK inclusive	233	232	232	232	232	229	223	225	228	231	233	237
Over 20 000 CZK – 30 000 CZK inclusive	87	87	91	96	96	110	104	102	103	105	106	108
Over 30 000 CZK – 50 000 CZK inclusive	72	72	73	70	71	59	62	62	61	62	63	62
Over 50 000 CZK – 100 000 CZK inclusive	56	55	56	57	58	61	60	60	62	63	62	65
Over 100 000 CZK	59	58	58	57	57	55	56	56	58	58	60	64
Number of codes	**8 592**	**8 565**	**8 571**	**8 598**	**8 586**	**8 626**	**8 695**	**8 749**	**8 719**	**8 700**	**8 718**	**8 813**

Overview of the Most Often Distributed Medicinal Products for Which Reimbursement from Health Insurance Was Changed

The overview clearly indicates that in the group of relatively expensive medicinal products with the highest volume of reimbursement from health insurance, there was a significant decrease in the reimbursement for individual packages of medicinal products. The highest reduction associated with the conduct of an abbreviated revision was seen in medicinal product ADVAGRAF (tab. 32).

Tab. 32 **Ten most often distributed medicinal products by financial volume in end-user prices reported in compliance with DIS-13, for which reimbursement was changed**

Code	ATC	Name	Name supplement	Financial volume in end-user prices	Original reimbursement (CZK)	New reimbursement (CZK)	Change in reimbursement In %
0210773	L01XC17	OPDIVO	10MG/ML INF CNC SOL 1X10ML	210 319 250	40 765,62	32 981,00	-19,1
0026794	A10AB05	NOVORAPID FLEXPEN	100U/ML INJ SOL 5X3ML	207 756 133	896,08	830,09	-7,4
0194246	L02BB04	XTANDI	40MG CPS MOL 112	206 538 604	91 923,84	77 944,64	-15,2
0028740	A10BH01	JANUVIA	100MG TBL FLM 28	205 320 008	1 062,21	953,48	-10,2
0168451	A10BH05	TRAJENTA	5MG TBL FLM 90X1	203 126 675	3 414,26	3 064,74	-10,2
0167653	M05BX04	PROLIA	60MG INJ SOL 1X1ML I	196 850 597	5 899,25	5 497,17	-6,8
0210118	J05AP07	DAKLINZA	60MG TBL FLM 28 KALBLI	174 665 474	244 203,40	244 041,50	-0,1
0026789	A10AB05	NOVORAPID PENFILL	100U/ML INJ SOL 5X3ML	173 906 291	848,35	830,09	-2,2
0029707	L04AD02	ADVAGRAF	1MG CPS PRO 60	173 567 522	4 546,07	2 484,52	-45,3
0026096	A16AB07	MYOZYME	50MG INF PLV CSL 1	169 664 476	13 035,91	13 794,71	+ 5,8

The group of medicinal products with the greatest distribution in respect of which reimbursement was changed contains particularly relatively cheap medicinal products. The reimbursements of the aforementioned products were mostly increased. In case of medicinal product KALNORMIN, the reimbursement of which was markedly decreased, the amount of supplies onto the market grew. In other evaluable cases (except for OMEPRAZOL STADA), however, the increased reimbursement was not principally reflected in the degree of interest and in the volume of medicinal product supplies (tab. 33).

Tab. 33 **Ten most often distributed medicinal products by number of packages reported in compliance with DIS-13 for which reimbursement was changed**

Code	ATC	Name	Name supplement	A (number of packages)	Original reimbursement (CZK)	New reimbursement (CZK)	B (number of packages)	Note
0200935	A12BA01	KALNORMIN	1G TBL PRO 30	164 905	63,7	42,51	199 360	*/
0215606	A02BC01	HELICID 20 ZENTIVA	20MG CPS ETD 90	378 859	31,65	35,18	268 339	
0214904	R03DA04	EUPHYLLIN CR N 200	200MG CPS PRO 50	305 162	34,6	34,15	294 372	
0101211	C09AA04	PRESTARIUM NEO	5MG TBL FLM 90	269 575	52,75	58,63	275 666	
0000269	H02AB07	PREDNISON 5 LÉČIVA	5MG TBL NOB 20	26 7848	36,54	48,42	266 466	
0069189	H03AA01	EUTHYROX	50MCG TBL NOB 100	24 8643	52,75	58,62	252 983	
0056976	C09AA05	TRITACE	2,5MG TBL NOB 20	227 088	30,56	32,81	240 278	
0187425	H03AA01	LETROX	50MCG TBL NOB 100	222 886	123,3	159,17	223 771	
0140192	A02BC01	OMEPRAZOL STADA	20MG CPS ETD 100	140 588	54,81	72,64	210 986	
0017189	A12BA01	KALIUM CHLORATUM BIOMEDICA	500MG TBL ENT 100	94 119	36,54	48,42	92 568	*/

** – the period of one quarter of a year, x – period cannot be assessed, A – number of packages distributed during 6 months prior to the change, B – number of packages distributed during 6 months after the change.*

Validation of Applications

The number of applications on the basis of which an administrative procedure pursuant to Part 6 of the Act on Public Health Insurance was commenced in 2017, remained on the same level as in 2016, again with a major share of submissions by health insurance companies whose share in the number of filed applications amounted to 30%. The number of administrative procedures discontinued by resolution as early as in the validation phase dropped by almost a half compared to 2016. The reason for discontinuation was, in particular, a barrier to the procedure (so called litispendency) or obvious legal unacceptability of the application.

In 2017, the reimbursement system was entered by 66 medicinal products on the basis of an application for transfer of the maximum price and the amounts and conditions of reimbursement from a reimbursed identical product code. In order to safeguard a greater comfort for the applicants and to standardise submissions, a new web form for transfer applications was published on the Institute's website.

Tab. 34 **Validation of applications for determination/change/cancellation of maximum prices and/or reimbursement amounts and conditions, for abbreviated revision of maximum price or reimbursement system – 2017**

Period	No. of submitted applications	Suspended due to defective submissions and deficiencies in applications	Discontinued in the validation phase
January	60	2	2
February	92	0	7
March	59	0	0
April	84	2	2
May	49	0	2
June	43	0	1
July	29	0	0
August	59	2	1
September	31	0	0
October	44	0	1
November	41	0	1
December	58	0	2
Total	**649**	**6**	**19**

Individually Prepared Medicinal Products (IPLP)

Individually prepared medicinal products (hereinafter referred to as "IPLP") were subjected to the conditions of material price regulation (hereinafter referred to as "VUC") set forth by the effective Price Regulation also in 2017. This regulation applies to the following groups of medicinal products: individually prepared radiopharmaceuticals (hereinafter referred to as "RF"), individually produced transfusion products (hereinafter referred to as "TP"), individually prepared medicinal products in pharmaceutical care facilities – extemporaneous products (hereinafter referred to as "MAG"), parenteral nutrition products for home therapy (hereinafter referred to as "DPV"), and advanced therapy products. The conditions for the determination of the amount and conditions of reimbursement by means of general measures (hereinafter referred to as "OOP") are set forth by Act No 48/1997 Coll., on Public Health Insurance, as amended, specifically in Section 15, paragraph 5. The drafting of general measures and the method of their publication are governed by Sections 171 to 174 of Act No 500/2004 Coll., the Administrative Code.

A change of payroll tariffs, stipulated by Government Regulation No 316/2016 Coll. of 9 October 2016, amending Government Regulation No 564/2006 Coll., on the salaries of public service and administration employees, as amended (hereinafter referred to as "Government Regulation No 316/2016 Coll.") effective as of 1 January 2017 was a stimulus for the adjustment of reimbursements for subgroup 14 DPV, subgroup 14 DPV, subgroup 13 RF, and subgroups 12 and 15 for TP.

General Measures

In 2017, 3 OOPs issued in 2016 became effective.

As of 1 January 2017, OOP 06-16 reflecting the increase in payroll tariffs of healthcare staff set forth by Government Regulation 316/2016 Coll. took effect. It is estimated that in the DPV group, the public health insurance costs were to grow by 0.5% compared to 2015.

As of 1 January 2017, OOP 07-16 reflecting the increase in payroll tariffs of healthcare staff set forth by Government Regulation 316/2016 Coll. and a change to the point value based on Decree No 348/2016 Coll., on the determination of the point value, amounts of reimbursement of reimbursed services, and regulatory measures for 2017 of 19 October 2016 coming into force on 1 January 2017 (hereinafter referred to as "Decree No 348/2016 Coll.), and amended Decree No 134/1998 Coll., setting forth the list of healthcare procedures and their point values, effective as of 1 January 2017, took effect. Furthermore, it reflected the amended amounts of reimbursement on the basis of a revision completed for 2015, which was published by the Institute in the revision report. Concurrently, the Institute removed code 0002023 – 99mTc Mefenin inj. – and code 0002024 – 99mTc Mebrofenin inj. from the list of reimbursed IPLP. The reason for this removal was the termination of marketing authorisation for products HIBIDA KIT (SÚKL code 0084116) and product TRIMETYL-HIDA KIT (SÚKL code 0091120). Despite the increase in the payroll funds and on the basis of other aforementioned changes, the costs from the public health insurance were estimated to decrease by 1 % compared to 2015.

As of 1 January 2017, OOP 08-16 reflecting the increase in payroll tariffs of healthcare staff set forth by Government Regulation 316/2016 Coll. and a change to the point value based on Decree No 348/2016 Coll., took effect; furthermore, procedure 11013 (follow-up by an internist) was removed and replaced with procedure 11023 (follow-up by an internist). With regard to the aforementioned changes, the annual costs from the public health insurance were estimated to grow by 7.5 % compared to 2015.

In the course of 2017, six OOP procedures were commenced and completed.

As of 1 April 2017, OOP 01-17 for subgroup 14 DPV took effect, reflecting a change to the composition of model DPV formulations which consisted of the deletion of item i. v. proton pump inhibitors from model formulations and its shift under Annex 5 – Products for pharmacological management of patients with intestinal failure. This change did not represent any economic impact upon subgroup 14 DPV.

Furthermore, as of 1 April 2017, OOP 02-17 for subgroup 13 RF took effect, reflecting changes regarding termination of manufacture of radiopharmaceuticals 6-MDP KIT and 8-MDP KIT and their replacement with radiopharmaceutical TECHNESCAN HDP, and termination of manufacture of radiopharmaceutical MAG 3 and its replacement with radiopharmaceutical TECHNESCAN MAG 3. With a view to these changes, the Institute removed product 99mTc Medronan inj. from the list of reimbursed IPLP RF, and for product 99mTc MAG 3 inj. it amended the reimbursement as per the price of the available radiopharmaceutical MAG 3 KIT.

As of 1 June 2017, OOP 03-17 for subgroup 13 RF took effect, reflecting new price source materials and the effective €/CZK exchange rate as per the source materials published by the Czech National Bank (ČNB); furthermore, the calculation for the determination of the reimbursement of radiopharmaceuticals reflected changes in association with the retrospective inclusion of IPLP RF 99mTc Etifenin inj. for product ROTOP-EHIDA. It was estimated that with regard to the aforementioned changes, the annual costs of the public health insurance would grow by 7.5% compared to 2015 in the 13 RF subgroup.

In the fourth quarter, three OOPs were prepared, with the effective date of 1 January 2017; these reflected the change to the payroll tariffs for healthcare staff based upon Government Regulation No 341/2017 Coll. of 19 October 2017, which came into force on 1 January 2018. In compliance with the VUC conditions and the effective Price Regulation,

reimbursements for IPLP subgroups were amended in the section of payroll costs associated with the time demands for IPLP preparation proper and were published in OOP 04-17 for TP, in OOP 05-17 for DPV, and in OOP 06-17 for RF so that the effective dates of the OOPs were consistent with the effect of the Government Regulation. A 0.7% increase in the costs is estimated in 2018 compared to 2017 in the TP group due to the changed payroll funds; in respect of the DPV, a 1% increase in costs and in respect of the RF group a 0.22% increase is foreseen. The conditions of reimbursement of subgroup MAG subject to the effective Price Regulation of the MoH 01/2013/FAR have not changed as of 1 January 2018.

Consumption and Costs of Individually Prepared Medicinal Products and Expenses from the Public Health Insurance

Chart 16 illustrates the distribution of costs of the public health insurance in the IPLP group for 2017 by individual subgroups. An overview of consumption of IPLP in DU for the period of 2015 to 2017 is provided in chart 18. The consumption of IPLP is evaluated in defined units (hereinafter referred to as "DU") by individual IPLP subgroups. In case of the transfusion product subgroup, incl. autologous transfusion products, the radiopharmaceuticals subgroups and the MAG subgroup, the consumption dropped; in the DPV subgroup the consumption of DU increased.

Chart 17 provides a comparison of costs of public health insurance for individual IPLP subgroups for the period of 2015 to 2017. Compared to the data specified in the Report for 2016, the values for the period of 2016 were updated as of 1 December 2017. Data on the consumption of IPLP for 2017 are available only as at 1 October 2017, due to a time shift in the hand-over of statistical data by health insurance companies, and hence incomplete data from the ÚZIS system. The fourth quarter of 2017 is therefore expressed as an estimate of the anticipated costs in the form of a future development prognosis using the least square method.

In 2017, the costs of individual IPLP groups were influenced by the increase in the payroll funds as of 1 January 2017 on the basis of Government Regulation No 316/2016 Coll., by the inclusion of new products in the list of reimbursed IPLP, and by changes to the €/CZK exchange rate. In respect of the TP and ATP subgroup, a slight increase in the costs despite dropping consumption of these products was seen, caused not only by the increased payroll funds for healthcare staff, but also by amendment to Decree No 348/2016 Coll. and Decree No 134/1998 Coll. effective as of 1 January 2017. In respect of the RF subgroup, despite dropping consumption, the costs grew. The reason for the growth of costs was the cancellation of code 00002016 and its replacement with code 0002073. The cost increase due to this change was estimated at 5.3 mil. CZK.

Another reason for increasing costs in the RF group was the submission of new price source materials for individual radiopharmaceuticals. The growth of costs due to this change was estimated at 4.76 mil. CZK. The growth in the consumption of DPV subgroup products is associated particularly with the extension of home therapy for patients with intestinal failure. In the MAG subgroup, including costs associated with cytostatic dilution, the growth in the consumption as well as costs associated with the increasing number of oncologically treated patients was seen.

The total costs paid for the IPLP group from the public health insurance funds for 2016 amounted to 2 912.7 mil. CZK, in 2017 it was 3 045.7 mil. CZK, which represents a cost increase by 133.0 mil. CZK or a 4.56% increase compared to 2016.

Chart 17 **Distribution of total costs of individually prepared medicinal products in 2017**

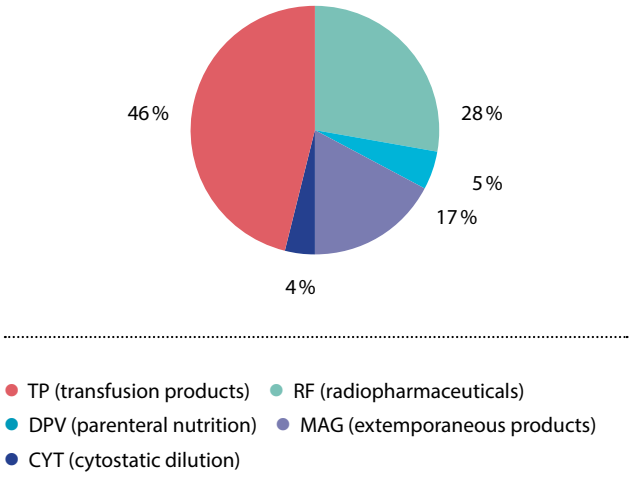


Chart 18 **Comparison of costs by groups of individually prepared medicinal products for the period from 2015 to 2017 in mil. CZK**

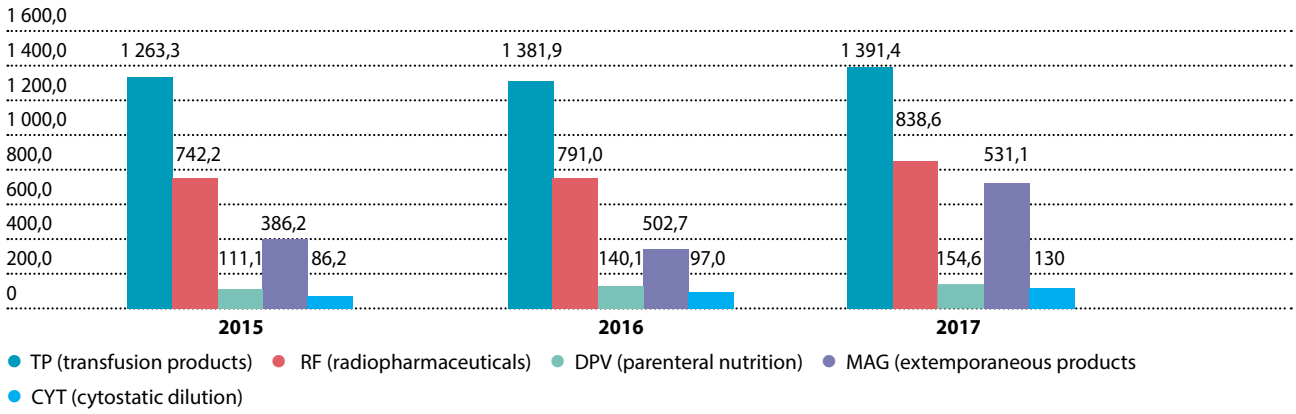
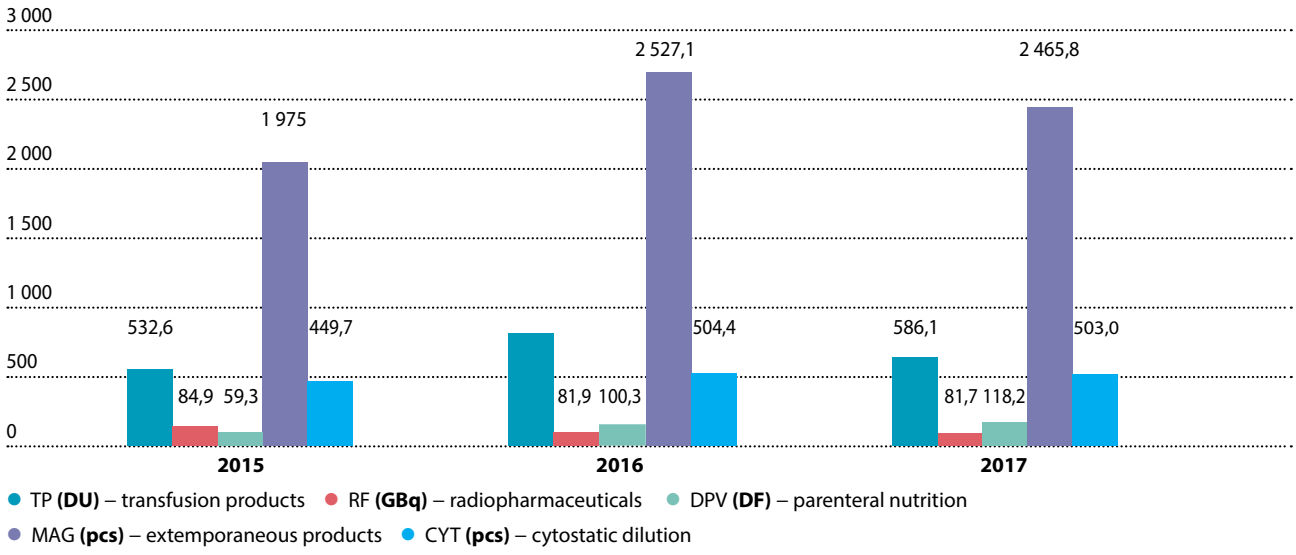


Chart 19 **Overview of consumption of individually prepared medicinal products for the period from 2015 to 2017 in thous. DU**



MEDICAL DEVICES BRANCH

4.15 Department of Clinical Trials and Medical Devices Vigilance

Clinical Evaluation

Pursuant to the obligation set forth for the sponsors of clinical investigations on medical devices (hereinafter referred to as "CIMD") by Act No 268/2014 Coll., on Medical Devices, 25 applications for authorisation of CIMD conduct and 15 applications for variations to CIMD conditions were submitted to the Institute in 2017 via the Registry of Medical Devices (hereinafter referred to as "RZPRO"). In compliance with Section 9(h) of Act No 268/2014 Coll., on Medical Devices, 21 favourable opinions authorising the conduct of CIMD were issued in administrative procedures, and one procedure was discontinued by resolution. Furthermore, 12 applications for authorisation of variations to the conditions of CIMD were granted.

Within the scope of control of the conduct of clinical investigations on medical devices at providers of healthcare services, 12 inspections were conducted, in which 11 types of investigational medical devices were inspected.

The selection of inspected sites was based upon issued decisions authorising the conduct of CIMD and previously commenced clinical investigations, taking into account the number of included subjects, the duration, and stage of the CIMD. On-site inspections identified 27 shortcomings in total, of which 3 were critical, 19 major, and 5 minor. The total of 61 serious adverse events (hereinafter referred to as "SAE") were reported from CIMD sites in the Czech Republic.

In 2017, the expert staff of the Department of Clinical Evaluations on Medical Devices (hereinafter referred to as "KHZP") were involved in the amendments and testing of amendments to the Clinical Investigations Module within RZPRO and in the development of forms relevant for the conduct of administrative procedures.

Within the scope of cooperation with domestic authorities in the sphere of medical devices, a representative of the KHZP Department was invited to participate in two inspections conducted by the Czech Office for Standards, Metrology and Testing due to specialisation in clinical investigations. The inspections were performed at two Czech notified bodies.

Within the scope of international cooperation in the sphere of clinical evaluations, in 2017, a KHZP representative participated in regular meetings of the expert WG on Clinical Investigation and Evaluation of the European Commission. The meetings focused upon basic information on new Regulation 2017/745 of the European Parliament and of the Council, the development of documents, and exchange of information among the EU Member States.

Medical Device Vigilance – Investigations into Serious Adverse Events and Monitoring of Safety Corrective Actions

Investigations into Serious Adverse Events and Monitoring of Safety Corrective Actions for Medical Devices: 469 adverse events (hereinafter referred to as "AEs") considered to be associated with the use of medical devices in the provision of healthcare services within the territory of the Czech Republic were reported to the Institute; furthermore, 2 adverse events arising outside the territory of the Czech Republic associated with medical devices of Czech manufacturers were notified. All of the cases were subjected to investigation. The development of the number of AE reports in 2010-2017 is provided in Chart 19.

The total number of received reports on safety corrective actions regarding medical devices from competent national authorities, manufacturers or their authorised representatives, distributors or importers, as applicable, amounted to 1 089. Of the total number of received reports, 485 concerned medical devices distributed to the Czech market. The development of the number of reports on safety corrective actions in 2010-2017 is provided in Chart 20.

In 2016, the Institute published 431 pieces of information for users – Field Safety Notices (FSN) via the Registry of Medical Devices. The FSN is disseminated by the manufacturer, authorised representative, or distributor in association with an adopted Field Safety Corrective Action (FSCA).

Within the scope of workshops organised by the Medical Device Branch, professionals were informed about the vigilance system focusing upon medical device manufacturers.

On the basis of medical device monitoring, one penalty was imposed for an administrative offence, amounting to 12 500 CZK. Furthermore, 80 proposals to commence an administrative procedure with a manufacturer or distributor of medical devices were forwarded to the Legal Support Department of the Medical Device Branch and 2 motions were filed with the Control Department for the conduct of an inspection at distributors and persons servicing medical devices.

Within the scope of monitoring of a safety corrective action adopted by a Czech manufacturer, 4 reports for competent national authorities (NCAR) were issued and disseminated via the European database of medical devices - EUDAMED.

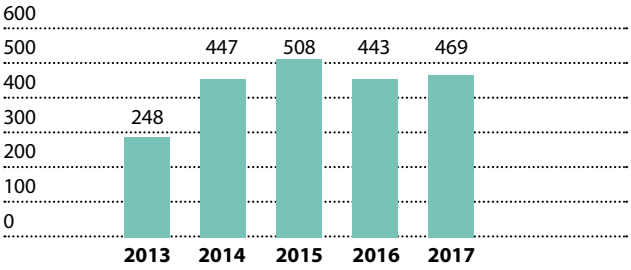
Within the scope of international cooperation in the field of medical device vigilance, in 2017, the inspectors of the Vigilance Department

participated in 12 teleconferences and 1 meeting of the Medical Device Expert Group (MDEG) on Vigilance focused upon the exchange of information among the EU Member States on current vigilance cases. Furthermore, they were involved in providing comments on the new version of an adverse event report form for manufacturers and attended a working group for the development of a specific vigilance guideline for breast implant manufacturers. In relation to the adoption of new European measures governing medical devices and in vitro diagnostic devices, a representative of the Vigilance Department took part in a two-day workshop focused upon the detection and management of vigilance signals – "Open Conceptual Framework for Signal Detection & Management". In the course of 2017, 14 questionnaires regarding vigilance issues which were sent by competent national authorities were completed.

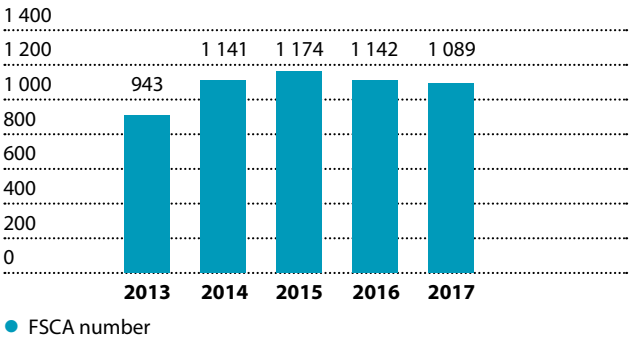
Within the scope of national cooperation, the inspectors from the Vigilance Department took part in 2 inspections conducted by the Czech Office for Standards, Metrology and Testing (hereinafter referred to as "ÚNMZ") with the Czech notified bodies, where they were invited due to their specialisation in medical device vigilance.

As part of adverse event investigation, inspectors from the Vigilance Department in two cases cooperated with enforcement authorities.

Chart 20 **Overview of notified adverse events in 2013–2017**



Graf 21 **Overview of safety corrective actions for medical devices adopted in 2013-2017**



4.16 Medical Device Registration and Notification Department

The Registration and Notification Section ("ORN") addresses regulations pursuant to Act No 268/2014 Coll., on Medical Devices and on Amendment to Act No 634/2004 Coll., on Administrative Fees, as amended, in respect of registration of persons, notifications of medical devices, and related activities. In 2017, the newly proposed structure of the Medical Device Branch was implemented. The activities in the field of expert opinions, borderline products, and free sale certificate issuance were separated from the Registration and Notification Department (RAN) and a Department of Issuance of Expert Opinions and Free Sale Certificates (OPC) was established. This department has been incorporated under ORN.

In the last year, the expert staff of the RAN Department were involved in the testing of RZPRO for the purposes of its development, in the development of new procedures in individual RZPRO modules, with some of these procedures within medical device notification being subject to an administrative procedure. They were creating instructions for use for RZPRO for external users and significantly extended the information base, incl. a FAQ tab on the Institute´s website. Due to the establishment of a general helpline (ext. 600) and e-mail address SZP_RZPRO_dotazy@sukl.cz, the Department continues to serve as the major contact point for general as well as professional queries in the area of RZPRO. In the last year, the OPC Department focused upon the drafting of opinions and assessments required externally, and upon immediate issuance of free sale certificates.

Title IV of the Act on Medical Devices – Chapter 1, Registration of Persons Handling Medical Devices

- **Notification of a Person**

In 2017, the Department completed 361 submitted notifications of persons.

- **Notification of Operation**

In 2017, 89 notifications concerning operations in general were completed; these concerned manufacturers of medical devices, distributors of medical devices, importers of medical devices, servicing persons, authorised representatives, and sponsors of clinical investigations.

- **Notification of Changes to Data**

In total, 399 notifications of changes to data were processed and completed.

- **Notifications of Extended Registration**

In total, 131 notified extensions were completed, where the obligation to file a notification of extended registration prior to 31 March 2016

pursuant to the Act on Medical Devices applied to entities which intended to continue their operation.

- **Notification of Deletion of a Person**

In 2017, the Department processed 21 notifications of person deletion. Out of the total number of 1 073 submitted notifications, in the last year, the Department completed 1 001 notifications in the Persons Module.

Title IV of the Act on Medical Devices – Chapter 2, Notification of Medical Devices

- **Application for Notification of a Medical Device**

In 2017, the Department completed 8 567 administrative procedures pertaining to applications for medical device notification, which is 21% more than in 2016.

- **Application for Extension of Medical Device Notification**

The Department completed 519 administrative procedures pertaining to extension of medical device notification.

- **Application for Changes to Medical Device Data**

In total, 738 applications for changes to medical device data were processed and completed.

- **Application for Deletion of a Medical Device**

Forty-two applications for medical device deletion were completed.

Title IV of the Act on Medical Devices – Chapter 3, Free Sale Certificate

- **Application for Issuance of a Free Sale Certificate**

Applications for the issuance of a free sale certificate (FSC) are associated with medical device notifications. Primarily, a medical device must be notified and subsequently, the free sale certificate may be issued. In 2017, 158 applications for FSC issuance were filed. The RAN Department, and in Q4 of 2017 already the new OPC Department which took this agenda over in October 2017, issued 181 free sale certificates in total.

Furthermore, in 2017, the RAN Department in close cooperation with the OPC Department was involved in the assessment of proper classification of medical devices and the nature of borderline products. In association with these activities, expert opinions were issued and professional support provided by the OPC Department for other departments of the Medical Device Branch.

- **Expert Opinion**

Expert opinions are issued on the basis of received applications for the issuance of an expert opinion from external entities as well as on the basis of motions from other departments of the Medical Device Branch, and also in reaction to submitted applications for medical device notification in RZPRO. In the last year, the OPC Department issued 105 expert opinions in respect of the nature of a product or medical device classification. In this area, when processing the opinion on the nature of the product, the Department cooperates also with the Department of Advertising Surveillance in the area of pharmaceuticals. Of the aforementioned number, 26 opinions were issued upon external request and 79 opinions were issued upon request of the Medical Device Legal Support Department (PPZ).

4.17 Medical Device Control Department

The Institute´s surveillance activity in respect of persons handling medical devices is set forth by Act No 268/2014 Coll., on Medical Devices and on Amendment to Act No 634/2004 Coll., on Administrative Fees, as amended, which defines the competences and control activities pursuant to this Act and Act No 22/1997 Coll., on Technical Requirements for Products and Amendments to Some Related Acts, as amended. These persons include providers of healthcare services in the area of medical device use as well as manufacturers, importers, distributors, persons servicing medical devices, vendors and dispensing persons in the area of medical devices. This surveillance activity includes also the area of assessments of proper placement of medical devices onto the market.

The purpose of scheduled and ad hoc inspections of the Institute is to make sure that medical devices which are supplied to the market in the Czech Republic were safe and functional, and, moreover, that health care were provided using adequate, safe, and effective medical devices in a manner preventing any damage to the health of users and patients upon their correct use for the purposes they are intended for. In 2017, the inspectors from the Medical Device Control Department completed 177 inspections in total, of which 57 were inspections at providers of healthcare services (both state and non-state healthcare facilities), and 120 were inspections at manufacturers, importers, distributors, vendors, persons dispensing medical devices, and servicing organisations. During these inspections, 859 medical devices were inspected. More detailed statistics on the total number of inspected medical devices and inspected persons is provided in the tables below.

Fifty-seven inspections at providers of healthcare services were completed, within the scope of which documentation evidencing compliance with the conditions of use of the medical device in the provision of health care was checked for 340 medical devices. Furthermore, 120 inspections took place within the scope of market surveillance, where 519 medical devices were inspected in terms of requirements of medical device supplies to the market. The number of shortcomings identified in respect of persons subjected to market surveillance was 293, and at providers of healthcare services 36 shortcomings were identified.

The Control Department forwarded 36 motions in total to the Medical Device Legal Support Department for further procedure.

Tab. 35 **Overview of inspections by the Control Department**

Number of inspections	177
Number of report-based inspections (of the total number of inspections)	42
Number of inspected medical devices	859
Number of inspected established meters (of the total number of inspected medical devices)	6
Number of inspected class IIb and III medical devices (of the total number of inspected medical devices)	298
Number of inspected medical devices without shortcomings (of the total number of inspected medical devices)	684*
Number of inspected medical devices with shortcomings (of the total number of inspected medical devices)	175*
Number of shortcomings	329*
Number of shortcomings in class IIb and III medical devices (of the total number of inspected medical devices with shortcomings)	102*
Number of reports forwarded to medical device Legal Support Department (proposal for initiation of an administrative procedure)	36

* As not all of the inspections have been concluded to date, this is a qualified estimate.

Tab. 36 **Rating of inspections conducted by the Control Department**

Entity	**Number of kontrol**	**Of which report -based**	**1**	**%**	**2**	**%**	**3**	**%**
Anaesthesiology & Resuscitation/Intensive Care Unit	4	0	3	75	1	25	0	0
Dialysis centres	1	1	1	100	0	0	0	0
Plastic surgery	3	3	3	100	0	0	0	0
Providers	18	3	12	66.7	5	27.8	1	5.6
Psychiatry	1	1	1	100	0	0	0	0
Radiology	7	0	5	71.4	0	0	2	28.6
Rehabilitation	8	0	5	62.5	3	37.5	0	0
Dentistry	1	1	0	0	0	0	1	100
Price controls	2	2	2	100	0	0	0	0
Distributors/importers	56	7	17	30.4	25	44.6	14	25
Vendors	4	2	3	75	1	25	0	0
Servicing entities	38	3	23	60.5	8	21.1	7	18.4
Dispensing persons	16	1	14	87.5	2	12.5	0	0
Manufacturers	4	2	1	25	2	50	1	25
Verification of corrective action implementation	14	14	14	100	0	0	0	0

Inspection rating is conducted in compliance with an internal classification of shortcomings, the inspector evaluates and classifies the shortcoming (MS – minor or no shortcomings - 1, SS – significant shortcoming – 2, CS – critical shortcoming – 3).

4.18 Penalties for Breach of Act on Medical Devices

In compliance with Act No 268/2014 Coll., on Medical Devices and Amendments to Act No 634/2004 Coll., on Administrative Fees, as amended, since 2015, the Institute, as the first-instance administrative authority, has been involved in the agenda of decision-making in the area of product nature and proper classification of medical devices.

Where the Institute identifies any doubt as to the proper classification of a medical device in terms of the degree of risk to health or as to whether the product meets the definition of a medical device during the assessment of an application for medical device notification, it commences an administrative procedure with the party in question.

In 2017, 89 proposals for the commencement of an administrative procedure on product nature and 58 proposals for the commencement of an administrative procedure on medical device classification were forwarded to the Legal Support Department of the Medical Device Branch.

In 2017, the Institute commenced 37 ex-officio administrative procedures on product nature, of which 27 were combined procedures pursuant to the Act on Medical Devices and Act on Pharmaceuticals. Furthermore, 10 ex-officio administrative procedures regarding medical device classification were commenced.

In 2017, the Institute received 2 applications for decision regarding product classification from a notified body.

In 2017, 1 decision on medical device classification and 1 decision on product nature were issued.

Chart 22 **Overview of administrative procedures commenced in 2017**

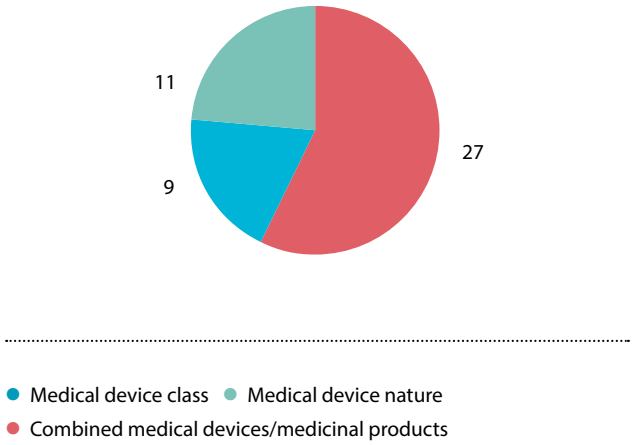
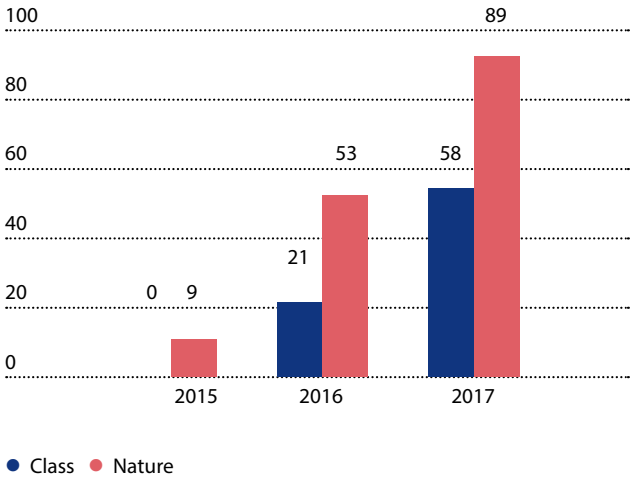


Chart 23 **Overview of forwarded proposals for commencement of ex-officio administrative procedures in 2015–2017**



Offences

The Institute, as a first-instance administrative authority, holds administrative procedures regarding administrative offences in case a breach of obligations imposed by the Act on Medical Devices is identified, particularly with reference to the inspection activity conducted at providers of healthcare services and distributors of medical devices.

In 2017, the Institute imposed fines for breach of the Act on Medical Devices amounting to the total of 284 500 CZK. The highest proportion of fines imposed in 2017 by the Institute for the breach of the Act on Medical Devices were fines imposed upon medical device distributors and healthcare service providers for the breach of their obligations in the provision of healthcare services. One fine was imposed upon a medical device distributor for failure to inform about the termination of an established safety corrective action.

Furthermore, one fine was imposed upon a medical device importer for failure to meet basic requirements applicable to the concerned medical device with regard to its defined purpose as per Act No 22/1997 Coll., on Technical Requirements for Products and on Amendment to Some Acts.

In compliance with the coming into force of the Act on Medical Devices (on 1 April 2015), the Legal Support Department has seen an increase in the proposals for commencement of an administrative procedure regarding administrative offences since 2016 within the scope of monitoring of adverse event investigations, particularly breach of the obligation laid down by Section 75 of the Act on Medical Devices, specifically to inform the Institute of established safety corrective actions and their termination in association with the establishment of a new actus reus in the Act.

Tab. 37 **Overview of forwarded motions for administrative procedure commencement in 2015–2017**

Overview for	**2015**	**2016**	**2017**
Clinical Trials Department	-	3	1
Vigilance Department	2	47	79
Control Department	22	69	64
Total	**24**	**119**	**144**

Appeals

In 2017, the Legal Support Department received 56 appeals in total for processing. In compliance with Section 88 of Act No 500/2004 Coll., the Administrative Code, as amended, these were forwarded via the Institute to the Ministry of Health of the Czech Republic as the appellate body.

Tab. 38 **Overview of received appeals to be forwarded to the Ministry of Health of the Czech Republic for 2017**

Department	Number of appeals	Of which returned for new consideration	Of which granted	Of which declined
Legal Support Department	12	2	5	1
Control Department	1	-	-	-
Clinical Trials Department	1	1	-	-
Department of Issuance of Expert Opinions and Free Sale Certificates	2	-	1	-
Department of Registration of Persons	20	1	18	-
Department of Medical Device Notification	20	-	12	-
Total number of appeals for 2017	**56**	**4x**	**36x**	**1x**

x – Number of MoH decisions sent back to the Institute.

STATE AGENCY FOR MEDICAL CANNABIS

In compliance with Act No. 167/1998 Coll., on Dependency-Producing Substances, as amended, the Institute performs the tasks of the State Agency for Medical Cannabis. The Department of the State Agency for Medical Cannabis (OSALK), which was established on 1 January 2013. Its activities are associated with the granting of licences to grow cannabis for medical use (hereinafter referred to as "medical cannabis"), controlling compliance of the cultivation, processing and storage with legislative requirements, ensuring purchases of grown and harvested cannabis and its safe storage, transport and distribution, and ensuring its export outside the territory of the Czech Republic, where applicable. In addition, it also fulfils all reporting obligations to the Ministry of Health and the Police of the Czech Republic.

4.19 Department of the State Agency for Medical Cannabis

In 2017, the Department of the State Agency for Medical Cannabis (OSALK) safeguarded processes and activities related to ensuring availability of the medical cannabis active substance for Czech patients from a domestic grower. In 2016, the Institute took over and placed in distribution 11.2 kg of medical cannabis from the winner of the first public contract for the supply of medical cannabis, Elkoplast Slušovice s.r.o. The Department supervised the organisation of safe storage, transportation, and distribution of medical cannabis to pharmacies via the Institute´s contract distributor, Alliance Healthcare s.r.o. It also mediated the process of framework contract conclusion on the transfer of medical cannabis between pharmacy operators and the Institute. In compliance with the Institute's statutory power, the Department organised the announcement of a tender for another supply of medical cannabis grown in the Czech Republic for the period of 2017–2021 in order to ensure its continuous availability on the market for Czech patients. On the basis of a successfully implemented public contract for the supply of medical cannabis, a framework contract with the supplier was concluded and the supplier was granted a licence for growing in compliance with the Act on Dependency-Producing Substances. OSALK was preparing expert source materials for issues regarding medical cannabis for the Press and Information Department, other expert units, and the management of the Institute. OSALK catered for the determination of the price of medical cannabis for operators of pharmaceutical care facilities and the administration of the published pricelist of medical cannabis. The Department safeguarded compliance with the Institute´s information and notification obligation towards the Czech Police and the MoH pursuant to Act No 167/1998 Coll., on Dependency-Producing Substances. As in 2016, it cooperated with the Inspectorate for Narcotic and Psychotropic Substances of the Czech Ministry of Health. As part of its operation, OSALK communicated and cooperated with major Czech and foreign experts in the field of medical cannabis, patient organisations, professional societies and chambers. The staff of the Department also gave lectures intended for professionals. In 2017, 21 doctors complying with the requirements of all applicable legal regulations and authorised to prescribe medical cannabis for patients in indications defined by law, and 33 pharmacies meeting the statutory requirements for the ordering, preparation, and dispensing of individually prepared medicinal products containing medical cannabis were registered. This, as well as other updated information relevant to the issues of medical cannabis, incl. up-to-date statistics, are published by OS

Tab. 39 **Cannabis dispensing in 2017 by month**

Month	1	2	3	4	5	6	7	8	9	10	11	12
Number of issued Rp.	49	0	0	0	3	29	17	2	0	0	0	0
No. of patients	43				3	29	17	2				
Dispensed amount (g)	830				15	206	156,76	20				

5 PROCESSING AND PROVISION OF INFORMATION

5.1 Information Technology

In 2017, the building of a new data centre was completed and the IT Department commenced data and system migration to the hardware of the new data centre. Concurrently with the migration, an upgrade of operating systems was performed in order to safeguard the security of IT technologies. Furthermore, the first stage of works on an upgrade of the MS Windows domain was commenced and completed in that year. As part of these works, the data in use were migrated to a new, more efficient hardware.

In 2017, migration of mail services to the Microsoft Office 365 cloud solution was also completed. Along with this migration, an upgrade of the Office package was performed for all employees of the Institute. This service has enhanced the security of e-mail communication in the form of a two-phase authentication and the possibility to encrypt selected documents sent by e-mail. Within the scope of this activity, a cycle of extensive training sessions for all employees of the Institute focusing upon work in the new system was completed.

In association with the preparations for the launch of a new electronic prescription system, the Institute's monitoring system was significantly upgraded.

In association with the preparations of the launch of the mandatory use of the electronic prescription of medicines system, a new web portal www.epreskripce.cz, which is the main information channel for this area both for professionals and for the general public, was prepared in 2017.

In 2017, several demanding projects were completed, such as the implementation of the new ePrescription system, the implementation of the SIEM security system, implementation of the new CDNÚ system for adverse drug reaction reporting or the implementation of a system for work with eCTD documentation. As part of the implementation of the CDNÚ system, an upgrade of the Axway gateway for communication with EMA was performed. Furthermore, a new risk management system was completed, the implementation of which had started as early as in 2016.

In mid-2017, the telephone operators providing telephone and mobile services of the entire Institute were replaced.

With regard to new requirements by EMA (European Medicines Agency), it was necessary to completely change the information system, which provides for the processing of the Central Database of Adverse Drug Reactions. For this reason, a completely new system was created, which was launched for routine operation in the autumn of 2017. The new system meets all of the (EMA) requirements for the exchange of information about adverse drug reactions in the EU.

On the basis of the preparation of the new ePrescription application, it was necessary to safeguard the development of other supporting subsystems as well. For this reason, a completely new system of external identities was created and put live, which stores information about all registered persons in its database. Concurrently, a system allowing for access to internal applications and systems of the Institute for authorised persons only on the basis of an issued and installed communication certificate of the Institute was modified and put into routine operation.

New systems for selected reports which have to be sent by pharmacies or other entities to the Institute in compliance with legislative rules were safeguarded and put live. It concerns, in particular, systems DIS13, HZ, LEK13, and REG13. Furthermore, the Institute began to create new web forms for the purposes of reports and notifications to be filed by entities with the Institute.

It may be stated that in 2017, the Information Technology Section provided for a number of measures which have enhanced the standard of security of operations and increased availability of the Institute's information systems. In compliance with Regulation (EU) 2016/679 of the European Parliament and of the Council on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation, GDPR), an analysis of the status of personal data processing was executed. Concurrently, measures to ensure full compliance of personal data processing with this Regulations have been gradually implemented.

ePrescription

Electronic prescriptions and the establishment of the Central Repository of Electronic Prescriptions (hereinafter referred to as "CÚER") are legislatively set forth by Act No 378/2007 Coll., on Pharmaceuticals, as amended. By means of the Central Repository of Electronic Prescriptions, the doctor issues an electronic prescription (ePrescription) to the patient; on the basis of this prescription the pharmacy dispenses the medicinal product. The Central Repository of Electronic Prescriptions, moreover, collects and stores all ePrescriptions under conditions set forth by effective legislation. The established electronic prescription system (ePrescription system) is one of the eHealth services and since 1 January 2018 has been operated in the Czech Republic mandatorily. Pursuant to Decree No 415/2017 Coll., exceptional situations when it is possible to continue to issue prescriptions in hard copies are permissible.

In relation to the requirement for mandatory electronic prescriptions, the process of modernisation of the entire system, also with a view to its inclusion in eHealth National Strategy of Electronic Healthcare and Strategic eGovernment Development Framework 2014+, commenced as early as in 2015. In 2017, a public contract for the development,

delivery, and implementation of the ePrescription information system was implemented. As of August 2017, a performance of a service contract on the provision of service support to this system for the period of 4 years commenced (the IS includes a Central Repository of Electronic Prescriptions, as defined by Section 81 of the Act on Pharmaceuticals, a Registry of Restricted Medicinal Products [hereinafter referred to as the "RLPO"] pursuant to Section 81a of the Act on Pharmaceuticals, and other components).

The implementation of the ePrescription IS project was conducted in accordance with the effective schedule and the project was completed in December 2017. From the beginning of 2017, so called interim ePrescription solution had been operable. The ePrescription IS was put live on 3 July 2017 and since then, a piecemeal migration of the existing systems to the new ePrescription IS had been under way and pilot operation was launched. As of 2 September 2017, a complete data migration was launched; on 2 September 2017, the interim ePrescription solution was switched off and the ePrescription IS was launched in full pilot operation, which lasted until the final acceptance on 21 December 2017. Since September 2017, the ePrescription IS was fully operable; in December 2017 the web and mobile applications for the patient, doctor, and pharmacist were launched. Via the application for doctors, the doctor has the possibility to prescribe an ePrescription outside his/her office. The patient application allows the patient to view a list of ePrescriptions issued for him/her, in respect of which the citizen's identity in the registry of inhabitants was unequivocally established. Via the application for pharmacists, the pharmacist can find out information about an ePrescription in case he/she does not have a functional standard communication with the CÚER.

To date, the ePrescription IS has been providing a wealth of benefits particularly for the patient – greater patient safety in the dispensing of medicines; as the ePrescription cannot be filled in incompletely or incorrectly, it cannot be counterfeited, there are four possibilities of handing the identifier to the patient (paper sheet, SMS, e-mail, patient application), the patient has an overview of all prescriptions electronically issued for him/her, the doctor has the possibility to view the medicines collected by the patient and to send the identifier to the patient in a remote manner.

During the implementation of the project, 11 workshops and webinars for the vendors of medical, hospital and pharmacy software were organised. The new www.epreskripce.cz website was launched which focuses completely on the area of ePrescriptions and it is updated on a regular basis. In the course of 2017, moreover, at least 130 events presenting the ePrescription were organised - these were seminars for doctors or pharmacists, conferences and congresses, or articles and presentations in the media.

Within the scope of operation of the electronic prescription system, the Institute provides support for applicants and users of the given system. Since September 2017, a free hotline has been available to applicants and users during working days from 7:00 a.m. to 7:00 p.m.

The Institute as the administrator ensures continuous access to data maintained in the RLPO for prescribing doctors and dispensing pharmacists, the purpose of which is to ensure the limitation of prescription and dispensing of the medicinal product to the quantity set forth by the marketing authorisation pursuant to Section 39, paragraph 4(c) or Section 39, paragraph 5 of Act No 378/2007 Coll., and the restriction set forth by Decree No 236/2015 Coll. To fulfil the provision of Section 43a, paragraph 2(b) of Act No 167/1998 Coll., on Dependency-Producing Substances, as amended, which stipulates the authority of the Czech Police to retrieve data from the RLPO via a defined contact site, the Institute ensures electronic access to this Registry for the Czech Police.

In 2017, 5 001 806 electronic prescriptions in total were issued. The average monthly number of issued electronic prescriptions in 2017 amounted to 416 817, which, compared to 2016, represents an almost 143% increase. The highest increase in the number of issued electronic prescriptions, however, was seen in the last three months of 2017, when 2 350 869 ePrescriptions were issued. In 2017, the total value of reimbursement for dispensed reimbursed medicinal products prescribed through the ePrescription system amounted to 3 775 799 thous. CZK, which is almost 2 471 448 thous. CZK more than in the previous year. Since the start of the ePrescription system operation till the end of 2017, the total of 52 341 doctors and 19 281 healthcare facilities applied for the possibility to issue electronic prescriptions, and the total of 9 462 pharmacists from 2 641 pharmacies applied for the possibility to dispense them.

In the course of the year, greater healthcare facilities were given the chance to submit multiple doctor applications, in order to simplify the agenda thereof. The highest increase in the number of submitted applications started in October 2017.

As of 31 December 2017, 32 294 doctors, 13 780 healthcare facilities, 7 883 pharmacists, and 2 641 pharmacies were actively involved. The ePrescription information system was fully operable and compliant with the currently effective legislation sufficiently in advance, in order to allow users to test it in practice prior to the start of the mandatory electronic prescription.

5.2 Database of Medicinal Products and Monitoring of Supplies to Pharmacies

On the basis of the obligation set forth by the Act on Pharmaceuticals, the Institute keeps a registry of authorised medicinal products and ensures the publication of selected information in its information media. For the purpose of this registry, an internal database of medicinal products (DLP) is used, which is updated on a continuous basis.

Registry of Active Substances

At present, the DLP database contains 19 936 components (incl. combined components). In 2017, 438 new components were entered.

- Furthermore, in 2017 an update of flagging of doping components and of products containing such substances in the DLP was carried out pursuant to the 2017 Prohibited List – The World Anti-Doping Code effective as of 1 January 2018.
- Czech Pharmacopoeia 2018 together with the corresponding data from the 9th edition of the European Pharmacopeia were entered.
- In cooperation with the Czech Pharmacopoeia staff, several changes to the titles of monographs were proposed and their subsequent implementation in the DLP performed.
- Components from lists proposed by INN WHO issued in 2017 were entered and an adjustment of components from the recommended INN WHO lists was performed.
- Data about psychotropic substances were updated and new components entered in compliance with the draft Government Regulation on the lists of narcotic and psychotropic substances.
- For the purposes of verification of correctness of data for herbal components, contacts with the Botanical Institute of the Czech Academy of Sciences in Průhonice continued to be availed of.
- The revision of the entire component library in the DLP has been underway and is still ongoing, on the basis of which 1 803 components were deleted, links among various components were updated, and changes were made to the numbering system of synonym lines, which is applied on an ongoing basis during component updates.
- Furthermore, a new list of literary sources was compiled, on the basis of which data in the component library were corrected.
- The names of most salts and esters and names of components used for pH adjustment were updated; names of hydrates and anhydrous substances were revised. Furthermore, on the basis of information provided by the staff of the Czech Language Institute of the Academy of Sciences, names of some aromas were corrected.

Registry of Medicinal Products

In 2017, the Institute granted 495 marketing authorisation (3 506 SÚKL codes). Authorisation was revoked for 399 marketing authorisation numbers, which corresponds to 3 396 codes. The authorisation was revoked either upon request of the marketing authorisation holder (257 marketing authorisation numbers), or due to the sunset clause (112 marketing authorisation numbers), or due to the fact that the holder did not apply for marketing authorisation renewal (30 marketing authorisation numbers). The validity of 4 404 codes in total expired (the period of final code sale expired or marketing authorisation was revoked).

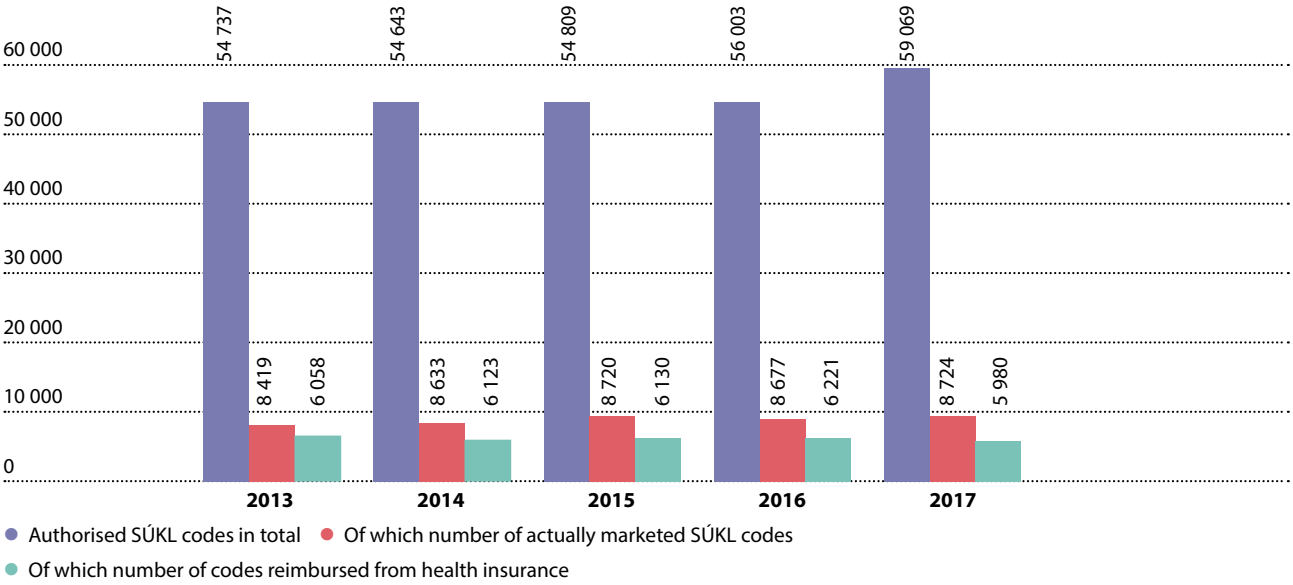
In the course of 2017, no distribution was reported for 50 345 codes (85%) of medicinal products, excluding homeopathic preparations. Hence despite having a valid marketing authorisation, these products were not placed on the market.

Authorised medicinal products contain 2 656 various active substances in total.

Tab. 40 **Selected subgroups of authorised medicinal products recorded in the Institute´s database as of 31 December 2017**

	Total no. of authorisation numbers / marketed authorisation numbers	**Total no. of SÚKL codes / marketed SÚKL codes**
Medicinal products in total (excl. homeopathic preparations)	17 439/5 956	59 069/8 724
Of which by MA numbers:		
MA numbers granted by the Institute	6 499/4 814	48 109/7 576
MA numbers of products authorised via Community Centralised Procedure	10 940/1 142	10 960/1 148
Single-component:		
Multi-component	14 070	47 346
Of which by type of dispensing:	3 369	11 712
Prescription-only medicinal products:		
OTC medicinal products	16 563/5 239	54 877/7 557
Single-component	923/730	4 120/1 158
Restricted OTC medicinal products	11/6	57/6
Restricted prescription-only medicinal products	3/3	15/3
Homeopathic preparations	284/265	777/330

Chart 24 **Authorised medicinal products in the period of 2013–2017**



Regular Outputs from the Database of Medicinal Products

For professionals as well as for the general public, the Institute regularly publishes information about authorised medicinal products, approved specific therapeutic programmes, and foods for special medical purposes with all details within the scope of the database of authorised medicinal products.

Since 2008, the Institute has been publishing the "List of Prices and Reimbursements of Medicinal Products and Foods for Special Medical Purposes", including updates thereof, on its website. In 2010, the system of so-called Control List publishing was established, which notifies professionals in advance of possible changes to maximum prices and reimbursements implied by final decisions which came into force. In 2011, in compliance with Act No. 298/2011 Coll., the name "Control List" was changed to "Draft List".

Information from the database is also utilised in the overview of reports on placement on the market or suspension or termination of supplies of medicinal products onto the market, in the overview of variations to marketing authorisations or in the overview of non-interventional post-marketing studies.

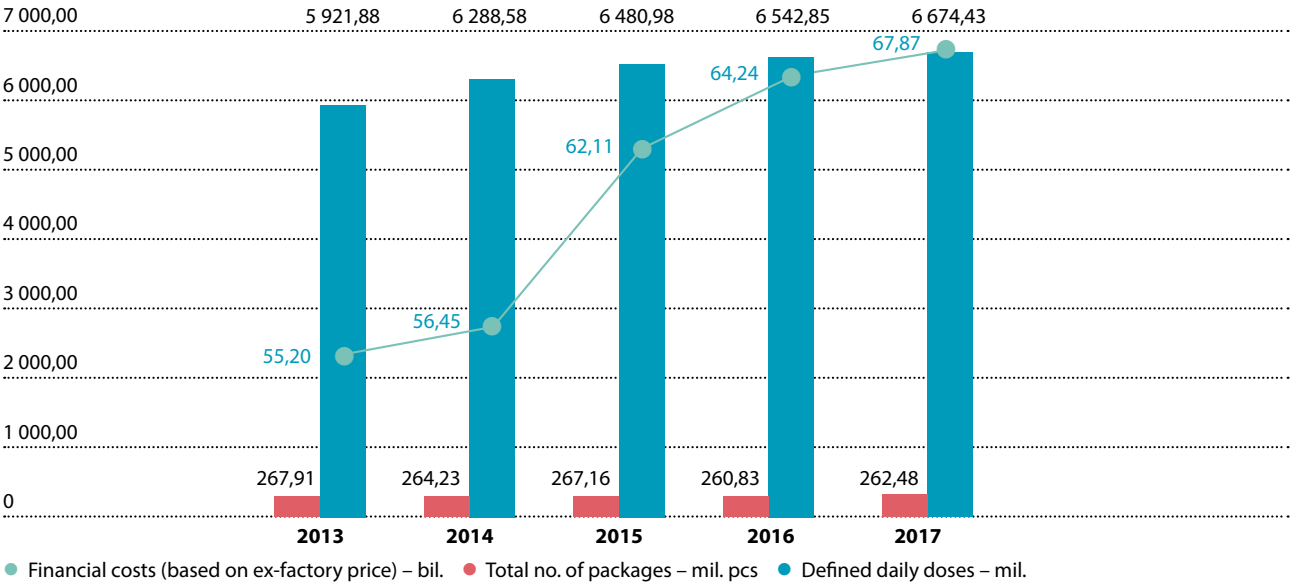
Evaluation of Deliveries of Distributed Medicinal Products

Evaluation of deliveries of distributed medicinal products based upon the mandatory reporting from entities authorised to distribute medicinal products in the Czech Republic was conducted on a monthly basis in 2017. The subject-matter of the reports concerned deliveries of medicinal products to pharmacies and other healthcare facilities in the Czech Republic and abroad. In addition to authorised medicinal products, also products included in specific therapeutic programmes and non-authorised products supplied on medical prescription for a specific patient were included in the evaluation.

Data on the volumes of distributed medicinal products in the number of packages, in financial volumes (in CZK), and in DDD (daily defined doses) were evaluated. With a view to the need to compare this value over the years, data on financial costs are provided in producer prices, i.e. ex-factory prices excl. VAT (VAT rates were changing over the years), and excl. the profit margin. Since 2008, the regular quarterly evaluation of deliveries of distributed products has been supplemented on the Institute´s website with a table showing deliveries for each active substance (further broken down by route of administration, where applicable). Furthermore, on a monthly basis, the Institute publishes summary information from monthly reports of entities authorised to distribute medicinal products in the Czech Republic on its website.

In 2017, 262.48 mil. packages of medicinal products were distributed, which corresponds to approx. 6 674.43 mil. DDD. The value of these deliveries amounted to 67.87 billion CZK (based on ex-factory price).

Chart 25 **Deliveries of medicinal products in 2013–2017**



Tab. 41 **Deliveries of distributed medicinal products in 2017**

Medicinal products in total	**Number**
Deliveries to pharmacies and healthcare facilities (mil. packages)	262.477
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	67 865.522
Deliveries to pharmacies and healthcare facilities (mil. DDD)	6 674.434
DDD/1 000 inhabitants/day	1 729.605
Prescription-only medicinal products	
Deliveries to pharmacies and healthcare facilities (mil. packages)	183.324
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	61 071.759
Deliveries to pharmacies and healthcare facilities (mil. DDD)	6 080.080
DDD/1 000 inhabitants/day	1 575.585
OTC and selected pharmaceuticals	
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. packages)	78.795
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. CZK based on ex-factory price)	6 750.600
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. DDD)	594.194
DDD/1 000 inhabitants/day	153.979
Restricted OTCs	
Deliveries to pharmacies and healthcare facilities (mil. packages)	0.357
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	43.163
Deliveries to pharmacies and healthcare facilities (mil. DDD)	0.159
DDD/1 000 inhabitants/day	0.041
Homeopathic preparations	
Deliveries to pharmacies (mil. packages)	1.928
Deliveries to pharmacies (mil. CZK based on ex-factory price) 2017	185.721

5.3 Information Activities

The major task of the Press and Information Department (TIO) is to provide information to the general and professional public. The most important sources of information about the Institute are the website www.sukl.cz, information portal for the public www.olecich.cz, and the website of the campaign Nebezpečné léky (Dangerous Drugs) www.nebezpecneleky.cz, which are administered by TIO and which serve both of the aforementioned groups. TIO is also in charge of Facebook profiles for the information portal for the public and for the Dangerous Drugs campaign.

On the information portal www.olecich.cz, patients may find information from the sphere of pharmaceuticals, such as a database of medicines, database of pharmacies, and database of clinical studies. Available is also a vaccination schedule with essential information regarding both mandatory and optional vaccination, incl. relevant vaccines. The general public may, for several years, avail of the "Ask Us" service, within which doctors and pharmacists answer the questions of the public.

Two issues of the publication for the general public called infoLISTY were published. This publication attempts to provide straightforward information about various issues in the sphere of medicines. In 2017, infoLISTY focused upon the topic of "Purchasing Medicines on the Internet" and "Treatment of Allergies and Asthma".

Via the "Ask Us" service, pharmacists and doctors – a general practitioner, a paediatrician, and three pharmacists – were answering questions from the public. In total, 305 patient questions were answered via this service. In 2017, the largest proportion of the questions concerned drug interactions.

In 2017, the "Don´t Throw Medicines in the Bin" campaign continued. The purpose of this campaign is to inform and educate the public in the sphere of proper handling of medicines in households. The campaign included lectures for patient organisations (7 in total), through which more than 270 patients were directly informed about this topic.

TIO administers a specialised library and is responsible for publication activities, represented by the preparation and publication of SÚKL´s Bulletin, the drug bulletin Farmakoterapeutické informace (Pharmacotherapeutic Information, a member of the International Society of Drug Bulletins – ISDB), and the Adverse Drug Reactions Bulletin. All of the above-mentioned publications are available from www.sukl.cz.

In 2017, TIO addressed 73 requests for information pursuant to Act No 106/1999 Coll., on Free Access to Information, as amended. Furthermore, it answered more 2 767 inquiries from the general public and from professionals which were sent via e-mail or post. Further approx. 3 360 inquiries were handled through the infoline.

The Department drafted responses to 463 inquiries from journalists and provided a statement for radio or TV broadcasting in 195 instances. Twenty-nine press releases/advices, and 7 reactions were published on the Institute´s website.

6 FINANCIAL AND MATERIAL RESOURCES OF THE INSTITUTE

6.1 Income and Expenditure Account for 2017

Income

In 2017, extra-budgetary income in the total amount of 497 546 thous. CZK was achieved. The major part of this income was generated by the reimbursement of costs of expert activities which were conducted by the Institute upon request from manufacturers, distributors, vendors, and other legal entities as well as natural persons. The major part of the overall volume was represented by income from applications related to marketing authorisations of medicinal products. The income from completed expert activities was used piecemeal by the Institute in compliance with Act No 378/2007 Coll., on Pharmaceuticals, as amended, Act No 296/2008 Coll., on Human Tissues and Cells, as amended, and Act No 268/2014 Coll., on Medical Devices and Amendment to the Act No 634/2004 Coll., on Administrative Fees, as amended, for the funding of payroll, operating and investment expenditures not covered by allocated financial resources from the state budget. In 2017, a total amount of 473 364 thous. CZK was used in this manner through permissible excess expenditure. Of this amount, 392 362 thous. CZK were used for non-investment expenditure and 81 002 thous. CZK for the financing of investment needs.

In addition to income from the reimbursement of costs of expert activities, another portion of income came from the revenues of the state budget, such as collected administrative fees for submitted applications amounting to 24 229 thous. CZK, income from fines imposed amounting to 6 052 thous. CZK, income from lease in the amount of 286 thous. CZK, income from the sale of goods amounting to 74 thous. CZK, income from the provision of services in the amount of 33 thous. CZK, refunds from excess advance payments made, related fully to the previous budgetary years, in the amount of 784 thous. CZK, etc. An overview of the reported budget income as of 31 December 2017 is shown in Table 44.

Tab. 42 **Funds and state budget**

	2015	2016	2017
Average converted number of employees	*433*	*446*	*458*
Funds allocated from the state budget for the operation of the Institute (in thousands CZK)	*122 798*	*128 977*	*138 748*
*Allocation of income in the state budget (in thousands CZK)**	*33 146*	*36 474*	*32 040*

** Without conversion from the reserve fund, from other own funds and from the National Fund.*

Expenditure

Data concerning expenditure incurred in 2017 by individual categories are provided in Table 44.

Total investment expenditure amounted to 80 992 thous. CZK from extra-budgetary resources. Investment resources were used to finance the building of the Institute's data centre (43 159 thous. CZK) and the ensuring of cyber-safety (9 151 thous. CZK). The costs of rights assessable on monetary terms amounted to 8 804 thous. CZK and those of software (CDNÚ, ERP, DMS and BPM system procurement and implementation, etc.) amounted to 12 871 thous. CZK. For laboratories, a control system for analytical instruments was purchased (1 083 thous. CZK) and an eCTD reader procured (3 666 thous. CZK). The attendance system was extended (129 thous. CZK); optical and metallic cables were extended (202 thous. CZK); and a new route of water pipes for Buildings no. 24 and 30 was completed (1 881 thous. CZK). Furthermore, retention money (Building Brno) and studies (Buildings no. 24 and 23) in the total amount of 46 thous. CZK were financed.

Non-investment expenditures were drawn in the total amount of 531 086 thous. CZK, of which 138 748 thous. CZK were funds from the state budget and 392 041 thous. CZK were utilised from extra-budgetary resources and 297 thous. CZK from claimed unused expenditures from previous years. Extra-budgetary resources included resources from abroad provided for the ARTHIQS project (127 887.54 CZK utilised), for the EURIPID project (174 576 CZK utilised), for the EUnetHTA project (27 449.18 CZK utilised). In 2017, the financing of the SCOPE project came from the funds of the Institute (40 498.92 CZK utilised).

Since 2014, the Institute has been involved in two Joint Actions within the scope of the second action programme of the Community in the area of health (2008-2013), co-funded by the European Commission and the EU Member States. The first of them focused upon the sphere of drug safety monitoring (Strengthening Collaborations for Operating Pharmacovigilance in Europe, SCOPE) and it was successfully completed in 2017. The other joint action focuses upon the sphere of assisted reproduction and haematopoietic cell transplantations (Assisted Reproductive Technologies and Haematopoietic Stem Cells Improvements for Quality and Safety throughout Europe, ARTHIQS) and is to be completed in May 2018. Member States contribute to co-funding by means of hours worked by their experts who fulfil the tasks defined under specialised areas, so called work packages.

The Institute has been involved in a joint action on healthcare technology assessment on the European Union level within the EUnetHTA project, Joint Action 3 (JA3 2016-2020). The objective of JA3 is to define and implement a sustainable model for multinational cooperation in the area of healthcare technology assessment (HTA) in Europe. Within the scope of Work Package 4, joint assessments of medicinal products or alternatively medical devices are carried out at various levels of cooperation, that is as dedicated reviewers. Within the

scope of the Work Package 7 activity, works on the implementation of HTA assessment of therapies/healthcare technologies on the national level are performed. Within the EUnetHTA project, the Institute is so called associated partner in cooperation with the MoH. In total, more than 78 organisations from 29 countries are involved in the project. This joint action is co-funded by the European Commission and the Member States, with the EC covering 60% of the project costs.

The EURIPID project has been under way since 2008. It represents a voluntary association of competent authorities for prices and reimbursements of medicinal products. The association was established for the purposes of setting up a joint database of reimbursed medicinal product prices. At present, more than 24 European countries take part. In 2015, the project obtained European support for the extension of the database and for the processing of technical and expert recommendations for the conduct of so called external price reference. Within the scope of this grant, in September 2016, the Institute organised a meeting of foreign participants – representatives of European industry associations, payers, patients, and the European Commission. An important output from the grant will be an open publication of a set of recommendations which will help to prevent or minimise the potential negative impact on the availability of medicinal products resulting from incompetent utilisation of foreign price references.

Assets

The total assets of the Institute as of 31 December 2017 amounted to 1 093 331 thous. CZK, of which fixed assets amount to 421 854 thous. CZK and current assets to 671 477 thous. CZK. Of the total liabilities of 1 093 331 thous. CZK, equity amounts to 1 056 504 thous. CZK and borrowed capital to 36 827 thous. CZK. Selected types of assets and liabilities of the Institute are listed in Table 43.

Other

A total of 3 778 thous. CZK from the Institute´s budget was used for foreign business trips. In 2017, 404 foreign business trips took place, of which 165 were fully covered by the Institute and 239 trips were fully or partially refunded by the organising institutions (EC, EU Council, EMA, etc.). The purpose of most business trips was participation in regular meetings of various committees and working groups resulting from membership in relevant bodies. the Institute has its members or alternates in more than 60 working groups across the EU institutions and international organisations. Other business trips were approved with regard to the Institute´s priorities, the relevance and benefits of the discussed topics for the Institute.

Auditing

In the period from 9 March 2016 to 25 September 2017, the Revenue Authority for the Capital City of Prague conducted an audit in the Institute to check whether a tax liability has arisen from a breach of budgetary discipline in the utilisation of funds from the state budget and funds from the state budget intended for pre-financing of expenditures to be covered from the budget of the European Union within the scope of the Human Resources and Employment Operational programme for the implementation of project "Increasing the Efficiency of the Institute´s Administrative Operation, reg. no. CZ.1.04/4.1.00/59.00009". The audit was commenced on the basis of and within the scope of a "Motion to initiate a procedure to investigate suspected breach of budgetary discipline", communicated by the Ministry of Interior of the Czech Republic, file no.: MV-77110-38/OSF-2010. The subject of the motion was tender 003, "SÚKL Agendas Electronisation Concept". The audit discovered that budgetary discipline as referred to by Section 44, paragraph 1(a) of the Act on Budgetary Rules was not breached.

In the period from 27 April 2017 to 13 June 2017, the Revenue Authority for the Capital City of Prague, territorial office for Prague 11, conducted an audit in the Institute focusing upon administrative fee management. The audit report concluded that no shortcomings have been identified and that in respect of all audited dossiers, administrative fees were established in compliance with Act No 634/2004 Coll., on Administrative Fees. No other audits performed by public administration bodies pursuant to the Act on Financial control or by the Supreme Audit office took place.

In 2017, no fines, penalties or costs of procedure were imposed upon the Institute.

Tab. 43 **Overview of selected types of assets and liabilities of the organisation in thousands of CZK**

Name of item	**Past period**	**Present period**
	2016	**2017**
ASSETS	1 038 083	1 093 331
A. Total fixed assets	393 142	421 854
of which:		
I. Long-term intangible fixed assets – total	115 990	119 734
II. Long-term tangible fixed assets – total	277 152	302 120
Lots	4 619	4 619
Buildings	226 163	246 991
Separate tangible movables and sets of tangible movables	45 410	50 274
Small tangible fixed assets	0	0
Unfinished tangible fixed assets	960	236
B. Total current assets	644 941	671 477
of which:		
I. Inventory - total	634	69
II. Short-term receivables - total	3 009	4 089
III. Short-term financial assets - total	641 298	667 319
LIABILITIES	1 038 083	1 093 331
C. Equity	1 007 943	1 056 504
of which:		
I. Assets of the accounting entity and adjustments	228 921	228 885
II. Funds of the accounting entity	612 006	636 896
Fund for cultural and social needs	1 976	2 016
Reserve fund	610 030	634 880
III. Economic result	-407 172	-490 139
Economic result for the current accounting period	-80 412	-82 966
Economic result for the previous accounting periods	-326 760	-407 173
IV. Income and expenditure account of the budget management	574 188	680 862
D. Total borrowed capital	30 140	36 827
of which:		
I. Total long-term liabilities	20	0
II. Total short-term liabilities	30 120	36 827

Tab. 44 **Budget income, budget expenditure and financing in thous. CZK**

BUDGET INCOME	**Budget for 2017**	**Real values for 2017**	
	Approved budget	**Corrected budget**	**Real values for 2017**
Administrative fees	19 800	19 800	24 229
Penalties received	1 000	1 000	6 052
Income from lease	0	0	286
Income from the sale of goods	0	0	74
Income from the provision of services	0	0	33
Non-equity contributions received	0	0	784
Insurance compensation received	0	0	12
Transfers from reserve fund	0	0	473 364
Transfers from other own funds	0	0	570
Total	**20 800**	**20 800**	**505 404**

Expenditure	**Budget for 2017**	**Real values for 2017**	
	Approved budget	**Corrected budget**	**Real values for 2017**
Employees´ salaries	20 497	36 787	36 787
Civil servants´ salaries	75 921	245 366	245 366
Other payments for performed work and severance pay	3 604	11 106	11 104
Mandatory premium	34 007	97 357	97 353
Contribution to the Fund of Social and Cultural Needs	1 928	5 654	5 653
Operating acquisitions and related expenditure	824	135 137	134 823
Acquisition of long-term tangible and intangible fixed assets	0	81 002	80 992
Total	136 781	612 409	612 078
of which: operating expenditure	136 781	531 407	531 086
capital expenditure	0	81 002	80 992

Tab. 45 **Expenditure statistics in the period of 2015–2017**

	2015	**2016**	**2017**
1 Total operating expenditure (in thous. CZK)	484 209	493 018	531 086
2 Non-investment expenditure (excluding salaries, insurance and fund for cultural and social needs) (in thous. CZK)	141 289	124 566	134 823
3 Investment expenditure (in thous. CZK)	76 172	61 603	80 992
4 Average converted number of employees	433	446	458
5 Expenses per employee (line 1/line 4) in thous. CZK	1 118	1 105	1 160

Organisational changes / **525 positions**

New competences / Mesures restricting re-exports of medicinal products

23 courses within which 162 employees were trained

Courses in the English, French, German, Spanish and Chinese language

Cicil-Service Exams / **Deepening of knowledge**

In 2017, the Inspectors of the Pharmacy and Distribution Section conducted 876 insopections in pharmaceutical care facilities - pharmacies

7 FOCUS UPON EMPLOYEES

7.1 Personnel Issues

In compliance with the Institute´s systemisation approved for 2017 pursuant to Act No 234/2014 Coll., on Civil Service, organisational changes have been implemented since 1 January 2017 in order to optimise the number of systemised positions and to increase the work effectiveness, in the total number of 525 positions, of which 433 are civil service positions and 92 work positions.

Within the scope of the organisational changes associated with the Institute´s systemisation effective as of 1 January 2017, in addition to the increased number of service and work positions compared to 2016, several substantial changes were implemented, particularly within the organisational structure of the Surveillance Branch and Medical Device Branch.

As of 1 June 2017, the systemisation was modified in relation to the changes arising from amended Act No 378/2007 Sb., on Pharmaceuticals and on Amendments to Some Related Acts (hereinafter referred to as the "Act on Pharmaceuticals"), which gave the Institute more powers consisting of the implementation of measures restricting re-exports of medicinal products outside the territory of the Czech Republic. For this reason, an organisational change was implemented, which despite not affecting the total number of staff, resulted in a change to the split of the total number of 525 positions into 434 civil service positions and 91 work positions, and a change within the scope of the organisational structure of the Service Activity Branch and the Surveillance Branch.

As at 31 December 2017, the total occupancy of systemised positions covered by the state budget amounted to 97%. The number of vacant positions, however, amounted to 50 in total.

The number of physical employees on payroll as of 31 December 2017 was 477 persons, of which 376 were women (i.e. 78.8%) and 101 were men (i.e. 21.2%).

Converted to FTEs worked under non-employment agreements (work agreement and agreement to perform work), a total of 31.8 employees were employed as of 31 December 2017.

Age structure of employees

The average age of all employees compared to 2016 increased by 1.6%, i.e. to 41.89 years.

Tab. 46 **Age structure of employees as of 31 December 2017 in %**

YEAR	Employees under 35 years (%)	Employees aged 36 to 55 years (%)	Employees over 55 years (%)
2016	38	45,2	16,8
2017	34,4	48,6	17

Working Hour Utilisation

Of the total amount of 987 041.7 hours worked, 3 262.39 were overtime hours. Overtime work mostly concerned employees from the workers' category (drivers), expert staff, and technical-economic staff.

In 2017, the employees were absent for the total of 1 861 working days due to sickness or nursing a family member, which is, compared to 2016, 329.50 working days less. Of the total number of employees, absence due to sickness or nursing a family member was observed for the total of 101 employees, of which:

- 94 were employees with absence up to 2 months;
- 3 employees with absence up to 3 months;
- 4 employees with absence exceeding 3 months.

Compared to year 2016, the total number of employees on sickness leave or nursing family members decreased by 26.

On the basis of amendments to the Higher-Degree Collective Agreement, a new Collective Agreement of the Institute was concluded in 2016, which includes particularly application of further obstacles to civil service (NV no. 135/2015 refers) and utilisation of sick days. In 2017, the employees utilised the total of 332 days of service leave (of which 87 were study service leave days) and 1 735 sick days.

Tab. 47 **Qualification structure of employees by achieved level of education as of 31 December 2017**

Highest achieved education	Primary	Secondary technical	Secondary general	Secondary technical with GCE	Technical colleges	University – bachelor degree	University – master degree	Postgraduate
Number of employees	1	5	8	81	6	12	351	13
% of the total number of employees	0,21	1,05	1,68	16,98	1,26	2,51	73,58	2,73

Staff Turnover

Tab. 48 **Overview of completed tenders pursuant to the Act on Civil Service (service positions) and pursuant to the Labour Code (work positions) and associated start-ups**

	Civil service		Employment	
Sekce/úsek	No. of positions to through tenders	Staffed	No. of positions to be staffed through tenders	Staffed
Director + Director's Office Section	6	3	-	-
Service Activity Branch	7	2	10	4
Surveillance Branch	46	18	16	6
Marketing Authorisation Branch	32	15	22	18
Price and Reimbursement Regulation Branch	15	4	4	4
Medical Device Branch	46	12	4	3
Total	152	54	56	35

The overall staff turnover, taking into account all start-ups and departures, is 9.9% (compared to the previous year 2016, a 2.17% decrease occurred).

Tab. 49 **Overview of employment and civil service terminations in 2017 by reason of employment/civil service termination**

	Employment	Civil service
Cancellation of employment/civil service in probationary period	3	3
Agreed time expiry	2	1
Termination by agreement (Labour Code)	5	-
Notices given by employees/termination of civil service upon request of the civil servant	3	23
Notices given due to organisational reasons/by decision of a service authority	2	0
UTermination of civil service performance with the Institute due to transfer of the civil servant to another civil service authority	-	4
Retirement	0	1
Total	15	32

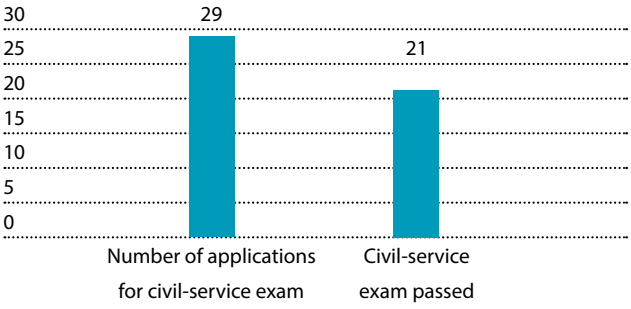
Civil-Service Exam

Pursuant to Section 35 of Act No 234/2014 Coll., on Civil Service, a civil servant is obliged to successfully complete a civil-service exam comprising of two parts – the general part and a specialised part (depending on the field of service).

As at 31 December 2017, 29 applications filed by the Institute´s employees were recorded. In 2017, 72.4% of the total number of employees successfully passed both parts of the civil-service exam. The remaining 27.6% of employees will take the exam in 2018 (within 12 months of their recruitment, as referred to in the Act on Civil Service).

Of the total number of civil-service exams taken, only 3 were unsuccessful at the first attempt (in the specialised part of the civil-service exam); by the end of 2017, all of them were successfully passed at a second attempt.

Chart 26 **Civil-service exams in 2017**



7.2 Employee Education

In 2017, in the area of employee education emphasis was placed both upon soft skill development and development of expert and language knowledge. Within the scope of initial education, all new members of the staff were trained in all topics set forth by legislation, i.e. particularly areas of employee evaluation, basic information about the Institute, information security, quality management, the Code of Ethics, internal regulation of conflict of interest, equality of men and women, environmental education, etc.).

Follow-up education focused particularly upon expert and foreign educational events, due to the high demands on expertise, implementation of legislative changes, and subsequent need for continuous deepening and increasing of qualification and knowledge of our staff in individual fields.

Concurrently, within the scope of follow-up education, the Institute implemented management courses intended for the education of senior and managerial staff, which were organised in the form of individual and group couching focused upon the development of personal qualities and using model situations, case studies, and results of research in the area of neuroscience and occupational psychology. The development of soft skills of the employees of the Institute took the form of open seminars which didactically combined the form of a presentation and workshop. They were, moreover, focused upon burnout prevention and personal quality development.

Language education for the employees was based upon the current needs, strategy, and objectives of the Institute. For this reason, it focused particularly upon specialised medical tuition. In 2017, 14 individual and 18 group courses in the English, French, German, Spanish, and Chinese language took place.

Within the scope of employee health support, courses in the sphere of care for the employees' health (such as seminars focused upon work environment ergonomics, upon cancer prevention, etc.) were scheduled and completed in 2017.

The total amount of funds spent on all types of education amounted to **3 042 000 CZK**.

Tab. 50 **Overview of educational activities in 2017 – follow-up education**

Type of event	Number of akcí	Number of hodin	Number of účastníků
PC training (expert + internal)	37	284	183
Language courses	32	2 082	158
Specialised courses and training	229	4 796	586
Managerial skills	27	216	266
Mandatory training	551	628	551
Foreign specialised training	44	1 232	61

Internal PC Training

With a view to savings of financial resources, established inhouse education focusing upon MS Office, (MS Excel and MS Word), on various levels of knowledge, continued in 2017. The courses have been held by internal tutors/staff with adequate level of knowledge.

In addition to substantial savings of funds, the advantage brought by inhouse trainings is particularly the possibility to adapt the content of the training to the actual needs of the Institute employees.

In 2017, 23 courses in total were completed within which 162 employees were trained.

Transparent documentation / **14 internal audits**

Quality management system ČSN EN ISO 9001:2016 / Expert assessment

EU Benchmarking of European Medicines Agencies cycle

Safe electronic prescription information system / **GDPR**

Inspection rating / Central Repository of Electronic Prescriptions

Information security management system (ISMS) / **External assessors**

In the Laboratory Control Section, 855 samples analyses were completed, the number of samples rated as non-compliant decreased...

8 FOCUS UPON QUALITY

The permanent intention of the Institute in the area of quality is to execute its activities at a high standard, in a predictable manner, with transparent documentation, in shortest practicable timelines and required quality, with openness to motions, while observing ethical rules, environmental conduct and safety at work, all with the objective to increase stakeholder satisfaction, to develop a positive image of the Institute, and striving to win international acknowledgement.

In 2017, the established quality management system was being developed in compliance with the new or extended requirements of the ČSN EN ISO 9001:2016 standard. In November 2017, the LL-C (Certification) Czech Republic s.r.o. certification body confirmed that the Institute's quality management system met the requirements of this standard and the Institute was granted a certificate for the following 3 years.

The functionality of the quality management system was verified on an ongoing basis also in the form of internal audits; in compliance with the annual plan, 14 internal audits took place in 2017.

In late 2017, the 4th EU Benchmarking of European Medicines Agencies (BEMA) cycle, focused upon the processes employed by medicines agencies in the sphere of management, marketing authorisation of medicinal products, pharmacovigilance, and inspections, was completed. This benchmarking is based upon self-assessment of process maturity and subsequent peer review by expertly trained assessors from other EU medicines agencies.

Within a three-day visit by external assessors from the Polish, Croatian, and Romanian medicines agency, the Institute's performance was independently assessed against assessment criteria and predefined indicators and the Institute achieved an average rating of 3.68 (of the maximum rating of 5). Compared to the previous assessment, a major improvement was seen, by almost one total grade (cf. the original 2.7).

The Institute will continue to be involved in the EU medicines agencies benchmarking.

9 INFORMATION SECURITY MANAGEMENT POLICY

In 2017, for the third time, the Institute successfully completed the information security management system (ISMS) (re)certification process in compliance with the ČSN/IEC ISO 27001:2014 standard. The Institute has been the holder of the respective certificate since 2007, which evidences the care and responsibility it dedicates to the protection of information as well as to the entire process of information system maintenance and development.

In the sphere of information security enhancement, 2017 was also a period when our efforts to prepare a reliable and safe electronic prescription information system, so called ePrescription, culminated. The technically flawless launch of full operation as at 1 January 2018 demonstrated that these efforts were successful. Following consultations with the National Cyber and Information Security Agency, the system became an element of critical information infrastructure in terms of severity classification.

Last, but not least, it is necessary to mention the commencement of the project of implementation of the requirements of Regulation (EU) 2016/679 on the protection of natural persons with regard to the processing of personal data - so called GDPR. This is not a completely new issue in respect of obligations of organisations, as personal data protection has already been laid down, in a rather similar manner, by the effective Act No 101/2000 Coll., on Personal Data Protection; nevertheless, within the scope of the project, the procedures applied were reviewed and fine-tuned, and preparations for some new processes for the protection of such data brought by the Regulation took place.

The Institute pays great attention to information security and in this respect has been closely cooperating with the National Cyber and Information Security Agency.

The Institute continues its effort to maintain a high degree of security and plausibility of data and information in its information systems and in the handling of information. Since 2007, it has continuously maintained and improved the Information Security Management System (ISMS) at a standard necessary for the Institute to be the holder of the certificate of compliance with the ČSN/IEC ISO 27001 standard, since 2015, as the ISO 27001:2014 version.

The Institute continues to enhance policy and implements processes and technical measures particularly with a view to personal data protection and adoption of legislation associated with cyber-security and legal regulations setting forth the conditions governing electronic communication and electronisation of activities.

10 OUTLOOK FOR 2018

The Institute's priority for 2018 is to develop and improve the operation of the ePrescription and to do everything to ensure that the entire medical and pharmaceutical field adopted it and that everybody were able to operate flawlessly. At present, the drug record is available to the patient and his/her treating doctor. In legislation, however, a shared drug record which could be shared by healthcare professionals is under preparation. The Institute has been involved in the activities of the MoH's workgroup addressing this issue. Another priority is the Regulation of the European Commission on combating counterfeit products and on security features shown on medicinal products, which is to come into force in February 2019. The Institute will have to enhance its surveillance activities over authorisation holders, distribution as well as pharmacies and carry out surveillance over the repository within the NMVO. The Institute has been actively involved in the drafting of national legislation and has been preparing a media campaign in order to inform all stakeholders to whom security features apply in due time.

In 2018, the issue of medical device notification, pricing and reimbursements will have to be addressed. In response to the ruling of the Constitutional Court, the legislative base was drafted very quickly. The manufacturers themselves will classify medical devices into reimbursement groups and the Institute will address only excess cases by means of administrative procedures.

Furthermore, attention has to be paid to reduced duration of administrative procedures concerning prices and reimbursements of pharmaceuticals. It will be necessary to process the results of an audit and cooperate in the drafting of legislation. When the legislation was being drafted, it did not count with biological medicines, highly innovative medicinal products, and medicines for orphan diseases. These very types of medicinal products are associated with extensively long administrative procedures. A complex change to the system of determination of prices and reimbursements for medicinal products is already being addressed by a MoH workgroup. Information will continue to be collected and a legislative change will begin to be prepared.

11 OVERVIEW OF ABBREVIATIONS

AMR	Antimicrobial resistance
ARTHIQS	Assisted Reproductive Technologies and Haematopoietic Stem Cells Improvements for Quality and Safety throughout Europe
ASRW	Assessment Report Worksharing
ATC	Anatomical Therapeutic Chemical group
BEMA	Benchmarking of European Medicines Agencies
BI	Business intelligence
BPM	Business process management
CAP	Centrally authorised product
CDFA	China Food and Drug Administration
CDNÚ	Central Database of Adverse Reactions
CD-P-PH	The European Committee on Pharmaceuticals and Pharmaceutical Care
CKS	End-user price
CKS NAP	Central Coordination Group for National Antibiotic Programme
CMS	Concerned Member State
CRS	Chemical reference substance
CTFG	Clinical Trials Facilitation Group
CÚER	Central Repository of Electronic Prescriptions
ČAV	Czech Academy of Sciences
CP	Czech Pharmacopoeia
DCP	Decentralised procedure
DU	Defined unit
DL	Diagnostic laboratory
DLL	Active substance importers
DMS	Data management software
DPV	Home parenteral nutrition
DSUR	Development Safety Update Report
ECDC	European Centre for Disease Prevention and Control
eCDT	Format for the submission of applications for marketing authorisations
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EFPIA	European Federation of Pharmaceutical Industries and Associations
EPC	European Pharmacopoeia Commission
EMA	European Medicines Agency
EUDAMED	European database of medical devices
EudraGMP	European Community of Manufacturing Authorisations and of Certificates of Good Manufacturing Practice
EUnetHTA	European Commission and Council of Ministers targeted Health Technology Assessment
EU-NTC	EU Network Training Centre
EURIPID	European Integrated Price Information Database
EV EWG	EudraVigilance Expert Working Group
FAQ	Frequently asked questions
FIH	First-in-human
FSC	Free sale certificate
FSCA	Field safety corrective action
FSN	Field safety notice
PV	Pharmacovigilance
GDPR	General Data Protection Regulation
GMP	Good Manufacturing Practice
HAV	Human autogenous vaccines
HMA	Heads of Medicines Agencies
HTA	Health Technology Assessment

CHMP	Committee for Medicinal Products for Human Use
IMPD	Investigational Medicinal Product Dossier
INN WHO	International nonproprietary name
IPLP	Individually prepared medicinal product
JVP	Joint Visit Programme
CT	Clinical trial
CIMD	Clinical Investigation of Medical Devices
LP	Medicinal product
HTC	Human tissues and cells
MAG	Magistral formulas
MC	Maximum price
MDEG	Medical Devices Expert Group
MHRA	Medicines & Healthcare Products Regulatory Agency (Great Britain)
MMR	measles, mumps, rubella
MOFCOM	Ministry of Commerce of the People's Republic of China
MRA	Medicine Regulatory Authority
MRP	Mutual recognition procedure
MoH	Ministry of Health of the Czech Republic
NCAR	National Competent Authority Report (medical devices)
NMVO	National Medicines Verification Organisation
OCABR	Official Control Authority Batch Release
OECD	Organisation for Economic Cooperation and Development
OMCL	Official Medicines Control Laboratory
ONM	Nuclear Medicine Department
OOP	General measure
OOVL	Detached pharmaceuticals dispensing units
OPC	Department of Issuance of Expert Opinions and Free Sale Certificates
ORN	Registration and Notification Section
OSALK	Department of the State Agency for Medical Cannabis
OZ	Donation Centre
Ph.Eu	European Pharmacopoeia
PhV	Pharmacovigilance
PhV BT	Pharmacovigilance Business Team
PhV IWG	Pharmacovigilance Inspectors Working Group
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PPZ	Medical Device Legal Support Department
PRAC	Pharmacovigilance Risk Assessment Committee
PSUR	Periodic Safety Update Report
PSUSA	Periodic Safety Update Single Assessment
RA	Rapid Alert
RAB	Rapid Alert System for Blood and Blood Components
RAN	Rapid Alert Network
RATC	Rapid Alert System for Human Tissues and Cells
RF	Radiopharmaceuticals
RLPO	Registry of Restricted Medicinal Products
RMS	Reference Member State
RSI	Reference Safety Information
RA	Rapid Alert
RZPRO	Registry of Medical Devices
SAE	Serious Adverse Event
SAKL	State Agency for Medical Cannabis

SCOPE	Strengthening Collaboration for Operating Pharmacovigilance in Europe
GDP	Good Distribution Practice
SEAI	List of Essential Anti-infectives
SKAP	Subcommission for Antibiotic Policy
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
SŘ	Administrative Procedure
SÚKL	State Institute for Drug Control
SUSAR	Suspected unexpected serious adverse reaction
GMP	Good Manufacturing Practice
SWP	Safety Working Party
CAFIA	Czech Agriculture and Food Inspection Authority
ŠÚKL	Slovak State Institute for Drug Control
TIO	Press and Information Department
TNK	Technical Standardisation Commission
TP	Transfusion Products
TC	Tissue Centre
ÚJČ AV	Czech Language Institute of the Academy of Sciences
ÚNMZ	Czech Office for Standards, Metrology and Testing
VHP	Voluntary Harmonisation Procedure
VILP	Highly innovative medicinal products
VUC	Material price regulation
WHO	World Health Organisation
SAR	Serious adverse reaction
SAE	Serious adverse event
ZoL	Act on Pharmaceuticals
ZoRR	Act on Advertising Regulation
ZP	Health insurance
ZP	Medical Device
ZTS	Blood centre

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