ANNUAL REPORT **2016**

SÚKL

STATE INSTITUTE FOR DRUG CONTROL

State Institute for Drug Control
Šrobárova 48
100 41 Praha 10
Czech Republic

phone: +420 272 185 111
fax: +420 271 732 377
e-mail: posta@sukl.cz

www.sukl.cz / **www.sukl.eu**

ANNUAL REPORT **2016**

STATE INSTITUTE FOR DRUG CONTROL

SÚKL

National Strategy of Electronic Healthcare / **Legal regulations**

International cooperation / Expert opinions

373 applications for authorisation/notification / **220 in-depth revisions**

Cooperation with EU / Central ePrescription Repository

Information of professionals and the general public / **Laboratory control**

CONTENT

INTRODUCTION

In 2016, the State Institute for Drug Control (hereinafter referred to as "SÚKL") 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 SÚKL´s operation. A more intensive cooperation between both institutions was developed also in the area of cooperation with the Chinese regulatory authorities, on the basis of signed regional as well as nation-wide contracts. Furthermore, SÚKL was actively involved in the operation of MoH´s workgroups for the development of the National Strategy of Electronic Health Care. In addition to activities associated with these major tasks, SÚKL also paid due attention to cooperation in the drafting of other legal regulations governing other areas of relevance for its operation. SÚKL continued to explain the statutory requirements for individual areas of its expert activities via published guidelines. In those guidelines, SÚKL 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 SÚKL. 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 namely 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, 540 applications were submitted to SÚKL for expert assessment in the sphere of regulatory issues. The total of 274 applications concerned marketing authorisation renewal and, furthermore, 391 applications for marketing authorisation revocation were settled.

In 2016, SÚKL received 373 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. A mild drop was seen in the sphere of DSUR (Development Safety Update Report) assessment and SUSAR control; 410 DSURs were submitted.

The Laboratory Control Section completed 695 sample analyses. The number of samples rated as non-compliant increased. These concerned primarily pharmacy samples queried by doctors and patients. Compared to 2015, the number of counterfeit and suspicious product samples analysed upon request of the Czech Police decreased.

In the course of 2016, the Price and Reimbursement Regulations Branch commenced 220 in-depth revisions (1 178 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. The maximum price was reduced in 54% of cases.

In 2016, 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 2016 is estimated at 1 227 133 738 CZK.

Furthermore, SÚKL, 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 2016, the Department of the State Agency for Medical Cannabis (hereinafter referred to as „OSAKL") 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. Medical cannabis in the amount of 11,2 kg was taken over from the winner of the first public contract on medical cannabis supply, Elkoplast Slušovice s.r.o., and placed in distribution.

With a view to the requirements for mandatory electronic prescription and the establishment of a Central ePrescription 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 eRecept information system (hereinafter referred to as "IS eRecept") and provision of service support for the system was announced and concluded. In December 2016, a contract with the tenderer whose offer was evaluated as the best one was signed and the implementation of the IS eRecept project commenced with much intensity. Pursuant to the effective schedule, the project is to be completed and the IS eRecept to go live on 16 November 2017. For SÚKL to be able to safeguard a flawless operation of electronic prescription (mandatory as of 1 January 2018), implementation of the Institute's data centre extension also started.

As part of its obligation to inform professionals and the general public, SÚKL 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 OSAKL website www.sakl.cz.

All of these activities reflect gradual fulfilment of goals defined in the Strategic Plan 2016-2020 which complies with the original objective and goals.

SÚKL´S ORGANISATIONAL STRUCTURE

In 2015, SÚKL´s systemisation was approved, within the scope of which organisational changes aimed at achieving a higher effectiveness of the work of the Marketing Authorisation Branch were implemented as of 1 January 2016; as part of these changes, the original large departments of pharmaceutical documentation assessment, administrative support, coordination of marketing authorisations, and clinical trials were transferred to sections with new individual departments.

The organisational structure effective from 1 January 2017 is provided below.

DIRECTOR

SURVEILLANCE BRANCH
- Advertising Regulation Dept.
- Quality Defects Dept.
- Legal Support and Enforcement 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 Clinical Trials Dept.
- Control Dept.
- Medical Device Branch Legal Support Dept.
- Vigilance Dept.
- **Marketing Authorisations and Notifications Section**
  - Marketing Authorisations and Notifications Dept.
  - Issuance of Expert Opinions and Free Sale Certificates 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.
  - Data Support Dept.
  - ePrescription Dept.
  - Business Analysis Dept.

Deputy Director

Director's Office
- EU Affairs Manager
- Legal and Legislative Service Dept.
- International Relations Dept.
- Human Resources and Education Dept.

Internal Audit and Control

Information Quality and Security Management

State Agency for Medical Cannabis

Press and Information 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.

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

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

In 2016, SÚKL 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 on the scope of SÚKL´s operation. A rather intensive cooperation between both institutions also developed in the sphere of collaboration with Chinese regulatory authorities, on the basis of signed regional as well as nation-wide agreements.

SÚKL was actively involved in the operation of the working groups of the MoH for the drafting of the National Strategy of Electronic Health Care. In addition to activities associated with these major tasks, SÚKL also paid due attention to cooperation in the drafting of other legal regulations governing other areas of relevance for its operation. SÚKL continued to explain the statutory requirements for individual areas of its expert activities via published guidelines. In those guidelines, SÚKL also informed the public about guidance published by the European Commission and the European Medicines Agency.

As in the previous years, cooperation with the Ministry of Foreign Affairs of the Czech Republic and the Ministry of Health of the Czech Republic 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, and newly, mutual contacts for cooperation with partners in the People´s Republic of China were developed.

SÚKL continued its cooperation with the Institute for State Control of Veterinary Biologicals and Medicines in Brno and the National Institute of Public Health. In the sphere of market surveillance, the Institute´s partners were the Czech Agriculture and Food Inspection Authority, Czech Trade Inspection, and the Customs Administration. 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.

Cooperation with EU Institutions and Other Foreign Partners

SÚKL is actively involved in international cooperation within more than 70 working groups and committees. These represent, in particular, groups 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 SÚKL 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, SÚKL 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. One 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 SÚKL also regularly participates. In total, 402 business trips abroad took place in 2016, of which 187 were paid for by SÚKL and 215 were fully or partially reimbursed by the organising institutions (European Commission, EU Council, EMA, etc.).

SÚKL´s international activities on the EU level include also involvement in the process of adoption of new European legislation falling under SÚKL´s responsibility. In 2016, the debate on the Medical Device Regulation in the EU Council was completed; SÚKL was actively involved in the debate. SÚKL´s representatives also participated in the discussion on the Council Conclusions on enhancing the balance of pharmaceutical systems in the European Union and its Member States and draft regulation amending regulation governing the procedures of marketing authorisation and surveillance over medicinal products.

SÚKL´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, SÚKL continued to develop contacts with the representatives of regulatory authorities of Shanghai, aimed at signing a similar memorandum in the course of 2017.

Relevant strategic information is transferred from international negotiations also onto the national level through membership in advisory boards of the Czech Government/MoH. One of the key issues addressed on the global international level is also the area of antimicrobial resistance. SÚKL continues to actively address this issue within the scope of its Advisory Body for Anti-infectives, through its membership in the Central Coordination Group for the National Antibiotic Program of the Czech Government and the Advisory Board for Antimicrobials of the Ministry of Agriculture of the Czech Republic. SÚKL´s involvement in the preparation of the new action plan of the National Antibiotic Programme was more intensive than in the previous years; the Institute became one of the guarantors of its drafting. The issue of antimicrobial resistance (hereinafter referred to as "AMR") also became one of the 11 key priorities of the HMA action plan for several years, approved in 2016, where SÚKL plans to become more actively involved through its membership in the respective working group. The implementation of plans to address AMR will be verified in 2017 by the European Commission in all EU Member States. This was also one of the reasons why SÚKL was actively represented in the AMR healthcare summit in Sweden and why it 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.

Projects

In the sphere of international projects, since 2014, SÚKL has been involved in two Joint Actions within the scope of the second programme of Community action in the field of health co-funded by the European Commission and the EU Member States. One of them focuses upon the area of pharmacovigilance (Strengthening Collaborations for Operating Pharmacovigilance in Europe, SCOPE), and the other upon 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.

In the SCOPE project, SÚKL has acted as an associated partner and in Work Package 4 it cooperated in the development of procedures for adverse drug reaction reporting. The Project is at its final stage; in the course of 2016, 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 ARTHIQS project started on 1 May 2014 and it will end in autumn 2017. SÚKL has been actively involved in both of its expert parts and, furthermore, acts 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, SÚKL has established and operates the www.arthiqs.eu website and caters for the printing and distribution of information materials and in October 2016, it 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.

In addition to the aforementioned workshop, SÚKL in 2016 hosted two other international events; the meeting of secretariats of pharmacopoeial commissions of the Council of Europe Member States in April 2016, and the meeting of the EURIPID project participants, focused upon cooperation among the EU Member States in the field of medicinal product pricing, in September 2016.

REGULATORY ACTIVITIES OF SÚKL

Record System

In 2016, the electronic record system of SÚKL, incl. its regional workplaces, registered 74 504 delivered documents and 60 168 dispatched documents (Tab. 1). SÚKL thereby continues the electronic processing of individual areas of its office work (Tab. 2).

Tab. 1 **Registration of documents in 2014–2016**

	2014	2015	2016
Received documents	71 494	73 925	74 504
Dispatched documents	36 697	50 016	60 168

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

	Mail room	E-mail messages	Data messages	Electronic notice board	Total
Received documents	25 434	41 715	7 355	-	74 504

	Dispatch room	E-mail messages	Data messages	Electronic notice board	Total
Dispatched documents	9 348	4 637	42 696	3 487	60 168

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.

SÚKL 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, issues opinions for project assessment as to whether clinical trials regulated by SÚKL are concerned, and 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.

Marketing Authorisation of Medicinal Products

Applications for New Marketing Authorisation

In 2016, following successful validation, 540 applications in total were forwarded for expert assessment. Most of them were applications for MRP/DCP marketing authorisations.

In the area of MRP/DCP marketing authorisations, the number of procedures with the Czech Republic as the Reference Member State is essential. In 2016, the number of submitted applications for MRP/DCP marketing authorisation with the Czech Republic as the Reference Member State grew from 65 applications in 2015 to 87 applications. The number of submitted applications for national marketing authorisations grew from 35 applications in 2015 to 51 applications in 2016.

Renewals of Marketing Authorisations

In 2016, following successful validation, 274 applications in total were forwarded for expert assessment. Most of them were applications for MRP/DCP marketing authorisation renewals; the number of applications for national marketing authorisation renewals decreased.

Variations to Marketing Authorisations

In 2016, the number of received applications for variations to MRP/DCP marketing authorisations as well as applications for variations to national marketing authorisations mildly decreased; concurrently, however, the number of submitted applications for transfers of MRP/DCP as well as national increased.

Parallel Import

In 2016, the number of received applications dropped; 73 parallel imports were authorised.

Revocation of Marketing Authorisation

In 2016, 391 applications for revocation of marketing authorisation were decided.

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

Process of marketing authorisation of medicinal products	**Submitted in 2015**	**Decided in total in 2015**	**Pending as of 31 December 2015**
New MAs	598	588	788
of which national	51	32	49
of which MRP-RMS	7	4	27
of which DCP-CMS	80	52	104
of which CMS (MRP and DCP)	460	500	608
MA renewals	276	635	731
of which national	28	274	247
of which RMS	35	46	47
of which CMS	213	315	437
National variations to MA	2673	2 725	454
of which MA transfers	112	115	7
of which PI and labelling	207	197	17
of which bulk NAR variations	2 354	2 359	405
MRP-RMS variations	377	407	66
of which MA transfers	13	13	0
of which PI and labelling	12	14	1
of which bulk MRP-RMS variations	352	380	65
MRP-CMS variations	3 996	4 000	1 200
of which MA transfers	121	105	11
of which PI and labelling	76	73	6
of which bulk MRP-CMS variations	3 799	3 822	1 183
MA revocations	402	391	15
Parallel import	40	73	17
Variation to parallel import	64	89	11
Parallel import renewals	15	10	5
Parallel import revocations	18	18	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 Authorisation

In 2016, SÚKL conducted 59 administrative procedures regarding the granting of exemptions from the Sunset Clause.

In the course of 2016, the Sunset Clause as referred to by Section 34a of the Act on Pharmaceuticals was applied to 128 marketing authorisation numbers and the marketing authorisation of these medicinal products expired.

Tab. 4 **Applications for exemption from the "Sunset Clause" in 2016**

Administrative procedures for granting of an exemption from the Sunset Clause	59
of which initiated based on application	51
of which ex officio initiated administrative procedures	8
granted	36
declined	12
suspended as undue	9
suspended as unjustified	0
suspended for failure to supplement	1
withdrawal of application	1

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

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"), SÚKL was involved in the assessment of centralised marketing authorisations as follows:

- Nine times as the Rapporteur/Co-Rapporteur;
- Eight times as the "Peer Reviewer";
- Three times assessed type I and II variations to centralised marketing authorisations;
- Once assessed a renewal of validity of a centralised marketing authorisation.

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

Clinical Trials

Compared to the previous year 2015, the total number of applications for notification/authorisation of a clinical trial submitted in 2016 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. Of the total number of 373 nationally submitted applications for authorisation/notification of a clinical trial, 25 clinical trials were submitted by non-commercial entities (academic research); 56 applications concerned orphan drugs (medicinal products for rare diseases); 33 involved clinical trials that included also children or were directly intended for paediatric population (paediatric trials), which is 21 less than in 2015 (Tab. 5); 6 clinical trials involved advanced therapy products (1 gene therapy, 4 somatic cell therapies, and 1 tissue engineering), 2 FIH (First-in-Human) applications. In the course of the assessment process, 29 applications for authorisation/notification of a clinical trial were withdrawn, which was less than in 2015; no application was declined.

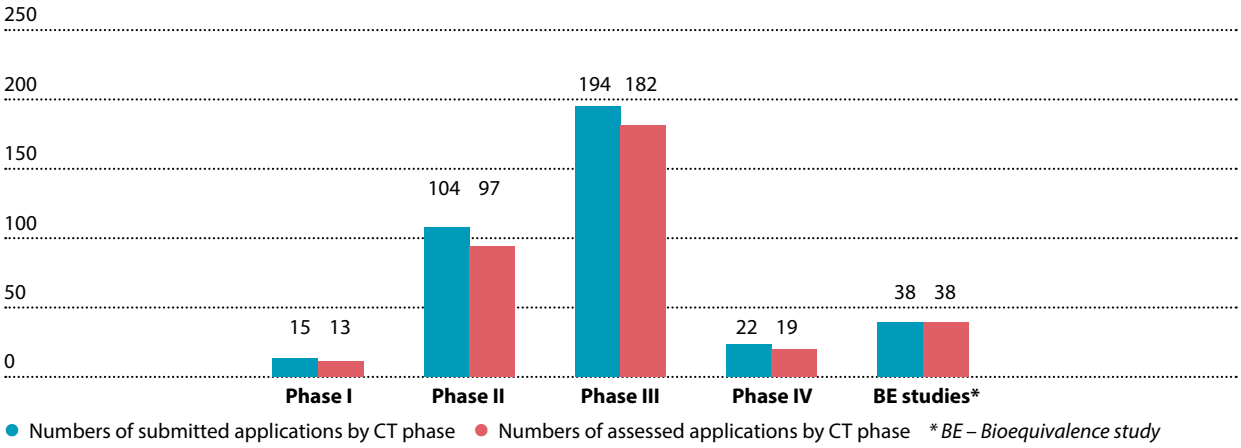
In 2016, the Institute continued its assessment of DSURs (Development Safety Update Reports) and checks of SUSARs. In 2016, 410 DSURs were submitted, which was slightly less than in 2015. In 2016, the project for DSUR assessment and drafting of Assessment Reports, with the participation of other Member States continued. The pilot project changed to Worksharing, the operation of which has been coordinated by the Czech Republic. In 2016, 12 Member States were involved, 49 Assessment Reports drafted, of which 10 by the Czech Republic. DSUR assessment and Assessment Report drafting, which is to continue also in 2017, will result 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.

In 2016, control of compliance with the obligations of the sponsor (submission of information on commencement, clinical trial progress reports, DSURs, and information on clinical trial completion/termination) continued.

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

	No. of applications received in 2016	**No. of decisions issued in 2016**	**Of which declined**	**Of which withdrawn**
Applications for CT authorisation	120	110	0	4
Notifications of CTs	253	239	0	25
Notifications of amendments to CTs	2 833	2 950	0	0

Fig. 1 **Numbers of applications submitted and assessed in 2016 by clinical trial phase**



Pharmacovigilance

In 2016, 3 695 primary reports of suspected adverse drug reactions (hereinafter referred to as "ADR") from the territory of the Czech Republic were received, and 1 767 follow-up reports thereto were made (verification or obtaining of additional information from the reporter). Each individual report received by SÚKL 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 identification of pharmacovigilance signals from reported adverse reactions from the Czech Republic, pharmacovigilance assessors are responsible for the evaluation of signals pertaining to 38 active substances on the European level. In 2016, 412 monthly adverse reaction excerpts from the EudraVigilance database regarding substances for which the Czech Republic is the pharmacovigilance signal rapporteur for the EU were assessed.

Periodic Safety Update Reports (hereinafter referred to as „PSURs") were assessed for nationally authorised medicinal products for all MA renewals and also in cases where a safety risk was identified or it was necessary to review the data on the medicinal product with a view to the EU regulatory procedures. In 2016, the involvement of SÚKL´s Department of Pharmacovigilance in the EU PSUR Single Assessment (so called PSUSA) procedure much intensified. While in 2015 we were the leading country for the assessment of 2 PSUSA procedures, in 2016, 12 PSUSA procedures were assessed.

Assessors from the Department of Pharmacovigilance were involved in the assessment of marketing authorisation dossiers where they reviewed their pharmacovigilance sections.

The conclusions of the Committee for (CHMP) and of the EMA Pharmacovigilance Committee (PRAC) were being transposed to the Czech clinical practice in cooperation with the Marketing Authorisation Department on an ongoing basis. In 25 cases, SÚKL 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 23 direct letters for healthcare professionals, focused upon enhanced safety of use.

SÚKL published 3 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. With a view to the interest of the entire society in the safety of vaccination, increased attention was again paid to the safety of vaccines.

55 notifications (commencement or termination) of post-marketing safety studies were processed. Furthermore, 12 inspections of the pharmacovigilance system of marketing authorisation holders took place.

In 2016, the Department of Pharmacovigilance continued to be actively involved in the SCOPE international project, the purpose of which was to facilitate the involvement of all EU Member States in the uniform execution of the European pharmacovigilance legislation. The Czech Republic is one of the topic leaders

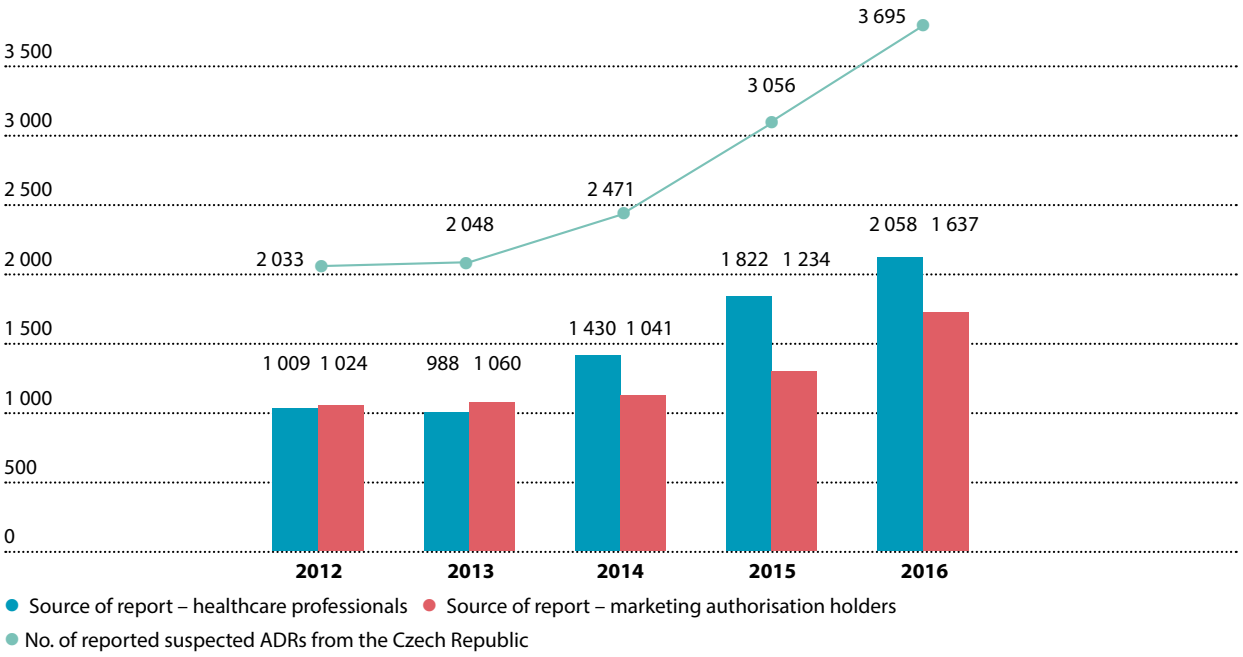
addressing the issue of adverse drug reaction reporting and the system of quality of pharmacovigilance work. In the course of the year, pharmacovigilance assessors participated in a number of training sessions, where information discovered within the scope of the project was presented and discussed.

Within the scope of the educational project to increase the reporting of suspected adverse drug reactions the Pharmacovigilance Department assessors gave 9 presentations at medical 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.

Furthermore, SÚKL has been involved in the education of pharmaceutical companies in good pharmacovigilance practice. In 2016, the Department of Pharmacovigilance organised 2 one-day workshops for these companies and, in addition thereto, gave 9 presentations on other occasions.

The Department of Pharmacovigilance has been actively involved in international pharmacovigilance activities. It took part in 11 meetings of the EMA Pharmacovigilance Committee (PRAC) and 10 teleconference meetings of the PRAC Committee. In the course of the year, SÚKL, as the rapporteur for the EU (chief pharmacovigilance assessor) for the newly authorised substance blinatomumab, conducted an evaluation of marketing authorisation renewal and an assessment of a post-marketing safety study protocol. Furthermore, it has been actively involved in the European Pharmacovigilance Inspectors Working Group (hereinafter referred to as „PhVIWG") and an expert group for the EudraVigilance system (hereinafter referred to as „EV EWG").

Fig. 2 **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 SÚKL 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 SÚKL 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 and Enforcement addresses quality defects of pharmaceuticals and excipients available on the market in the Czech Republic. Furthermore, the Department is involved in the identification and penalising 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, SÚKL cooperates with other institutions in the Czech Republic as well as abroad (particularly with the Police of the Czech Republic, Customs Administration, Czech Agriculture and Food Inspection Authority, control authorities of the EU Member States).
The exercise of supervision 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.

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 SÚKL units). This includes, in particular, addressing of quality defects of medicinal products, analyses of pharmacy samples, suspected counterfeit and illegal medicines, 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 (hereinafter referred to as „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 2016, 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 2016 by both laboratory departments of the Laboratory Control Section are summarised in the tables below.

Tab. 6 **Supervision over the quality of pharmaceuticals on the market by means of laboratory analyses according to predefined projects (projects concluded in 2016)**

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
3/2015 – Pharmacy samples*	57	210	186	24	1
6/2015 – Therapy days	6	16	16	0	0
Flue vaccines 2015/2016	4	4	4	0	0
LAL in infusions	15	30	30	0	0
Verification of microbiological quality of medicinal products containing live microorganisms	4	7	7	0	0
Herbal teas – microbiological quality	24	47	47	0	0
Total (ex. 3/2015)	**53**	**104**	**104**	**0**	**0**

** Samples from these products included in 2015*

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 SÚKL's Quality Team. In 2017, works on the following projects will take place: Verification of microbiological quality of products for nasal and auricular use; Verification of microbiological quality of lozenges against sore throat; Quality control of generic products (products containing meloxicam, montelucast, escitalopram, cetirizine hydrochloride, paracetamol); Control of products containing capillary stabilisers; Control of products in the form of creams and gels; and Control of medicinal products containing corticosteroids. The project of Braill labelling of medicinal products was concluded and the final report was submitted to the Quality Team for approval. At present, sampling for new laboratory control projects is under way, particularly for the following ones: Control of vasodilators; Control of medicinal products containing telmisartan, loratadine, betaxolol, and salicylic acid. Furthermore, the Control of medicinal products containing diclofenac project has been approved. Pharmaceutical samples continue to be controlled and analyses of identified counterfeit products carried out.

Tab. 7 **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	57	900	882	18	900	0
Vaccines	30	465	465	0	465	0

**Some batches were released repeatedly.*

Tab. 8 **Laboratory control of pharmaceuticals and excipients requested by other units of SÚKL, other state administration organisations or EDQM**

	Number of samples	Of which compliant	Of which non-compliant
Suspected quality defect of a pharmaceutical	110	97	13
Suspected counterfeit, illegal samples*	49	-	-
Pharmacy samples	202	173	30
International studies within OMCL*	6	-	-
Internal quality control of purified water	146	145	1
Samples taken by the INS section	1	1	0
Spectrum library development (Raman, IR)*	50	-	-
Other analyses**	9	9	0
Total	**573**	**425**	**44**

* *Sample compliance cannot be evaluated.*

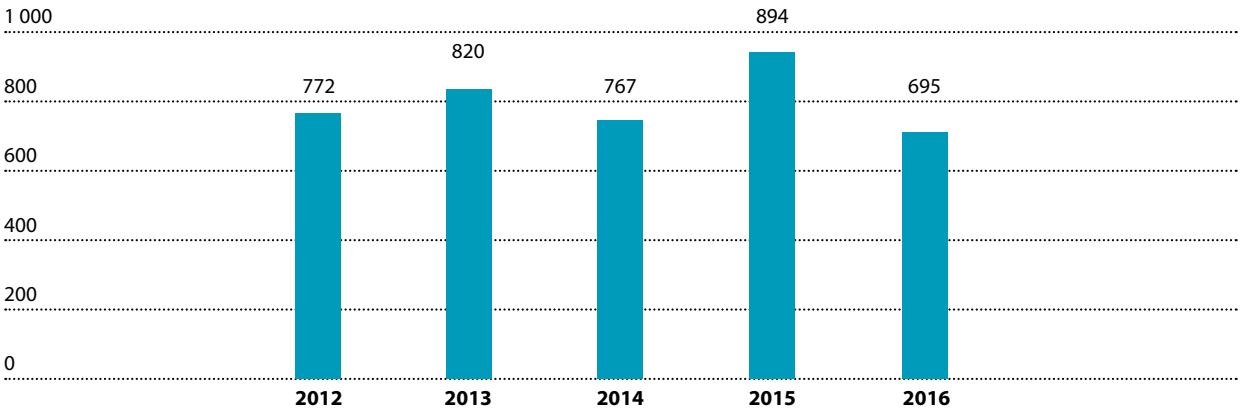
** *E.g. requested microbiological controls, other requested analyses, etc.*

In the Laboratory Control Section, 695 sample analyses were completed. The reduced number of samples has been caused primarily by large sampling projects carried out by the Section in 2016, which are at the stage of final report preparation and have not been concluded to date. Compared to 2015, the number of samples of counterfeit products and suspicious medicinal products analysed upon request of the Czech Police also dropped. Nevertheless, the number of these requests cannot be influenced on the part of the Section.

The number of samples rated as non-compliant (ex. counterfeits and illegal products, samples from international studies, and samples for the spectrum library development) again increased compared to the last year and amounted to 6.3% (5.3% in 2015; 4.8% in 2014; 3.5% in 2013). This concerned primarily pharmacy samples and samples queried by doctors and patients. The number of addressed suspected quality defects has been increasing over the past few years in a stable manner. Confirmed defects of pharmaceuticals involved primarily the content of active substances, adjustments, and purity, incl. microbiological purity. The Section will continue this trend of projects focused particularly upon risk groups of medicinal products.

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.

Fig. 3 **Number of sample analyses in 2012–2016**



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 2016, the Laboratory Control Section participated in collaborative international studies listed in Table 9.

Tab. 9 **Involvement in international studies**

Study	Study title	Rating
PTS 159	Dissolution	Good
PTS 160	Liquid Chromatography	Good
PTS 165	Volumetric Titration	Good
PTS 166	Loss on Drying	Good
CAP 16/02	Ammonaps Granules	Good
CRS	Sodium Alendronate Trihydrate	Good

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.

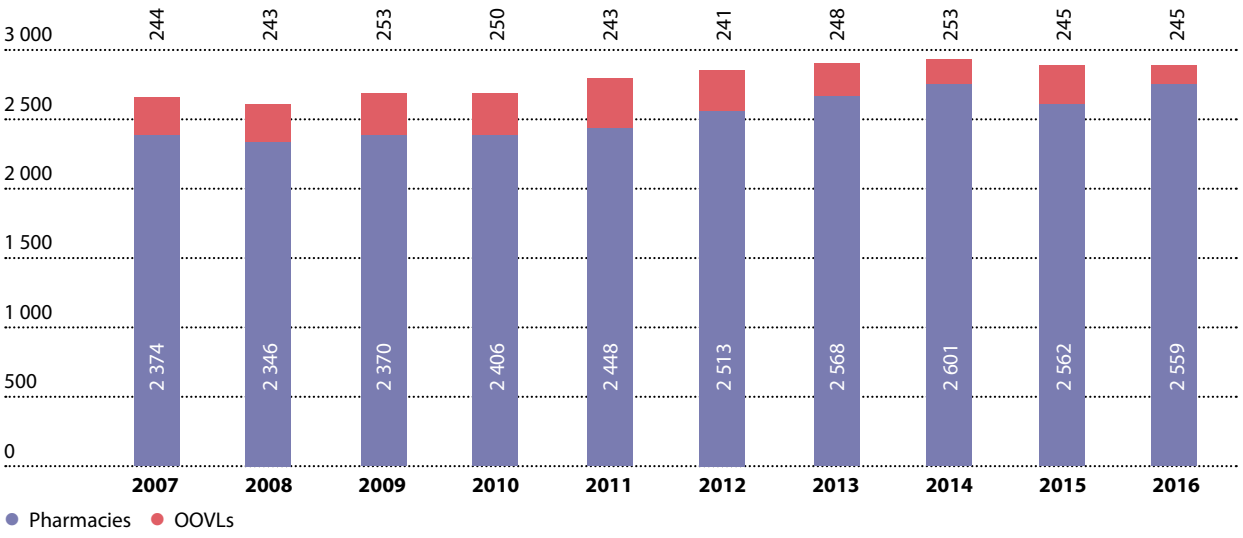
CRS – Verification of the quality of the reference substance for EDQM/ Chemical Reference Substance.

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 SÚKL 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 2016, SÚKL kept a record on a total of 2 559 pharmacies, of which 4 fell within the scope of powers of the Ministry of Defence of the Czech Republic; moreover, SÚKL kept a record on 245 detached pharmaceuticals and medical device dispensing units (hereinafter referred to as "OOVL"), 402 medical device dispensaries, 2 212 vendors of selected medicinal products, 45 nuclear medicine departments of healthcare facilities, and 443 wholesale distributors of medicinal products. The stagnation in the total number of pharmacies continued; compared to 2015, the total number of pharmacies decreased by 3 entities, the number of OOVLs remained the same (Fig. 4).

Fig. 4 **Number of pharmacies and OOVLs in the period of 2007–2016 (as of the last day of each concerned year**



In 2016, the inspectors of the Pharmacy and Distribution Section conducted 877 inspections in pharmaceutical care facilities – pharmacies, in total, of which 30 were hospital pharmacies of inpatient care providers. Of the total number of inspected pharmacies, 43 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 468 pharmacies.

Price control focusing upon compliance with the Act on Prices and rules of price regulation was conducted in 99 pharmacies, of which 12 inspections were targeted, and at 13 wholesale distributors´.

On the basis of facts identified during the conducted inspections, in total, 94 final decisions to impose a fine for breach of obligations stipulated by the Act on Pharmaceuticals in the total amount of 7 350 000 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 11 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, in particular, non-compliance with the rules of good pharmacy practice in the preparation and control of medicinal products, e.g. the use of active substances and excipients after their shelf-life expiry; failure to perform prescribed checks of apparatuses

and devices used for preparation; preparation without technological regulations; and insufficient records on 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 and dispensed; storage and dispensing of medicinal products which should have been withdrawn from the market based on a decision of the marketing authorisation holder or whose marketing authorisation expired; transfers of medicinal products between pharmacies and illegal export of medicinal products abroad; non-compliance with the storage conditions of medicinal products.

Within the scope of inspections of the handling of dependency-producing substances in pharmacies, identification of major breaches of the Act on Dependency-Producing Substances resulted in the total of 17 final decisions on fine imposition to pharmacy operators amounting to 429 000 CZK in total, of which 100 000 CZK concerned penalties imposed for failure to comply with the notification duty regarding the stock and movement of dependency-producing substances and products.

In 2016, the operators of pharmacies were imposed the total of 11 final decision on a fine amounting to 203 000 CZK in total for major breaches of the Act on Precursors.

As in the previous year, the main reasons for the issue of the decision on fine imposition included, in particular, failure to submit the annual report on the stock and movement of dependency-producing substances and products; incorrect or incomplete data in the annual report; major breaches of the Act on Dependency-Producing Substances regarding record-keeping and documentation of dependency-producing substances and products; handling of precursors without a special licence; failure to keep documents and records of the activities with precursors and their storage and protection from abuse contrary to the Act on Precursors.

Inspections focusing on compliance with price regulation rules in pharmacies identified a breach of price regulations in the total of 43 cases. Pharmaceutical care providers were issued 40 final decisions on fine imposition pursuant to the Act on Prices amounting to 970 000 CZK in total and 1 final fine for failure to provide cooperation during the inspection in the amount of 100 000 CZK. Most often, failure to observe the binding procedure governing the determination of the sales price of magistral formulas and proprietary medicinal products treated prior to dispensing; failure to observe officially fixed maximum prices during sales; disregard for the conditions and procedures for their application stipulated in the price regulations of the MoH; and failure to specify or keep price records were identified.

A breach of the ban on offering and provision of advantageous sale in respect of reimbursed medicinal products dispensing was identified in 18 cases. This concerned, in particular, 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, the offer and provision of discounts or vouchers for future buys and financial bonuses for a prescription.

On the basis of the inspection findings, 16 final decisions on fine imposition were issued pursuant to the Act on Public Health Insurance, with the fines amounting to the total of 480 000 CZK.
Furthermore, un 2016, 304 inspections of the handling of medicinal products in healthcare facilities were conducted. The inspections were carried out in 22 inpatient hospital departments and in 282 separate outpatient offices of general practitioners and medical specialists, and in other healthcare facilities. On the basis of reports received by SÚKL in connection with the operation of healthcare facilities, where health care is provided, a total of 38 targeted inspections took place. A total of 9 final decisions on fine imposition in the total amount of 1 405 000 CZK were taken for the identified violations of the Act on Pharmaceuticals.

The major reasons for the issue of the decision on fine imposition included, in particular, the storage and dispensing of medicinal products in the doctor´s office; handling of medicinal products contrary to the summary of the product characteristics; incorrect storage of medicinal products past their expiry date; 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 2016 involved 106 outlets in total; 9 final decisions on fine imposition in the total amount of 95 000 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 2016 are provided in Table 10.

Tab. 10 **Inspection surveillance over pharmacies, nuclear medicine departments, healthcare facilities, and vendors of selected medicinal products in 2016**

			Classification of shortcomings						Penalties		
Inspected entity	**Type of inspection**	**Number**	**1**	**%**	**2**	**%**	**3**	**%**	**A**	**B**	**C**
Pharmacies	Regular inspections	877	454	51,8	261	29,8	162	18,4	1 1	-	94
	Price inspections	99	Not rated by classification of shortcomings						-	-	40
	Inspections of dependency-producing substances	468	290	61,9	129	27,6	49	10,5	-	-	28
Nuclear medicine departments		15	12	80,0	3	20,0	-	-	-	-	-
HAV		3	1	33,4	1	33,3	1	33,3	-	-	-
Healthcare facilities		304	189	62,2	80	26,3	35	11,5	-	-	9
Vendors of selected medicinal products		106	91	85,8	8	7,6	7	6,6	-	-	9

Classification of shortcomings

1 – None or minor shortcomings identified

2 – Major or repeated shortcomings

3 – Critical shortcoming or serious breach of law

Penalisation

A – Suspended preparation

B – Suspended operation

C – Fine imposed (final decision)

In 2015, inspectors from the Pharmacy and Distribution Section took a total of 202 samples of medicinal products during inspections in pharmacies, of which 110 were pharmaceutical products intended for the preparation of extemporaneous products in the pharmacy. Out of 92 pharmacy samples (medicinal products prepared in pharmacies), 4 in total were out-of-specification, the shortcomings being out-of-specification content, total weight of the sample, and inadequate galenic processing. In respect of 23 samples intended for dispensing, defects in their labelling were identified. The number of samples taken has not practically changed over the past few years and it corresponds with the decreasing internal preparation of medicinal products in pharmacies.

Comparison of occurrence of monitored shortcomings in out-of-specification pharmacy samples in the last years is provided in Table 11.

Tab. 11 **Occurrence of monitored types of shortcomings in % (of the total number of non-compliant samples)**

Type of shortcoming	**2014**	**2015**	**2016**
Out-of-specification content of active substance	50,0	42,9	25,0
Out-of-specification total weight	37,5	42,9	50,0
Out-of-specification purified water Microbiological compliance	-	-	-
Out-of-specification galenic processing	12,5	-	25,0
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 2016, a total of 321 applications for issuance of an opinion were received from pharmacy operators and 322 positive binding opinions were issued. In the case of dispensaries of medical devices, a total of 13 operators applied for a binding opinion and 13 positive binding opinions were issued.

In 121 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 13 cases with an inspection of OOVLs (Table 12). Furthermore, in this context, 12 initial inspections of medical device dispensaries and 243 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 12 also provides data on newly established and defunct pharmacies/OOVLs.

Tab. 12 **Other activities of the Pharmacy and Distribution Section**

Initial pharmacy inspections	Establishment of a new pharmacy/OOVL	Defunct pharmacies/OOVLs
121	81/17	84/17
Initial OOVL inspections	**Initial medical device dispensary inspections**	**Consultations**
13	12	243

Distribution of Medicinal Products

In 2016, the number of distributors decreased by 12 entities to the total of 440 medicinal products distribution authorisation holders. Of the total number of approved distributors, 162 entities were both a pharmacy operator and a distribution authorisation holder.

In 2016, 37 new distribution authorisations and 145 decisions on variations to distribution authorisations were issued, and 46 authorisations were revoked upon request of their holders. In one case, the distribution authorisation expired in compliance with Section 76, paragraph 4 of the Act on Pharmaceuticals. In two other cases, the authorisation was revoked by the decision of SÚKL pursuant to Section 76, paragraph 3 of the Act on Pharmaceuticals. The total of 9 entities applied for entry into the Register of Brokers of Human Medicinal Products in 2016; one application was rejected. As of 31 December 2016, the Register included the total of 19 entities.

Table 13 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. 13 **Distribution and intermediation of pharmaceuticals in 2016**

	Received applications	Authorisations issued/register entries made
Application for distribution authorisation	36	37
Application for variation to distribution authorisation	140	145
Application for revocation of distribution authorisation	41	46
Application for entry in the Register/variation to entry in the Register	9	8

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

In 2016, the total of 318 inspections of distributors and 2 inspections of brokers took place, of which 13 were targeted inspections carried out on the basis of internal and external reports. In total, 22 reports were received and investigated; in 4 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 SÚKL guidelines.

Of the total number of 243 rated inspections of distributors (follow-up and targeted inspections), 71.2% were rated with grade 1 (good), 22.2% with grade 2 (satisfactory), and 6.6% with grade 3 (not satisfactory).

Following the completed inspections, the total of 192 post-inspection good distribution practice certificates were issued, of which 37 certificates were of limited validity (one year in 11 cases; 2 years in 26 cases). In respect of one certificate, the scope of certified activities of the distributor was restricted on the basis of the inspection findings. 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 one investigation of suspected quality defect of a medicinal product and, with the authorisation of the Strasbourg EDQM inspectorate and SÚKL´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 9 paid consultations regarding the application of good distribution practice principles.

In 2016, 13 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 6 cases and 5 proposals to initiate an administrative procedure regarding fine imposition were submitted. The reason was failure to comply with the officially established maximum price of medicinal products, non-observation of the conditions and procedures for its application, and breach of the obligation to keep price records. One fine amounting to 100 000 CZK was finally imposed for failure to provide cooperation during price inspection.

On the basis of facts identified during the completed inspections, distributors were imposed the total of 22 final decisions on fine for breach of obligations set forth by the Act on Pharmaceuticals and its implementing regulations amounting to 3 396 000 CZK (incl. also finalised administrative procedures based on inspections conducted in the previous period).

The main reasons for the proposed fine imposition were, in particular, non-observance of the obligation to provide SÚKL with complete and correct data about distributed medicinal products; deliveries to unauthorised customers; the breach of ban on distribution and export of medicinal products on the basis of an extraordinary measure issued by the MoH; 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 four 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 2016 are provided in Table 14.

Comparison of the number of regulated entities, conducted inspections and imposed penalties for the last 3 years is illustrated by Fig. 5.

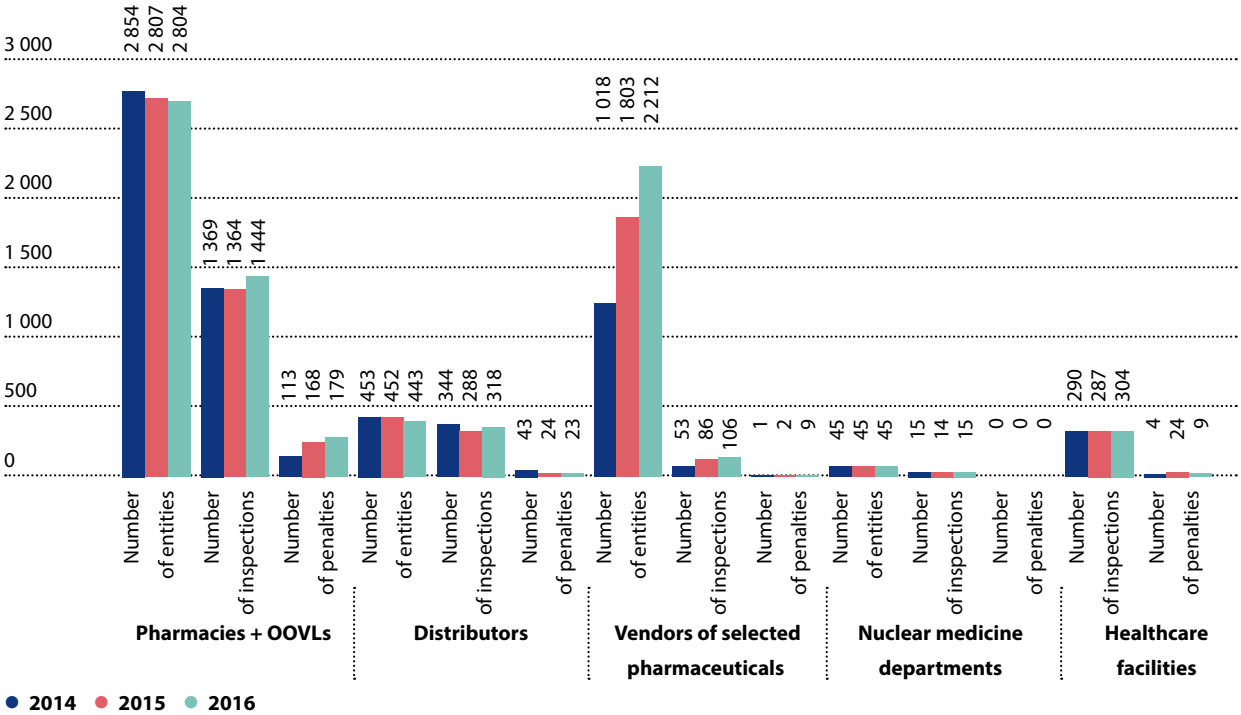
Tab. 14 **Inspection surveillance over distributors**

	Number of inspections				Inspection rating			Measures	
Total	Initial	Follow-up	Targeted	Variation	1	2	3	Breach of law	Proposed fine
318	36	231	13	38	173	54	16	82	49

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

Fig. 5 **Information on surveillance activities in 2014–2016**



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 SÚKL´s website. In the sphere of manufacturers (incl. blood centres) the total of 91 applications for manufacturing authorisation or variations thereto were received (Tab. 15). 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 15% less than in 2015.

Human Tissues and Cells

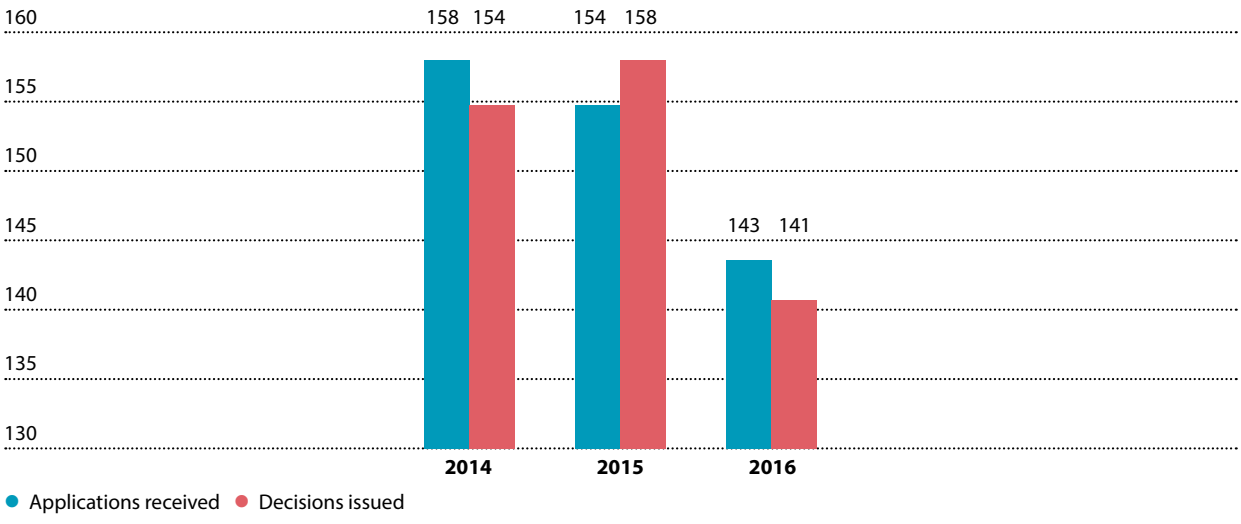
This is an area regulated by SÚKL pursuant to Act No. 296/2008 Coll., on Human Tissues and Cells.

In 2016, 52 applications for operating authorisation and applications for variations to operating authorisations were received. The number of submitted applications was 18% more than in 2015.

Tab. 15 **Activities associated with applications in the sphere of manufacture of pharmaceuticals and in the sphere of human tissues and cells**

Application type		2014		2015		2016	
		Received applications	Issued decisions	Received applications	Issued decisions	Received applications	Issued decisions
Application for manufacturing authorisation	Manufacturer of medicinal products	0	3	1	0	3	2
	Control laboratory	3	3	2	3	2	1
	Blood centre	0	0	0	0	1	0
Application for variation to manufacturing authorisation	Manufacturer of medicinal products	67	65	63	61	55	55
	Control laboratory	3	5	4	3	5	4
	Blood centre	35	35	29	36	23	26
Application for revocation of manufacturing authorisation	Manufacturer of medicinal products	2	2	2	2	2	3
	Control laboratory	2	1	4	2	0	2
	Blood centre	4	4	5	5	0	0
Application for operating authorisation	Tissue centre	4	5	4	4	1	1
	Donation centre	1	1	0	0	0	0
	Diagnostic laboratory	1	0	1	1	0	0
Application for variation to operation	Tissue centre	30	25	28	26	41	37
	Donation centre	0	0	0	0	0	0
	Diagnostic laboratory	5	4	10	9	8	8
Application for revocation of operation	Tissue centre	1	1	1	1	2	2
	Donation centre	0	0	0	0	0	0
	Diagnostic laboratory	0	0	0	0	0	0
Total		**158**	**154**	**154**	**158**	**143**	**141**

Fig. 6 **Numbers of received and concluded applications**



In 2016, the Institute carried out 340 inspections in total, of which 171 inspections were associated with the regulated area of tissues and cells. Their nature and results of rating are provided in Table 16. 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 2016 is provided in Table 17 and Fig. 7 and 8.

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 or active substances, 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 (hereinafter referred to as "GMP") proper, contains also manufacture risk assessment and other criteria. Inspections related to a variation are carried out only if the conditions under which the activities were permitted 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 102 inspections at manufacturers of medicinal products, active substances, and control laboratories, a breach of the Act on Pharmaceuticals was identified in five 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.

Tab. 16 **Inspections conducted in 2016 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	71	6	45	6	14	51	0	3	1
Manufacturers of active substances	18	3	10	3	2	13	0	2	1
Control laboratories	9	2	6	1	0	8	0	0	0
Medicinal product importers	4	1	3	0	0	4	0	0	0
Blood centres	47	0	42	1	4	0	0	0	0
Blood banks	22	1	20	0	1	21	0	1	0
GCP inspections – Ethics Committees	0	0	0	0	0	0	0	0	0
GCP inspections - other	16	0	1	14	1	1	0	7	0
TC, DC, DL inspections	104	8	88	3	5	104	0	1	1

TC – tissue centre, DC – donation centre, DL – diagnostic laboratory; 1) –rates only for initial and follow-up inspections

Tab. 17 **Inspections conducted in 2014–2016**

	2014		2015		2016	
	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
Manufacturers of active substances	27	0	15	0	18	2
Control laboratories	11	0	23	0	9	0
Medicinal product importers	-	-	-	-	4	0
Blood centres	46	0	47	0	47	0
Blood banks	11	0	17	0	22	0
GCP inspections + Ethics Committees	21	0	15	0	16	7
Tissue centres, donation centres, diagnostic laboratories	107	0	171	0	104	1
Total	**294**	**1**	**340**	**0**	**295**	**13**

Fig. 7 **Number of manufacturers of medicinal products, active substances and control laboratories and an overview of conducted inspections in 2014-2016**

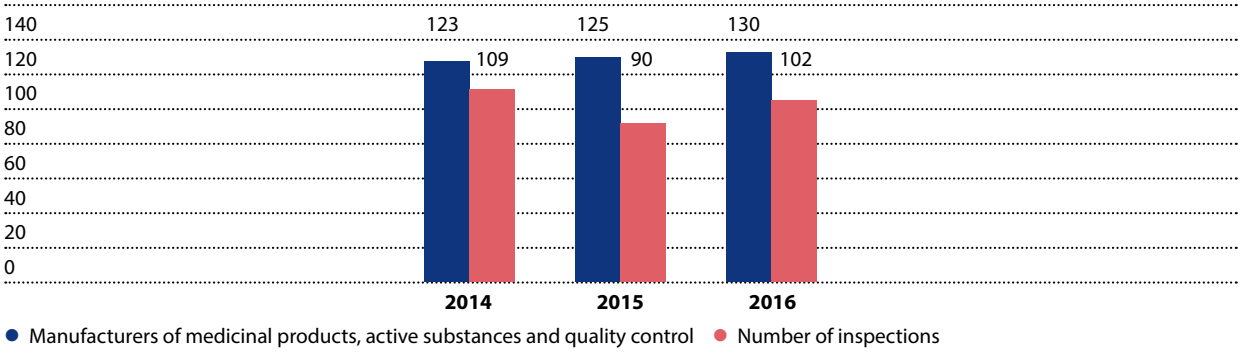
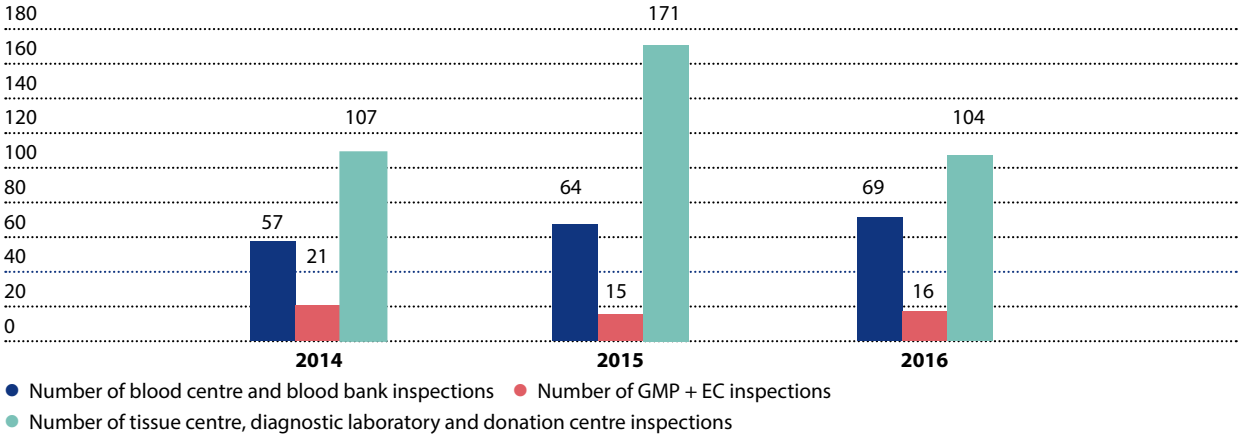


Fig. 8 **Overview of inspections conducted by Clinical Practice and Surveillance over Biological Material Processing Dpt. in 2014–2016**



Haemovigilance

In 2016, 19 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 8 regulated entities, i.e. blood centres or blood banks, were received. Of this, 4 cases of SAR concerned donors of blood or blood components, 11 cases of SAR involved a post-transfusion reaction in TP recipients, and 4 cases did not constitute a SAR. In case of SARs experienced by TP recipients, in 9 cases full recovery followed, in 1 case the TP recipient died for cause other than the transfusion, 1 SAR resulted in the death of the patient. Pin all of the 4 cases of SARs regarding blood or blood component donors, full recovery followed. Furthermore, 11 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, 3 cases concerned a product defect; 3 cases a human error; in 1 case the SAE was associated with the storage of the TP; and 4 cases did not concern a SAE. Each report 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. On an ongoing basis, educational activities to raise the awareness of regulated entities regarding the importance of suspected SAR and SAE reporting was carried out. In cooperation with the Transfusion Medicine Society, a document containing recommendations on how to evaluate and report adverse reactions, is being drafted. Within the scope of its involvement in RAB, SÚKL in 2016 received 7 reports from 6 countries. 5 cases involved an epidemiological situation (twice associated with the occurrence of the West Nile virus; twice with the occurrence of malaria; and once with the occurrence of the Zika virus) and 2 cases constituted a warning regarding the use of a medical device by a TP manufacturer.

Good Laboratory Practice (GLP)

In 2016, a total of 8 holders of Good Laboratory Practice Certificates issued by SÚKL were listed, with prevailing scope of activities in toxicological studies; these are included in the National GLP Programme. In the same year, 7 follow-up inspections were completed.

Good Clinical Practice (GCP)

In the course of the year, the total of 16 national inspections of good clinical practice were conducted, of which 14 concerned a targeted inspection of a trial site (a GCP inspection at the investigator´s); one case concerned a systemic inspection of a contract research organisation, and one case concerned a systemic inspection based upon an application for a GCP certificate issuance. In the total of 7 cases, a possible breach of an obligation set forth by Act No. 378/2007 Coll., on Pharmaceuticals, was identified.

In 2016, the GCP inspectors were involved in one international inspection conducted by EMA and, within the scope of the PIC/S – JVP programme, participated in an international inspection in Great Britain.

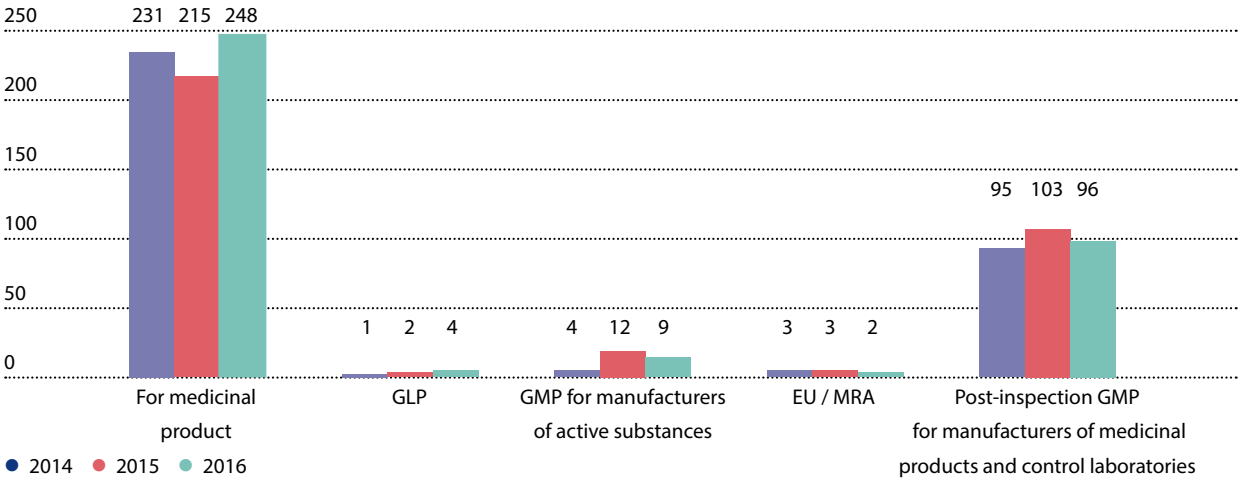
Actions and Penalties

In 2016, a breach of the Act on Pharmaceuticals and the Act on Tissues and Cells was identified in 13 cases.

Certification

In total, 257 various certificates were issued. Post-inspection good manufacturing practice certificates are subsequently entered in the EudraGMP database maintained by the EMA. All of the certificates for medicinal products were issued within the 30-day timeline, and all good manufacturing practice certificates within the 90-day timeline.

Fig. 9 **Issued certificates**



Assessment of GMP Compliance within the Scope of Marketing Authorisation Activities

A total of 1 287 cases were received (a 34% increase compared to 2015), all of them were processed within the timelines.

Foreign Inspections

In 2016, 3 good manufacturing practice inspections at foreign entities in Turkey, the U.S. and Canada were performed

Tab. 18 **Foreign inspections**

	2014	2015	2016
Number of inspections	2	7	3
Certificate issuance	2	3	3
Issued non-compliance	0	1	0

Quality Defects of Pharmaceuticals

Between 2009 and 2013, there was a rapid increase in the number of reports in the area of quality defects. A relatively significant increase in the number of reports compared to 2014 and 2015 can be seen also in 2016. The amount of received reports is comparable to 2013 (Tab. 19).

In 2016, the reports concerned not only authorised medicinal products 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, SÚKL received and evaluated the total of 96 reports on quality defects of pharmaceuticals. Compared to previous years, in 2015 and 2016, SÚKL saw a marked increase in the number of reports regarding the occurrence of counterfeit medicinal products in the legal network.

Mutual exchange of information with the Slovak State Institute for Drug Control (hereinafter referred to as „ŠÚKL") in Bratislava continued and the Institute collaborated with ŠÚKL in Bratislava on several occasions in 2016.

Reports received from abroad also included reports on noncompliance of the manufacturing site of a medicinal product or an active substance with the GMP (Good Manufacturing Practice) principles. The Quality Defects Department received a total of 55 such reports in 2016.

Tab. 19 **Number of received reports**

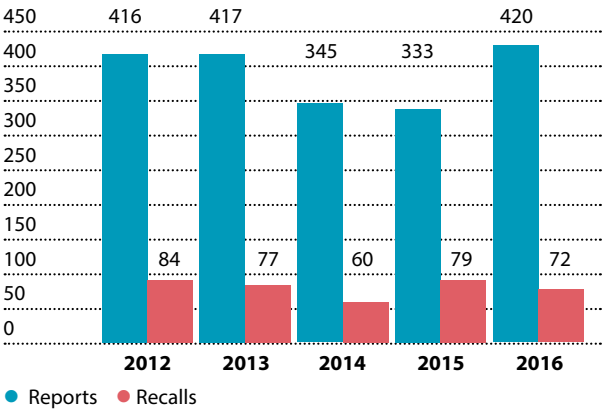
Quality Defects	**2012**	**2013**	**2014**	**2015**	**2016**
Reports received in total	416	417	345	333	420
Reports from the Czech Republic	294	210	181	181	243
Reports from abroad	122	207	164	152	177
Resulted in recall	84	77	60	79	72
Issued RWs	4	1	6	16	18
Issued RAs	7	3	6	11	17

RW – Rapid Warning, RA – Rapid Alert

Tab. 20 **Actions taken in 2016 (in SÚKL codes)**

Action taken	**Number**
Recalls from distributor level	0
Recalls from healthcare facility level	64
Recalls from patient level	8
Suspended distribution, dispensing and therapeutic use	2
Released distribution, dispensing, and therapeutic use	2

Fig. 10 **Number of reports and recalls of medicinal products in 2012–2016**



Within the scope of the solution of quality defects, effective actions have been taken to reduce the impact of the quality defect on patient health. Table 20 gives an overview of actions adopted as part of addressing the quality defects in individual medicinal products (related to SÚKL codes) in 2016. In all cases, the actions were adopted by the operators themselves, with SÚKL solely monitoring or adjusting those measures.

The Quality Defects Department, moreover, monitored recalls of medicinal products due to variations to marketing authorisation (such as a shortened shelf-life, changed method of dispensing, changes to the summary of the product characteristics, labelling or package leaflet, etc.). For these reasons, in 2016, 21 medicinal products were recalled in total.

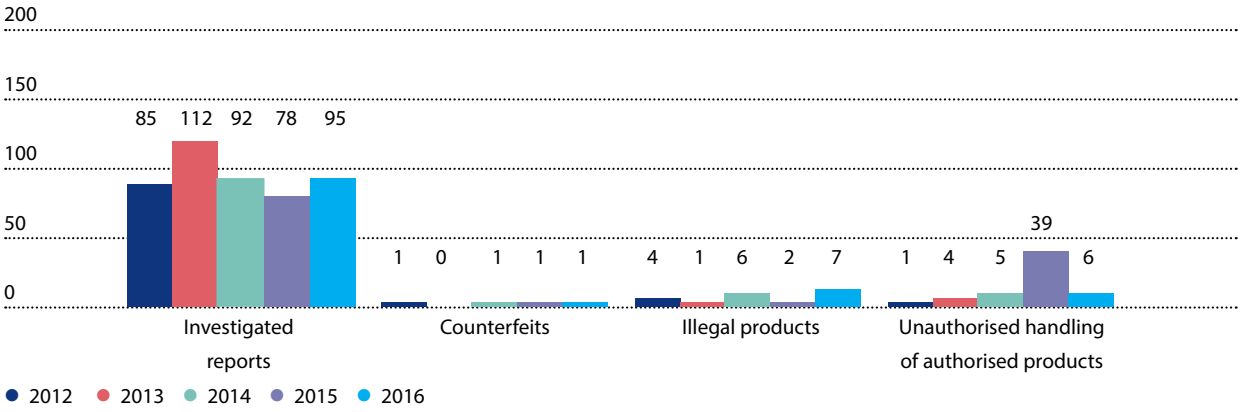
The Quality Defects Department also focused upon supervision over compliance with the obligation of marketing authorisation holders stipulated under the provisions of Section 33, paragraph 2 of Act No. 378/2007 Coll., on Pharmaceuticals and on Amendments to Some Related Acts (Act on Pharmaceuticals), as amended, which requires marketing authorisation holders to notify SÚKL datum of the date of the actual placing of the medicinal product on the market in the Czech Republic by pack size and packaging type, no later than within 2 months of the actual placing on the market; in the same manner, they are also required to notify SÚKL of a suspension or termination of placing the medicinal product on the market in the Czech Republic at least 2 months in advance. If the medicinal product is re-introduced to the market, the marketing authorisation holder is obliged to forthwith inform SÚKL of this fact. In the last year, SÚKL addressed 50 such reports.

Enforcement

In 2016, 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, SÚKL closely cooperates with the Customs Administration, Czech Police, Czech Trade Inspection, Czech Agriculture and Food Inspection Authority (hereinafter referred to as „CAFIA"), and the Trade Licensing Offices. 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.

Fig. 11 **Control activities in of SÚKL in the period of 2012–2016**



In 2015, a total of 95 reports (either SÚKL's own or received reports) were investigated. In 2016, SÚKL much focused upon the monitoring and detection of illegal offers of medicinal products in the internet environment and checked 439 websites and executed 13 control buys, in which 7 cases of handling of unauthorised medicinal products and 6 cases of unauthorised handling of authorised medicinal products were identified.

In 2016, SÚKL prepared a total of 151 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 in compliance with the applicable legislation.

Tab. 21 **Results of investigated cases**

Cases concluded by:	**2012**	**2013**	**2014**	**2015**	**2016**
Administrative procedure with proposed penalty imposition	2	1	5	2	6
Reports of crime	2	3	4	2	2
Cases forwarded to other authorities (CAFIA, etc.)	4	3	1	1	1

Surveillance in the Area of Regulation of Advertising for Medicinal Products

In 2016, SÚKL investigated a total of 201 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 2015, the Institute received 1 more new report in 2016 (130 newly received reports in 2015). In 2016, 7 administrative procedures were completed that resulted in the imposition of 8 fines in the aggregate amount of 2 970 000 CZK.

Tab. 22 **Overview of investigated reports of suspected breaches of the Act on Advertising Regulation**

	Reports brought forward from 2015	**Newly received reports in 2016**	**Total**
Number of reports	75	131	206
Investigation completed	63	107	170
Forwarded for commencement of administrative procedure	12	6	21
Pending	3	2	5
Completed administrative procedure	3	2	5

The subject of investigation into advertising was printed advertising matter (21%), websites (67%), sponsorship (7%), and promotional samples (4%).

Advertising for prescription-only medicines accounted for 70% of the investigated cases, advertising for over-the-counter medicines represented 30% of cases.

Pharmaceutical companies or their legal representatives filed 8% of reports on suspected breaches of law, 4% of reports were filed anonymously, 7% were lodged by private individuals, 1% by state administration bodies, and 80% by SÚKL.

Fig. 12 **Overview of investigated reports of suspected breaches of the Act on Advertising Regulation for the period of 2012–2016 (in %)**

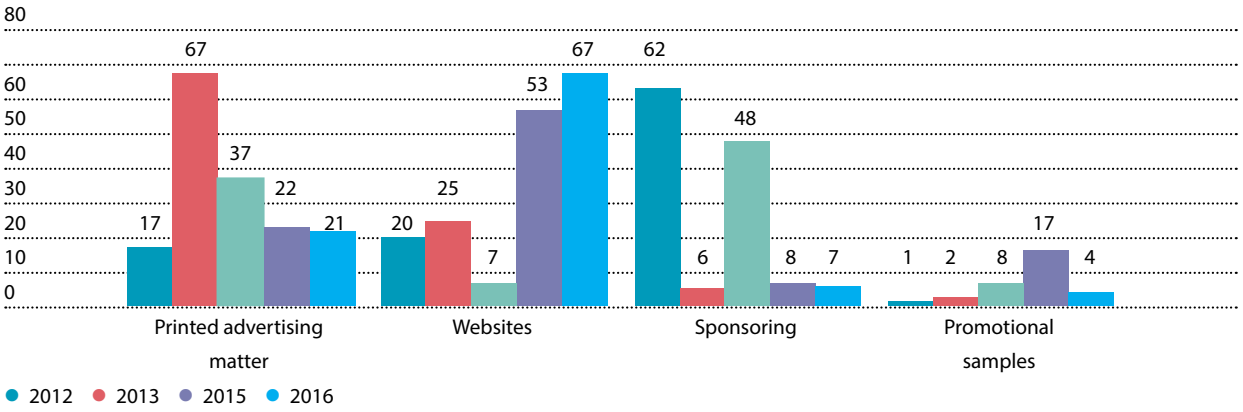
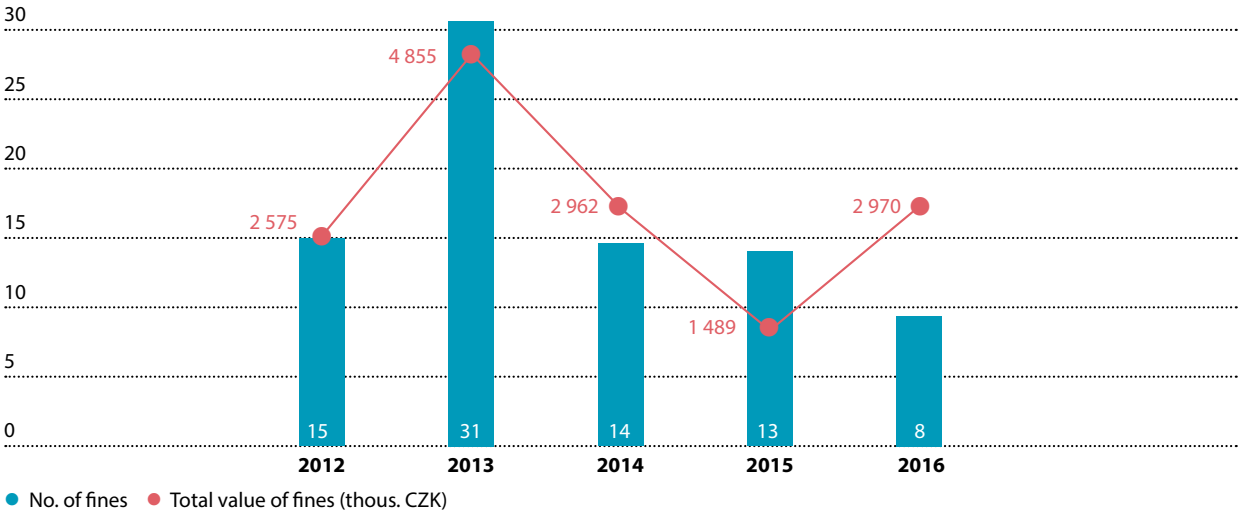


Fig. 13 **Overview of fines imposed for violating the Act on Advertising Regulation in the period of 2012–2016**



Upon request, SÚKL 42 issued/provided 42 expert opinions/consultations on the issue of proposed advertising for medicinal products for human use.

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

In 2016, SÚKL commenced investigation into 40 cases of various products, most often dietary supplements and cosmetic products, for suspected classification as a medicinal product; it processed 11 applications for the issue of a decision on the nature of a product and 17 opinions. In 4 cases, an administrative procedure regarding the nature of the product was initiated ex officio. In 2016, SÚKL reclassified 4 products in total to the group of medicinal products.

Standardisation and Pharmacopoeial Activities

The Pharmacopoeia and Pharmaceuticals Standardisation Department prepared a manuscript of a new edition of the Czech Pharmacopoeia 2017 (hereinafter referred to as "CP 2017").

The complete edition of all texts allowed for the approximation of the titles of monographs and names of reagents to the European Pharmacopoeia (hereinafter referred to as "Ph. Eur.") and to carry out a number of minor text adjustments reflecting new scientific and technical trends in the given fields. The names of salts or organic compounds in reagents as well as in monographs were amended so as to be consistent with the European Pharmacopoeia as well as with the effective rules of the Czech organic terminology based upon IUPAC rules. In the Reagents section, original names referring to the new ones were also maintained to facilitate navigation. The amended names were always supplemented with the original ones in the form of synonyms, so as to facilitate work with pharmacopoeial texts for healthcare professionals. The aforementioned amendments were reflected also in the National Part of CP 2017.

In the European Part, this edition contains translations of the texts of the 9th edition of 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, i.e. approximately 30% of amended texts.

The National Part of CP 2017 in its general section contains an overview of updated reagents used in national monographs (where the "RN" labelling continues to be used) and reference substances used in national monographs which are available upon order through the website www.sukl.cz. Furthermore, the general section contains 15 tables. Tables I, II, III, IV, V, VI, IX, XII have been amended with data on newly included substances or products, while substances which have been deleted from any of the previous editions of the Pharmacopoeia, are no longer provided here. Table 23 has been amended with data on newly included Standard Terms for pharmaceutical forms, methods of administration and packaging/ closures in a structure consistent with the European Database.

In the special section of the National Part, the included monographs are no longer structured into groups of Active Substances and Medicinal Products; monographs are listed in alphabetic order here. Some monographs, such as monograph Dronabinolum (no longer up to date), monographs Aminophenazonum, Pix fagi and Pix lithanthracis (evidenced carcinogens, currently obsolete) and articles related thereto – Carbonis detergens tinctura and Gelatum Holt have been deleted from the National Part of CP 2017. Deleted have been also monographs Glyceroli suppositorium (has been reclassified as a medical device) and Solutio Galli-Valerio (not a medicinal product, either). Monograph Butamirati citras has been revised, the impurity limits being harmonised with the general texts of the European Part of the Pharmacopoeia.

Tab. 23 **Number of texts in CP 2009 – Suppl. 2017**

	General articles, general monographs, tables	**Monographs**	**Total**
European part	358	2 329	2 687
National Part	17	145	162
Total	**375**	**2 474**	**2 849**

In coordination with the Pharmacopoeia and Pharmaceuticals Standardisation Department, also other experts of the Institute contributed to the preparation of SÚKL. CP 2017 will be published in three volumes and will become binding as of 1 December 2017.

Cooperation with the European Pharmacopoeia Commission (hereinafter referred to as "EPC") in the preparation of another edition of Ph. Eur. and in the preparation of Czech translations and revisions of the "Standard Terms" database continued. The Department of Pharmacopoeia and Pharmaceuticals Standardisation informs about the binding nature of the Ph. Eur. editions in the information media of SÚKL. The Department regularly took part in the meetings of EPC and of the secretariats of national pharmacopoeial commissions.

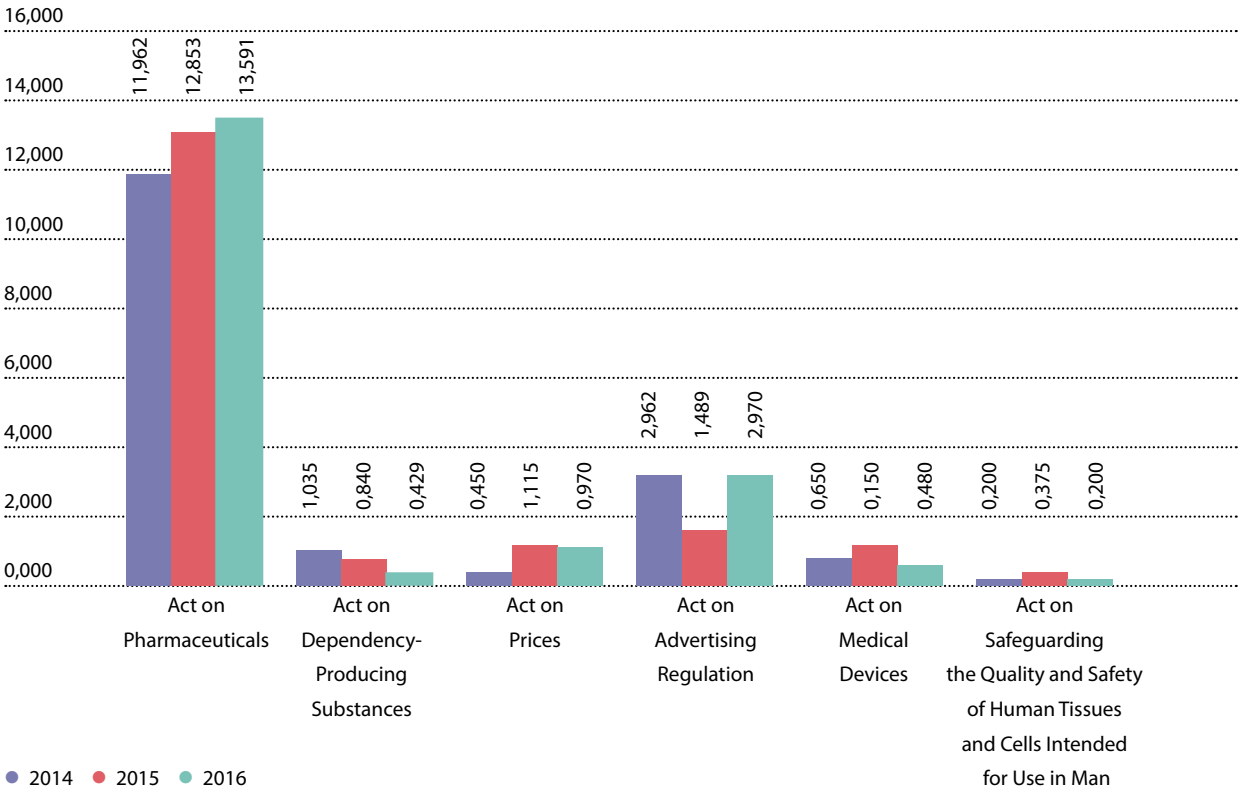
Standardisation

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 SÚKL´s website. In 2016, a representative from the Vigilance Department was actively involved in the work of the TNK 81 Technical Standardisation Commission for Medical Devices.

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 supervision of advertising and based on reports, SÚKL initiates administrative procedures on administrative offences within which penalties referred to in the applicable laws are imposed according to the severity of the identified problem. Since August 2011, SÚKL 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 2016. Since January 2015, SÚKL 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. A new feature in the area of penalisation in 2016 was the imposition of penalties in the form of so called summary fines for committed administrative offences governed to several laws within the powers of SÚKL in the sphere of medicinal products.

Fig. 14 **Decisions on imposed penalties which became final in 2014–2016 (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 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.

Determination of Prices and Reimbursements

In the course of 2016, the Branch continued in the initiation of in-depth reimbursement revisions in accordance with the schedule. For 2016, the initiation of 234 in-depth revisions was scheduled, of which 220 administrative procedures (1 178 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.).

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 2016.

In 2016, SÚKL was completing in-depth revisions of maximum prices of all medicinal products regulated by the maximum price, which were commenced in the second half of 2015. Within the scope of in-depth revisions, SÚKL assessed whether the determined maximum prices did not exceed the restrictions imposed by the Act on Public Health Insurance. In those cases, where it was established that the determined maximum price exceeds the restrictions set forth by this Act, the maximum price of the medicinal product was reduced. To date, all of the initiated in-depth revisions of maximum prices (493 administrative procedures in total, 4 639 SÚKL codes) have been decided (of which 104 administrative procedures held for 1 455 codes were decided in 2016). The maximum price was reduced in 54% of the cases.

Compared to 2015, 39% less administrative procedures on a change of maximum ex-factory price were initiated. With a view to the fact that the aforementioned in-depth revisions caused a change to the maximum price reflecting the current price references, the number of applications for maximum price change filed by marketing authorisation holders was no longer so high in 2016. Applications for maximum price change filed by marketing authorisation holders were submitted particularly in those cases where the in-depth revision revealed that the determined maximum price does not exceed the restrictions set forth by this Act. Therefore, in administrative procedures for change of the maximum price commenced in 2016 on the basis of applications filed by marketing authorisation holders, the maximum price was mostly increased.

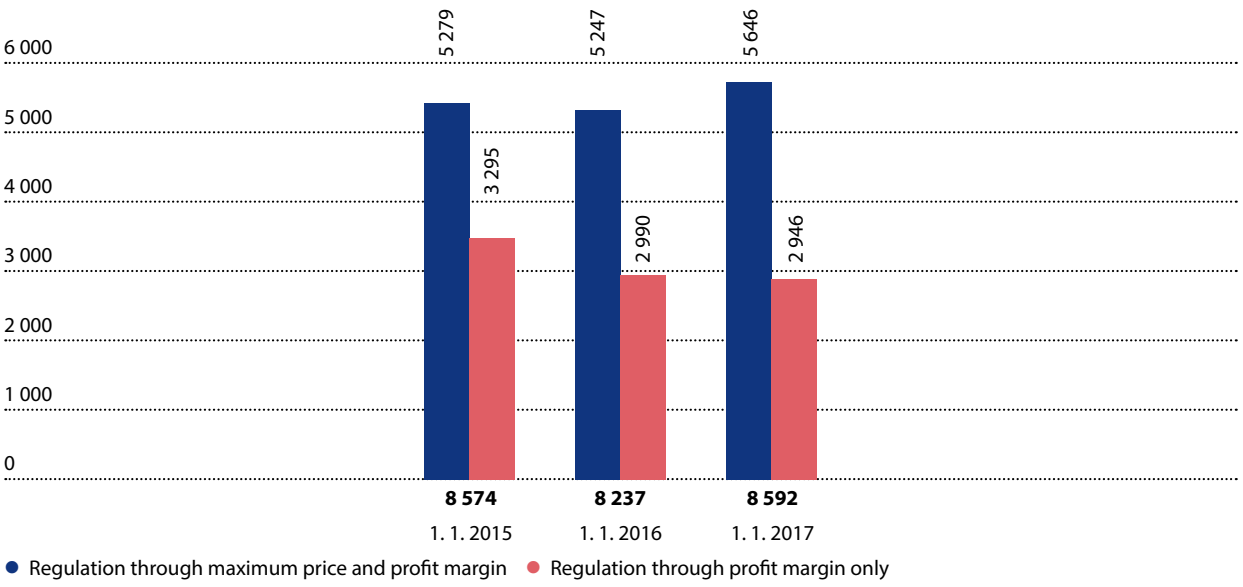
Tab. 24 **Overview of administrative procedures in 2016**

Applications for determination of maximum ex-factory price	**No. of SÚKL codes**
Initiated	9
Decided	9
Appeal procedure pending	0
Came into force	9
Applications for maximum ex-factory price change	
Initiated	135
Decided	121
Appeal procedure pending	7
Came into force	108
Applications for maximum ex-factory price reduction – abbreviated procedures	
Initiated	36
Decided	36
Appeal procedure pending	0
Came into force	36
Applications for maximum ex-factory price cancellation	
Initiated	11
Decided	11
Appeal procedure pending	0
Came into force	11

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 2015. 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 variations of existing medicinal products in the reimbursement system (Fig. 15).

With a view to the structure of medicinal products (tab. 25), it may be stated that the numbers of medicinal products in the below listed zones by maximum price mostly increased in 2016. The most pronounced increase was seen in the above 30 000 CZK zone. A drop in the number of medicinal products occurred only in three zones (up to 20 CZK, above 300 CZK and above 3 000 CZK).

Fig. 15 **Structure of reimbursed products by the type of price regulation**



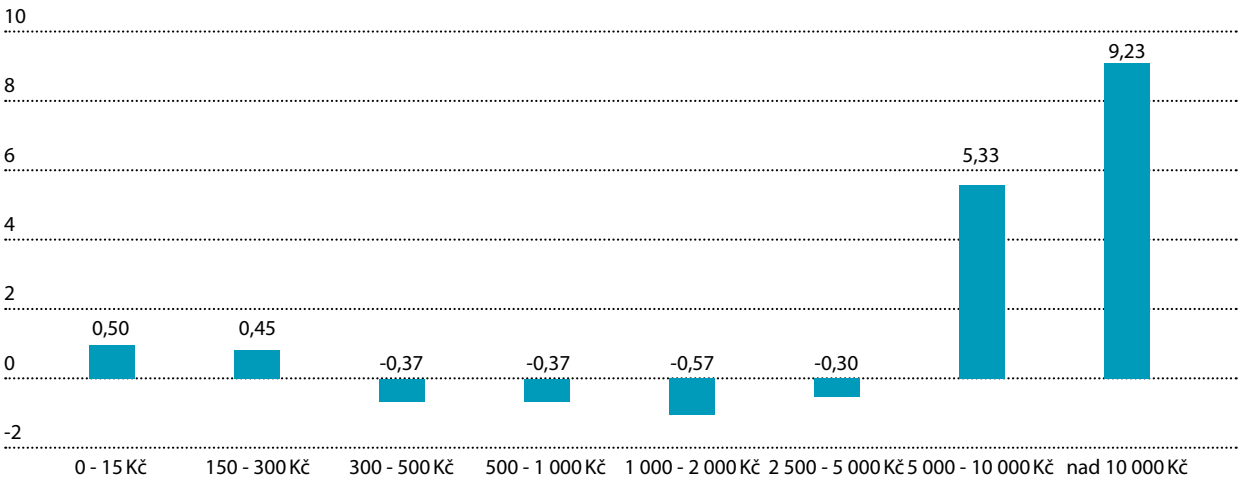
Tab. 25 **Overview of the number of codes of medicinal products/foods for special medical purposes in the maximum price zones as per the List of Prices and Reimbursements (SCAU) by month**

Price regulation zone	1/2016	2/2016	3/2016	4/2016	5/2016	6/2016	7/2016	8/2016	9/2016	10/2016	11/2016	12/2016
Up to 20 CZK inclusive	24	23	23	23	24	24	24	22	21	21	21	21
Over 20 CZK – 50 CZK inclusive	340	351	349	378	386	384	383	381	377	374	375	373
Over 50 CZK – 100 CZK inclusive	635	682	695	705	691	691	693	698	694	694	706	704
Over 100 CZK – 200 CZK inclusive	836	877	897	893	918	917	908	909	909	910	912	914
Over 200 CZK – 300 CZK inclusive	441	430	422	431	456	460	470	477	477	481	483	496
Over 300 CZK – 500 CZK inclusive	550	536	531	522	514	511	513	526	527	535	530	538
Over 500 CZK – 1 000 CZK inclusive	636	662	665	662	660	656	665	676	676	675	683	693
Over 1 000 CZK – 2 000 CZK inclusive	604	572	566	587	593	609	612	620	618	621	629	640
Over 2 000 CZK – 3 000 CZK inclusive	226	234	240	242	226	226	232	234	238	244	242	244
Over 3 000 CZK – 5 000 CZK inclusive	337	328	336	328	306	304	309	312	311	308	313	314
Over 5 000 CZK – 10 000 CZK inclusive	254	245	248	244	241	245	247	248	253	251	254	256
Over 10 000 CZK – 20 000 CZK inclusive	160	161	162	170	172	174	178	187	193	189	192	196
Over 20 000 CZK – 30 000 CZK inclusive	72	70	62	64	66	68	70	71	72	75	76	78
Over 30 000 CZK – 50 000 CZK inclusive	47	49	49	49	50	50	53	53	61	61	61	64
Over 50 000 CZK – 100 000 CZK inclusive	46	47	47	47	47	48	50	50	51	52	52	53
Over 100 000 CZK	40	39	39	40	40	41	41	42	44	44	45	46
Number of codes	5 248	5 306	5 331	5 385	5 390	5 408	5 448	5 506	5 522	5 535	5 574	5 630

Development of Average End-User Prices

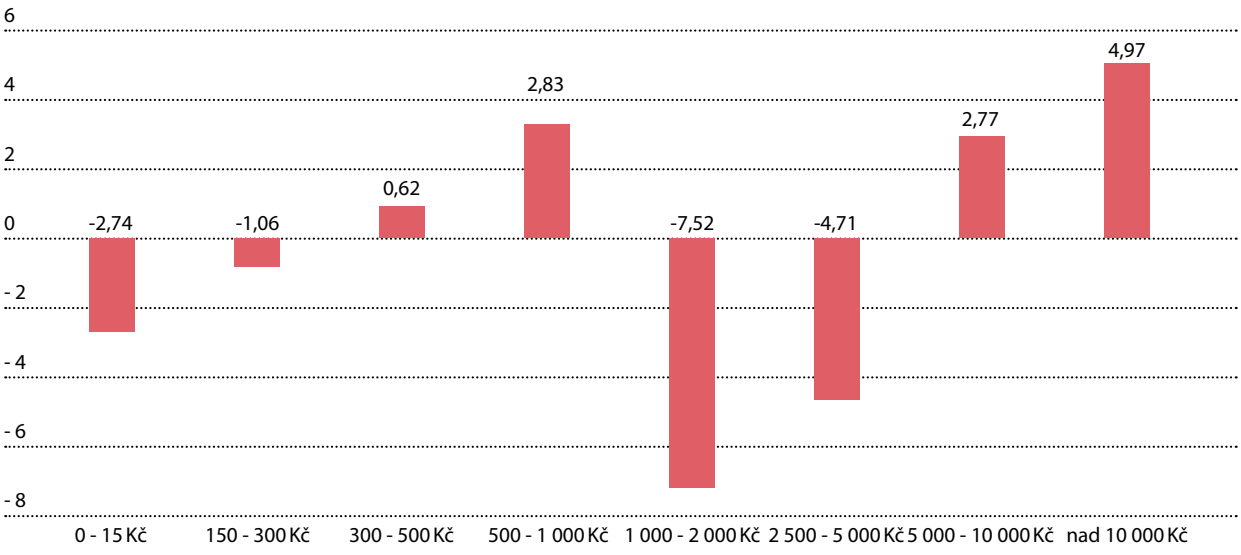
In 2016, there was not change to the profit margins or to the VAT, which for medicinal products was 10% in 2016. In respect of medicinal products regulated by the determined maximum price (maximum price determined by an administrative procedure and profit margin as per the Price Regulation), the average end-user price increased by 6.6%. The increase 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 1.4%. The situation in ex-factory price levels (ex. profit margin and VAT) focusing upon comparison of the latest quarters is provided below.

Fig. 16 **Prices of pharmaceuticals regulated by maximum price and profit margin – comparison of average prices in Q4 2015 and Q4 2016 by price zones**



Kč = CZK

Fig. 17 **Prices of pharmaceuticals regulated by profit margin only – comparison of average prices in Q4 2015 and Q4 2016 by price zones**



Kč = CZK

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 medicinal products with the highest financial volume by the ex-factory price, for which the maximum ex-factory price was changed.

In 2016, the maximum prices both increased and decreased in the group of the most often distributed 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. In the case of relatively expensive medicinal products (PRESTARIUM NEO and CIPRALEX), the price, on the contrary, decreased (tab. 26).

Tab. 26 **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 %
0101211	C09AA04	PRESTARIUM NEO	5MG TBL FLM 90	529 567	433,50	394,85	-8,9
0002479	R06AX	DITHIADEN	2MG TBL NOB 20	507 648	56,62	58,45	3,2
0000168	C03AA03	HYDROCHLOROTHIAZID LÉČIVA	25MG TBL NOB 20	493 992	33,92	38,45	13,4
0083318	C01AA05	DIGOXIN 0,125 LÉČIVA	0,125MG TBL NOB 30	470 354	20,99	20,81	-0,9
0001066	D06AX	FRAMYKOIN	250IU/100IU/G UNG 10G	455 905	35,63	45,18	26,8
0000536	C01CA03	NORADRENALIN LÉČIVA	1MG/ML INF CNC SOL 5X1ML	422 260	109,25	111,27	1,8
0009709	H02AB04	SOLU-MEDROL	40MG/ML INJ PSO LQF 40MG+1ML	417 642	30,76	32,84	6,8
0094114	B01AA03	WARFARIN ORION	5MG TBL NOB 100	398 185	122,59	122,58	-0,01
0214427	A02BC02	CONTROLOC I.V.	40MG INJ PLV SOL 1	389 712	112,85	81,45	-27,8
0020132	N06AB10	CIPRALEX	10MG TBL FLM 28 I	336 961	364,04	205,15	-43,6

Medicinal products with the highest financial volume are distributed almost across the entire price zone spectrum. For all of the aforementioned medicinal products, however, the maximum price was reduced, also due to the enforceability of the maximum price revision carried out by SÚKL in 2016 (Tab. 27).

Tab. 27 **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 %
0025566	L04AB04	HUMIRA	40MG INJ SOL 2X0,8ML I	701 030 286	22 686,51	22 646,93	-0,2
0028397	L01XC07	AVASTIN	25MG/ML INF CNC SOL 1X16ML	617 519 948	27 319,27	26 585,50	-2,7
0027283	L04AB02	REMICADE	100MG INF PLV CSL 1	584 423 336	12 481,78	11 595,82	-7,1
0027918	L04AB04	HUMIRA	40MG INJ SOL 2X0,8ML	349 504 527	22 686,55	22 646,93	-0,2
0194345	L04AB02	REMSIMA	100MG INF PLV CSL 1	332 025 526	10 209,17	8 099,32	-20,7
0149868	J07AL02	PREVENAR 13	INJ SUS 1X0,5ML+1SJ	303 497 361	1 196,21	1 172,14	-2,0
0028740	A10BH01	JANUVIA	100MG TBL FLM 28	235 354 257	795,12	792,77	-0,3
0027905	L04AB01	ENBREL	50MG INJ SOL ISP 4X1ML	229 558 185	22 651,83	21 106,42	-6,8
0193870	L01XC13	PERJETA	420MG INF CNC SOL 1X14ML	229 529 572	74 720,77	72 713,60	-2,7
0149770	L03AA13	NEULASTA	6MG INJ SOL 1X0,6ML II	203 178 802	20 290,00	19 086,70	-5,9

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. 28 **Overview of administrative procedures in 2016**

Applications for determination or change of the amount and conditions of reimbursement	**No. of SÚKL codes**
Initiated	404
Decided	258
Appeal procedure pending	13
Came into force	185
Applications for determination or change of maximum prices and the amount and conditions of reimbursement	
Initiated	214
Decided	43
Appeal procedure pending	0
Came into force	36
Applications for reimbursement cancellation	
Initiated	39
Decided	34
Appeal procedure pending	1
Came into force	26
Applications for maximum price and reimbursement cancellation	
Initiated	69
Decided	59
Appeal procedure pending	0
Came into force	50
Procedures initiated ex officio	
Initiated	1 393
Decided	679
Appeal procedure pending	86
Came into force	357
Procedures on similar products	
Initiated	529
Decided	455
Appeal procedure pending	0
Came into force	455

In 2016, 18 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, SÚKL 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 and cost effectiveness and comparison with the original goals of pharmacotherapy. This process takes place within so-called in-depth revision of the reimbursement system. SÚKL initiates also other types of administrative procedure ex officio, such as abbreviated revisions or individual administrative procedures to change or cancel the amounts and conditions of reimbursement.

In 2016, 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 2016 is estimated at 1 227 133 738 CZK.

Tab. 29 **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**
1/2016	170	33	580 639 717
2/2016	701	26	921 645 792
3/2016	305	24	462 951 356
4/2016	337	21	224 821 037
5/2016	137	25	128 665 883
6/2016	135	22	154 512 441
7/2016	172	21	247 011 904
8/2016	187	36	349 625 874
9/2016	392	24	713 984 137
10/2016	255	27	997 467 897
11/2016	217	19	242 608 303
12/2016	47	20	10 523 883

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

The overview includes also administrative procedures imitated ex-officio in order to level up the amount of reimbursement with the legally determined basic reimbursement of therapeutically interchangeable medicinal products.

Tab. 30 **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	1/2016	2/2016	3/2016	4/2016	5/2016	6/2016	7/2016	8/2016	9/2016	10/2016	11/2016	12/2016
Up to 20 CZK inclusive	195	195	192	194	194	194	193	190	189	189	181	179
More than 20 CZK – 50 CZK inclusive	791	801	853	858	866	868	867	866	864	868	862	867
Over 50 CZK – 100 CZK inclusive	1 146	1 145	1 162	1 162	1 245	1 242	1 248	1 253	1 254	1 252	1 268	1 269
Over 100 CZK – 200 CZK inclusive	1 476	1 499	1 439	1 446	1 404	1 409	1 417	1 420	1 423	1 428	1 433	1 448
Over 200 CZK – 300 CZK inclusive	682	682	696	696	669	675	684	691	690	682	678	688
Over 300 CZK – 500 CZK inclusive	713	699	694	695	661	664	670	676	678	687	689	692
Over 500 CZK – 1 000 CZK inclusive	1 033	1 042	1 044	1 046	1 037	1 050	1 041	1 043	1 042	1 036	1 041	1 053
Over 1 000 CZK – 2 000 CZK inclusive	811	818	836	839	840	850	861	881	877	884	891	909
Over 2 000 CZK – 3 000 CZK inclusive	290	298	289	294	300	295	300	302	294	295	301	304
Over 3 000 CZK – 5 000 CZK inclusive	321	320	328	325	324	326	332	334	340	334	340	334
Over 5 000 CZK – 10 000 CZK inclusive	348	343	349	350	352	342	341	338	338	337	338	341
Over 10 000 CZK – 20 000 CZK inclusive	195	201	202	215	217	202	211	225	230	228	225	230
Over 20 000 CZK – 30 000 CZK inclusive	75	80	74	74	76	75	77	78	83	85	84	85
Over 30 000 CZK – 50 000 CZK inclusive	52	53	53	54	55	56	59	58	63	64	66	69
Over 50 000 CZK – 100 000 CZK inclusive	51	51	51	51	51	52	54	54	55	56	55	56
Over 100 000 CZK	59	59	54	55	55	57	57	58	60	58	60	61
Number of codes	8 238	8 286	8 316	8 354	8 346	8 357	8 412	8 467	8 480	8 483	8 512	8 585

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 was seen in medicinal products SYMBICORT TURBUHALER, TOUJEO, and LANTUS SOLOSTAR (tab. 31).

Tab. 31 **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 reimb. (CZK)	New reimb. (CZK)	Change in reimb. in %
0185368	L01XC03	HERCEPTIN	600MG INJ SOL 1	639 671 866	44 809,55	42 879,48	-4,3
0028397	L01XC07	AVASTIN	25MG/ML INF CNC SOL 1X16ML	617 519 948	31 102,43	29 117,23	-6,4
0168462	L04AA27	GILENYA	0,5MG CPS DUR 28	457 572 774	37 744,15	36 175,21	-4,2
0027184	L04AA23	TYSABRI	300MG INF CNC SOL 1X15ML	422 828 305	38 203,25	38 823,24	1,6
0027953	A10AE04	LANTUS SOLOSTAR	100U/ML INJ SOL 5X3ML	402 284 702	1 577,75	1 285,80	-18,5
0168904	B01AF01	XARELTO	20MG TBL FLM 98 II	390 513 878	6 177,80	6 167,15	-0,2
0180087	R03AK07	SYMBICORT TURBUHALER 200 MIKROGRAMŮ / 6 MIKROGRAMŮ / INHALACE	160MCG/4,5MCG INH PLV 1X120DÁV	386 053 743	1 179,50	802,48	-32,0
0210402	A10AE04	TOUJEO	300U/ML INJ SOL 3X1,5ML	263 517 419	1 498,86	1 157,22	-22,8
0194569	S01LA04	LUCENTIS	10MG/ML INJ SOL 1X0,165ML	244 301 189	23 424,48	22 912,71	-2,2
0029248	L01XC08	VECTIBIX	20MG/ML INF CNC SOL 1X5ML	243 640 940	11 672,89	11 498,17	-1,5

The group of medicinal products with the greatest distribution in respect of which reimbursement was changed contains particularly relatively cheap medicinal products. In all of the aforementioned cases, the reimbursements were both increased and decreased. In case of medicinal product FURON, the reimbursement of which was decreased, the amount of supplies increased. In other evaluable cases, however, a major change in reimbursement was not principally reflected in the volume of medicinal product supplies (tab. 32).

Tab. 32 **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 reimb. (CZK)	New reimb. (CZK)	B (number of packages)	Note:
0098219	C03CA01	FURON	40MG TBL NOB 50	299 337	63,7	42,51	345 624	*/
0125114	B01AC06	ANOPYRIN	100MG TBL NOB 3X20	538 174	31,65	35,18	514 742	
0012023	A11CC05	VIGANTOL	0,5MG/ML POR GTT SOL 1X10ML	210 509	34,6	34,15	203 675	*/
0155782	B01AC06	GODASAL 100	100MG/50MG TBL NOB 100	337 658	52,75	58,63	334 121	
0017187	M01AX17	NIMESIL	100MG POR GRA SUS 30		36,54	48,42		x/
0188850	B01AC06	STACYL	100MG TBL ENT 100 I	310 714	52,75	58,62	265 391	
0000168	C03AA03	HYDROCHLOROTHIAZID LÉČIVA	25MG TBL NOB 20	119 496	30,56	32,81	123 408	*/
0087076	R05CB15	ERDOMED	300MG CPS DUR 20	219 674	123,3	159,17	211 007	
0119672	M01AB05	DICLOFENAC DUO PHARMASWISS	75MG CPS RDR 30 I		54,81	72,64		x/
0012892	M01AX17	AULIN	100MG TBL NOB 30		36,54	48,42		x/

** – 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 submitted in 2016 did not much differ from the submission in 2015 (a 3.5% increase), with the share of submissions by health insurance companies increasing as well as it did in the last year, and representing almost 15% of the total number of submissions. The number of administrative procedures which had to be discontinued by resolution as early as in the validation phase increased compared to 2015, the number of discontinued procedures being more than treble compared to 2015. The reason for discontinuation was a barrier to the procedure (so called litispendency) or withdrawal of the application. The proportion of suspended administrative procedures due to defective submission remains on the same level as in 2015.

Tab. 33 **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**

Period	No. of submitted applications	Suspended due to defective submissions and deficiencies in applications	Discontinued in the validation phase
January	44	2	1
February	52	1	0
March	64	1	2
April	41	5	2
May	51	0	0
June	56	0	3
July	42	0	1
August	85	0	17
September	44	2	6
October	81	1	1
November	31	1	1
December	57	1	2
Total	**648**	**14**	**36**

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") also in 2016. 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.

In the first half of 2016, SÚKL focused upon the addressing of IPLP – MAG issues in relation to a new Decree No. 236/2015 Coll. of 4 September 2015 laying down the conditions of prescribing, preparation, distribution, dispensing, and use of individually prepared medicinal products containing cannabis for medical use. By the end of the first six months of the year, moreover, a list of items used for the preparation of DPV was updated. As of 1 August 2016, group 13 RF was addressed with a view to new price source materials, the effective €/CZK exchange rate, and inclusion of newly authorised products used for the preparation of RF, and as of 1 December 2016, the group was supplemented with a newly authorised product intended for the preparation of RF. 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 13 RF, and subgroups 12 and 15 for TP.

In the second half of the year, two revisions focused upon verification of correctness of defined parameters were conducted in compliance with effective methodology. A revision of subgroup RF was done through a comparison of data from the statistics of health insurance companies, provided to SÚKL by the Institute of Health Information of the MoH (hereinafter referred to as "ÚZIS"). In addition to the statistics of health insurance companies, data about the distribution of radiopharmaceuticals based on source materials monitored by SÚKL were used for the control and evaluation. All of the source materials form part of the revision report (file no. sukls226172/2016) published on SÚKL´s website. In respect of seven products, deviations were identified and settled by OOP 07–16. In the DPV subgroup, the revision focused upon the legitimacy of the prescribed drug coverage for a patient with DPV. The identified facts form part of the revision report (file no. sukls185838/2016) published on SÚKL´s website and were handled through OOP 06-16.

General Measures

In the course of 2016, eight OOP procedures were initiated and duly completed.

As of 1 January 2016, three OOPs issued in 2015 took effect, which reflected the change to the payroll tariffs of healthcare professionals stipulated by Government Regulation No. 278/2015 Coll of 19 October 2015, 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."), as of 1 January 2016. In compliance with the conditions of VUC and the effective Price Regulation, the reimbursements for IPLP subgroups were amended in the section of payroll costs associated with the IPLP preparation proper and were published for RF (OOP 04-15), for TP (OOP 05-15), and for DPV (OOP 06-15) in a manner allowing for consistency between the effective dates of individual OOPs and the effective date of the Government Regulation. Compared to 2015, a price increase associated with the increase in payroll tariffs, for group RF (by 0.2%), for DPV (by 0.15%) and for (by 0.2%) was anticipated. The costs of MAG preparation are defined by an effective Price Regulation of the MoH 01/2013/FAR, in the amount fully implied by taxa laborum (TXL). The anticipated total IPLP cost increase associated with the new payroll conditions was estimated at 3.77 mil. CZK.

As of 1 April 2016, OOP 01-16 for IPLP subgroup 11 MAG took effect, addressing the issue of prepared medicinal products containing cannabis for medical use in pharmacy care facilities, on the basis of a stimulus from Patient Association for Cannabis Treatment (hereinafter referred to as "KOPAC"). The proposed change suggesting removal of cannabis from the list pf phytopharmaceutical and placement into a separate IPLP subgroup was accepted and on the basis thereof, the IPLP group was extended with a new subgroup 19. This subgroup was addressed by OOP 02-16, which specified only IPLP with the content for cannabinoids – cannabis for medical use.

As of 1 July 2016, OOP 03-16 took effect, reflecting a change to the composition of model DPV formulations which consisted of the replacement of nutritional component ADDAMEL, whose marketing authorisation was revoked, with newly authorised components ADDAVEN L and NUTRYELT. This change represented a 0.7% increase in the costs of subgroup 14 DPV.

As of 1 August 2016, OOP 04-16 for subgroup 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, newly authorised 99mTc POLTECHNET generators were included in the source materials for the determination of reimbursements of 99mTc-labelled radiopharmaceuticals. The amendment implied a 0.1% increase in the costs of subgroup 13 RF.

As of 1 December 2016, OOP 05-16 took effect, extending subgroup 13 RF with a new code 0002100 99mTcTektrotyd inj., which represents an economically more beneficial alternative. The shorter time of radioactive transformation with the use of 99mTc implies a lower radiation burden for the patient. The inclusion of this economically more beneficial alternative is expected to bring savings which may be assessed only after one year, due to the date of inclusion of the product in the list of reimbursed radiopharmaceuticals as of 1 December 2016.

In the third quarter, three OOPs were prepared, with the effective date of 1 January 2017; these reflected the change to the payroll tariffs for healthcare professionals based upon Government Regulation No. 316/2016 Coll. 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 07-16 for RF, in OOP 08-16 for TP, and in OOP 06-16 for DPV so that the effective dates of the OOPs were consistent with the effect of the Government Regulation. In the radiopharmaceuticals group, a 1% decrease of the total costs is anticipated due to the recommended changes in the revision resulting in savings, as well as in connection with the increase in payroll tariffs; in the case of DPV, a 0.5% increase in the costs is estimated in 2017 compared to 2016 due to the changed payroll funds; and in respect of TP, a 7% increase in costs is foreseen. The conditions of reimbursement of subgroup MAG are subject to the effective Price Regulation of the MoH 01/2013/FAR and have not changed as of 1 January 2017.

Consumption and Costs of Individually Prepared Medicinal Products

The consumption of IPLP is evaluated in defined units (hereinafter referred to as "DU") by individual IPLP subgroups. In the case of the transfusion products subgroup, incl. autologous transfusion products, and in the case of the radiopharmaceuticals subgroup, the consumption dropped; in respect of the DPV and MAG subgroups, the consumption of DU grew. Fig. 18 provides distribution of costs for the IPLP group in 2016 by individual subgroups. The overview of the IPLP consumption in DU for the period 2014-2016 is provided in Fig. 20.

In 2016, the costs of individual IPLP groups were influenced by the increase in the payroll funds as of 1 January 2016 on the basis of Government Regulation No. 278/2015 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 drop in the costs corresponding to the decrease in the consumption of these products was seen; in respect of the RF subgroup, despite dropping consumption, the costs grew. The reason for the growth of costs was the inclusion of new radiopharmaceuticals intended for the detection of amyloid plaques in Alzheimer´s disease as well as the inclusion of the product XOFIGO intended for the treatment of bone metastases. The anticipated increase in costs upon the inclusion of these products into reimbursement from the public health insurance funds was estimated at 35 mil. CZK. The cost increase above the aforementioned estimate for new RF was caused also by the increase in the number of PET centres, and hence the increasing consumption of PET radiopharmaceuticals. The increase in the consumption of products from subgroup DPV is associated particularly with the extension of home therapy for patients with intestinal failure. In subgroup MAG, including costs associated with the dilution of cytostatic agents, the growth in the consumption as well as in costs was obvious in relation to the increasing number of oncologically treated patients. Fig. 19 shows the comparison of costs in the period from 2014 to 2016 for individual IPLP subgroups. The values for 2015 specified in the 2015 Report were updated as of 1 December 2016. Data on the consumption of IPLP for 2016 are available only as at 1 October 2016, due to the time shift in the submission of statistical data by health insurance companies, and hence incomplete data from ÚZIS; Q4 of 2016 is therefore expressed as an estimate of anticipated costs through an average conversion from the three quarters of 2016. The total costs paid for the IPLP group from the public health insurance funds in 2015 amounted to 2 589.2 mil. CZK, in 2016 it was 2 640.8 mil. CZK, which represents a cost increase by 51.8 mil. CZK or a 1.99% increase compared to 2015.

Fig. 18 **Distribution of total costs of individually prepared medicinal products in 2016**

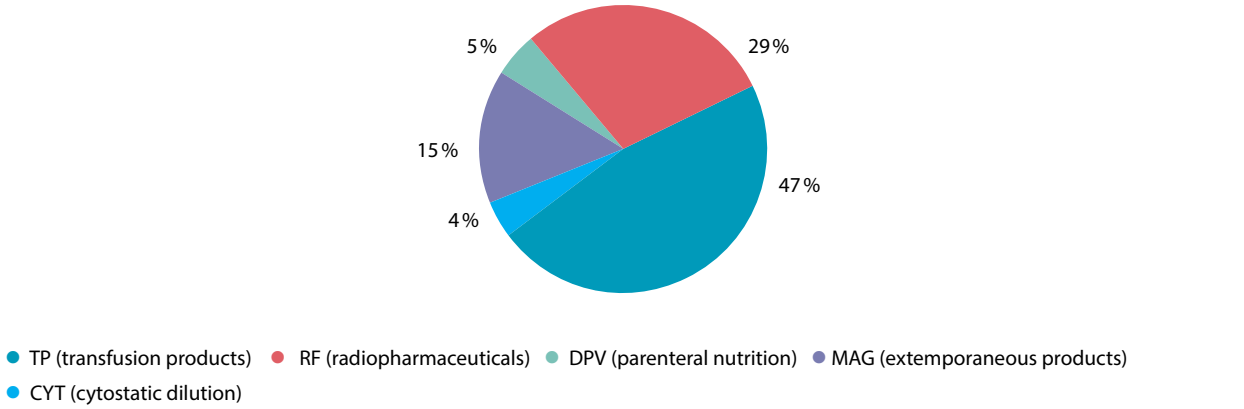


Fig. 19 **Comparison of costs by groups of individually prepared medicinal products for the period from 2014 to 2016 in mil. CZK**

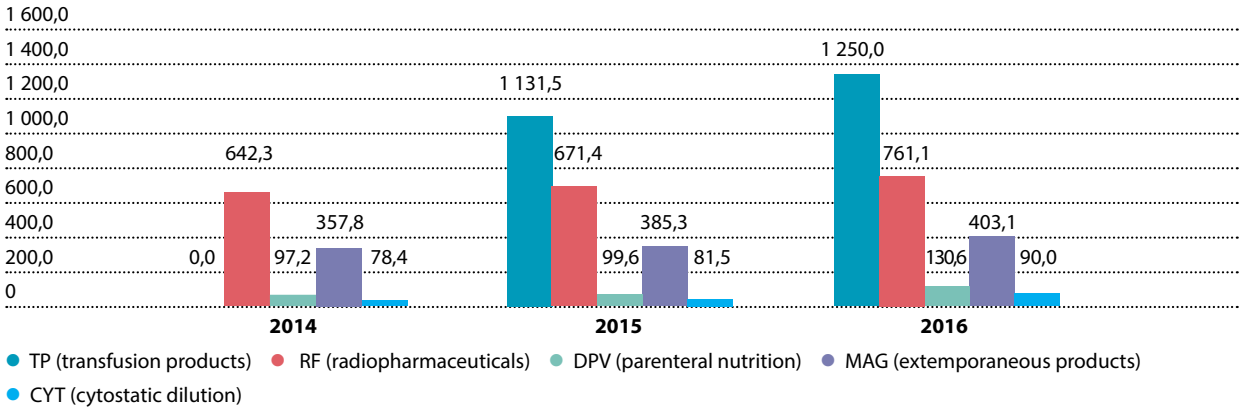
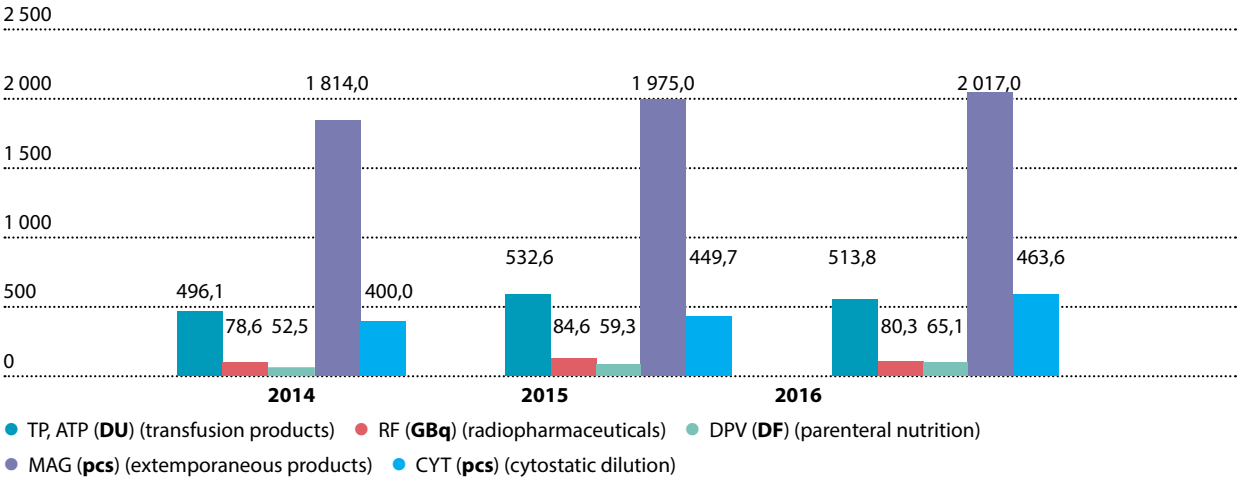


Fig. 20 **Overview of consumption of individually prepared medicinal products for the period from 2014 to 2016 in thous. DU**



MEDICAL DEVICES BRANCH

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, applications for authorisation of CIMD conduct were submitted to SÚKL in 2016 only via the Registry of Medical Devices (hereinafter referred to as "RZPRO"), Clinical Investigation Module.

Through this route, 28 applications were filed. In compliance with Section 9(h) of Act No. 268/2014 Coll., on Medical Devices, 21 positive opinions authorising the conduct of CIMD were issued in administrative procedures, 6 procedures were discontinued by a resolution, and 1 application was rejected. Furthermore, 15 applications for authorisation of changes to the conditions of CIMD were filed, of which 13 were granted and 1 was withdrawn.

Within the scope of control of the conduct of clinical investigations on medical devices at providers of healthcare services, 22 inspections were conducted, in which 16 types of investigational medical devices were inspected.

The selection of inspected sites was based upon the positive opinions issued by SÚKL on the intention to carry out a clinical investigation, and upon issued decisions authorising the conduct of CIMD. All of the inspections were performed on the basis of a transitional provision in Act No. 268/2014 Coll., on Medical Devices governing CIMD initiated prior to the coming into force of this Act and still pending. On-site inspections identified 24 shortcomings in total, of which 3 were critical, 15 major and 6 minor.

The total of 95 serious adverse events (hereinafter referred to as "SAE") were reported from 81 CIMDs conducted at sites in the Czech Republic.

In 2016, 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 international cooperation in the sphere of clinical evaluations, in 2016, a KHZP representative participated in a meeting of the expert WG on Clinical Investigation and Evaluation of the European Commission focused upon the development of documents and exchange of information among the EU Member States. Furthermore, two representatives took part in a Workshop organised by the European Commission which concentrated on the assessment of CIMD documentation across the EU Member States.

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

443 adverse events (hereinafter referred to as "AEs") associated with the use of medical devices in the provision of healthcare services within the territory of the Czech Republic were reported to SÚKL; furthermore, 5 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 2012-2016 is provided in Fig. 21.

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 1 142. Of the total number of received reports, 476 concerned medical devices distributed to the Czech market. The development of the number of received reports on corrective actions in 2012-2016 is provided in Fig. 22.

In 2016, SÚKL published 438 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 importers, distributors, and healthcare service providers.

On the basis of the results of investigations into medical device adverse events, one penalty was imposed for administrative offences, amounting to 80 000 CZK. Furthermore, 34 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 one motion was filed with the Control Department of the Medical Device Surveillance Section for the conduct of an inspection at healthcare service providers.

Within the scope of monitoring of a safety corrective action adopted by a Czech manufacturer, one report for concerned national authorities (NCAR) was issued and disseminated via EUDAMED.

Within the scope of international cooperation in the field of medical device vigilance, in 2016, the inspectors of the Vigilance Department participated in 11 teleconferences, 2 meetings of the Medical Device Expert Group (MDEG) on Vigilance focused upon the exchange of information among the EU Member States on current vigilance cases, 15 teleconferences focused upon the adoption of field actions regarding medical devices from the Brazilian manufacturer Silimed, for which the EC certificate validity was suspended. In the course of 2016, inspectors addressed 18 questionnaires regarding vigilance issues sent by concerned authorities.

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. One inspection was conducted in the Mandatory Joint Assessment NB mode.

Fig. 21 **Overview of notified adverse events in 2012–2016**

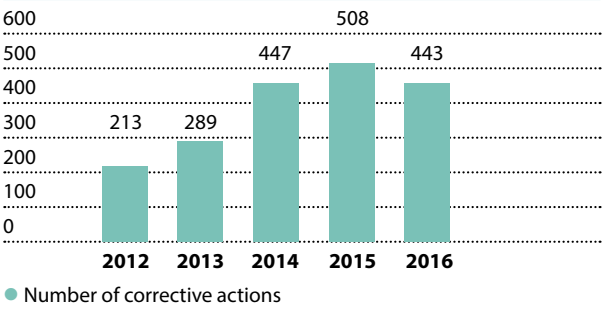
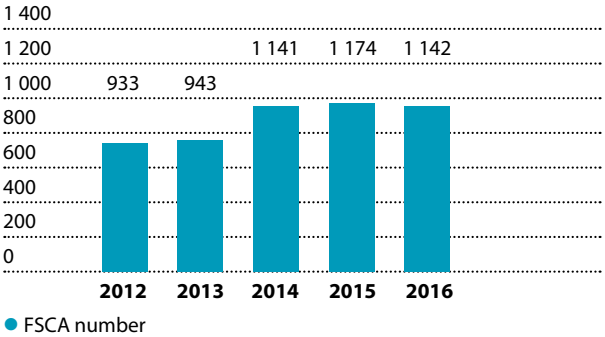


Fig. 22 **Overview of corrective actions for medical devices adopted in**



Medical Device Registration and Notification Department

The Department 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 (hereinafter referred to as the "Act on Medical Devices"), in respect of registration of persons, notifications of medical devices, and related activities. In the last year, the expert staff of the 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 being subject to administrative procedure. They were creating instructions for use for RZPRO and educating the public via three workshops and six consultations. They participated in two meetings of foreign workgroups under the European Commission and in five teleconferences. Due to the establishment of a general helpline and e-mail address, the Department serves also as the major contact point for general as well as professional queries in the area of medical devices and RZPRO.

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

Notification of a Person

In 2016, the Department completed 745 submitted notifications of persons.

Notification of Operation

In 2016, 124 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, 697 notifications of changes to data were processed and completed.

Notifications of Extended Registration

In total, 1 829 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 2016, the Department processed four notifications of person deletion.

Out of the total number of 4 049 submitted notifications, in the last year, the Department completed, accepted, or requested amendment of the total of 3 399 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 2016, the Department completed 2 659 administrative procedures pertaining to applications for medical device notification.

Application for Extension of Medical Device Notification
The Department completed 2 071 administrative procedures pertaining to extension of medical device notification.

Application for Changes to Medical Device Data
In total, 2 152 applications for changes to medical device data were processed and completed.

Application for Deletion of a Medical Device
Ninety-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 are associated with medical device notifications. Primarily, a medical device must be notified and subsequently, the free sale certificate may be issued. In the last year, the Department issued 118 free sale certificates.

In total, the Department completed, i.e. accepted or requested amendment of 7 092 applications in the Medical Device Module out of the total number of 22 022 applications submitted in the last year.

Furthermore, in 2016, the 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 to 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 Department issued 82 expert opinions in respect of the nature of a product or its 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, 43 opinions were issued on the basis of an opinion from the Department of Advertising Surveillance.

In 2016, also a new structure of the Medical Device Branch was created. As of 2017, the activities of expert opinions, borderline products and issuance of free sale certificates will be excluded from the Registration and Notification Department and will be transferred to a newly established Department of Issuance of Expert Opinions and Free Sale Certificates. Both of these Departments will form part of the Registration and Notification Section.

Medical Devices Control Department

SÚKL´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 SÚKL inspections 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 2016 the inspectors from the Control Department completed 176 inspections in total, of which 96 were inspections at providers of healthcare services (both state and non-state healthcare facilities), and 80 were inspections at manufacturers, importers, distributors, vendors, persons dispensing medical devices and servicing organisations. During these inspections, 1 564 medical devices were inspected. More detailed statistics on the total number of inspected medical devices is provided in the tables below.

Ninety-six 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 831 medical devices. Furthermore, 80 inspections took place within the scope of market surveillance, where 733 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 468, and at providers of healthcare services 188 shortcomings were identified.

The Control Department forwarded 69 motions in total to the medical device Legal Support Department for further procedure. Moreover, the Control Department received 73 reports submitted in the sphere of market surveillance by natural or legal persons both from the Czech Republic and from abroad for processing.

Tab. 34 **Overview of inspections by the Control Department**

Number of inspections	176
Number of report-based inspections (of the total number of inspections)	30
Number of inspected medical devices	1 564
Number of inspected established meters (of the total number of inspected medical devices)	35
Number of inspected class IIb and III medical devices (of the total number of inspected medical devices)	375
Number of inspected medical devices without shortcomings (of the total number of inspected medical devices)	1 047 *
Number of inspected medical devices with shortcomings (of the total number of inspected medical devices)	517 *
Number of shortcomings	656 *
Number of shortcomings in class IIb and III medical devices (of the total number of inspected medical devices with shortcomings)	201 *
Number of reports forwarded to other authorities	8
Number of reports forwarded to medical device Legal Support Department (proposal for initiation of an administrative procedure)	69

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

Tab. 35 **Rating of inspections conducted by the Control Department**

Entity	**Number of inspections**	**Of which report-based**	**1**	**%**	**2**	**%**	**3**	**%**
Anaesthesiology & Resuscitation/Intensive Care Unit	4	3	1	25	2	50	1	25
Medical transport service	1	0	0	0	0	0	1	100
Gastroenterology	28	0	26	93	1	4	1	4
Gynaecology	2	2	0	0	0	0	2	100
Inspection of sterile medical devices in hospitals	3	3	0	0	1	33	2	67
Plastic surgery/dermatology/surgery	21	0	14	67	7	33	0	0
Sexology	1	1	0	0	1	100	0	0
Dentistry	36	1	25	69	10	28	1	3
Manufacturers	8	5	2	25	4	50	2	25
Distributors/importers	36	12	10	28	14	39	12	33
Servicing	18	1	9	50	3	17	6	33
Dispensing persons	10	0	6	60	3	30	1	10
Vendors	8	1	4	50	3	38	1	13
Total	**176**	**29**	**97**	**55**	**49**	**28**	**30**	**17**

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). The inspection is rated on the basis of the most serious shortcoming, the number of which becomes the inspection rating.

Penalties for Breach of Act on Medical Devices

SÚKL, 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.

In 2016, SÚKL imposed fines for breach of the Act on Medical Devices amounting to the total of 899 000 CZK. The highest proportion of fines imposed in 2016 by SÚKL for the breach of the Act on Medical Devices were fines imposed upon healthcare service providers for the breach of their obligations implied by Act No. 268/2014 Coll., on Medical devices, and the preceding Medical Device Act No. 123/2000 Coll.

One fine was imposed upon a distributor for failure to comply with the rights and obligations of an inspected person pursuant to Section 10 of Inspection Code No. 255/2012 Coll.

Furthermore, one fine was imposed upon a manufacturer of medical devices for breach of manufacturer's obligations associated with the placement of medical devices onto the market pursuant to Section 19a of Act No. 22/1997 Coll., on Technical Requirements for Products, and Government Regulation No. 54/2015 Coll., on Technical Requirements Governing Medical Devices.

Information on Administrative Procedures Concerning Product Nature and Medical Device Classification

SÚKL, as a first-instance administrative authority, holds administrative procedures on the nature of products and classification of medical devices pursuant to the Act on Medical Devices.

In 2016, SÚKL issued 8 decisions on product nature pursuant to Section 41 of the Act on Medical Devices, and 2 decisions on medical device classification pursuant to Section 40 of the Act on Medical Devices.

Furthermore, 11 administrative procedures on product nature and 4 administrative procedures on medical device classification were commenced.

STATE AGENCY FOR MEDICAL CANNABIS

In compliance with Act No. 167/1998 Coll., on Dependency-Producing Substances, as amended, SÚKL performs the tasks of the State Agency for Medical Cannabis. The Department of the State Agency for Medical Cannabis was established on 1 January 2013. Its activities are associated with the granting of licenses 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.

Department of the State Agency for Medical Cannabis

In 2016, the Department of the State Agency for Medical Cannabis (OSAKL) safeguarded processes and activities related to ensuring availability of the medical cannabis active substance for Czech patients from a domestic grower.

OSAKL took over and placed in distribution 11.2 kg of medical cannabis from the supplier 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 SÚKL´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 SÚKL.

Furthermore, the Department safeguarded compliance with SÚKL´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 the previous year, it cooperated with the Inspectorate for Narcotic and Psychotropic Substances of the Ministry of Health. As part of its operation, OSAKL communicated and cooperated with major Czech and foreign experts in the field of medical cannabis, a patient organisation, professional societies and chambers. The staff of the Department also gave lectures intended for professionals.

In 2016, 16 doctors complying with the requirements of all relevant legal regulations and authorised to prescribe medical cannabis for patients in indications defined by law, and 25 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, were published by OSAKL on a regular basis on their website at www.sakl.cz and on the website www.sukl.cz (Medical Cannabis).

Tab. 36 **Overview of issued prescriptions, number of patients, and amounts of dispensed cannabis in 2016**

Period (month/year)	1 / 2016*	2 / 2016*	3 / 2016	4 / 2016	5 / 2016	6 / 2016	7 / 2016	8 / 2016	9 / 2016	10 / 2016	11 / 2016	13 / /2016
Number of issued Rp.	-	-	0	13	41	30	24	33	27	24	38	42
No. of patients	-	-	0	13	39	28	24	31	26	24	35	39
Dispensed amount (g)	-	-	0	154	422,5	218	214	294,5	375	179,5	418,3	303

** Not on the market*

PROCESSING AND PROVISION OF INFORMATION

Information Technology

In 2016, the Information Technology Department (hereinafter referred to as„OIT") continued to replace obsolete IT equipment and proceeded in the preparation and execution of the first stage of the building of a new data centre. Within the scope of this first stage, new HW has been procured and it will be located in the new data centre once its non-IT part is completed. In relation to this, primary preparations for the migration of virtual servers from the existing HW to the new one which is to be located within the premises of the new data centre were carried out. These preparations constituted of planning and upgrading the operating systems of some servers. This upgrade will continue also in the following year, so as to achieve the desired target situation in the new data centre. Concurrently, an extensive migration of a shared document repository to the new HW was performed.

In early 2016, the Operations Department commenced the operation of a new service-desk tool for the collection of requests from users. The objective of putting this tool in operation was to increase the effectiveness in resolving users´ requests and to create a uniform contact point for communication between IT and other users. The new tool serves not only for the purposes of request collection, but also as an important help for IT staff in their routine work. The tool incorporates essential processes for the management of IT services within the scope of requirements set forth by the ISO 27001 standard and the ITIL methodological framework. In the first year of operation of this system, almost 10 000 user requests were collected and resolved. Concurrently with this tool, a uniform contact point (Contact Centre) to cater for communication between external entities and SÚKL in relation to the development of the new systems ERP, LEK-13, and DIS-13 was established.

In summer 2016, the contract registry internal application was connected to the Contract Register System which was established pursuant to Act No. 340/2015 Coll. In association with this Act, an obligation to publish contracts with financial volumes in excess of 50 000 CZK in this Register arose.

In 2016, the transfer of SÚKL mail services to the Office 365 cloud solution commenced. This solution will bring SÚKL a wealth of benefits, such as protection of data through encryption, two-factor authentication, skype communication application, and the latest version of the Office package.

In late 2016, the development of an internal risk management application began. This application is to replace the current solution which exists in the form of record-keeping in MS Excel tables. The solution includes also an integrated record-keeping of audit records integrated with a register of non-conformities and shortcomings identified during audits. The integration constitutes also of safeguarding links between associated data from the aforementioned registers. The proposed solution will enable to interconnect the monitored data, to create overviews and reports, to capture the history of changes, and to set up authorisations for work with the data.

In the course of 2016, the Pilsen and Hradec Králové branches were physically relocated to new premises. During this event, OIT safeguarded the development of a new data infrastructure and organised the relocation of IT technology. In this year, several larger projects started, for which OIT provided technical support and cooperation.

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 (hereinafter referred to as „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, to date, it operates on a voluntary basis in the Czech Republic. On 19 November 2014, Act No. 255/2014 Coll., effective as of 31 December 2014, was published in the Collection of Laws, which postponed the obligation to issue electronic prescriptions to 1 January 2018.

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 2016, a public contract was announced and concluded for the development, delivery, and implementation of the ePrescription information system and the provision of service support to this system for the period of 4 years (the IS includes a Central Repository of Electronic Prescriptions, as defined by Section 81 of the Act on Pharmaceuticals, a Register of Restricted Medicinal Products pursuant to Section 81a of the Act on Pharmaceuticals, and other components). Since December 2016, when a contract was signed with the winner of the tender, the ePrescription IS project has been intensively executed. According to the effective schedule, the project should be completed and the ePrescription IS put live on 16 November 2017. Concurrently, the implementation of SÚKL´s data centre began. All of the activities are aimed at a flawless safeguarding of electronic prescription in the following period, when an increase in the number of users, and hence also the number of issued electronic prescriptions, is expected with the approaching timeline for mandatory electronic prescription. Within the scope of operation of the electronic prescription system,

New Data Centre / **Upgrade of Operating Systems**

Risk Management Application / IT Services according to ISO 27001

10 000 User Requests resolved / **ePrescription**

eHealth / Connection to the Contract Register System

Protection of Data through Encryption / **Two-factor Authentication**

SÚKL provides support for applicants and users of the given system. One of the important activities is the operation of a free hotline which is available to applicants and users during working days from 8:00 a.m. to 5:00 p.m.

Concurrently, SÚKL as the administrator ensures continuous access to data maintained in the Register of Restricted Medicinal Products (hereinafter referred to as "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, SÚKL ensures electronic access to this Register for the Czech Police.

A separate area which is being addressed on a continuous basis is the security of the entire system. With the coming into force of Act No. 181/2014 Coll., on Cybernetic Security, the CÚER and RLPO systems were included among important public administration information systems. With respect to this, adequate measures to help fulfil the requirements of the aforementioned Act were adopted in 2016.
Despite temporary non-functionality of the ePrescription IS in the first few months of 2016, caused by restricted operation of some information systems at the end of 2015, the functionality of the RLPO, and subsequently also a substitute solution for the prescription and dispensing of medicinal product was safeguarded in early 2016 and launched on 30 March 2016. At present, this solution works within the same scope as in autumn 2015. Concurrently, the numbers of doctors and pharmacists working in the system as well as the numbers of issued ePrescriptions reaching the daily and monthly maximums for the entire operation keep growing.

In 2016, 1 541 135 electronic prescriptions were issued. The average monthly number of issued electronic prescriptions in 2016 was 171 237, which, compared to 2015, represents an almost 18% increase. Despite this increase, a major proportion of prescriptions is still issued in the form of paper copies. In 2016, the total value of reimbursement for dispensed reimbursed medicinal products prescribed through the ePrescription system amounted to 1 304 351 422 CZK, which is 561 948 685 CZK more than in the previous year.
Since the start of the ePrescription system operation till the end of 2016, the total of 6 297 doctors in 983 healthcare facilities applied for the possibility to avail of electronic prescriptions, and the total of 6 031 pharmacists from 1 886 pharmacies applied for the possibility to dispense them.

Database of Medicinal Products and Monitoring of Supplies to Pharmacies

On the basis of the obligation set forth by the Act on Pharmaceuticals, SÚKL 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 (hereinafter referred to as „DLP") is used, which is updated on a continuous basis.

Registry of Active Substances

As at the end of 2016, the DLP database contained 23 375 components (incl. combined components); in 2016, 378 new components were entered and records were updated for 1 456 components. Furthermore, in 2016, an update of flagging of doping components and of products containing such substances in the DLP was carried out pursuant to the 2016 Prohibited List – the World Anti-Doping Code effective as of 1 January 2016. The 2015 and 2016 Supplements to Czech Pharmacopoeia together with the corresponding data from the European Pharmacopeia were entered. Components from lists proposed by INN WHO issued in 2016 were entered and an adjustment of components from the recommended INN WHO lists was performed. Some data about psychotropic substances were updated 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. In cooperation with the Czech Pharmacopoeia staff, several changes to the titles of monographs and their subsequent implementation in the DLP were proposed. The revision of selected groups of components is still under way.

Registry of Medicinal Products

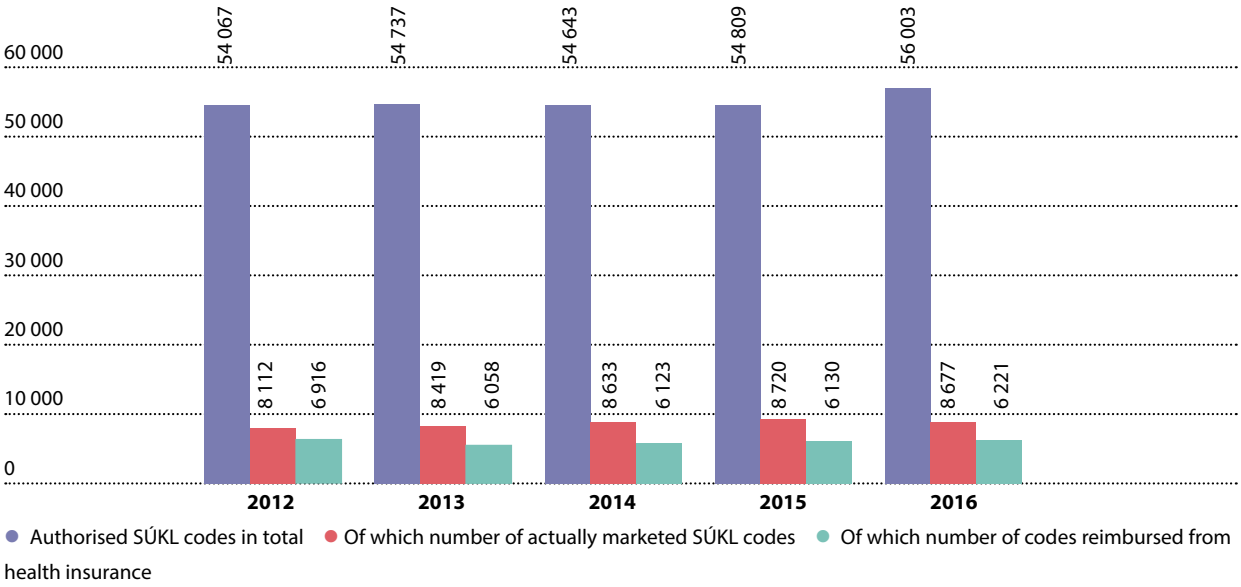
In 2016, SÚKL granted 507 (3 552 SÚKL codes). Authorisation was revoked for 529 marketing authorisation numbers, which corresponds to 4 784 codes. The authorisation was revoked either upon request of the marketing authorisation holder (388 marketing authorisation numbers), or due to the sunset clause (128 marketing authorisation numbers), or due to the fact that the holder did not apply for marketing authorisation renewal (13 marketing authorisation numbers). The validity of 4 986 codes in total expired (the period of final code sale expired or marketing authorisation was revoked).

In the course of 2016, no distribution was reported for 47 326 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 2 615 various active substances in total.

Tab. 37 **Selected subgroups of authorised medicinal products recorded in the SÚKL database as of 31 December 2016**

	Total No. of authorisation numbers/marketed authorisation numbers	Total No. of SÚKL codes/marketed SÚKL codes
Medicinal products in total (excl. homeopathic preparations)	**16 698/5 919**	**56 003/8 677**
Of which by MA numbers:		
MA numbers granted by SÚKL	6 393/4 820	45 680/7 574
MA numbers of products authorised via Community Centralised Procedure	10 305/1 099	10 323/1 103
Of which by content:		
Single-component	13 365	44 909
Multi-component	3 333	11 094
Of which by type of dispensing:		
Prescription-only medicinal products	15 827/5 215	51 933/7 572
OTC medicinal products	915/718	4 008/1 096
Restricted OTC medicinal products	12/5	47/6
Restricted prescription-only medicinal products	3/3	15/3
Homeopathic preparations	271/256	723/321

Fig. 23 **Authorised medicinal products in the period of 2012–2016**



Regular Outputs from the Database of Medicinal Products

For professionals as well as for the general public, SÚKL 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, SÚKL 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.

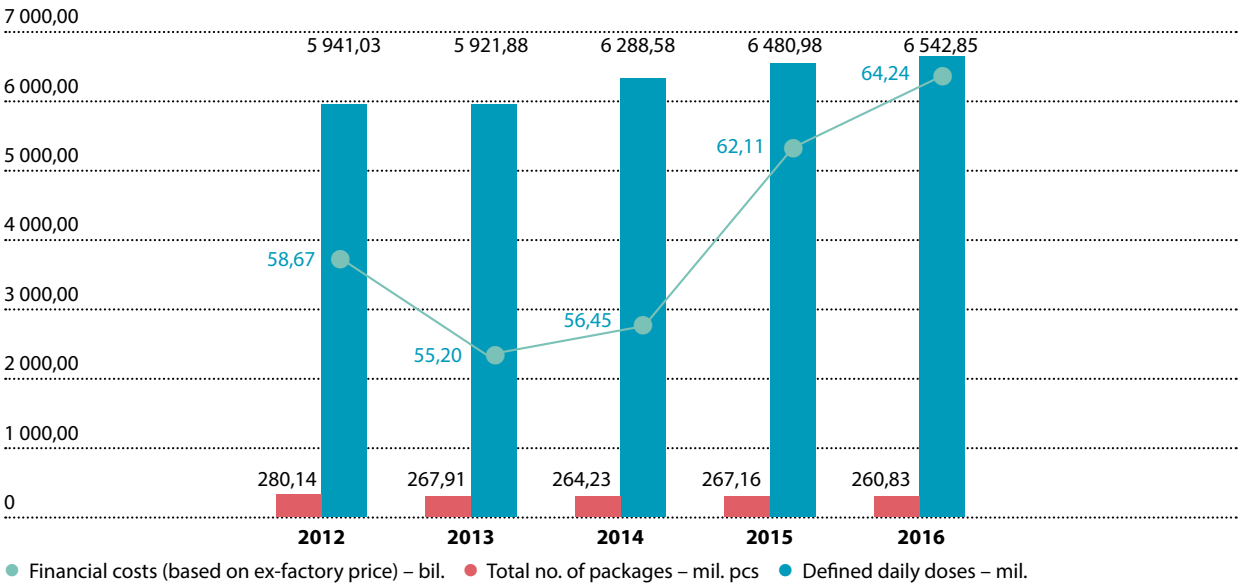
Evaluation of Deliveries of Distributed Medicinal Products

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 2016. 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 the authorised medicinal products, also products included in specific therapeutic programmes and non-authorised products supplied on medical prescription to 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 SÚKL´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, SÚKL publishes summary information from monthly reports of entities authorised to distribute medicinal products in the Czech Republic on its website.

In 2016, 260.83 mil. packages of medicinal products were distributed, which corresponds to approx. 6 542.85 mil. DDD. The value of these deliveries amounted to 64.25 billion CZK (based on ex-factory price).

Fig. 24 **Deliveries of medicinal products in 2012–2016**



Tab. 38 **Deliveries of distributed medicinal products in 2016**

Medicinal products in total	**Number**
Deliveries to pharmacies and healthcare facilities (mil. packages)	260,826
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	64 254,212
Deliveries to pharmacies and healthcare facilities (mil. DDD)	6 542,849
DDD/1 000 inhabitants/day	1 700,486
Prescription-only medicinal products	**Number**
Deliveries to pharmacies and healthcare facilities (mil. packages)	181,942
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	57 745,088
Deliveries to pharmacies and healthcare facilities (mil. DDD)	5 938,724
DDD/1 000 inhabitants/day	1 543,474
OTC and selected pharmaceuticals	**Number**
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. packages)	78,517
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. CZK based on ex-factory price)	6 467,879
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. DDD)	603,932
DDD/1 000 inhabitants/day	156,962
Restricted OTCs	**Number**
Deliveries to pharmacies and healthcare facilities (mil. packages)	0,367
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	41,245
Deliveries to pharmacies and healthcare facilities (mil. DDD)	0,194
DDD/1 000 inhabitants/day	0,050
Homeopathic preparations	**Number**
Deliveries to pharmacies (mil. packages)	1,874
Deliveries to pharmacies (mil. CZK based on ex-factory price)	176,199

Information Activities

The major task of the Press and Information Department (hereinafter referred to as „TIO“) is to provide information to the general and professional public. The most important sources of information about SÚKL 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.

In 2016, the website for professionals www.sukl.cz was visited by 3.1 million visitors who viewed more than 14.2 million pages.

O the information portal www.olecich.cz, patients may find information from the sphere of pharmaceuticals, such as a database 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. Information on the www.olecich.cz portal was searched by 226 thousand visitors who viewed almost 761 thousand pages.

Four 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 2016, infoLISTY focused upon the topic of "Medical Cannabis", "Availability of Medicines", and "Advertising for Medicines", with the last topic being split into two issues.

Via the "Ask Us" service, pharmacists and doctors – a general practitioner and a paediatrician, and three pharmacists – were answering questions from the public. In total, 310 patient questions were answered via this service. In 2016, the largest proportion of the questions concerned drug interactions.

In 2016, 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 (11 in total), through which more than 300 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 the SÚKL 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 2016, TIO addressed 70 requests for information pursuant to Act No. 106/1999 Coll., on Free Access to Information, as amended. Furthermore, it answered more 3240 inquiries from the general public and from professionals which were sent via e-mail or post. Further 3 500 inquiries were handled through the infoline.
The Department drafted responses to 212 inquiries from journalists and provided a statement for radio or TV broadcasting in 153 instances. Twelve press releases/advices, and 6 reactions were published on SÚKL´s website.

Tab. 39 **Number of processed inquiries from journalists and outputs in media in 2014–2016**

	Answers to inquiries from journalists (printed and web)	Source materials and outputs for TV or radio broadcasting
2016	212	153
2015	188	126
2014	225	86

FINANCIAL AND MATERIAL RESOURCES OF SÚKL

Income and Expenditure Account for 2016

Income

In 2016, extra-budgetary income in the total amount of 480 992 thous. CZK was achieved. The major part of this income was generated by the reimbursement of costs of expert activities which were conducted by SÚKL 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 SÚKL 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 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 2016, a total amount of 425 742 thous. CZK was used in this manner through permissible excess expenditure. Of this amount, 364 123 thous. CZK were used for non-investment expenditure and 61 619 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 5 296 thous. CZK, income from the sale of goods amounting to 253 thous. CZK, income from lease in the amount of 311 thous. CZK, income from the sale of other tangible long-term assets of 206 thous. CZK, refunds from excess advance payments made, related fully to the previous budgetary years, in the amount of 711 thous. CZK, etc. An overview of the reported budget income as of 31 December 2016 is shown in Table 42.

Tab. 40 **Funds and state budget**

	2014	2015	2016
Average converted number of employees	409,44	433	446
Funds allocated from the state budget for the operation of SÚKL (in thousands CZK)	114 907	122 798	128 977
Allocation of income in the state budget (in thousands CZK)*	36 703	33 146	36 474

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

Expenditure

Data concerning expenditure incurred in 2016 by individual categories are provided in Table 42.

Total investment expenditure amounted to 61 603 thous. CZK from extra-budgetary resources. Investment resources were used to finance the interior reconstruction of building no. 30 (3 867 thous. CZK), air-conditioning at a remote worksite in Brno (1 995 thous. CZK), data networks and electronic security systems at sites OKL Litoměřice, OKL Plzeň and OKL Hradec Králové (621 thous. CZK), reconstruction of substation in building no. 24 and a transformer station (623 thous. CZK). For laboratories, laboratory apparatuses in the total value of 906 thous. CZK were purchased (titrator balances, nitrogen generator, freezer box). Two cars (1 812 thous. CZK) and a data projector (61 thous. CZK) were procured. For technology renewal purposes, the total of 11 061 thous. CZK was incurred, for valuable rights the total of 33 693 thous. CZK, and for software the total of 6 740 thous. CZK (KLP RIS-module; web form implementation; CÚER replacement solution; data warehouse and BI implementation; etc.). Furthermore, studies for the following projects were funded: Brno – construction of a lift, completion of the basement (83 thous. CZK); new routing of water pipelines for buildings no. 24 and 30 (48 thous. CZK); building no. 24 – community hall reconstruction (33 thous. CZK); data centre construction - NON IT Stage 1 (27 thous. CZK); and building no. 23A (33 thous. CZK).

Non-investment expenditures were drawn in the total amount of 493 018 thous. CZK, of which 128 977 thous. CZK were from the state budget and 364 041 thous. CZK were utilised from extra-budgetary resources. Extra-budgetary resources included resources from abroad provided for the ARTHIQS project (196 583.20 CZK utilised), for the EURIPID project (288 550 CZK utilised), for the EUnetHTA project (39 089.68 CZK utilised), and for the SCOPE project (funds utilised in total: 255 674.70 CZK, of which 74 000 CZK were funds from abroad).

Since 2014, SÚKL 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.

SÚKL 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 (hereinafter referred to as „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, SÚKL 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. SÚKL has been involved since the start of the project and at present chairs the association´s executive commission. 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, SÚKL 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 SÚKL as of 31 December 2016 amounted to 1 038 083 thous. CZK, of which fixed assets amount to 393 142 thous. CZK and current assets to 644 941 thous. CZK. Of the total liabilities of 1 038 083 thous. CZK, equity amounts to 1 007 943 thous. CZK and borrowed capital to 30 140 thous. CZK. Selected types of assets and liabilities of the Institute are listed in Table 41.

Other

A total of 3 548 thous. CZK from SÚKL´s budget was used for foreign business trips. In 2016, 402 foreign business trips paid for by SÚKL took place, of which fully covered were 187; in respect of others (215 trips), the costs were partly 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. SÚKL 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 SÚKL´s priorities, the relevance and benefits of the discussed topics for the Institute.

Auditing

In the period from 9 March 2016 to 31 May 2016, the Revenue Authority for the Capital City of Prague conducted an audit in SÚKL 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 SÚKL´s Administrative Operation, reg. no. CZ.1.04/4.1.00/59.00009". The audit was performed 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 the reimbursement of an invoice for office supplies and exceeded prices for specified items and their classification as another type of costs. The audit discovered that funds were used in an unauthorised manner as referred to under the provision of section 3 (e) of Act No. 218/2000 Coll., on Budgetary Rules and on Amendment to Some Related Acts (hereinafter referred to as the "Act on Budgetary Rules") and budgetary discipline breached in respect of a total amount of 47 237.20 CZK, as referred to under Section 44, paragraph 1 (a) of the Act on Budgetary Rules.

On the basis of an issued tax adjustment notice for breach of budgetary discipline, amounts of 40 152 CZK and 7 086 CZK were paid to the account of the Revenue Authority for the Capital City of Prague. Concurrently, SÚKL paid a penalty for late payment of tax for the breach of budgetary discipline for the period from 28 February 2013 to 8 June 2016 pursuant to the provision of Section 44a, paragraph 10 of Act No. 218/2000 Coll., on Budgetary Rules and on Amendment to Some Related Acts in the amount of 40 152 CZK and 6 909 CZK to the account of the Revenue Authority for the Capital City of Prague.

In the period from 9 March 2016 to 31 May 2016, the Revenue Authority for the Capital City of Prague conducted an audit in SÚKL 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 SÚKL´s Administrative Operation, reg. no. CZ.1.04/4.1.00/59.00009". The audit was performed 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-matter of the motion were personal costs claimed for the said period and a difference between claimed and worked hours associated with the project. The audit discovered that funds were used in an unauthorised manner as referred to under the provision of section 3 (e) of Act No. 218/2000 Coll., on Budgetary Rules and on Amendment to Some Related Acts (hereinafter referred to as the "Act on Budgetary Rules") and budgetary discipline breached in respect of a total amount of 4 533 CZK, as referred to under Section 44, paragraph 1 (a) of the Act on Budgetary Rules.

On the basis of an issued tax adjustment notice for breach of budgetary discipline, amounts of 3 854 CZK and 680 CZK were paid to the account of the Revenue Authority for the Capital City of Prague. Concurrently, SÚKL paid a penalty for late payment of tax for the breach of budgetary discipline for the period from 10 November 2012 to 7 April 2016 pursuant to the provision of Section 44a, paragraph 10 of Act No. 218/2000 Coll., on Budgetary Rules and on Amendment to Some Related Acts in the amount of 3 454 CZK to the account of the Revenue Authority for the Capital City of Prague. In the period from 9 March 2016 to 31 May 2016, the Revenue Authority for the Capital City of Prague conducted an audit in SÚKL 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 SÚKL´s Administrative Operation, reg. no. CZ.1.04/4.1.00/59.00009". The audit was performed 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 public contract 002 "Increasing the Efficiency of SÚKL´s Project Management". The audit discovered that funds were used in an unauthorised manner as referred to under the provision of section 3 (e) of Act No. 218/2000 Coll., on Budgetary Rules and on Amendment to Some Related Acts (hereinafter referred to as the "Act on Budgetary Rules") and budgetary discipline breached in respect of a total amount of 240 000 CZK, as referred to under Section 44, paragraph 1 (a) of the Act on Budgetary Rules. With a view to the judicature and assessment of the scope of the breach of budgetary discipline, the nature and severity of the fault, a sanction in the amount of 1% from the amount of 240 000 CZK, i.e. 2 400 CZK, was established.

On the basis of issued tax adjustment notices for breach of budgetary discipline, amounts of 2 040 CZK and 360 CZK were paid to the account of the Revenue Authority for the Capital City of Prague. Concurrently, SÚKL paid a penalty for late payment of tax for the breach of budgetary discipline for the period from 18 January 2013 to 8 June 2016 pursuant to the provision of Section 44a, paragraph 10 of Act No. 218/2000 Coll., on Budgetary Rules and on Amendment to Some Related Acts in the amount of 2 040 CZK to the account of the Revenue Authority for the Capital City of Prague. On 9 March 2016, the Revenue Authority for the Capital City of Prague initiated an audit 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 SÚKL´s Administrative Operation, reg. no. CZ.1.04/4.1.00/59.00009". The audit was initiated 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 public contract 003 "Conception of Electronisation of SÚKL´s Activities". The audit has not been completed to date.

On 29 June 2016, a meeting was held at the Revenue Authority for the Capital City of Prague, territorial office for Prague 10, to verify the tax base and value-added tax for tax period of April 2016. The meeting resulted in verification of the submitted source documentation, in respect of which no shortcomings were identified, and excess VAT deduction was refunded to SÚKL.

In the period from 28 January 2016 to 22 April 2016, the Revenue Authority for the Capital City of Prague conducted an audit in SÚKL to check whether a tax liability has arisen from a breach of budgetary discipline in the utilisation of funds from the state budget and EU funds in 2011 within the scope of the Human Resources and Employment Operational Programme for the implementation of the project "Implementation of process effectiveness (performance) measurement in SÚKL and its individual organisational units", reg. no.: CZ.1.04/4.1.00/59.00023, associated with implemented public contract VZ19/2011 "Process Effectiveness Measurement System" (due to failure to observe the transparency principle and equal approach to tenderers), the provision of Section 6 of Act No. 137/2006 Coll., on Public Contracts was breached, funds from the state budget were used in an unauthorised manner as referred to under the provision of section 3 (e) of Act No. 218/2000 Coll., on Budgetary Rules and on Amendment to Some Related Acts (hereinafter referred to as the "Act on Budgetary Rules") and budgetary discipline was breached in respect of a total amount of 1 768 800 CZK, as referred to under Section 44, paragraph 1 (a) of the Act on Budgetary Rules. With a view to the judicature and assessment of the scope of the breach of budgetary discipline, the nature and severity of the fault,

a sanction in the amount of 25% from the amount of 1 768 800 CZK, i.e. 442 200 CZK, was established.

On the basis of issued tax adjustment notices for breach of budgetary discipline in the amount of 375 870 CZK and 66 330 CZK, a request for tax payment deferral was filed with the General Financial Directorate, which was granted by decisions of 19 December 2016 establishing the timeline for tax payment no later than by 15 June 2018. On 16 November 2016, requests for tax waiver for breach of budgetary discipline were filed (kept under files sukls261791/2016 and sukls261802/2016). Concurrently, on 13 January 2017, SÚKL filed a request for deferral of payment of the penalty for late tax payment for breach of budgetary discipline in the amount of 375 870 CZK and 66 330 CZK and on 10 January filed a request for waiver of the penalty for late tax payment for breach of budgetary discipline for the period from 16 May 2012 to 15 December 2016, in respect of which an opinion is awaited (kept under files sukls261791/2016 and sukls261802/2016).

In 2016, fines and penalties amounting to the total of 106 727 CZK were paid to the account of the Revenue Authority.

In the period from 14 June 2016 to 19 December 2016, an audit was performed in SÚKL by the Supreme Audit Office, focusing upon assets and monetary funds of the state which may be utilised thereby in the period of 2013–2015, previous and future periods, where materially justified, until the completion of the audit. The audit has not been concluded in 2016.

Tab. 41. **Overview of selected types of assets and liabilities of the organisation in thousands of CZK**

Name of item	**Past period**	**Present period**
	2015	**2016**
ASSETS	**990 072**	**1 038 083**
A. Total fixed assets	**403 673**	**393 142**
of which:		
I. Long-term intangible fixed assets – total	132 666	115 990
II. Long-term tangible fixed assets – total	271 007	277 152
Lots	4 619	4 619
Buildings	218 375	226 163
Separate tangible movables and sets of tangible movables	41 367	45 410
Small tangible fixed assets	0	0
Unfinished tangible fixed assets	6 646	960
B. Total current assets	**586 399**	**644 941**
of which:		
I. Inventory - total	74	634
II. Short-term receivables - total	4 016	3 009
III. Short-term financial assets - total	582 309	641 298
LIABILITIES	**990 072**	**1 038 083**
C. Equity	**936 907**	**1 007 943**
of which:		
I. Assets of the accounting entity and adjustments	226 285	228 921
II. Funds of the accounting entity	555 599	612 006
Fund for cultural and social needs	1 311	1 976
Reserve fund	554 288	610 030
III. Economic result	-326 760	-407 172
Economic result for the current accounting period	-53 827	- 80 412
Economic result for the previous accounting periods	-272 933	- 326 760
IV. Income and expenditure account of the budget management	481 783	574 188
D. Total borrowed capital	**53 165**	**30 140**
of which:		
I. Total long-term liabilities	20	20
II. Total short-term liabilities	53 145	30 120

Tab. 42. **Budget income, budget expenditure and financing in thous. CZK**

BUDGET INCOME	**Budget for 2016**		**Real values for 2016**
	Approved budget	**Corrected budget**	**Real values for 2016**
Administrative fees	19 800	19 800	29 092
Penalties received	1 000	1 000	5 296
Income from lease	0	0	311
Income from the sale of other long-term tangible assets	0	0	206
Income from the sale of goods	0	0	253
Income from the provision of services	0	0	23
Non-equity contributions received	0	0	711
Transfers from reserve fund	0	0	425 742
Transfers from other own funds	0	0	582
Operating transfers from the National Fund	0	0	0
Total	**20 800**	**20 800**	**462 216**
Expenditure	**Budget for 2016**		**Real values for 2016**
	Approved budget	Corrected budget	Real values for 2016
Employees´ salaries	19 521	32 571	32 571
Civil servants´ salaries	70 784	229 823	229 822
Other payments for performed work and severance pay	3 603	10 986	10 985
Mandatory premium paid by employer	31 929	91 130	91 130
Contribution to the Fund of Social and Cultural Needs	1 297	3 944	3 944
Operating acquisitions and related expenditure	824	124 646	124 566
Acquisition of tangible and intangible fixed assets	0	61 619	61 603
Total	**127 958**	**554 719**	**554 621**
of which: operating expenditure	127 958	493 100	493 018
capital expenditure	0	61 619	61 603

Tab. 43. **Expenditure statistics in the period of 2014–2016**

	2014	**2015**	**2016**
Total operating expenditure (in thous. CZK)	470 816	484 209	493 018
Non-investment expenditure (excluding salaries, insurance for cultural and social needs) (in thous. CZK)	160 980	141 289	124 566
Investment expenditure (in thous. CZK)	56 268	76 172	61 603
Average converted number of employees	409,44	433	446
Expenses per employee (line 1/line 4) in CZK	1 150	1 118	1 105

FOCUS UPON EMPLOYEES

Personnel Issues

Organisational Structure

In compliance with the SÚKL systemisation approved for 2016 pursuant to Act No. 234/2014 Coll., on Civil Service, organisational changes have been implemented since 1 January 2016 in order to optimise the number of systemised positions and to increase the work effectiveness, in the total number of 510 positions, of which 420 are service positions and 90 work positions.

Within the scope of the organisational changes, in addition to the increased number of service and work positions compared to 2015, several substantial changes were implemented, particularly within the organisational structure of the Marketing Authorisation Branch, specifically the opening of 3 new sections: Section of Clinical Trials and Non-authorised Medicinal Products, Section of Administrative and Process Support, and Section of Coordination and Regulation.
As at 31 December 2016, the total occupancy of systemised positions amounted to 92 %. The number of vacant systemised positions was 41 (of which 35 were service positions and 6 work positions).
The number of physical employees on payroll as of 31 December 2016 was 471 persons, of which 365 were women (i.e. 77.5%) and 106 were men (i.e. 22.5%).

Converted to FTEs worked under non-employment agreements (work agreement and agreement to perform work), a total of 29.5 employees were employed as of 31 December 2016. Compared to 2015, this was a 14.34% increase.

Age structure of employees

The average age of all employees compared to 2015 increased by 0.64%, i.e. to 41.24 years.

Tab. 44 **Age structure of employees as of 31 December 2016 in %**

	Employees under 35	Employees aged 36 to 55 years	Employees over 55 years
2015	40,3	44,7	15,0
2016	38,0	45,2	16,8

Working Hour Utilisation

Of the total amount of 958 841.4 hours worked, 2 934.04 were overtime hours. Overtime work mostly concerned employees from the workers' category (drivers), expert staff and technical-economic staff.

In 2016, the employees were absent for the total of 2 190.5 working days due to sickness or nursing a family member, which is, compared to 2015, 341 working days less. Of the total number of employees, absence due to sickness or nursing a family member was observed for the total of 127 employees, of which:

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

Compared to the previous year 2015, the total number of employees on sickness leave or nursing family members decreased by 8.

On the basis of amendments to the Higher-Degree Collective Agreement, a new SÚKL Collective Agreement 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 2016, the employees utilised the total of 393 days of service leave (of which 182 were study service leave days) and 1 439 sick days.

Tab. 45 **Qualification structure of employees by achieved level of education as of 31 December 2016**

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	9	78	6	13	346	13
% of the total number of employees	0,21	1,06	1,91	16,56	1,28	2,76	73,46	2,76

Staff Turnover

The overall staff turnover, taking into account all start-ups and departures, is 9.69% (compared to 2015, a 3.97% decrease occurred).

Tab. 46 **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**

	Service positions		Work positions	
	No. of tenders	Start-ups	No. of tenders	Start-ups
Tenders for vacancies	74	48	54	41
Tenders – existing occupied positions (so-called re-tendering)	47	47	-	-
Total	**121**	**95**	**54**	**41**

Tab. 47 **Overview of employment and service terminations in 2016 by reason of employment/service termination**

	Cancellation in probationary period	Agreed time expiry	Termination by agreement	Notices given by employees	Notices given due to organisational reasons/by decision of a service authority	Death of the employee	Total
Employment	0	1	4	13	3	0	21
Service	2	6	0	14	1	1	24

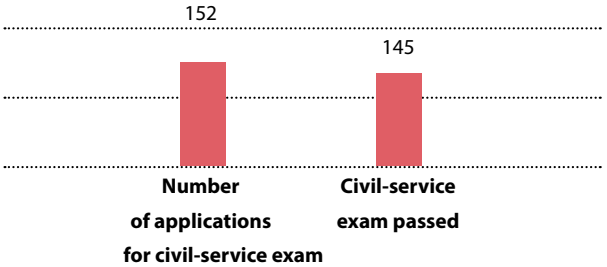
Civil-Service Exam

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 2016, 152 SÚKL´s applications were filed. In 2016, 95.4% of obliged employees successfully passed the civil-service exam. The remaining 4.6% of employees will take the exam in 2017 (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 2 were unsuccessful at the first attempt, of which one has already been successfully passed.

Fig. 25 **Civil-service exams**



Employee Education

In 2016, in the area of employee education emphasis was placed not only on initial education, but within the scope of follow-up education and education of managers 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.

The total amount of funds spent on all types of education amounted to 3 657 500 CZK.

Internal PC Training

With a view to savings of financial resources, inhouse education focusing upon MS Office, particularly MS Excel, on various levels of knowledge, was established in 2016. The courses have been held by internal 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 SÚKL staff.

In 2016, 17 courses were completed within which 163 employees were trained.

Tab. 48 **Overview of educational activities in 2016 – follow-up education**

Type of event	Number of events	Number of hours	Number of attendees
PC training (expert + internal)	25	204	173
Language courses	32	794	162
Specialised courses and training	276	5 672	429
Managerial skills	35	280	307
Mandatory training	556	643	556
Foreign specialised training	46	1 152	60

Environmental conduct / **Ethical rules**

Surveillance audits / **Transparent documentation**

Quality Management System / **ISO 9001:2009**

Project BEMA / **CSQ-CERT certification authority of the Czech Society for Quality**

Customer Satisfaction Questionnaire / **26 internal audits**

FOCUS UPON QUALITY

SÚKL continues to develop the certified quality management system in compliance with the requirements of the ČSN EN ISO 9001 standard and, for the Laboratory Control Section, in compliance with the ČSN EN ISO/IEC 17025 standard, striving to continuously improve the system.

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

In 2016, two regular surveillance audits of the quality management system completed by the CSQ-CERT certification authority of the Czech Society for Quality (ČSJ) took place and confirmed conformity with the requirements of the concerned certification criteria of the ČSN EN ISO 9001:2009 standard for the quality management system. Furthermore, a regular verification of the established quality system of the Laboratory Control Section was conducted by a group of EDQM auditors. The certificate is to be issued in early 2017.

SÚKL continues its involvement in the "BEMA" project where, for the fourth time, the benchmarking of the quality system standard among the European medicines agencies is being conducted. In 2016, a preparation for self-assessment began, which will be followed by assessment by external assessors in the 4th quarter of 2017.

In the course of the year, 26 internal audits of the quality management system were completed, in which the set-up and effectiveness of the quality management system as applied to the individual processes (activities) of SÚKL were assessed.

In late 2016, an updated Customer Satisfaction Questionnaire was published on SÚKL´s website which helped to identify customer needs and evaluate the effectiveness of processes.

INFORMATION SECURITY MANAGEMENT POLICY

SÚKL 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 (hereinafter referred to as „ISMS") at a standard necessary for SÚKL to be the holder of the certificate of compliance with the ČSN/IEC ISO 27001 standard, since 2015, as the ISO 27001:2014 version.

SÚKL 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.

OVERVIEW OF ESSENTIAL CONTACTS FOR INDIVIDUAL SPHERES OF SÚKL´S OPERATION

Updated as of 31 March 2017. A comprehensive updated overview of contacts is available from SÚKL´s website.

Prefix: 272 185	**Extension**	**e-mail**
Director		
Zdeněk Blahuta	199	zdenek.blahuta@sukl.cz
Deputy Director		
Irena Storová	344	irena.storova@sukl.cz
Director of Director's Office		
David Přinesdom	354	david.prinesdom@sukl.cz
Quality Manager		
Lenka Jeglová	955	lenka.jeglova@sukl.cz
Internal Audit and Control		
Kamila Hrušková	225	kamila.hruskova@sukl.cz
State Agency for Medical Cannabis		
Marcela Škrabalová	856	marcela.skrabalova@sukl.cz
Press and Information Department		
Head of Press and Information Department		
Lucie Přinesdomová	756	lucie.prinesdomova@sukl.cz
Information Centre	333	infs@sukl.cz

ECONOMIC ISSUES AND INFORMATION TECHNOLOGY DIVISION

Director of Service Activities Branch		
Vilibald Knob	873	vilibald.knob@sukl.cz
Economic Section		
Head of Section		
Jana Přerovská	810	jana.prerovska@sukl.cz
Operations Section		
Director of Section		
Tereza Kotherová	808	tereza.kotherova@sukl.cz
Mail room and dispatch room	806, 789	posta@sukl.cz fax: 271 732 377
Information Technology Section		
Director of Section		
Petr Koucký	898	petr.koucky@sukl.cz

REGULATORY DIVISION

Surveillance Branch		
Director of Branch		
Apolena Jonášová	706	apolena.jonasova@sukl.cz
Marketing Authorisation Branch		
Director of Branch		
Jana Mladá	729	jana.mlada@sukl.cz
Price and Reimbursement Regulation Branch		
Director of Branch		
Lenka Vostalová	420	lenka.vostalova@sukl.cz
Medical Devices Branch		
Director of Branch		
Věra Janderová-Kopečná	927	vera.janderovakopecna@sukl.cz

www.sukl.cz / www.sukl.eu