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1. Introduction

In 2014, the State Institute for Drug Control (hereinafter referred to as the "Institute") intensively cooperated with the Ministry of Health of the Czech Republic in the implementation of tasks within the scope of cooperation with the EU, particularly 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 activities of the Institute. As a result of this close cooperation, on 24 November 2014, the Act on Medical Devices was published in the Collection of Acts under No. 268/2014 Coll., with effective date of 1 April 2015. The scope of changes prepared in the area of legal amendments to the Act on Pharmaceuticals, which will have to be made due to the adaptation of Regulation No 536/2014 on Clinical Trials, will not be negligible, either; therefore, this joint preparation was given much attention in the last year. Furthermore, intensive cooperation with other state institutions was carried out, e.g. with the Ministry of Foreign Affairs, the Institute for State Control of Veterinary Biologicals and Medicines in Brno, the State Office for Nuclear Safety and the Czech Agriculture and Food Inspection Authority.

On the international level, the Institute continued its active participation in working groups and committees, especially within groups of the EU Council, the European Commission and the European Medicines Agency (EMA), as well as in the working bodies of the World Health Organisation (WHO) or the European Council and its European Directorate for the Quality of Medicines and Health Care (EQDM) or the Organisation for Economic Cooperation and Development (OECD).

In 2014, Institute commenced or successfully implemented several projects. Major projects include, for example, "Website – SAKL" as well as the "2014 Medical Device Agenda" project, the purpose of which is to safeguard activities of the newly created medical device area. In the sphere of international projects, SÚKL was involved in two Joint Actions within the scope of the second Community action programme in the area of health (2008–2013). Within the SCOPE project, the Institute is so called associated partner and in the ARTHIQS project, Institute actively participates in both professional parts and is also one of the five leaders.

In the area of medicines licensing, more than 600 applications for new marketing authorisation of a medicinal product were submitted for professional assessment. Compared to 2013, the number of applications for extension of existing marketing authorisations dropped – 459 cases in total (655 applications in 2013) and so did the number of applications for revocation of marketing authorisation – 368 cases (516 in 2013). In 2014, 97 parallel imports were authorised.

In 2014, the Institute continued to assess borderline products, received applications for authorisation/notification of a clinical trial, issued opinions on specific therapeutic programmes, and filed notifications of use of non-authorised products. In the area of pharmacovigilance, the number of primary reports of suspected adverse drug reactions from the territory of the Czech Republic positively grew by more than 400 reports compared to 2013–2471 reports in total.

The Institute continued its supervisory activities covering the areas of laboratory testing, pharmacies and wholesale distribution, manufacturing of medicines, good clinical and laboratory practices, quality defects, advertising for medicinal products and safety of medical devices. The Institute intensively focused upon the field of illegal and counterfeit medicines, issued opinions for the release of medicinal products imported from third countries and opinions for the Police of the Czech Republic and the Customs Administration.

In the area of advertising regulation, the Institute concluded 14 administrative procedures that resulted in 14 fines amounting to almost 3 mil. CZK.

Via its Price and Reimbursement Regulation Branch, the Institute continued to commence in-depth reimbursement revisions in the course of the year. The commencement of 362 in-depth revisions was planned for 2014, of which 354 administrative procedures were actually initiated.

As a first-instance authority, the Institute initiated administrative procedures regarding administrative offences where breach of obligations set forth by the Act on Medical Devices was identified; in 2014, the Institute imposed fines amounting to the total of 1,955,000 CZK for breaches of the Act on Medical Devices.

In 2014, the Department of the State Agency for Medical Cannabis announced a tender for public contract "Supply of Cannabis for Medicinal Use". The timeline for first round completion of the tender was established at 1 September 2014 and it was entered by 16 candidates in total. 4 candidates who met the required first-round qualification prerequisites were shortlisted for the second round, where the main assessment criterion was the lowest quoted price. The evaluation of the price quotations submitted in the second round of the tender was completed on 16 December 2014. On the website of the State Agency for Medical Cannabis www.sakl.cz, information relevant to medical cannabis was gradually completed. This concerns, in particular, information for patients, doctors and pharmacists as well as for future growers.

Professionals as well as the general public may avail of the database of medicinal products (DLP). This database where information about authorised medicinal products, approved specific therapeutic programmes and foods for special medical purposes is available, with any necessary details, has been regularly updated by the Institute.

As part of its obligation to inform professionals and the general public, the Institute administered websites www.sukl.cz, www.olecich.cz and www.nebezpecneleky.cz, including two Facebook profiles. It also administered the website of the ARTHIQS project www.arthiqs.eu and the website of the State Agency for Medical Cannabis www.sakl.cz. Furthermore, the Institute published 3 issues of the infoLISTY publication for the general public and some 437 people placed their questions on the "Ask Us" ("Zeptejte se") web service. In 2014, the total of 18 talks on safe use of medicines were organised in cooperation with the author of the book "Stories of medicines" for public libraries and senior clubs throughout the country.

SÚKL STATE INSTITUTE FOR DRUG CONTROL

2. Organisational Structure of the Institute


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Agilent Technologies
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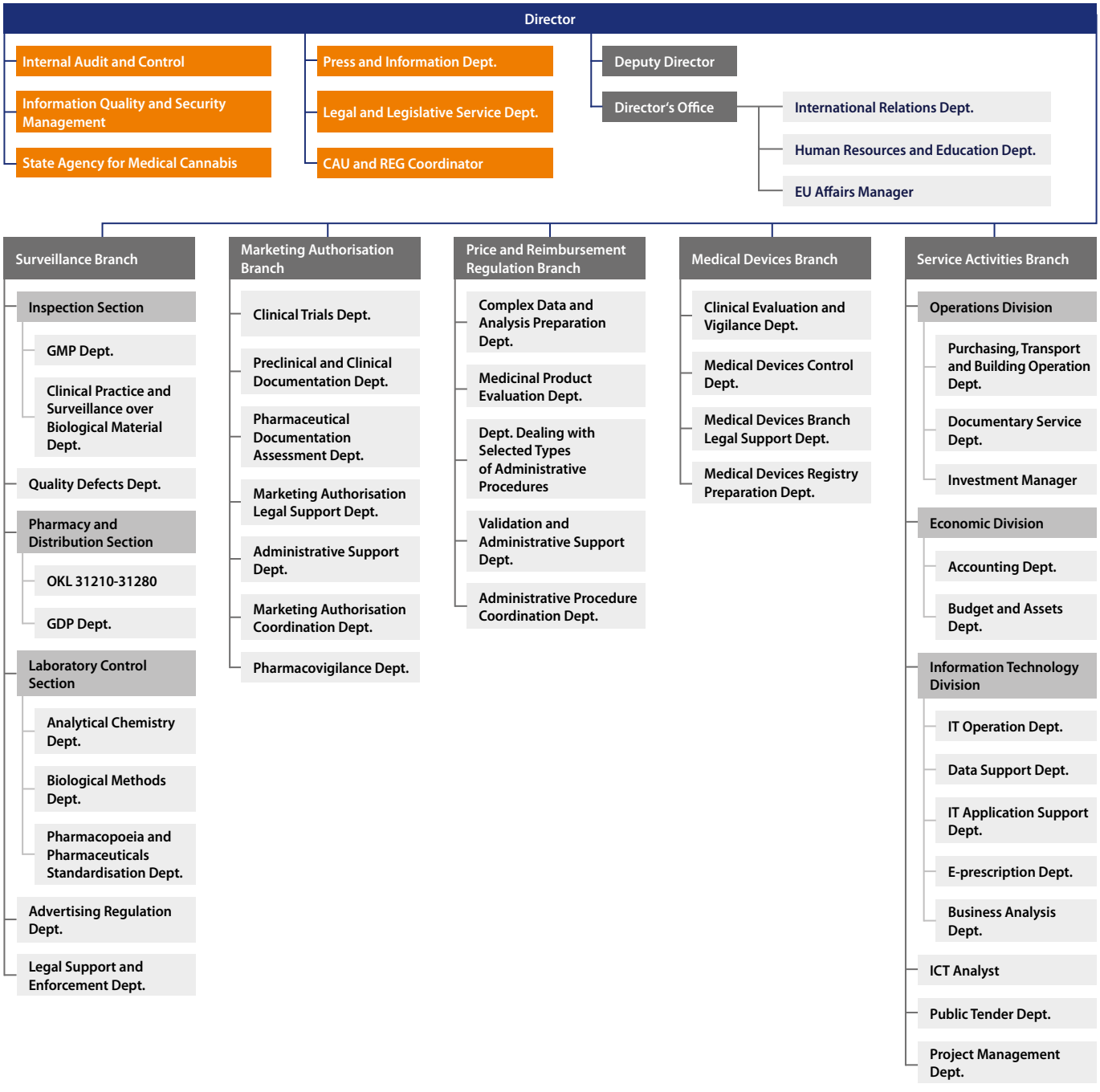
Infinitely better.

In order to increase the efficiency of work, organisational changes were implemented in the Institute in 2014. As of 1 April 2014, the positions of Deputy Directors were completely abolished and their areas of work and powers were taken over by the heads of individual branches. They report directly to the Director of the Institute. Furthermore, Quality and Safety Department, Press and Information Department, Legal and Legislative Service Department, originally operating under the Director's Office, were transferred to the direct managerial power of the Director of the State Institute for Drug Control.

The newly established Operations Section, Economic Section, and Information Technology Section report directly to the Service Activity Branch.

Within the scope of the preparation of work associated with the coming into force of the new Act on Medical Devices (No. 268/2014 Coll.), the Medical Device Branch was extended by the Medical Device Inspection Department, Department of Legal Support for the Medical Device Branch, and the Medical Device Registry Preparation Department.

The organisational structure effective as of 31 December 2014 is noted below. The organisational structure is provided on the website of the Institute.



SÚKL STATE INSTITUTE FOR DRUG CONTROL

3. Involvement in the Network of National, EU and Other International Institutions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3.1 Cooperation with the Ministry of Health of the Czech Republic and Other State Institutions in the Czech Republic

In 2014, the Institute very closely cooperated with the Ministry of Health of the Czech Republic, particularly in the implementation of tasks within the scope of cooperation with the EU, namely in the field of pharmaceuticals and medical devices as well as in the preparation and subsequent legislative process of adoption of new legal regulations with significant impact upon the scope of operation of the Institute.

A close cooperation continued in the legislative process concerning the drafting of the Act on Medical Devices. At the turn of 2013/2014, the preparatory works and progress in the legislative process were slightly delayed due to the dissolution of the Chamber of Deputies; nevertheless, in the first weeks of 2014, the draft of the act was re-submitted to the Chamber of Deputies of the Parliament. On 24 November 2014, the Act on Medical Devices was published in the Collection of Acts under No. 268/2014 Coll., with effective date of 1 April 2015. Cooperation in this field still continues in the preparation of implementing legal regulations for this Act.

In 2014, joint activities of the Institute and the Ministry of Health of the Czech Republic focusing upon the preparation of adaptation of Regulation No 536/2014 on Clinical Trials became much intensive. This adaptation will require amendment to the Act on Pharmaceuticals and its implementing regulations. The scope of amendments in this area of legislation will not be negligible; hence much attention was paid to the preparation in the last year.

Despite the activities associated with these major tasks, the Institute did not neglect its involvement in the preparation of other legal regulations governing other areas of relevance to the operation of the Institute, either.

Legal requirements governing individual areas of professional activities were further explained by the Institute in the guidelines issued thereby. In these guidelines, the Institute also familiarised the public with guidelines issued by the European Commission and the European Medicines Agency.

In the course of the last year, cooperation with the Ministry of Foreign Affairs of the Czech Republic and the Ministry of Health of the Czech Republic in particular continued in the preparation of opinions of the Czech Republic on preliminary questions raised by the European Court of Justice related to the sphere of competence of the Institute.

The Institute continued its cooperation with the Institute for the State Control of Veterinary Biologicals and Medicines in Brno. Like in the previous years, the Institute's partners for the sphere of market surveillance were the Czech Agriculture and Food Inspection Authority, Czech Trade Inspection and the Czech Customs Administration. Cooperation with the Czech Office for Standards, Metrology and Testing involved the preparation of standards governing the area of medical devices.

3.2 Cooperation with EU Institutions and Other Foreign Partners

The Institute is actively involved in international cooperation within more than 70 working groups and committees. These represent, in particular, groups of the EU Council, European Commission and the European Medicines Agency (EMA), but also the working bodies of the World Health Organisation (WHO), Council of Europe and its European Directorate for the Quality of Medicines and Health Care (EDQM), or the Organisation for Economic Cooperation and Development (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. Last but not least, the Institute is also actively involved in informal groups that bring together experts from various countries specialised in the area of regulation of pharmaceuticals and medical devices or human tissues and cells. One of these informal groups is a network of the Heads of Medicines Agencies (HMA) based on voluntary membership, in whose activities the Institute also regularly participates.

The activities of the Institute on the EU level, moreover, include involvement in the legislative process of adoption of new European legislation, which is under the responsibility of the Institute. In 2014, the Institute actively participated in the discussions regarding the regulation on medical devices in the EU Council and implementing regulations for the Directive on Pharmaceuticals in the working bodies of the European Commission. In total, 435 business trips abroad took place in 2014, of which 232 were paid for by the Institute and 203 were fully or partially refunded by the organising institutions (EC, EU Council, EMA, etc.).

The links among strategic international issues within the executive support of the Heads of Medicines Agencies (HMA) with clearly established responsibilities, the Management Board of the European Medicines Agency, the European Commission's Pharmaceutical Committee and others, which was established as a result of introducing the position of the Manager for European Affairs (MEU), ensures proper continuity, consistency and timeliness of administration of international issues at the strategic level and commitments of the Czech Republic arising therefrom, in the professional area as well as in terms of drug policy.

Through its membership in the operating groups for sustainability of the network of EU regulatory authorities and HMA/EMA strategy for 2016–2020, the Czech Republic became one of the Member States directly involved in the preparation of the first joint strategy of HMA national agencies, and the European Medicines Agency; on the European Commission level it, moreover, participated as an observing member in the preparation of agendas for the meeting of the IPRF global regulatory forum.

The major topics on the EMA Management Board level, in which the Czech Republic is actively involved, are the solution of the current crisis caused by the annulment of the 2011 EMA Director elections by the European Court of Justice, the negative result

of the IT management audit by the European Commission, the preparation of an adequate revision of Commission Regulation No 297/95 (so called "Fees Regulation"), joint strategy with HMA for 2016–2020, implementation of the Regulation of the European Parliament and of the Council (EU) 536/2014 on clinical trials on medicinal products for human use, increasing the transparency by publishing data from clinical studies serving as source materials for authorisation of medicinal products.

Relevant strategic information is in the appropriate extent transferred also to the national level through membership in advisory boards of the Government/Ministry of Health of the Czech Republic for the National Antibiotic Program, of the Ministry of Agriculture of the Czech Republic for antimicrobials and other advisory boards. Professional cooperation with the field in the area of anti-infectives is implemented through leading the Advisory Council for Anti-Infectives.

In 2014, the global level of cooperation was extended by establishing relationships with partners in the People's Republic of China.

3.3 Projects

In 2014, the Institute commenced or successfully implemented several projects. Major projects include, for example, "Website – SAKL", the outcome from which has been the implementation of the website of the State Agency for Medical Cannabis, as well as the "2014 Agenda for Medical Devices" projects, the purpose of which is to safeguard the operation of the newly established medical device area of work.

In the area of international projects, the Institute became involved in two Joint Actions within the scope of the second programme of Community action in the field of health (2008–2013), co-funded by the European Commission and the EU Member States. One of them 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 worked hours by their experts, who fulfil the tasks established in expert parts, so called Work Packages.

In the SCOPE project, the Institute acts as an associated partner and in Work Package 4 it cooperates in the development of procedures for adverse drug reaction reporting. The project was commenced in November 2013, and its anticipated duration is 36 months.

The ARTHIQS project started on 1 May 2014 and will last until April 2017. The Institute 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, specifically safeguarding communication with the public and submission of information about the outputs from the project. Within the scope of the ARTHIQS project, the Institute has established and operates website www.arthiqs.eu and caters for the printing and distribution of information materials.

SÚKL STATE INSTITUTE FOR DRUG CONTROL

4. Regulatory Activities of the Institute

4.1 Record System

In 2014, the electronic record system of the Institute, incl. its regional workplaces, registered 71,494 delivered documents and 36,697 sent documents (Table 1). The priority of official document delivery is delivery via data mailboxes and the Institute thereby continues in the electronic processing of individual areas of its office work (Table 2).

MARKETING AUTHORISATION BRANCH

Prior to their placement on the market in the Czech Republic, proprietary medicinal products are subject to marketing authorisation granted by the Institute. Within the scope of the marketing authorisation procedure, the Marketing Authorisation Branch assesses dossiers, in which the applicant for marketing authorisation evidences the safety, efficacy and quality of the product. A medicinal product may be placed on the market only in case the benefits associated with its use prevail over the potential risks. Upon the issuance of the marketing authorisation, the new marketing authorisation holder is informed about the approved Summary of the Product Characteristics and package leaflet, which serve both professionals and the general public as a key source of information about the medicinal product.

In case of doubts as to whether a product is a medicinal product subjected to marketing authorisation or an active substance or another product or homeopathic preparation, the Institute issues its opinion/decision. The decision of the Institute is essential for the regulatory regimen of the assessed product and for the subsequent procedure to be employed by the applicant prior to the placement of the product onto the market in the Czech Republic.

Furthermore, the Institute issues opinions on applications for specific therapeutic programmes of the Ministry of Health of the Czech Republic. Specific therapeutic programmes allow for the use, distribution, and dispensing of non-authorised medicinal products for human use, if specific 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 whether clinical trials regulated by the Institute are concerned, and keeps records on the use of non-authorised medicinal products.

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

4.2 Marketing Authorisation of Medicinal Products

Applications for New Marketing Authorisation

In 2014, following successful validation confirming the completeness of the dossier, 614 applications in total were forwarded for expert assessment. Most of them were applications for MRP/DCP marketing authorisation (MA), which confirms the trend from the previous years when the number of applications for national marketing authorisation was gradually decreasing.

In 2014, 80 applications for MRP/DP procedures with the Czech Republic as the Reference Member State were submitted.

Renewals of Marketing Authorisation

In 2014, following successful validation, 459 applications in total were forwarded for expert assessment. Most of them were applications for MRP/DCP marketing authorisation renewals. The number of

Table 1 Registration of documents in 2012–2014

	2012	2013	2014
Received documents	**84,232**	**76,979**	**71,494**
Sent documents	**59,554**	**47,524**	**36,697**

Table 2 Overview of communication channels in 2014

	Mail room	E-mail messages	Data messages	Electronic notice board	Total
Received documents	**41,530**	**24,257**	**5,707**	–	**71,494**
	Dispatch room	**E-mail messages**	**Data messages**	**Electronic notice board**	**Total**
Sent documents	**8,638**	**1,932**	**21,655**	**4,472**	**36,697**

applications for renewals decreased due to the amendment to the Act on Pharmaceuticals of 2008, which sets forth the obligation to submit the application for marketing authorisation renewal only after the first five years. Thereafter, marketing authorisation is renewed for an indefinite period of time.

Variations to Marketing Authorisations

In 2014, the number of received applications for variations to MRP/DCP marketing authorisations slightly grew, and the number of received applications for variations to national marketing authorisations slightly decreased.

Parallel Import

In 2014, the number of received applications decreased; 97 parallel imports were authorised.

Revocation of Marketing Authorisation

In 2014, 368 applications for revocation of marketing authorisation were decided.

Expiry/Non-expiry of Marketing Authorisations

In 2014, the Institute conducted 71 administrative procedures regarding the granting of exemptions from the Sunset Clause.

Table 3 Marketing authorisation applications

Process of marketing authorisation of medicinal products	Submitted in 2014	Decided in total in 2014	Pending as of 31 December 2014
New MA	**672**	**575**	**872**
▪ of which national	47	44	70
▪ of which MRP-RMS	15	19	22
▪ of which DCP-CMS	65	31	49
▪ of which CMS (MRP and DCP)	545	481	731
Switch from national to MRP/DCP	**1**	**0**	**2**
MA renewals	**468**	**1,098**	**1,654**
▪ of which national	99	640	1,006
▪ of which RMS	39	28	27
▪ of which CMS	330	430	621
National variations to MA	**2,823**	**3,127**	**581**
▪ of which II	0	364	196
▪ of which bulk NAR variations	2,597	2,534	352
▪ of which PI and labelling, transfers	226	229	33
MRP variations	**4,350**	**4,244**	**1,683**
▪ of which IA	0	2	0
▪ of which IB	83	78	17
▪ of which II	0	7	1
▪ of which PI and labelling	88	102	9
▪ of which bulk MRP variations	4,179	4,055	1,656
MA revocations	**413**	**368**	**39**
Parallel import	**60**	**97**	**36**
Variation to parallel import	**90**	**77**	**23**
Extension of parallel import	**2**	**3**	**0**
Revocation of parallel import	**21**	**21**	**0**

Note: 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

In the course of 2014, the Sunset Clause as referred to by Section 34a of the Act on Pharmaceuticals was applied to 171 marketing authorisation numbers and the marketing authorisation of these products expired.

4.3 Cooperation with the European Medicines Agency and CHMP

In 2014, within the scope of cooperation with the European Medicines Agency (EMA) and its Committee for Medicinal Products for Human Use (CHMP), the Institute was involved in the assessment of centralised marketing authorisations as follows:

- 3 times as the Rapporteur/CoRapporteur;
- 3 times as the "Peer Reviewer";
- 2 times assessed Type II centralised variations;
- 2 times assessed renewals for previously authorised centralised products;
- 3 times as the Rapporteur/assessor in European arbitrations pursuant to the provisions of Directive 2001/83/EC, which were addressed on the CHMP level.

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

4.4 Clinical Trials on Pharmaceuticals

On 27 May 2014, Regulation (EU) No 536/2014 of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (hereinafter referred to as the "Regulation") was published. Subsequently, preparatory works on the adaptation of the Regulation commenced. A working group for the adaptation of the Regulation was established in the Institute. It includes subgroups for legislative amendments, changes to the system of ethics committees, indemnification-insurance, working group under EMA for the development of a portal and a new EU CT database. The Institute took part in 15 meetings in EMA, 34 teleconferences, and organised 21 working meetings. Preparations for the adaptation of the Regulation will continue also in the next year.

The Institute has continued its active involvement in international expert working groups. The Institute attended 11 meetings of the CAT (Committee for Advanced Therapies) working group, of which 6 were meetings held in EMA, 2 were informal meetings, 3 virtual meetings; 6 working meetings of the CTFG Group (Clinical Trials Facilitation Group); and 1 meeting of the Ad Hoc Group for Implementation of Directive 2001/20/EC.

Since January 2014, the Institute has restored its involvement in the Voluntary Harmonisation Procedure (VHP), which is a voluntary harmonisation process of joint assessment of clinical trial documentation managed by the EMA Clinical Trial Facilitation Group (CTFG). Within the VHP, 53 clinical trials were received for assessment in the Czech Republic. With a view to experience from previous years and the growing number of applications submitted within the VHP procedure, a transparent system of application acceptance has been developed. Conditions for acceptance of the VHP procedure are provided and regularly updated on the website of the Institute.

Compared to the previous years 2013 and 2012, the total number of applications for notification/authorisation of clinical trial submitted in 2014 slightly dropped and went back to the numbers of applications submitted in 2010 and 2011. 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 374 applications for authorisation/notification of clinical trial, 20 clinical trials were submitted by non-commercial entities (academic research); 53 applications concerned orphan drugs (medicinal products for rare diseases), 36 cases involved clinical trials that included also children or were directly intended for paediatric population (paediatric trials), and 7 clinical trials were advanced therapy studies. During the assessment

Table 4 Applications for exemption from the "Sunset Clause"

	Procedures conducted in 2014
Administrative procedures for granting of an exemption from the Sunset Clause	**71**
▪ **of which initiated based on application**	**54**
▪ **of which ex officio initiated administrative procedure**	**17**
▪ granted	46
▪ declined	5
▪ suspended as undue	2
▪ suspended as unjustified	11
▪ suspended for failure to supplement	2
▪ withdrawal of application	2

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

process, 31 applications for authorisation/notification of clinical trial were withdrawn, which was 2 applications more than in 2013. No application has been declined.

In 2014, attention focused more upon pharmacovigilance reporting from clinical trials; the assessment of DSURs (Development Safety Update Report) was started; and control of SUSAR (Suspected Unexpected Serious Adverse Reactions) reporting. In 2014, 475 DSURs were submitted.

In 2014, systematic 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) was initiated.

In 2014, 11 ethics committees for multicentric clinical trials were operating. Four joint working meetings of the Working group of representatives of multicentric ethics committees and representatives of the Department of Clinical Trials of the Institute took place.

Two meetings with the representatives of regulated entities and interest groups were summoned (Association of Innovative Pharmaceutical Industry (AIFP), Czech Association of Pharmaceutical Companies (ČAFF), professional associations, ethics committees, contract organisations, Ethics Committee Forum, representatives of the Union of Patients).

The Institute addressed 87 patient organisations and offered them cooperation in the sphere of not only clinical trials, but also the use of non-authorised medicinal products. One workshop for patient organisation representatives was organised.

Other 2 workshops were prepared for sponsors, contract organisations, and monitors. The Institute participated in 4 external workshops for academic research, investigators and study team members as well as in 1 workshop for pharmacies and one for qualified persons.

In 2014, 112 applications (particularly grant projects) for project assessment were assessed as to whether they involved a clinical trial regulated by the Institute or not.

Specific Therapeutic Programmes

53 applications for the issue of opinion on proposed specific therapeutic programmes were submitted. An opinion was issued for 56 applications, 5 were pending and brought forward to the next year.

Non-authorised Medicinal Products

In 2014, 3,983 notifications of the use of non-authorised medicinal products were received, which is 56% more than in 2013.

In 2014, the Institute provided 26 consultations and issued 12 written opinions on issues regarding the activities of the Department of Clinical Trials.

4.5 Pharmacovigilance

In 2014, the Institute received 2,471 primary reports of suspected adverse reactions from the territory of the Czech Republic, and 1,180

Figure 1 Numbers of applications submitted and assessed in 2014 by clinical trial phase

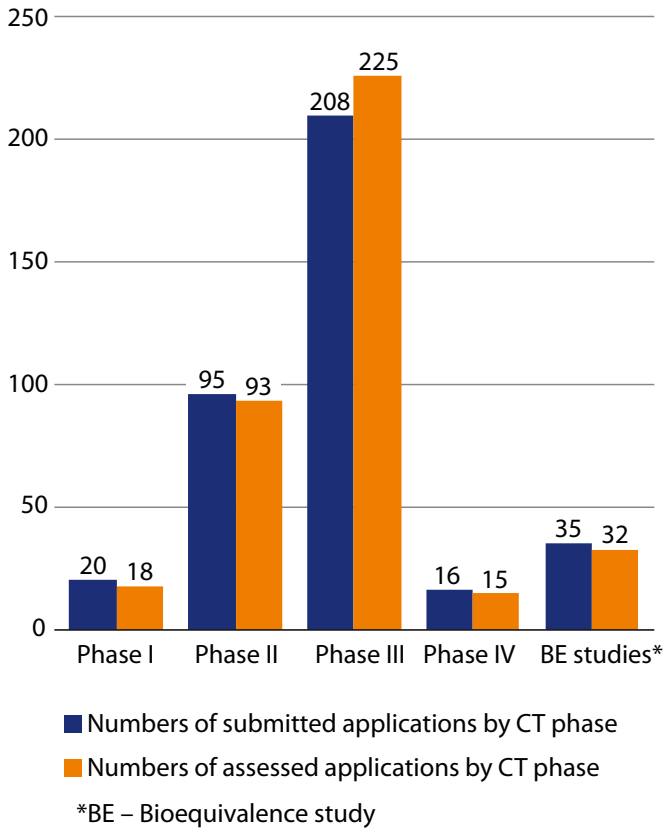


Table 5 Clinical trials (CT)

	No. of applications received in 2014	No. of decisions issued in 2014	Of which declined	Of which withdrawn
Application for CT authorisation	103	107	0	5
Notification of CTs	271	277	0	25
Notification of amendments to CTs	2,213	2,674	0	0

follow-up reports thereto were made (verification or obtaining of additional information from the reporter). Each individual report delivered to the Institute is processed, individually assessed, and entered into the database of adverse reactions from the Czech Republic (CDNÚ), and, concurrently, sent to the European EudraVigilance database as well as to the global WHO database. Records in databases of adverse reactions are regularly checked and evaluated using statistical as well as qualitative methods in order to be able to identify 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 37 active substances on the European level.

As in the previous year, Periodic Safety Update Reports (PSURs) for individual products were assessed only for products in respect of which a safety risk was identified or where it was necessary to review the necessary data about the medicinal product in relation to the regulatory procedures of the EU or in case of marketing authorisation renewals. 930 reports were submitted in 2014.

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

The conclusions of the Committee for Human Medicinal Products (CHMP) and of the PRAC Pharmacovigilance Committee were transposed to the Czech clinical practice in cooperation with the Marketing Authorisation Department. In 43 cases, the Institute published information intended for healthcare professionals or for the general public regarding the safety of medicinal products on its website, in the Farmakoterapeutické informace (Pharmacotherapeutic Information, FI) or in other media. In cooperation with marketing authorisation holders, it published 41 letters for healthcare professionals regarding updated information on the safe use of medicinal products, and 154 educational materials on 59 active substances, focused upon enhanced safety of use.

The Institute published 4 issues of the Information Bulletin "Adverse Reactions to Medicines", which provided current information on the safe use of medicinal products, including a new column called

Table 6 Indication groups of clinical trials assessed in 2014

Indication groups	Number
Oncology	79
Respiratory + Allergology	32
Healthy volunteers	41
Neurology	35
Cardiovascular system	39
Rheumatology	25
Other	17
Psychiatry	1
Diabetology	19
Infectious	3
Urogenital diseases	11
Gastrointestinal diseases	18
Haematology	11
Metabolism disorders + Endocrinology	3
Dermatology	10
Transplantation	5
Ophthalmology	5
Gynaecology	8
Otolaryngology	2
Emergency	1
Pain	6
Examination procedures	1
Internal medicine	6
Paediatrics	6

"You reported to us" where specific cases of adverse drug reactions reported from the Czech Republic are published.

50 notifications (commencement or termination) of post-marketing safety studies were processed. Furthermore, 11 inspections of the pharmacovigilance system of marketing authorisation holders took place.

In 2014, the Department of Pharmacovigilance became actively involved in the SCOPE international project, the purpose of which is to facilitate the involvement of all EU Member States in the uniform execution of the European pharmacovigilance legislation.

At the end of 2014, a new educational project to increase the reporting of suspected adverse drug reactions was commenced. The project continues also in 2015. The objective of the project is to extend and improve the provision of information for healthcare professionals as well as patients not only about the importance of adverse reaction reporting, but also to generally raise the awareness of pharmacovigilance and on where to obtain information and how to use medicinal products as safely as possible.

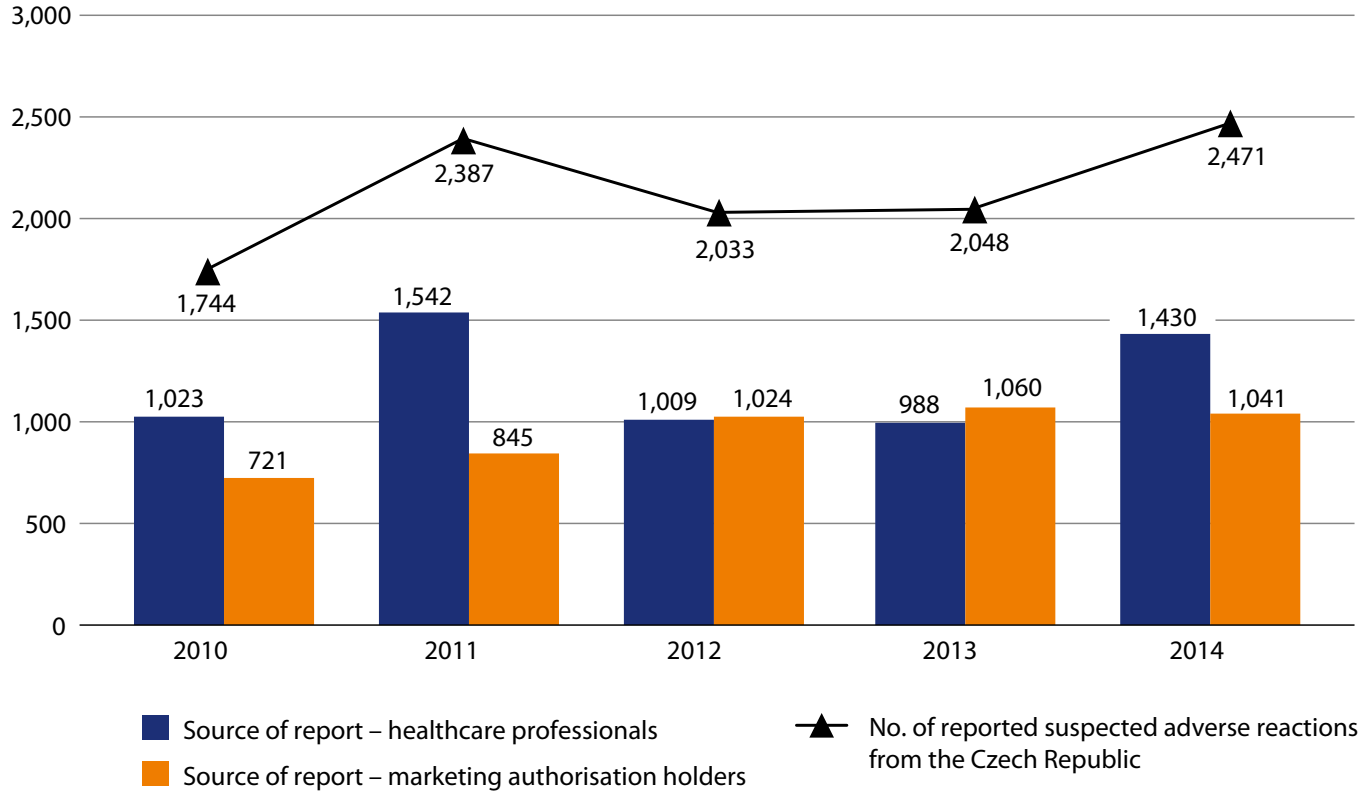
SURVEILLANCE BRANCH

The Laboratory Control Section conducts analyses of pharmaceuticals required by the law (e.g. random inspections of pharmaceuticals on the market, or batch release), upon request of other units of the Institute or state administration bodies and within the scope of international cooperation. The laboratories are integrated into the international General Network of Official Medicines Control Laboratories. The laboratories do not perform analyses upon request of 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 European Pharmacopoeia.

The Pharmacy and Distribution Section safeguards monitoring of 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 is conducted also in any other healthcare facilities. The inspection is safeguarded by individual regional units of the Institute according to their territorial competence.

The Inspection Section ensures supervisory activities in the area of manufacture of pharmaceuticals, good clinical and laboratory practices, issuing of binding opinions on the import and export of

Figure 2 Number of reported suspected adverse reactions from the Czech Republic and the source of the report



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 applicable law are concerned.

The Department of Quality Defects 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, the Institute 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, supervisory authorities of the EU Member States).

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

The Institute also performs activities implied by legislation governing the safety of medical devices marketed in the Czech Republic. It conducts investigations of adverse events of medical devices and their evaluation, inspects the conduct of clinical evaluations or clinical trials on medical devices. It controls medical devices at the sites of healthcare providers where it focuses primarily upon record-keeping and documentation of medical devices.

4.6 Laboratory Control

Laboratory control is conducted by the Laboratory Control Section both within the scope of requirements defined by the Act on Pharmaceuticals, i.e. it controls the quality of pharmaceuticals placed on the market pursuant to predefined projects and releases batches of defined medicinal products, and on the basis of internally submitted requirements (requirements of other units of the Institute). This includes, in particular, addressing of quality defects of medicinal products, analyses of pharmaceutical 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. 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 2012, a regular verification of the established quality system by a group of EDQM auditors took place. The Certificate was issued in 2013. 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.

Table 7 Supervision over the quality of pharmaceuticals on the market by means of laboratory analyses according to predefined projects (projects closed in 2014)

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
3/2013 pharmacy samples*	63	214	199	15	1
2/2013 counterfeits*	140	140	-	-	-
1c/2012 glimepiride	16	42	42	0	2
1d/2012 donepezil hydrochloride	16	39	39	0	0
7/2012 extended-release products	39	86	84	2	1
Verification of extemporaneous product shelf-life	4	12	12	1	0
Verification of microbiological quality of selected eye products	27	53	53	0	2
Total (ex. 2/2013 and 3/2013)	102	232	230	3	5

**Samples from these products included in 2013*

The results of sample analyses conducted in 2014 by both laboratory departments are summarised in the tables below.

Projects are prepared on the basis of "risk-based" analysis. The criterion is, in particular, high consumption of the controlled products, less common dosage forms or routes of administration, target patient group, or frequent complaints filed by patients or medical and pharmaceutical professionals. Drafts of these projects and reports on completed projects are approved by the Institute's Quality Team. In 2014, works on the following projects were taking place: Microbiological control of medicinal products for gastrointestinal treatment; Microbiological control of medicinal products carrying live microorganisms; Generic product quality control (products containing simvastatin, sumatriptan, topiramate, fenofibrate, clopidogrel); Quality control of hot drinks, anti-flu products; Effects of storage upon selected medicinal products (expectorants). Furthermore, pharmacy samples were inspected and captured counterfeits analysed.

According to the Figure 3, 767 sample analyses were completed in the Laboratory Control Section. The number of counterfeit products captured in the Czech Republic in 2014 only seems to have dropped, as the ANA dept. began to address an instigation of December 2014 filed by the Czech Police, which requested an expert opinion on more than 150 samples captured during criminal investigations. The number of samples rated as non-compliant (ex. counterfeit products and samples from international studies), slightly increased compared to the previous year, and amounted to 4.8% (3.5% in 2013; 0.9% in 2012). This concerned particularly pharmacy samples and samples in respect of which doctors and patients filed a complaint. Defects of pharmaceuticals involved primarily the content of active substances and their purity. The increase in the number of non-compliant pharmacy samples is particularly due to adjustment defects, which were newly included in this number.

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 the timelines stipulated by the law.

International Cooperation within the Area of Laboratory Control

In addition to other cooperations within the OMCL EDQM network, the Section participates in joint studies on the control of the quality of marketed pharmaceuticals, 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 – programme CAP).

Table 8 Batch release for defined medicinal products

Type of product	Number of reported medicinal products	Number of reported batches	Released on the basis of certificate*	Number of laboratory-verified samples	Total number of released batches*	Not released
Blood derivatives	52	588	672	30	702	0
Imported vaccines	37	263	400	0	400	0
Czech vaccines	1	2	0	1	1	1

**Some batches were released repeatedly*

Table 9 Laboratory control of pharmaceuticals and excipients requested by other units of the Intitute, other state administration organisations or EDQM

	Number of samples	Of which compliant	Of which non-compliant
Suspected quality defect of pharmaceutical	75	71	4
Suspected counterfeit, illegal samples*	39	–	–
Pharmacy samples	200	179	21***
International studies within OMCL*	6	–	–
Internal quality control of purified water	136	126	10
Verification of proposed pharmacopoeial monographs	6	6	0
Other analyses**	41	39	2
Total	**503**	**421**	**37**

** Sample compliance cannot be evaluated*
*** E.g. LAL tests, requested microbiological controls, other requested analyses, etc.*
**** Non-compliant pharmacy samples newly include also those which bear incorrect labelling*

In 2014, the Laboratory Control Section participated in collaborative international studies mentioned in Table 10.

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

The principal activities of the Pharmacy and Distribution Section include supervision in the area of medicinal product handling conducted by the Institute in pharmacies, at vendors of selected medicinal products, in healthcare facilities (including their specialised departments) and wholesale distributors of pharmaceuticals. The Pharmacy and Distribution Section is also entrusted with the performance of price inspections of medicinal products and foods for special medical purposes as well as with the inspection 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 regulated entities with the exception of healthcare facilities.

Figure 3 Number of samples analysed by the Laboratory Control Section

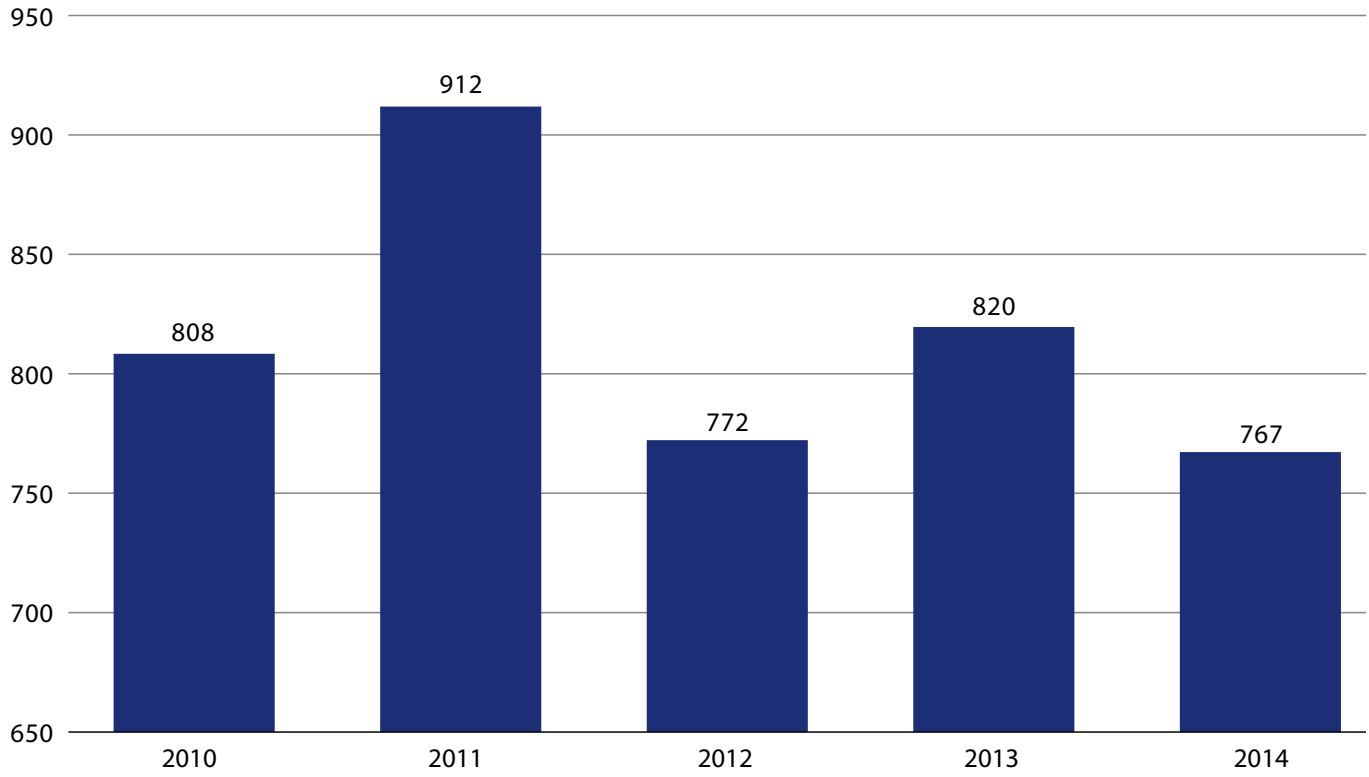


Table 10 Involvement in international studies

Study	Study title	Rating
PTS 141	Liquid Chromatography	good
PTS 147	Potentiometric Titration	good
PTS 148	Relative Density	good
PTS 149	Dissolution Testing	good
CAP 14/42	Xalkori	good
CRS	Moxidectine	good

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

At the end of 2014, the Institute registered a total of 2,601 pharmacies, of which 4 fell within the scope of powers of the Ministry of Defence of the Czech Republic; moreover, the Institute registered 253 detached pharmaceutical and medical device dispensing units (hereinafter referred to as OOVL), 395 medical device dispensaries, 1,018 vendors of selected medicinal products, 45 nuclear medicine departments of healthcare facilities, and 453 wholesale distributors of medicinal products. The trend from previous years in the form of the slightly growing number of pharmacies continued and, compared to 2013, the total number of pharmacies increased by 33 entities and the number OOVLs decreased by 5 entities (Figure 4).

In 2014, the inspectors of the Pharmacy and Distribution Section conducted 883 inspections in pharmaceutical care facilities – pharmacies, of which 19 were hospital pharmacies of inpatient care providers. Of the total number of inspected pharmacies, 40 inspections were targeted inspections, carried out on the basis of reports.

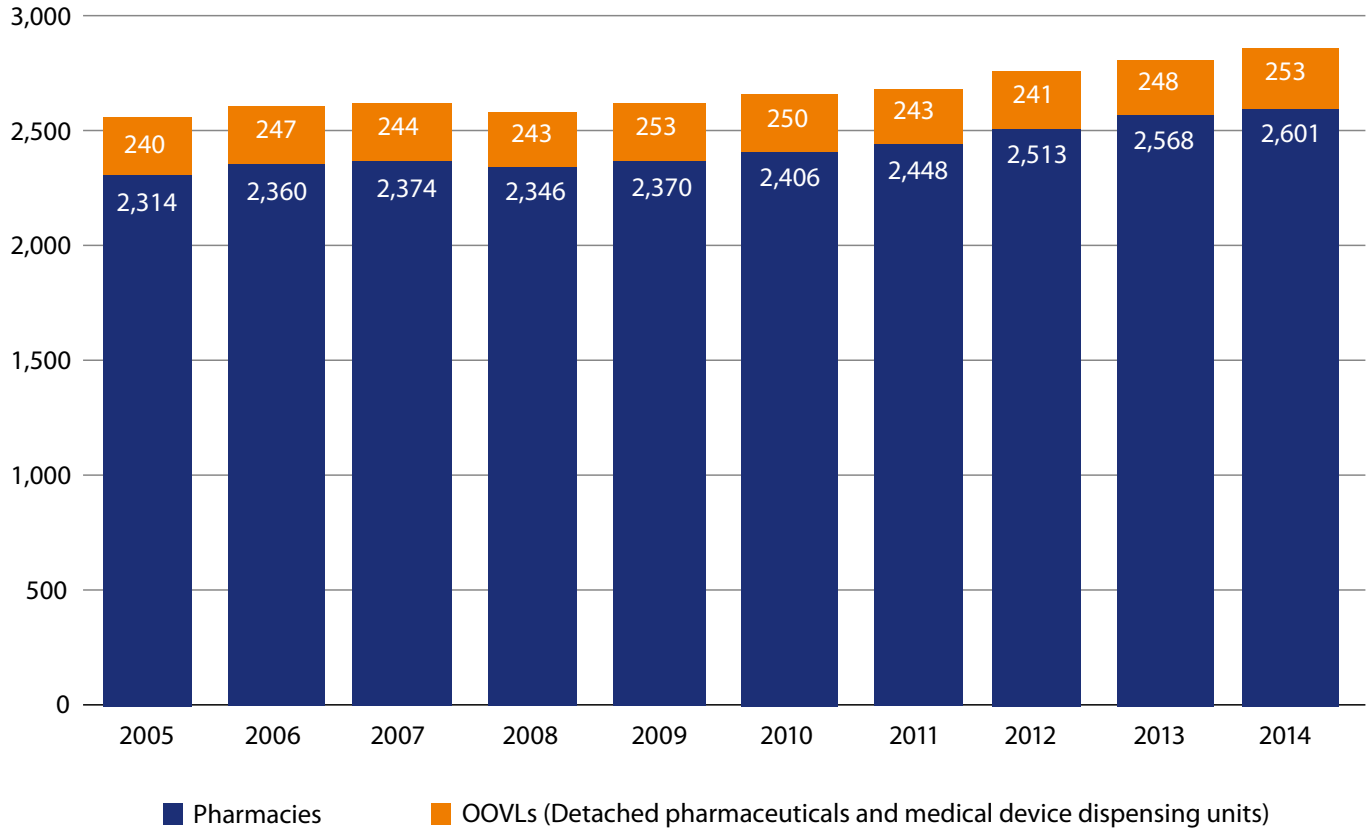
Specific inspections aimed at handling of dependence-producing substances and precursors were carried out in 402 pharmacies, of which 377 inspections were planned inspections and 25 inspections were targeted inspections.

Price control focusing upon compliance with the Act on Prices and rules of price regulation was conducted in 84 pharmacies, of which 3 inspections were targeted, and in 9 wholesale distributors.

On the basis of facts identified during the inspections, 73 final decisions to impose a fine for breach of obligations stipulated by the Act on Pharmaceuticals in the total amount of 6,750,000 CZK were issued (this includes also finalised administrative procedures based upon inspections conducted in the previous period). The preparation of medicinal products was suspended for a pharmacy in 11 cases (non-verified weights, inadequate equipment, use of starting materials without a certificate of their quality for preparation), and in 1 case the operation of the entire pharmacy was suspended.

The main reasons for the issuance of a decision imposing a fine included, in particular, dispensing of medicinal products without a prescription or with an invalid prescription, including foreign prescriptions; 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; use of active substances and excipients for the preparation of medicinal products after the expiry date or without a proof of

Figure 4 Number of pharmacies and OOVLs in the last 10 years (as of 31 December 2014)



their quality; dispensing of prescription-only medicinal products by a pharmaceutical assistant; violation of the principles of good pharmaceutical practice and serious deficiencies in file-keeping on the operation and records of the pharmacy.

Within the scope of inspections of the handling of dependency-producing substances and precursors in pharmacies, identification of major breaches of the Act on Dependency-Producing Substances or the Act on Precursors resulted in the total of 32 final decisions on fine imposition to pharmacy operators in the total amount of 1,055,000 CZK. This concerned, in particular, failure to send the annual report on the status and movements of dependency-producing substances and products within the timeline; incorrect or incomplete data in the report; in other cases, serious breaches of the Act on Dependency-Producing Substances regarding record-keeping and documentation, or handling of precursors without a special licence.

Inspections focusing on the compliance with price regulation rules identified a breach of price regulations in the total of 16 cases and pharmaceutical care providers were issued 8 final decisions on fine imposition pursuant to the Act on Prices amounting to 350,000 CZK in total. Further 3 fines in the amount of 65,000 CZK were imposed upon wholesale distributors of medicinal products. Most often, failure to observe the officially fixed prices during sales and disregard for the conditions and procedures for their application stipulated in the price regulations of the Ministry of Health of the Czech Republic were identified.

In 2014, 290 inspections of the handling of medicinal products in healthcare facilities in total were conducted; in one case it was not possible to carry out the planned inspection due to failure to provide cooperation. The inspections were carried out in 25 inpatient hospital departments and in 265 separate outpatient offices of general practitioners and medical specialists, and in other healthcare facilities. On the basis of reports received by the Institute in connection with the operation of healthcare facilities, where health care is provided, a total of 33 targeted inspections took place. A total of 4 final decisions on fine imposition in the total amount of 390,000 CZK were taken for the identified violations of the Act on Pharmaceuticals.

Inspections of vendors of selected medicinal products in 2014 involved 53 outlets in total; in one case a fine of 5,000 CZK for breach of the Act on Pharmaceuticals was imposed.

In other healthcare facilities authorised to prepare medicinal products (Nuclear Medicine Departments and workplaces preparing autogenous vaccines for human use – HAV), a total of 19 inspections were carried out; the findings from the inspections did not result in the need for the imposition of any penalty.

In 2014, the dispensing and handling of medicinal products by unauthorised entities was identified in 3 cases; in this respect, final decisions on fine imposition in the total amount of 316,000 CK were issued.

Summary results from inspections completed in 2014 are provided in Table 11.

In 2014, inspectors from the Pharmacy and Distribution Section took a total of 200 samples of medicinal products during inspections in pharmacies, of which 117 were pharmaceutical products intended for the preparation of extemporaneous products in the pharmacy. Out of the 83 pharmacy samples (medicinal products prepared in pharmacies), 8 in total were out-of-specification, the shortcomings being out-of-specification content of the active substance in the

Table 11 Inspection surveillance over pharmacies, nuclear medicine departments, healthcare facilities, and vendors of selected medicinal products in 2014

			Classification of shortcomings						Penalties		
Inspected entity	**Type of inspection**	**Number**	**1**	**%**	**2**	**%**	**3**	**%**	**A**	**B**	**C**
Pharmacies	Regular inspections	883	508	57.5	226	25.6	149	16.9	11	1	73
	Price inspections	84	Not rated by classification of shortcomings						–	–	8
	Inspections of dependency-producing substances	402	279	69.4	92	22.9	31	7.7	–	–	32
Nuclear medicine departments		15	8	53.3	–	–	7	46.7	–	–	–
HAV		4	1	25.0	3	75.0	–	–	–	–	–
Healthcare facilities		290	182	62.8	80	27.6	28	9.6	–	–	4
Vendors of selected medicinal products		53	41	77.4	10	18.8	2	3.8	–	–	1

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*

medicinal product, galenic processing, and the total weight of the sample. Shortcomings in the labelling were detected in 4 other pharmacy samples. The low number of samples taken corresponds to the long-term trend of decreasing preparation of medicinal products in pharmacies proper.

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

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 2014, a total of 361 applications for issuance of an opinion were received from pharmacy operators; 349 positive binding opinions were issued and 6 applications declined. In the case of dispensaries of medical devices, a total of 23 operators applied for a binding opinion and 22 positive binding opinions were issued.

In 157 cases, the issuance of the binding opinion was associated with an inspection in the pharmacy (on-the-spot check of the technical and material equipment) and in 9 cases with an inspection of OOVLs (Table 13). In this context, 15 initial inspections of medical device dispensaries and 143 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 implementing regulations for the Act on Pharmaceuticals or Act on Dependency-Producing Substances and Act on Precursors took place. Table 13 also provides data on newly established and defunct pharmacies/OOVLs.

Distribution of Medicinal Products

In 2014, the number of distributors increased by 28 entities to the total number of 453 medicinal product distribution authorisation holders. Of the total number of approved distributors, 203 entities are both a pharmacy operator and a distribution authorisation holder.

In 2014, 53 new distribution authorisations and 132 decisions on variations to distribution authorisation were issued, and 25 authorisations were revoked upon request of their holders. Within the scope of the administration of the register of brokers of medicinal products, 5 new entities in total were entered.

Table 12 Occurrence of monitored types of shortcomings in % (of the total number of non-compliant samples)

Type of shortcoming	2010	2011	2012	2013	2014
Out-of-specification content of active substance	51.9	50.0	40.0	63.6	50.0
Out-of-specification total weight	29.6	30.0	40.0	9.1	37.5
Out-of-specification purified water Microbiological compliance	–	–	–	–	–
Out-of-specification galenic processing	7.4	–	–	18.2	12.5
Out-of-specification microbiological compliance	–	10.0	20.0	9.1	–
Active substance and excipient identity confusion	11.1	10.0	–	–	–

Table 13 Other activities of the Pharmacy and Distribution Section

Initial pharmacy inspection	Establishment of a new pharmacy/OOVL	Defunct pharmacies /OOVLs
157	93/12	79/11
Initial OOVL inspection	**Initial medical device dispensary inspection**	**Consultations**
9	15	143

Table 14 Distribution and intermediation of pharmaceuticals in 2014

	Received applications	Authorisations issued/register entries made
Application for distribution authorisation	53	53
Application for variation to distribution authorisation	121	132
Application for revocation of distribution authorisation	26	25
Application for entry in the register/variation to entry in the register	6	5

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

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

In the second half of 2014, the entry of all distributors in the EudraGMDP central European database of distributors was completed on the basis of the issued certificates and decisions on distribution authorisations or variations thereto in the uniform EU format. Good distribution practice certificates issued by the Institute following the completed inspections of distribution warehouses are also being entered into this database. In 2014, 220 post-inspection GDP certificates in total were issued.

In 2014, a total of 344 inspections of distributors took place. Compared to 2013, an increase in follow-up inspections in particular is apparent (by 20 inspections) as well as an increase in targeted inspections based on reports and complaints. The number of such inspections increased by 15.

With a view to facts identified during the conduct of inspections, 43 final decisions on imposition of a fine for breach of the obligations set forth by the Act on Pharmaceuticals and its implementing regulations amounting to 2,563,000 CZK in total were issued for distributors (this includes also finalised administrative procedures based upon inspections conducted in the previous period). In one case, distribution authorisation was suspended (distribution from non-authorised storage facilities).

In 2014, the conduct of distribution of medicinal products without effective authorisation for such operation was identified in 4 cases; in this respect, 3 final decisions on the imposition of fine amounting to 1,050,000 CZK were issued.

The main reasons for the imposition of fines were, in particular, the breach of ban on distribution and export of some medicinal products outside the territory of the Czech Republic, distribution of suspended medicinal products, the conduct of distribution activities in non-authorised facilities, sourcing medicinal products from unauthorised suppliers and supplies to non-authorised customers, failure to comply with the obligation to provide the Institute with data about distributed medicinal products in compliance with SÚKL guideline DIS-13, failure to comply with the rules of good distribution practice and inadequately effective quality assurance system, including risk management measures.

The results of distributor inspections in 2014 are provided in Table 15.

Comparison of the number of regulated entities, conducted inspections and imposed penalties over the last 5 years is provided in Figure 5.

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

Manufacture of Pharmaceuticals

In the sphere of manufacturers (incl. blood centres) the total of 116 applications for manufacturing authorisation or variations thereto were received (Table 16). The number of cases brought forward from one year to another corresponds to the intervals for application processing. The number of decisions issued for variation to manufacturing authorisation was very similar to that in 2013. The number of applications for revocation of authorisations for blood centres increased.

Human Tissues and Cells

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

In 2014, 42 applications for operating authorisation and applications for variations to operating authorisations were received, which represents a drop compared to 2013.

In 2014, the Institute carried out 294 inspections in total, of which 107 were associated with the regulated area of tissues and cells. Their nature and results of evaluation are provided in Table 17. 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 individual years 2011–2014 is provided in Table 18 and Figure 7 and 8.

An initial inspection was carried out in connection with an application for operating authorisation under Section 63 (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

Table 15 Inspection surveillance over distributors

Number of inspections					Inspection rating			Measures	
Total	Initial	Follow-up	Targeted	Variation	1	2	3	Breach of law	Fine
344	52	226	26	40	202	27	23	106	43

Rating from the Inspection

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

Figure 5 Information on surveillance activities 2010–2014

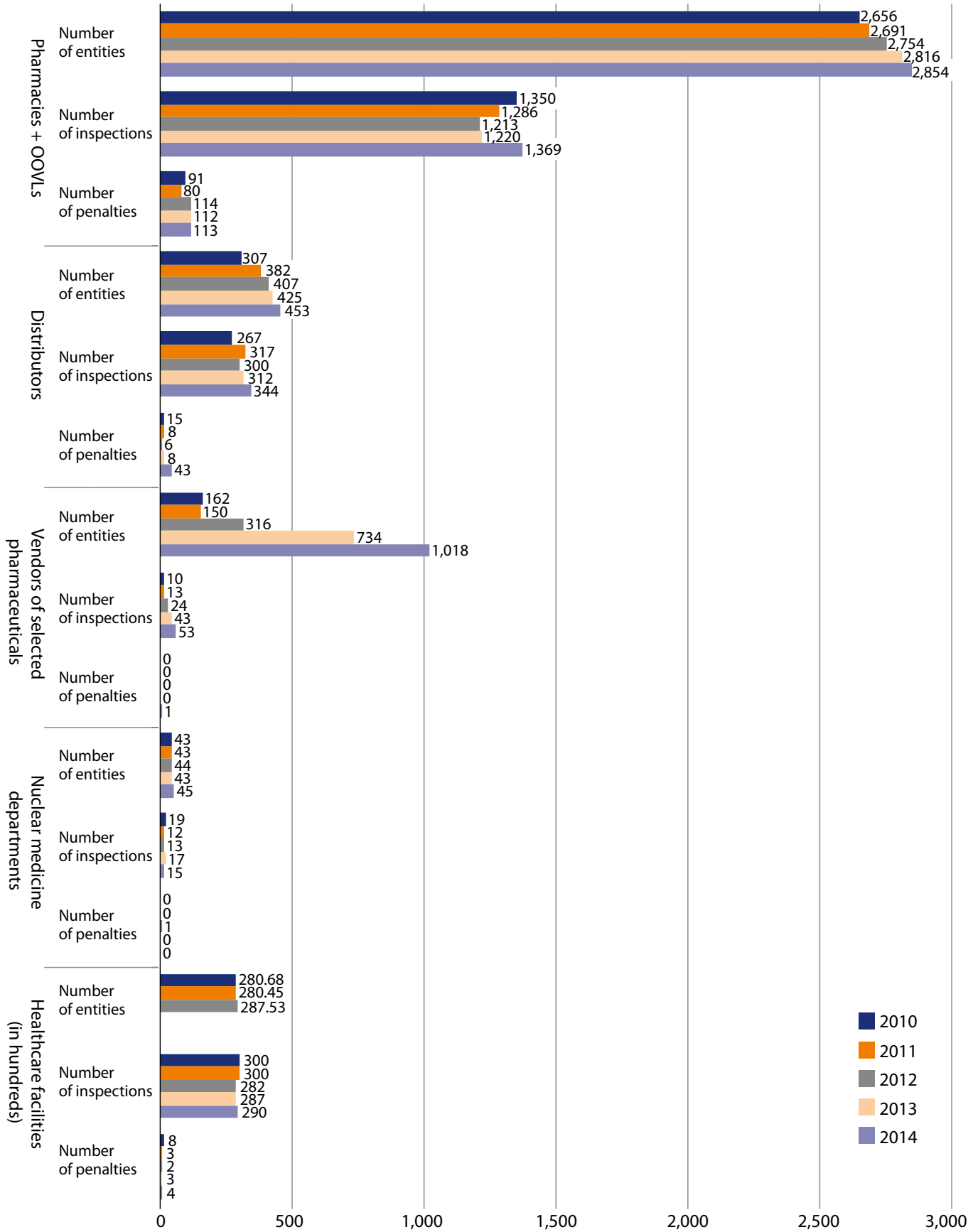
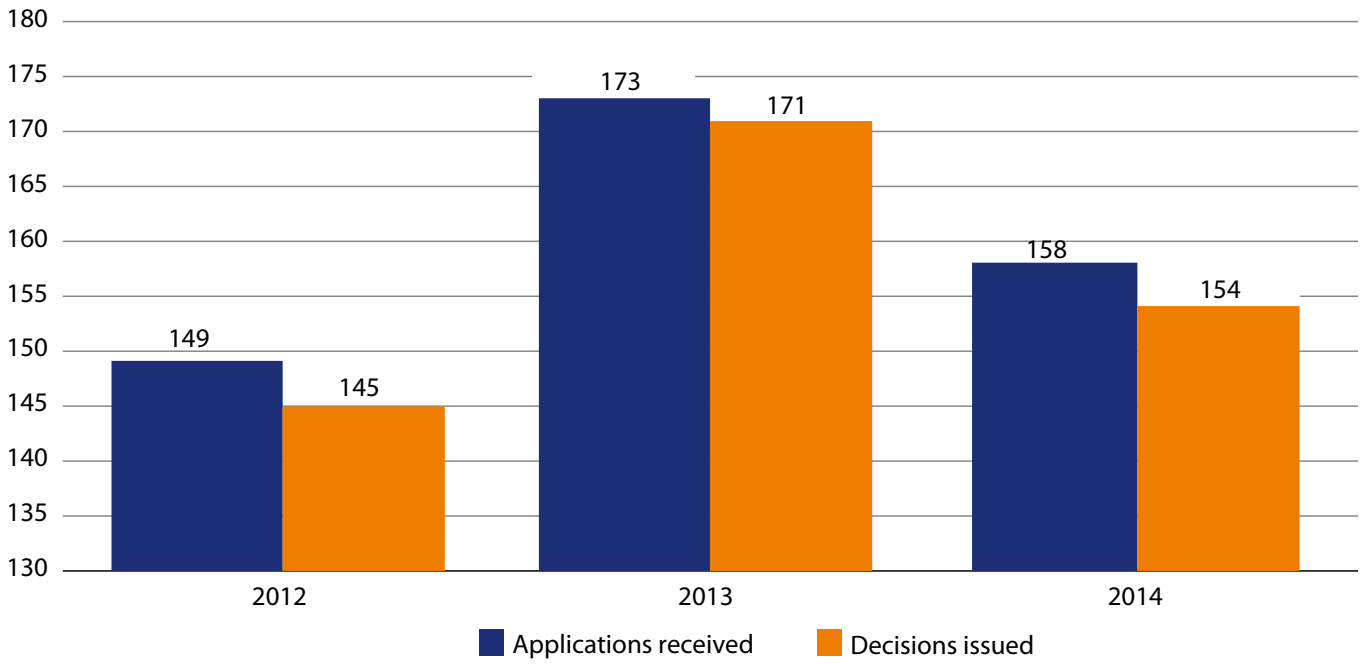


Table 16 Applications in the sphere of manufacture of pharmaceuticals and in the sphere of human tissues and cells

Application type		2012		2013		2014	
		Received applications	Issued decisions	Received applications	Issued decisions	Received applications	Issued decisions
Application for manufacturing authorisation	Manufacturer of medicinal products	7	7	6	4	0	3
	Control laboratory	4	4	5	4	3	3
	Blood centres	1	1	1	1	0	0
Application for variation to manufacturing authorisation	Manufacturer of medicinal products	45	41	68	66	67	65
	Control laboratory	2	1	5	6	3	5
	Blood centres	19	17	33	31	35	35
Application for revocation of manufacturing authorisation	Manufacturer of medicinal products	5	5	3	3	2	2
	Control laboratory	–	–	–	–	2	1
	Blood centres	–	–	1	1	4	4
Application for operating authorisation	Tissue centre	18	12	7	6	4	5
	Donation centre	2	0	0	1	1	1
	Diagnostic laboratory	5	4	3	3	1	0
Application for variation to operation	Tissue centre	16	15	34	35	30	25
	Donation centre	2	2	1	1	0	0
	Diagnostic laboratory	7	7	6	9	5	4
Application for revocation of operation	Tissue centre	–	–	–	–	1	1
	Donation centre	–	–	–	–	0	0
	Diagnostic laboratory	–	–	–	–	0	0
Total		**145**	**116**	**173**	**171**	**158**	**154**

Figure 6 Numbers of received and completed applications



Decree No. 229/2008 Coll. and for blood centres pursuant to Decree No. 143/2008 Coll. An inspection related to a variation is 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 109 inspections at manufacturers of medicinal products, active substances, and control laboratories, a breach of the Act on Pharmaceuticals was established in 1 case. The level of good manufacturing practice (GMP) in blood centres was rated 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.

Good Laboratory Practice (GLP)

In 2014, a total of 9 holders of Good Laboratory Practice Certificates issued by the Institute were registered, with prevailing scope of activities in toxicological studies; these are included in the National GLP Programme. In the same year, 3 follow-up inspections and 2 initial inspections of an applicant for the Good Laboratory Practice Certificate, and 1 targeted inspection were conducted.

Good Clinical Practice (GCP)

In the course of the year, 11 follow-up systemic inspections of local ECs and 10 good laboratory practice inspections were carried out. In case of GCP, no decision on operating authorisation of the inspected entities is issued.

Table 17 Inspections conducted in 2014 and their outcomes

	Number of inspections					Rating from the inspection			
	Total	Initial	Follow-up	Targeted	Variation	Compliant	Non-compliant	Breach of law	Fine/Order
Manufacturers of medicinal products	**71**	3	49	6	13	71	0	1	0
Manufacturers of active substances	**27**	1	16	3	7	27	0	0	0
Control laboratories	**11**	3	8	0	0	11	0	0	0
Blood centres	**46**	0	42	0	4	46	0	0	0
Blood banks	**11**	0	11	0	0	11	0	0	0
GCP inspections – Ethics Committees	**11**	0	11	0	0	11	0	0	0
GCP inspections – other	**10**	10	0	0	0	10	0	0	0
TC, DC, DL inspections	**107**	18	75	7	7	107	0	0	0

TC – tissue centre, DC – donation centre, DL – diagnostic laboratory

Table 18 Inspections conducted in 2012–2014

	2012		2013		2014	
	No. of inspections	Breach of law	No. of inspections	Breach of law	No. of inspections	Breach of law
Manufacturers of medicinal products	57	1	68	1	71	1
Manufacturers of active substances	25	0	15	0	27	0
Control laboratories	12	0	17	0	11	0
Blood centres	44	0	45	0	46	0
Blood banks	22	0	17	0	11	0
GCP inspections + Ethics Committees	26	0	20	0	21	0
Tissue centres, donation centres, diagnostic laboratories	102	12	132	1	107	0
Total	**288**	**15**	**314**	**2**	**294**	**1**

Figure 7 Number of manufacturers of medicinal products, active substances and control laboratories and an overview of conducted inspections

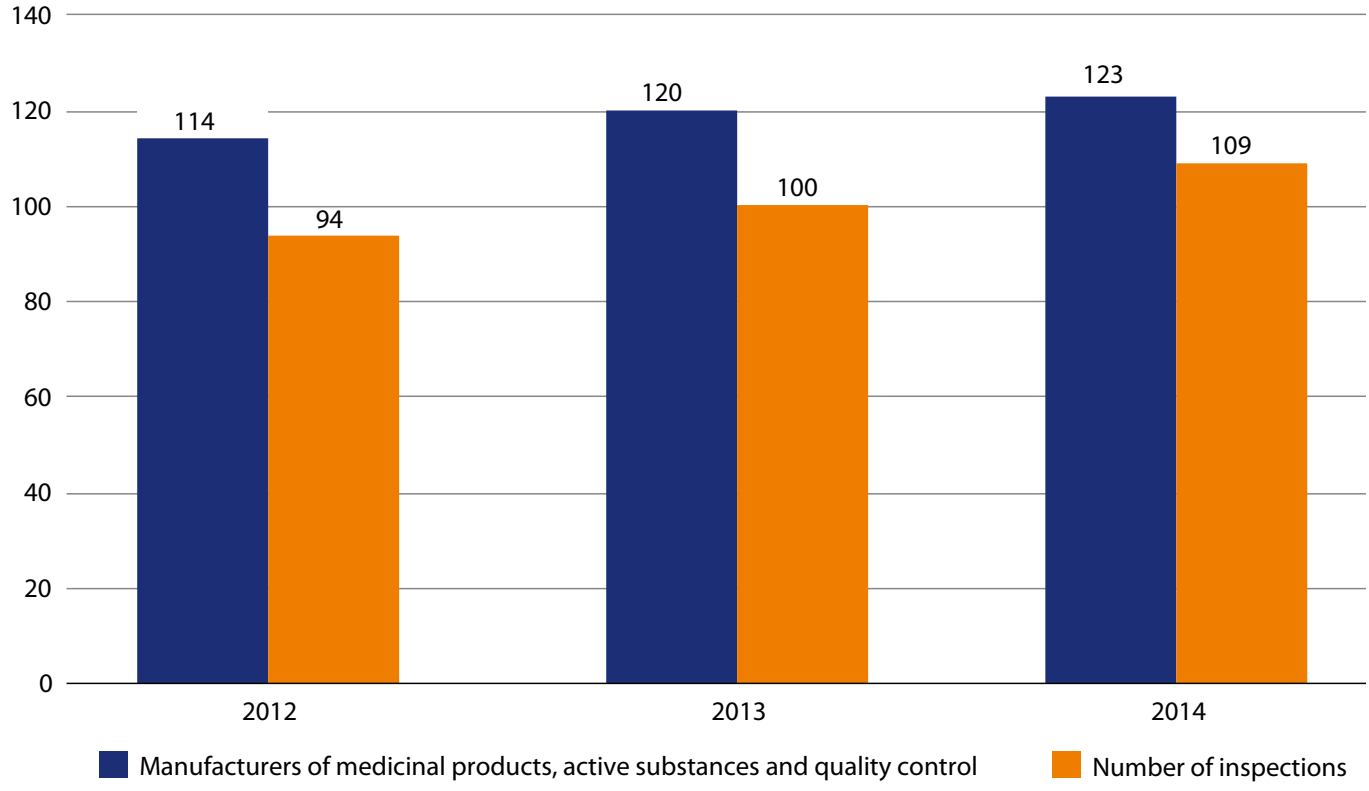
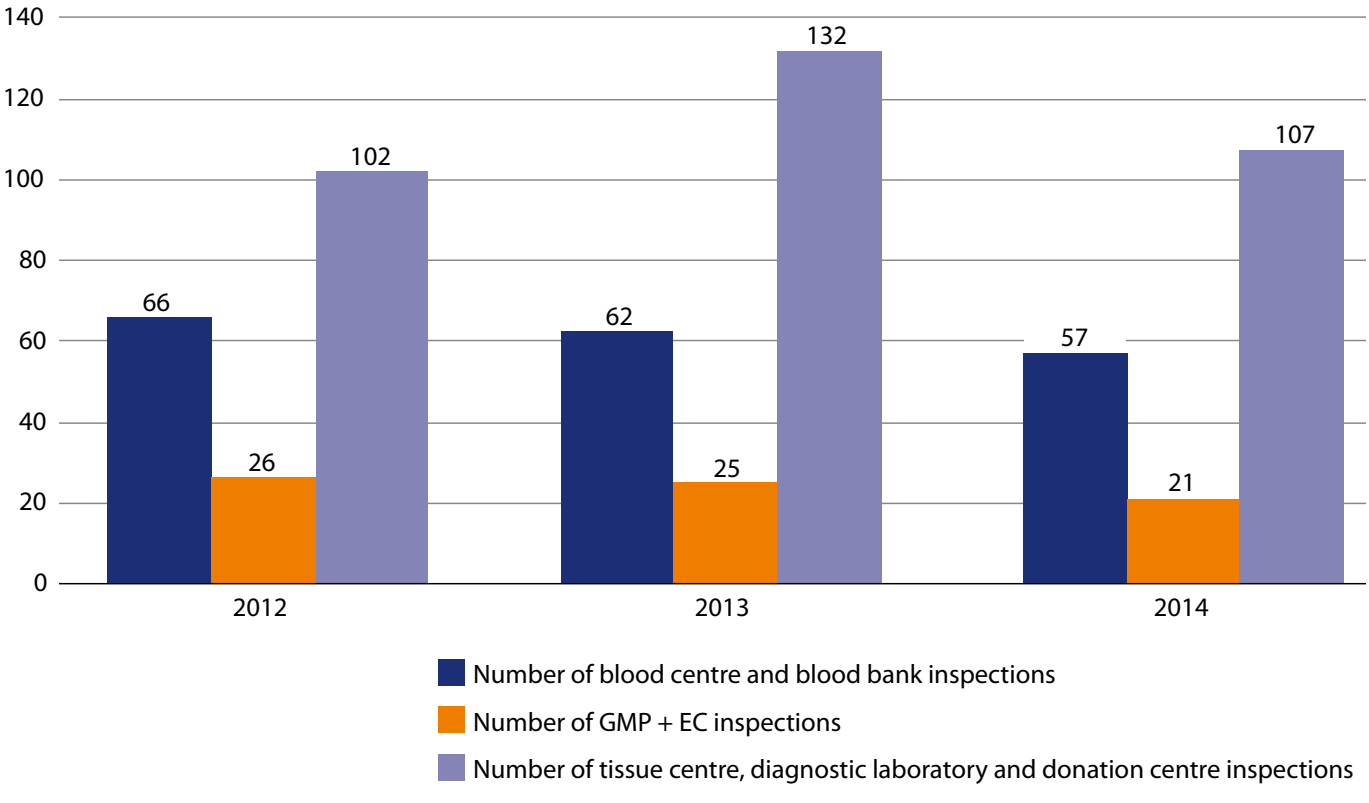


Figure 8 Overview of inspections conducted by Clinical Practice and Surveillance over Biological Material Processing Dpt. in 2012–2014



Actions and Penalties

In 2014, one breach of the Act on Pharmaceuticals was identified and the entity's operation was suspended. The Act on Tissues and Cells was not violated.

Certification

In total, 346 various certificates were issued (415 in 2013), of which, like in the previous years, the highest number was the number of certificates issued for medicinal products (231). Post-inspection good manufacturing practice certificates are entered in the EudraGMP database maintained by EMA. All certificates of medicinal products were issued within the 30-day period, and all good manufacturing practice certificates within the 90-day period.

Assessment of GMP Compliance within the Scope of Marketing Authorisations

A total of 1,056 cases (a 6.4% decrease compared to 2013) were received, all of them were processed within the timelines.

4.9 Quality Defects of Pharmaceuticals

Between 2009 and 2013, there was a major increase in the number of reports in the area of quality defects. The number of reports received in this year is comparable to 2011 (Table 19).

In 2014, 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 EU countries, MRA PIC/S, the Institute received and evaluated the total of 127 reports on quality defects of pharmaceuticals.

Mutual exchange of information with the State Institute for Drug Control (ŠÚKL) in Bratislava continued.

Reports received from abroad also include reports on noncompliance of the manufacturing site of a medicinal product or an active substance with GMP (Good Manufacturing Practice) principles. The Department received a total of 37 such reports in 2014.

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 taken as part of addressing the quality defects in individual medicinal products (SÚKL codes) in 2014.

In seven cases, patient-level recalls were conducted. It concerned several batches of medicinal products Calcium pantothenicum, drm. ung. 30 and 100mg as they did not comply with the

Figure 9 Issued certificates

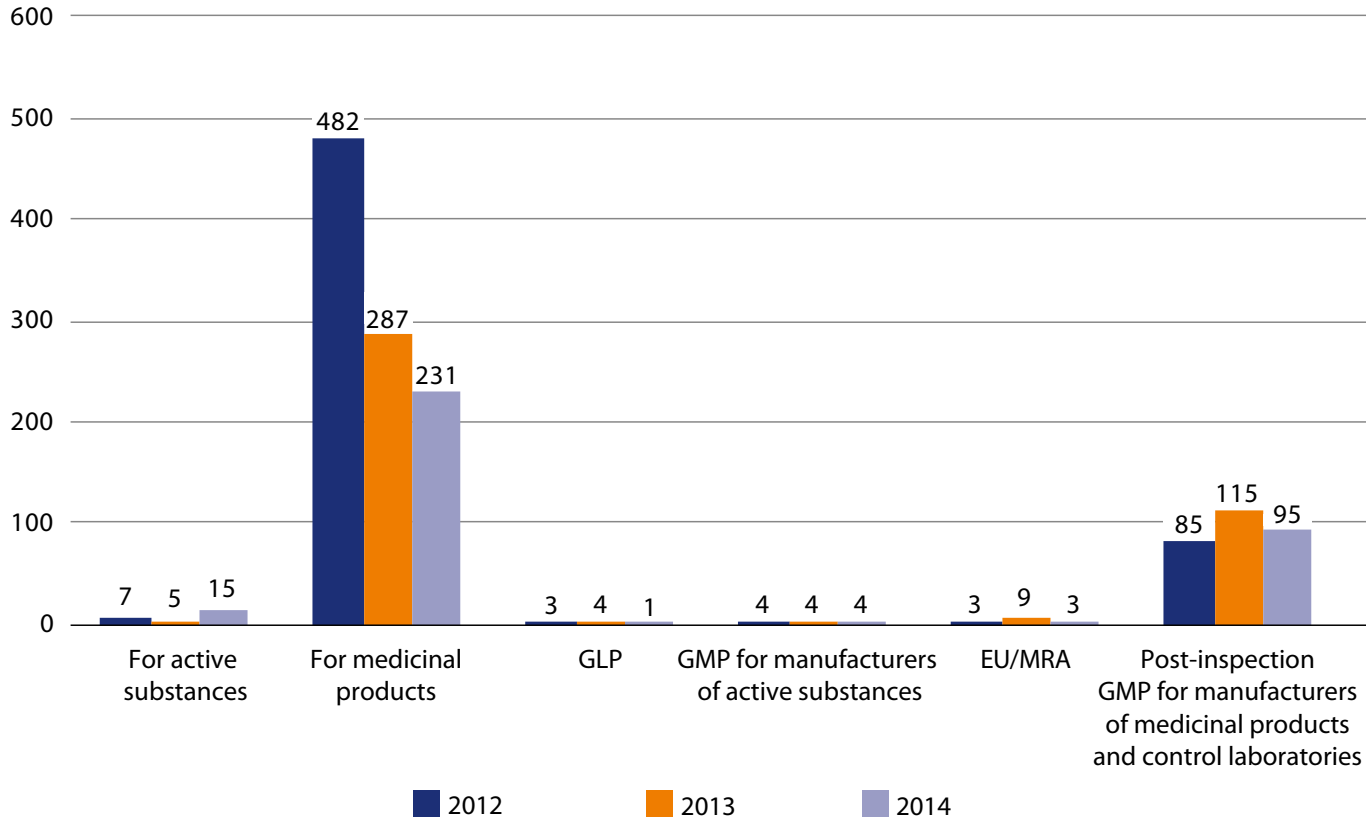


Table 19 Number of received reports

Quality Defects	2010	2011	2012	2013	2014
Reports received in total	248	357	416	417	345
Reports from the Czech Republic	150	203	294	210	181
Reports from abroad	98	124	122	207	164
Resulted in recall	47	129	84	77	60
Issued RWs	5	2	4	1	6
issued RAs	1	5	7	3	6

RW – Rapid Warning, RA – Rapid Alert

requirements governing microbial quality. For the same reason, also products Ibuberl for children 100mg/5ml oral suspension, por. sus. 1× 100ml/2gm, batch no. 21003, 22009, 23013 and Sirupus Simplex 650 g, batch no. 211013 were subjected to recall.

Batch no. 251113 of product Aqua Carminativa Rubra 1000g was then recalled because it was manufactured from a starting material which was not compliant with the requirements for microbiological quality.

Furthermore, the following products were recalled from the patient level: Thiogamma 600 Injekt, inf. cnc. sol., batch nos. 13J077 and 12J154 due to occurrence of particles in the concentrate, and medicinal product Jox, orm. spr. 1x30ml, batch nos. 3B101034, 3A102006, 3B104118, and 3A104006 due to the risk of a hidden mechanical defect of the plastic applicator which could cause non-functionality of the product or a break-down of the applicator to small parts implying a risk of swallowing thereof.

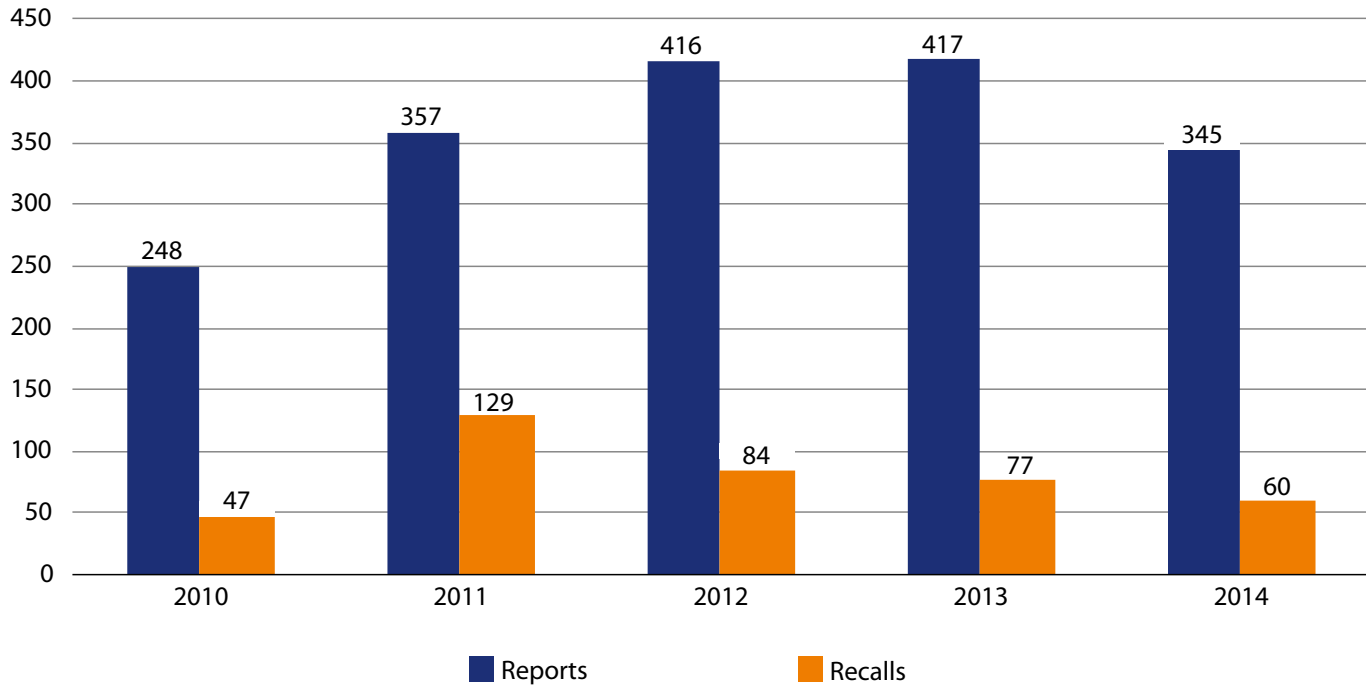
In all cases, interventions were made by the operators themselves, with the Institute merely monitoring or adjusting their actions.

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, the total of 98 medicinal products was recalled in 2014.

Table 20 Actions taken in 2014

Action taken	Number
Recalls from distributors	0
Recalls from healthcare facility level	52
Recalls from patient level	7
Suspended distribution, dispensing and therapeutic use	2

Figure 10 Number of reports and recalls of medicinal products



The Department also focused upon supervision over compliance with the obligation of marketing authorisation holders stipulated in Section 33 (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 the Institute of the date of the actual placing of the medicinal product on the market in the Czech Republic by package size and packaging type after the issue of the marketing authorisation, specifically within 2 months of the actual placing on the market; in the same manner, they are also required to notify the Institute 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 must inform the Institute of this fact immediately. In 2014, the Institute addressed 49 such reports.

4.10 Enforcement

In 2014, active surveillance in the area of illegal handling of medicinal products focused, in particular, upon the identification, investigation, and penalisation of the cases of distribution and sales by unauthorised persons and upon monitoring the internet, where illegal sale of medicinal products is being carried out.

In the sphere of enforcement, the Institute closely cooperates with the Czech Customs Administration, Czech Police, Czech Trade Inspection, Czech Agriculture and Food Inspection Authority (CAFIA), and the Trade Licensing Offices.

Cooperation also includes foreign partners, not only in the exchange of information, but also in the investigation of individual cases with potentially international impact.

In 2014, a total of 92 reports (either the Institute's own or received reports) were investigated. During control activities on the Internet, the employees of the Institute identified and investigated 6 cases of unauthorised medicinal products and 5 cases of unauthorised handling of authorised medicinal products.

In 2014, the Institute prepared a total of 107 expert opinions for the customs authorities for the purposes of release/non-release of medicinal products imported from third countries. These opinions 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. For the Czech Police and the Customs Administration, the Institute prepared 7 expert opinions for the purposes of identification of medicinal products and for clarification of legislation governing the dispensing, distribution, import, and export of medicinal products.

Figure 11 Control activities in 2010–2014

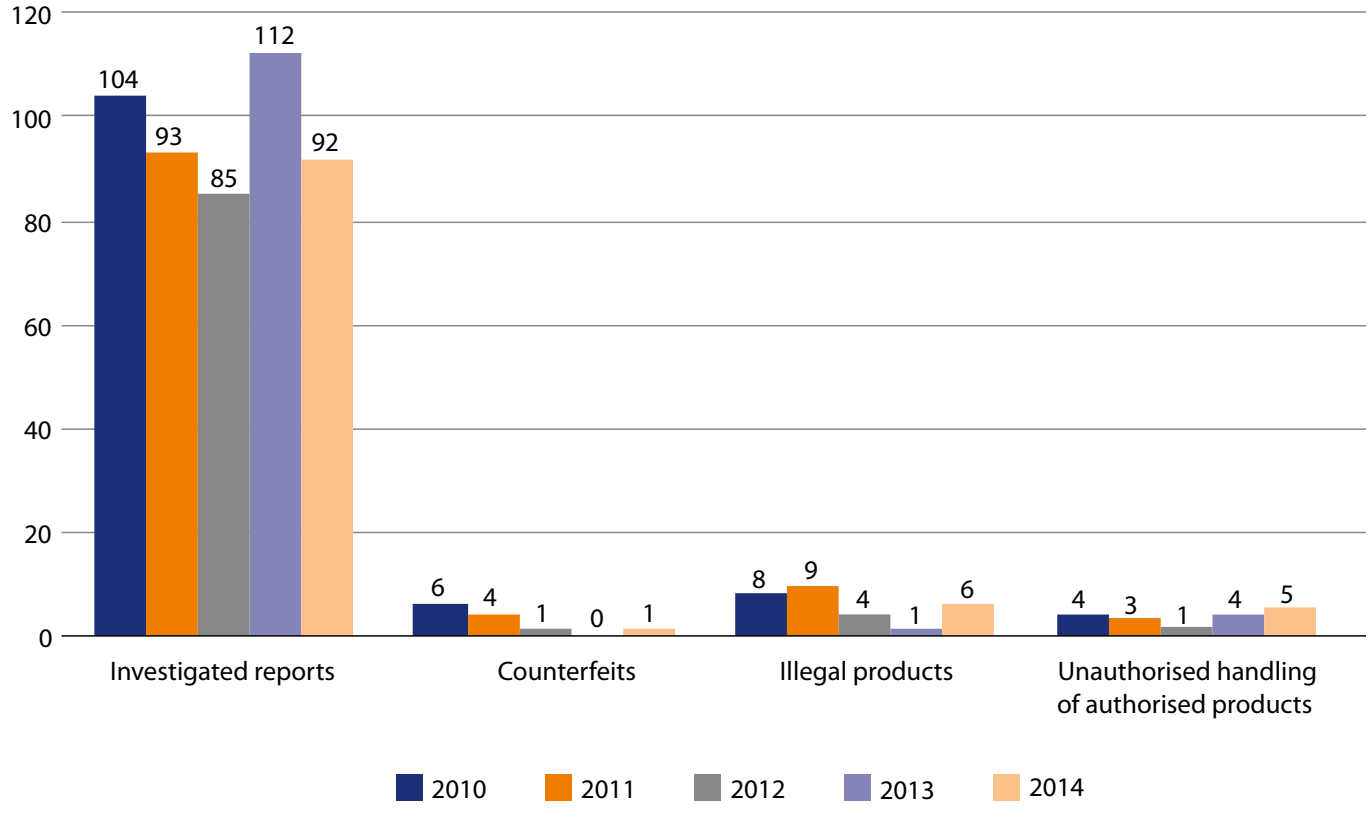


Table 21 Results of investigated cases

Cases concluded by:	2010	2011	2012	2013	2014
Administrative procedure with proposed penalty imposition	10	2	2	1	5
Reports of crime	8	6	2	3	4
Case forwarded to other authorities (CAFIA, etc.)	2	3	4	3	1

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

In 2014, the Institute investigated a total of 128 reports of suspected breaches of Act No. 40/1995 Coll., on Advertising Regulation, as amended (Act on Advertising Regulation). Compared to 2013, the Institute received 17 more new reports in 2014 (103 newly received reports in 2013). In 2014, 14 administrative procedures were completed that resulted in the imposition of 14 fines in the aggregate amount of 2,962, 000 CZK.

Investigation of advertising applied to printed advertising matter (37%), websites (7%), sponsorship (48%) and promotional samples (8%).

Advertising for prescription-only medicines accounted for 84% of the investigated cases, advertising for over-the-counter medicines represented 16% of cases.

Pharmaceutical companies or their legal representatives filed 14% of reports on suspected breaches of law, 4% of reports were filed anonymously, 14% were lodged by private individuals, 2% by state administration bodies, and 66% by the employees of the Institute.

Upon request, the Institute issued/provided 28 expert opinions/consultations on the issue of the proposed advertising for medicinal products for human use.

Table 22 Overview of investigated reports of suspected breaches of the Act on Advertising Regulation

	Reports brought forward from 2013	Newly received reports in 2014	Total
Number of reports	8	120	128
Investigation completed	8	97	105
Forwarded for commencement of administrative procedure	0	19	19
Pending	0	14	14
Completed administrative procedure	0	5	5
Number of final decisions on fines	0	5	5

Figure 12 Overview of investigated reports of suspected breaches of the Act on Advertising Regulation (2010–2014)

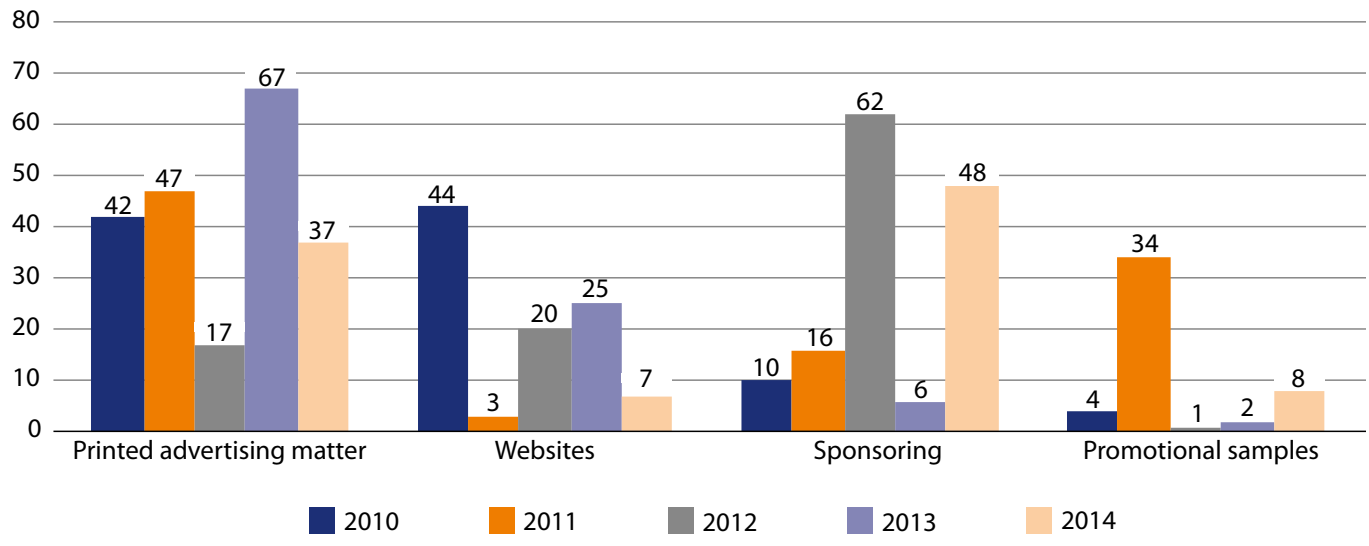
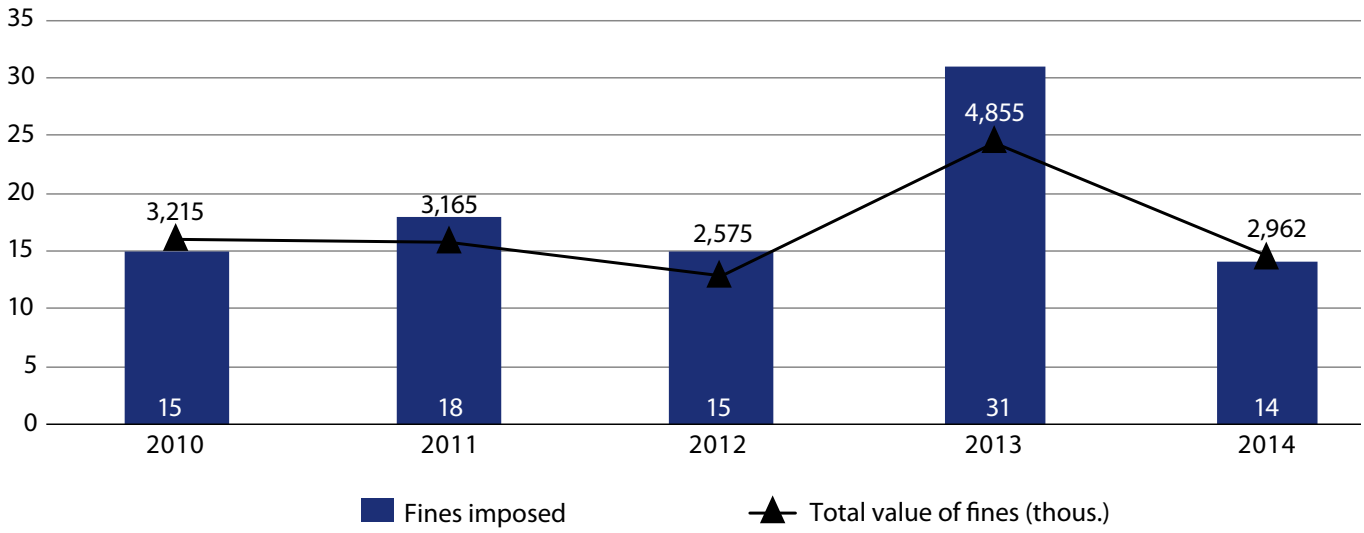


Figure 13 Overview of fines imposed for violating the Act on Advertising Regulation (2010–2014)



4.12 Inspections of Medical Devices of Healthcare Providers

Since 2014 Medical Devices Branch has taken over surveillance of medical devices of healthcare providers. This activity relates to surveillance and therefore this chapter has been left as a part of the "Surveillance Branch" section.

In 2014, inspectors from the Medical Device Branch carried out a total of 94 inspections of healthcare providers (both state and non-state healthcare facilities), of which 92 inspections were planned and 2 inspections were completed upon instigation. The inspections focused upon the provision of health care in the field of surgery and plastic surgery, dialysis, gynaecology and obstetrics, ophthalmology, and dentistry.

Table 23 shows the numbers of inspections by healthcare specialty, their overall rating using the 1–3 classification scale based on the nature of the inspection, and occurrence and severity of identified defects.

In total, 696 medical devices were inspected, of which 286 (i.e. 41.1%) were classified by the degree of risk for users as Class IIb or III, 84 medical devices (i.e. 12.1%) of the total number were established measuring devices. 601 medical devices (i.e. 86.3%) were rated as flawless or with minor shortcomings. In 97 medical devices (i.e. 14.0%) of the total number, 113 shortcomings were identified, of which 52 medical devices were classified by the degree of risk for users as Class IIb or III. Documents evidencing compliance with the conditions governing usage of medical devices in the provision of healthcare services were checked for all of the 696 medical devices.

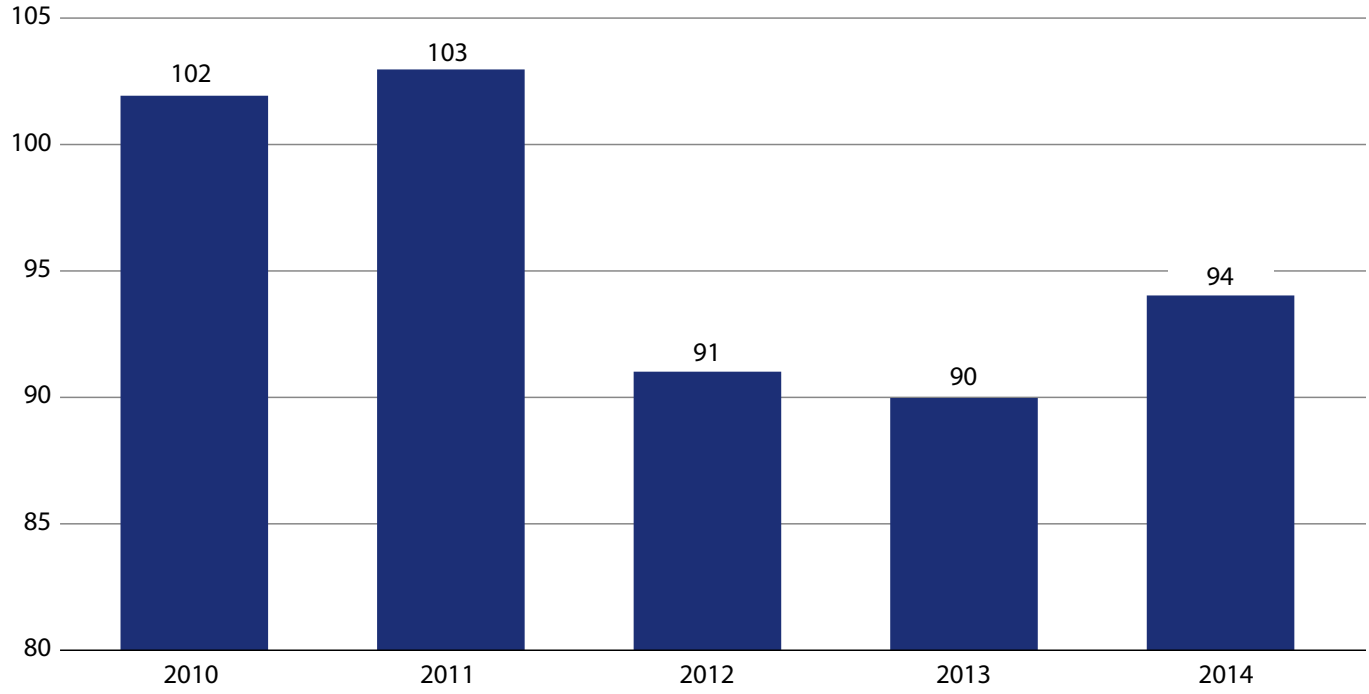
47 reports from the conclusions of inspections were forwarded to other administrative authorities (Czech Trade Inspection, public

Table 23 Inspections of medical devices carried out at providers of healthcare services in 2014

Field of provided care	Number of inspections	General rating of all inspections					
		1	%	2	%	3	%
Surgery	17	8	47.1	8	47.1	1	5.8
Dialysis	23	11	47.8	11	47.8	1	4.4
Gynaecology	15	8	53.3	7	46.7	0	0
Ophthalmology	15	7	46.7	8	53.3	0	0
Dentistry	22	11	50.0	11	50.0	0	0
Other (upon instigation)	2	1	50.0	1	50.0	0	0
Total	**94**	**46**	**48.9**	**46**	**48.9**	**2**	**2.1**

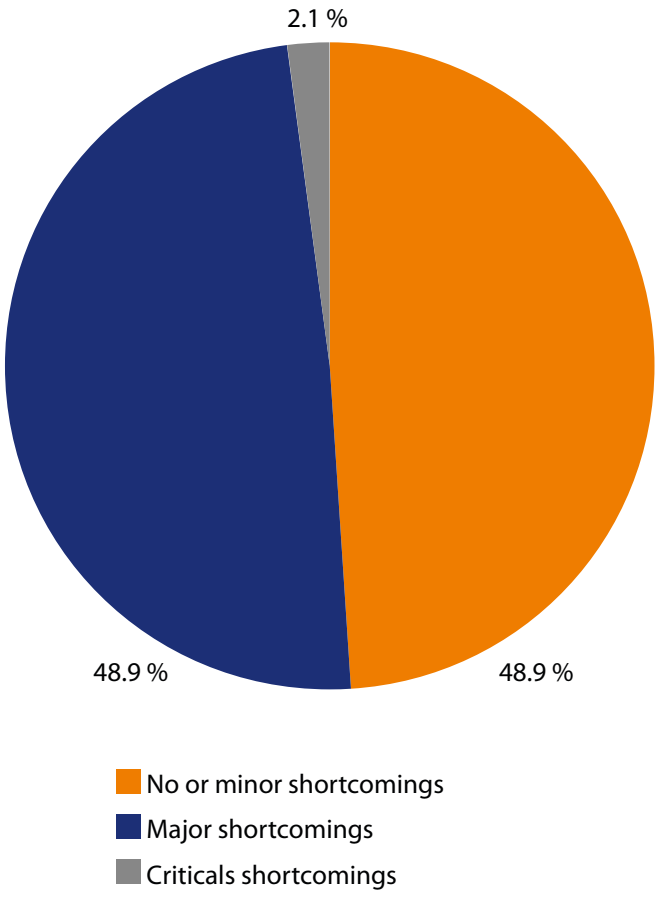
Classification
1 – No defects or minor defects, 2 – Major defects, 3 – Critical defects

Figure 14 Number of medical device inspections



health protection authorities, revenue authorities); 81 reports were proposed for submission to the Ministry of Health of the Czech Republic due to failure to comply with the notification duties of manufacturers, importers, distributors or persons servicing medical devices.

Figure 15 Ratio of defects in inspected medical devices



4.13 Standardisation and Pharmacopoeial Activities

The Pharmacopoeia and Pharmaceuticals Standardisation Department prepared a copy of the Czech Pharmacopoeia 2009 – Supplement 2015 (hereinafter referred to as the CP 2009 – Suppl. 2015) for printing.

In the European part, this edition contains translations of other supplements (8.3 to 8.5) of the European Pharmacopoeia (hereinafter referred to as "Ph. Eur."). The European part of CP 2009 – Suppl. 2015 contains also article *Antithrombinum III humanum densatum*, which was adopted at the November meeting of the European Pharmacopoeial Commission (hereinafter referred to as "EPC") as binding through rapid procedure with effective date of 1 January 2015; its translated text has been published also on the website of the Institute.

The general part – the National Part of the CP 2009 – Suppl. 2015 – includes the full version of tables II, III, IV, V, VI, and XII that were supplemented with information about newly added substances and also include active substances specified in CP 2009 and subsequent supplements. Revised Table X containing effective Standard Terms for pharmaceuticals dosage forms, methods of administration and packaging, is also provided in its

full version. Table XVI: Storage and expiry of products prepared in pharmacies, which was processed in cooperation with the analytical department of the Institute and selected hospital pharmacies, was revisited and extended with newly tested products.

The Special Section of the National Part newly includes 21 articles, some of them reflecting data acquired from stability monitoring; these revised texts were submitted for public review (notified) and were reported under No. 2014/0651/CZ in compliance with Directive 98/34/EC of the European Parliament and of the Council of 22 June 1998 laying down a procedure for the provision of information in the field of technical standards and regulations, and the rules on information society services, as amended by Directive 98/48/EC. National articles which were adjusted to reflect deletion of the Dispensing Provision the inclusion of which was not compliant with Section 11 (d) of Act No 378/2007 Coll., on Pharmaceuticals and on Amendments to Some Related Acts, as amended, passed the notification process in the past years.

In coordination with the Pharmacopoeia and Pharmaceuticals Standardisation Department, also other experts of the Institute contributed to the preparation of CP 2009 – Suppl. 2015. Czech Pharmacopoeia 2009 – Supplement 2015 will be binding as of 1 September 2015.

Cooperation with the EPC in the preparation of another edition of Ph. Eur. and in the preparation of 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 the Institute. The employees of the Department regularly took part in the meetings of EPC and of the secretariats of national pharmacopoeial commissions.

Standardisation

In 2014, two draft translations of Czech technical standards for medical devices were commented on within the scope of standardisation activities.

In 2014, a representative of the Clinical Trials and Vigilance (KHV) department actively participated in the work of the TNK 81 Technical Standardisation Commission for Medical Devices.

4.14 Penalties imposed by the Institute

Based on its ex-officio findings and breaches of legislative requirements identified in the course of inspections or in the supervision of advertising and based on reports, the Institute initiates administrative procedures within which penalties referred to in the applicable laws are imposed according to the severity of the identified problem. Since August 2011, the Institute has been availing also of the option to impose penalties on the basis of so called administrative order, under the Administrative Code. The Institute observed this practice also in 2014.

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 in accordance with 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 holder in the case of an authorised medicinal product; importer or domestic manufacturer of medicinal products if the medicinal product imported or produced by it is used in the Czech Republic within a specific therapeutic programme or another person applying for a specific therapeutic programme; importer or domestic manufacturer of foods for special medical purposes; health insurance company). The request to initiate an administrative procedure ex officio may be submitted by any person.

4.15 Determination of Prices and Reimbursement

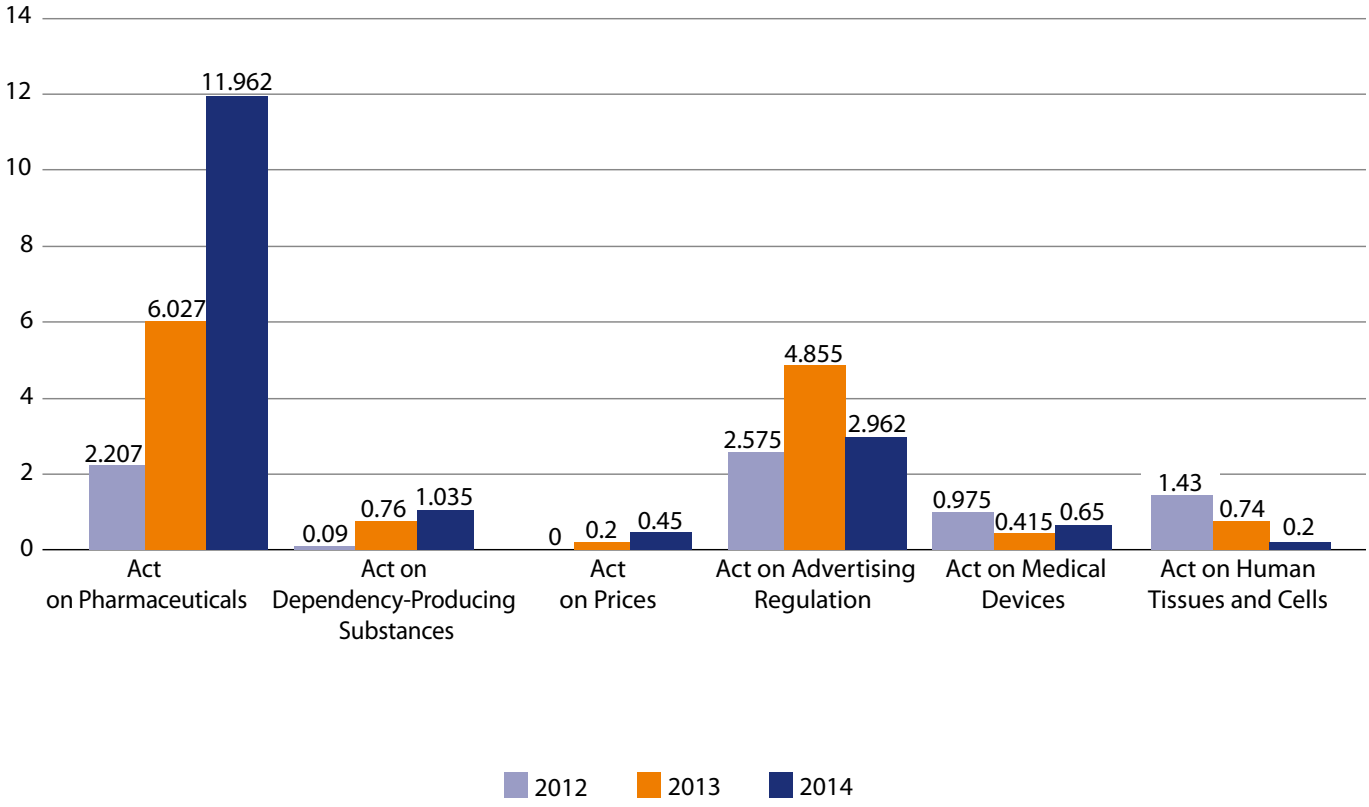
In the course of 2014, the Branch continued in the initiation of in-depth reimbursement inspections in accordance with the schedule. For 2014, initiation of 362 in-depth revisions was scheduled, of which 354 administrative procedures were actually commenced.

At the start of 2014, administrative procedures concerning cancellation of the maximum price and/or the amount and conditions of reimbursement for products which had not been traded on the market in the Czech Republic for more than one year were initiated.

Table 24 Number of texts in CP 2009 – Suppl. 2015

	General articles, tables	Articles	Total
European part	31	219	250
National Part	10	21	31
Total	41	240	281

Figure 16 Final decisions on penalties imposed by the Institute in 2014 (in mil. CZK)



In addition to the planned administrative procedures, administrative procedures on the establishment, change or cancellation of the maximum price and/or the amount and conditions of reimbursement upon request and abbreviated revisions were initiated.

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 dosage 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 2014. For this reason, in 2014, a drop in the number of administrative procedures on the determination of the maximum ex-factory price compared to 2013 is apparent (in 2013, the procedure was initiated for 772 codes of medicinal products which were subjected to new maximum price regulation as of 1 January 2013).

Compared to 2013, three times more administrative procedures on change of maximum ex-factory price were initiated (92 administrative procedures in 2013 vs. 281 administrative procedures in 2014), particularly due to the change in the CZK/€ exchange rate change resulting from the intervention of the Czech National Bank at the end of 2013. In the aforementioned administrative procedures, the ex-factory price was mostly increased due to the change in the exchange rate.

In 2014, the total number of reimbursed medicinal products decreased, due to administrative procedures on the cancellation of the maximum price and/or amount and conditions of reimbursement, in which reimbursement was cancelled for 1,118 codes. Due to the entry of a higher number of maximum-price regulated medicinal products, the relative ratio of deregulated products dropped (Figure 17).

Development of Average End-User Prices

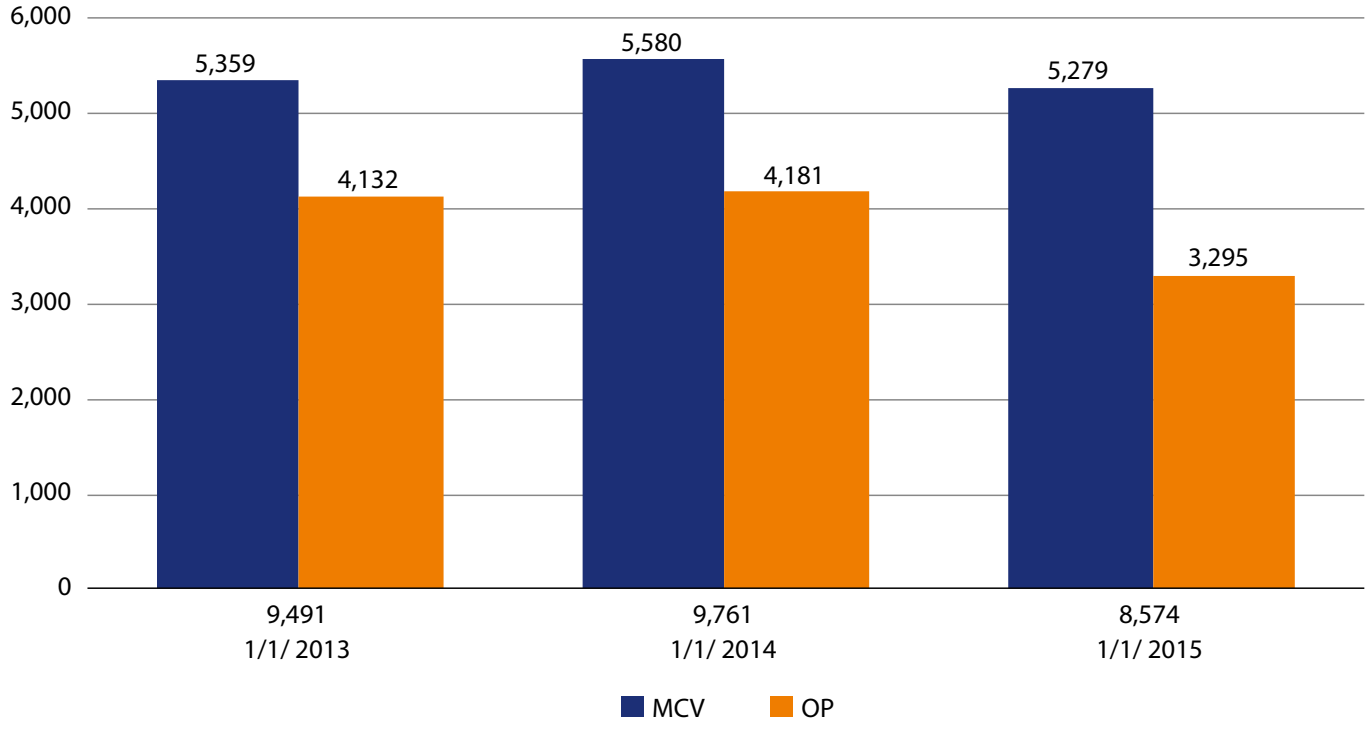
In 2014, profit margins and VAT did not change. VAT continued to be applied in the rate of 15%.

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 producer price increased by 5.29% (comparison of the last quarters of 2013 and 2014 exhibits as much as a 6.97% increase), which may be caused by the change in the CZK/€ exchange rate. In case of medicinal products regulated by notified price and profit margin (as per the Price Regulation and Price Decision), the average producer price dropped by 11.43% (comparison of the last quarters exhibits only a 6.16% drop).

Table 25 Overview of administrative procedures in 2014

Applications for establishment of maximum ex-factory price	No. of SÚKL codes
Initiated	10
Decided	4
Appeal procedures pending	0
Came into force	4
Applications for maximum ex-factory price change	
Initiated	431
Decided	401
Appeal procedures pending	1
Came into force	378
Applications for maximum ex-factory price reduction – abbreviated procedures	
Initiated	2
Decided	0
Appeal procedures pending	0
Came into force	0
Applications for maximum ex-factory price cancellation	
Initiated	1
Decided	1
Appeal procedures pending	0
Came into force	1

Figure 17 Structure of reimbursed products by the type of price regulation



MCV – maximum ex-factory price, OP – profit margin

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

Price regulation zone	01/2014	02/2014	03/2014	04/2014	05/2014	06/2014	07/2014	08/2014	09/2014	10/2014	11/2014	12/2014
Up to 20 CZK inclusive	43	42	42	41	41	37	32	32	32	31	31	31
Over 20 CZK – 50 CZK inclusive	445	421	415	411	403	371	359	358	353	351	351	345
Over 50 CZK – 100 CZK inclusive	702	700	710	704	690	660	655	655	654	655	660	647
Over 100 CZK – 200 CZK inclusive	826	835	837	839	833	808	812	817	815	824	836	833
Over 200 CZK – 300 CZK inclusive	446	454	457	460	451	424	435	438	445	450	453	458
Over 300 CZK – 500 CZK inclusive	580	585	590	596	579	540	532	537	542	545	553	558
Over 500 CZK – 1,000 CZK inclusive	671	670	671	675	660	618	600	609	618	633	634	632
Over 1,000 CZK – 2,000 CZK inclusive	621	623	628	630	615	566	553	563	576	571	562	570
Over 2,000 CZK – 3,000 CZK inclusive	251	254	253	253	244	214	213	216	216	215	212	213
Over 3,000 CZK – 5,000 CZK inclusive	343	348	347	347	339	340	336	354	364	362	362	361
Over 5,000 CZK – 10,000 CZK inclusive	305	304	308	306	295	282	282	283	283	281	281	284
Over 10,000 CZK – 20,000 CZK inclusive	189	185	185	182	178	164	159	164	163	165	167	168
Over 20,000 CZK – 30,000 CZK inclusive	64	65	66	66	66	62	61	61	60	61	64	64
Over 30,000 CZK – 50,000 CZK inclusive	39	39	38	37	37	31	31	35	35	35	38	38
Over 50,000 CZK – 10,0000 CZK inclusive	39	40	40	40	39	37	38	38	38	38	42	42
Over 100,000 CZK	16	17	19	19	19	19	19	19	21	21	22	22
Number of codes	5,580	5,582	5,606	5,606	5,489	5,173	5,117	5,179	5,215	5,238	5,268	5,266

Figure 18 Maximum ex-factory price and notified-price regulated prices of medicinal products – comparison of average prices in Q4 2013 and Q4 2014 by price zones

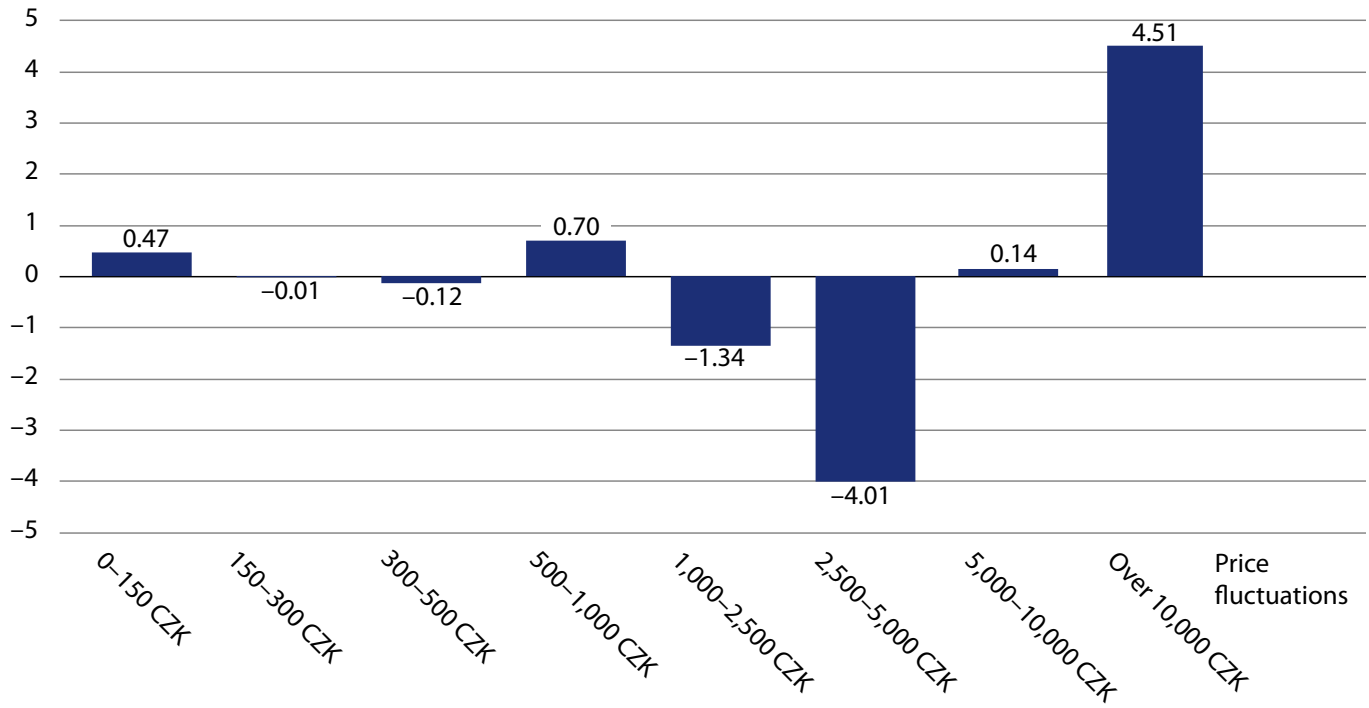
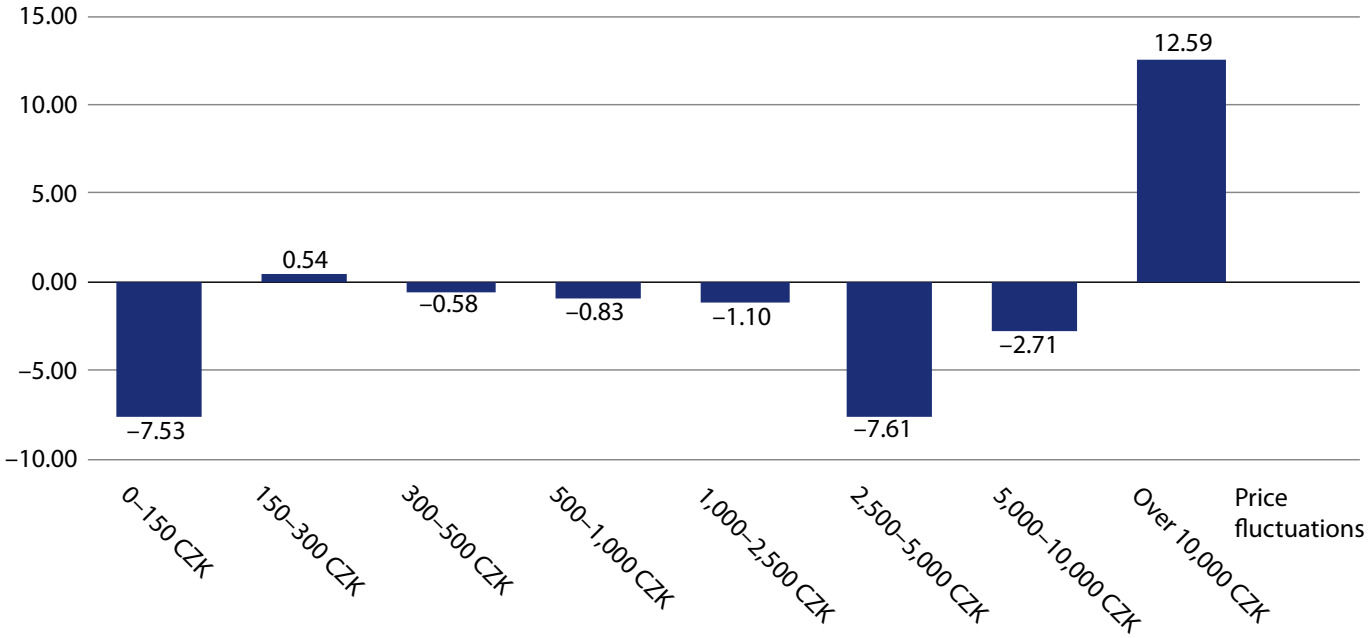


Figure 19 Notified-price only regulated prices of pharmaceuticals – comparison of average prices in Q4 2013 and Q4 2014 by price zones



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

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

All of the ten most often distributed products where the maximum price was changed fall within the first price zone (Table 27). An increase in the maximum price occurred in 8 of the 10 specified cases due to the change in the CZK/€ exchange rate caused by the intervention of the Czech National Bank at the end of 2013.

Medicinal products with the highest financial volume fall most often into the last price zone. The maximum price grew for all medicinal products (Table 28).

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

Code	ATC	Name	Name supplement	No. of packages	Original price (CZK)	New price (CZK)	Change of profit margin in %
0002592	M04AA01	MILURIT 100	POR TBL NOB 50× 100MG	956,921	52.34	55.81	6.6
0000536	C01CA03	NORADRENALIN LÉČIVA	INJ SOL 5× 1 ml/1 mg	652,944	103.07	109.49	6.2
0001066	D06AX	FRAMYKOIN	DRM UNG 1× 10 GM	600,487	33.32	35.40	6.2
0001710	M04AA01	MILURIT 300	POR TBL NOB 30× 300 mg	475,939	56.33	58.34	3.6
0125599	A12BA01	KALNORMIN	POR TBL PRO 30× 1 GM	452,392	15.37	43.47	182.8
0076064	B03BB01	ACIDUM FOLICUM LÉČIVA	POR TBL OBD 30× 10 mg	447,833	58.90	63.11	7.2
0176954	A03DA02	ALGIFEN NEO	POR GTT SOL 1× 50 ml	436,434	77.90	85.06	9.2
0096696	C03BA11	INDAP	POR CPS DUR 30× 2.5 mg	428,982	33.03	41.59	25.9
0017189	A12BA01	KALIUM CHLORATUM BIOMEDICA	POR TBL FLM 100× 500 mg	354,415	33.60	36.50	8.6
0093109	N01BB58	SUPRACAIN 4%	INJ SOL 10× 2 ml	345,470	91.04	134.69	48.0

Amounts and Conditions of Reimbursements from Health Insurance

Since the end of 2011, parties to procedures 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 establishment, change or cancellation of the amounts and conditions of reimbursement can be also requested by the parties to procedures 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.

In 2014, 11 applications for the determination of temporary reimbursement for highly innovative products were filed. Temporary reimbursement was determined for four of these, in one case the application was withdrawn and in 6 cases the administrative procedure is still pending.

Pursuant to the provisions of Section 39l of the Act on Public Health Insurance, the Institute is required, among other things, to assess the amount of the basic reimbursement, the consistency of the amounts of reimbursements for all principally therapeutically interchangeable medicinal products with the basic reimbursement, the uniformity and effectiveness of the determined conditions of reimbursement, and compliance of the determined amounts and conditions of reimbursement with this Act, specifically meeting the expected results and reasons for pharmacotherapy, the effectiveness of the establishment of reference groups, the amount of basic reimbursement, conditions of reimbursement, assessment of the clinical 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. The Institute initiates also other types of administrative procedures ex officio, such as abbreviated revisions or individual administrative procedures to change or cancel the amounts and conditions of reimbursement. In 2014, 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 2014 is estimated at 1.1 bill. CZK.

In 2014, the Institute also conducted ex-officio administrative procedures concerning the cancellation of maximum prices and/or the amounts and conditions of reimbursement for products which had not been placed on the Czech market for more than one year. This concerned 116 administrative procedures (1,119 codes in total), all of which have been finalised. With a view to the fact that it concerns products not placed on the market, the cancellation of the maximum price or the amount and conditions of reimbursement does not influence clinical practice in the Czech Republic.

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

It is clear from the overview that there was a decrease in the reimbursement for individual packages of medicinal products in the group of medicinal products with the greatest volume of reimbursement from health insurance (Table 32).

Validation of Applications

In 2014, the number of submitted applications decreased. The reason is the fact that no legislative change occurred, as against the start of 2013 when the marketing authorisation holders were obliged to submit applications for the determination of maximum prices of medicinal products which were transferred back to

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

Code	ATC	Name	Name supplement	Financial volume in end-user price	Original price (CZK)	New price (CZK)	Change of profit margin in %
0025566	L04AB04	HUMIRA 40 mg	INJ SOL 2× 0.8 ml	835,493,548	22,170.50	22,686.51	2.3
0027283	L04AB02	REMICADE 100 mg	INF PLV CSL 1× 100 mg	822,765,106	12,010.79	12,481.78	3.9
0025555	L01XC03	HERCEPTIN 150 mg	INF PLV SOL 1× 150 mg	602,042,902	12,808.27	13,498.86	5.4
0026544	L01XC02	MABTHERA 500 mg	INF CNC SOL 1× 50 ml	569,252,122	27,507.52	28,952.62	5.3
0028028	L01XE01	GLIVEC 400 mg	POR TBL FLM 30× 400 mg	504,350,091	51,568.32	53,960.82	4.6
0105385	L03AX13	COPAXONE 20 mg/ml	INJ SOL ISP 28× 20 mg/ml	493,364,571	16,261.37	16,679.93	2.6
0027953	A10AE04	LANTUS 100 JEDNOTEK/ml	SDR INJ SOL 5× 3 ml SOLOSTAR	433,055,844	1,110.61	1,154.97	4.0
0149868	J07AL02	PREVENAR 13	INJ SUS 1× 0.5 ml+SJ	273,927,985	1,112.30	1,196.21	7.5
0027918	L04AB04	HUMIRA 40 mg	SDR INJ SOL 2× 0.8 ml	269,210,661	22,170.50	22,686.55	2.3
0029740	A10BD08	EUCREAS 50 mg/1000 mg	POR TBL FLM 60	231,175,504	914.15	933.75	2.1

maximum ex-factory price regulation on the basis of the Price Decision of the Ministry of Health of the Czech Republic 1/13-FAR.

The highest number of applications for 2014 was filed in April, and concerned particularly applications for changes to the maximum price due to the intervention of the Czech National Bank. The change in the CZK/€ exchange rate impacted particularly procedures initiated in the second quarter of 2014.

The proportion of the number of administrative procedures suspended due to defective submissions and shortcomings in applications which were, however, subsequently eliminated, dropped by half compared to 2013 (from 16.48% in 2013 to 8.94% in 2014), the proportion of administrative procedures stopped for these reasons copied the level from 2013.

Individually Prepared Medicinal Products

Individually prepared medicinal products (IPLP) were subjected to the conditions of material price regulation (VUC) pursuant to the Price Regulation also in 2014. This regulation applies to the following groups of medicinal products: individually prepared radiopharmaceuticals (RF), individually produced transfusion products (TP), individually prepared medicinal products in pharmaceutical care facilities – extemporaneous products (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 (5). The drafting of general measures and the method of their publication

Table 29 Overview of administrative procedures in 2014

Applications for determination or change of the reimbursement amount and conditions	No. of SÚKL codes
Initiated	142
Decided	80
Appeal procedures pending	0
Came into force	65
Applications for determination or change of maximum prices and reimbursement amount and conditions	
Initiated	184
Decided	79
Appeal procedures pending	0
Came into force	70
Applications for reimbursement cancellation	
Initiated	15
Decided	15
Appeal procedures pending	0
Came into force	15
Applications for maximum price and reimbursement cancellation	
Initiated	59
Decided	57
Appeal procedures pending	1
Came into force	56
Procedures initiated ex officio	
Initiated	4,144
Decided	1,761
Appeal procedures pending	67
Came into force	1,438
Procedures on similar products	
Initiated	519
Decided	460
Appeal procedures pending	0
Came into force	460

are governed by Act No 500/2004 Coll., the Administrative Code (the course of the procedure is described in Sections 171 to 174 thereof).

In the first half of 2014, the Institute conducted two revisions focused upon the verification of correctness of issued methodologies for the determination of reimbursement amounts for two subgroups of individually prepared medicinal products,

Table 30 Overview of final decisions on the revision of reimbursements and the impact on public health insurance funds

Effective date	No. of administrative procedures	No. of SÚKL codes	Impact on health insurance funds
1/2014	17	77	–36,128,910.00 CZK
2/2014	35	290	64,476,147.00 CZK
3/2014	35	125	–11,345,875.00 CZK
4/2014	35	268	281,689,941.00 CZK
5/2014	23	358	401,575,603.00 CZK
6/2014	25	423	173,161,747.00 CZK
7/2014	18	175	176,921,225.00 CZK
8/2014	17	176	154,731,349.00 CZK
9/2014	23	119	84,359,476.00 CZK
10/2014	18	106	35,522,673.00 CZK
11/2014	12	94	146,139,070.00 CZK
12/2014	25	192	222,441,735.00 CZK

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

Table 31 Overview of the number of codes of medicinal products/foods for special medical purposes in reimbursement price zones according to the List of Prices and Reimbursements by month

Price zones	01/2014	02/2014	03/2014	04/2014	05/2014	06/2014	07/2014	08/2014	09/2014	10/2014	11/2014	12/2014
Up to 20 CZK inclusive	182	180	178	181	189	143	152	153	151	150	157	181
More than 20 CZK – 50 CZK inclusive	766	757	778	811	792	747	751	752	753	749	749	724
Over 50 CZK – 100 CZK inclusive	1,307	1,285	1,309	1,333	1,290	1,223	1,188	1,210	1,219	1,217	1,200	1,200
Over 100 CZK – 200 CZK inclusive	1,640	1,637	1,637	1,647	1,606	1,518	1,489	1,576	1,569	1,573	1,574	1,577
Over 200 CZK – 300 CZK inclusive	932	926	913	960	928	854	805	734	732	740	743	763
Over 300 CZK – 500 CZK inclusive	1,014	1,005	993	904	884	815	766	776	784	779	790	793
Over 500 CZK – 1,000 CZK inclusive	1,379	1,373	1,369	1,333	1,301	1,207	1,138	1,113	1,123	1,130	1,137	1,142
Over 1,000 CZK – 2,000 CZK inclusive	923	926	925	919	899	806	769	768	767	776	783	771
Over 2,000 CZK – 3,000 CZK inclusive	390	386	387	378	356	317	312	313	319	320	316	307
Over 3,000 CZK – 5,000 CZK inclusive	351	350	354	354	339	321	315	320	329	330	333	328
Over 5,000 CZK – 10,000 CZK inclusive	394	397	400	395	388	359	352	367	369	368	370	373
Over 10,000 CZK – 20,000 CZK inclusive	280	263	268	266	262	226	222	228	231	233	236	232
Over 20,000 CZK – 30,000 CZK inclusive	95	95	92	92	92	84	85	85	80	81	85	84
Over 30,000 CZK – 50,000 CZK inclusive	51	51	51	50	49	36	38	41	42	42	40	40
Over 50,000 CZK – 100,000 CZK inclusive	40	41	40	40	39	37	38	39	39	39	42	42
Over 100,000 CZK	17	18	20	20	20	20	20	20	22	22	25	25
Number of codes	9,761	9,690	9,714	9,683	9,434	8,713	8,440	8,495	8,529	8,549	8,580	8,582

specifically for the parenteral nutrition products for home therapy subgroup and for prepared radiopharmaceuticals. In these subgroups, the revision confirmed compliance with the effective methodology. In the second half of 2014, a revision of the transfusion product and extemporaneous product groups was carried out. In the subgroup of transfusion products, changes were identified; following verification, these will be addressed in 2015 by means of a separate general measure. In the extemporaneous product subgroup, only the development of year-to-years costs is being monitored, as this subgroup concerns

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

Code	ATC	Name	Name supplement	Financial volume in end-user prices	Original reimbursement (CZK)	New reimbursement (CZK)	Change in reimbursement in %
0025566	L04AB04	HUMIRA 40 mg	INJ SOL 2× 0.8 ml	835,493,548	25,770.86	22,121.29	–14.2
0027283	L04AB02	REMICADE 100 mg	INF PLV CSL 1× 100 mg	822,765,106	15,595.89	13,387.25	–14.2
0025555	L01XC03	HERCEPTIN 150 mg	INF PLV SOL 1× 150 mg	602,042,902	15,093.55	15,615.41	3.5
0028397	L01XC07	AVASTIN 25 mg/ml	INF CNC SOL 1× 16 ml	425,391,120	32,632.97	32,516.17	–0.4
0027918	L04AB04	HUMIRA 40 mg	SDR INJ SOL 2× 0.8 ml	269,210,661	25,770.86	22,121.29	–14.2
0027905	L04AB01	ENBREL 50 mg	INJ SOL 4× 1 ml/50 mg	215,986,045	26,167.89	22,462.10	–14.2
0054316	B01AB06	FRAXIPARIN MULTI	INJ SOL 10× 5 ml/47.5KU	204,942,558	7,290.38	6,035.83	–17.2
0028761	L01XC06	ERBITUX 5 mg/ml	INF SOL 1× 20 ml	194,643,189	6,119.55	6,146.62	0.4
0029248	L01XC08	VECTIBIX 20 mg/ml	IVN INF CNC SOL 1× 5 ml	179,459,192	12,235.63	12,203.48	–0.3
0026096	A16AB07	MYOZYME 50 mg	INF PLV CSL 1× 50MG/LAH	168,462,366	13,194.46	13,628.45	3.3

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

Code	ATC	Name	Name supplement	A (number of packages)	Original reimbursement (CZK)	New reimbursement (CZK)	B (number of packages)	Note:
0125114	B01AC06	ANOPYRIN 100 mg	POR TBL NOB 3× 20× 100 mg	330,913	36.78	33.09	332,928	*/
0002592	M04AA01	MILURIT 100	POR TBL NOB 50× 100 mg	538,741	47.63	44.80	440,871	
0020132	N06AB10	CIPRALEX 10 mg	POR TBL FLM 28× 10 mg I	186,919	201.75	128.80	174,890	*/
0155782	B01AC06	GODASAL 100	POR TBL NOB 100	147,544	61.29	55.14	170,698	*/
0044305	R03DA04	EUPHYLLIN CR N 200	POR CPS PRO 50× 200 mg	339,776	110.66	84.64	340,459	
0012023	A11CC05	VIGANTOL	POR GTT SOL 1× 10 ml	309,492	23.72	36.17	,	x/
0000536	C01CA03	NORADRENALIN LÉČIVA	INJ SOL 5× 1 ml/1 mg	317,076	155.59	162.39	326,905	
0014957	N03AE01	RIVOTRIL 0,5 mg	POR TBL NOB 50× 0.5 mg	150,310	55.71	24.69	166,774	*/
0000168	C03AA03	HYDROCHLORO-THIAZID LÉČIVA	POR TBL NOB 20× 25 mg	315,403	26.97	31.95	308,366	
0163137	C07AB02	VASOCARDIN 50	POR TBL NOB 50× 50 mg	298,191	49.92	28.75		x/

** – period of one quarter of a year, x - period cannot be assessed, A – number of packages distributed during 6 months before change, – number of packages distributed during 6 months after change.*

individual preparation in pharmacies where the individual components entering the preparation are variable.

The revisions worked with revised CZK cost items for individually prepared medicinal products based upon data provided by health insurance companies. In the subgroup of parenteral nutrition for home therapy, the results of statistics of health insurance companies were compared to the data maintained in the Registry of Home Nutritional Support (REDNUP); for transfusion products, the revision was conducted as a comparison of data about the transfusion service production which were provided to the Institute by the Czech Society for Transfusion Medicine of the Czech Medical Society of J. E. Purkyně and form part of the revision report published on the website of the Institute. In case of radiopharmaceuticals, in addition to the statistics of health insurance companies, data about the distribution of radiopharmaceuticals as per the source materials monitored by the Institute were used.

General Measures

Four procedures regarding general measures were initiated and duly completed in the course of 2014.

In the first quarter of 2014, changes to reimbursements were made in association with the change in the CZK/€ exchange rate resulting from the intervention of the Czech National Bank in November 2013. The changes influenced those groups of individually prepared medicinal products the components for the preparation of which are mostly imported from the EU countries. It involved, in particular, the subgroup of individually prepared radiopharmaceuticals, where, with a view to the usability and time of transformation of radioactive components, long-term storage was not possible. The said change was addressed by OOP 01–14 together with the inclusion of a new radiopharmaceutical – 223Ra-Radium-dichloride – for the treatment of bone metastases in castration-resistant prostate carcinoma. The anticipated increase of costs associated with the change in the exchange rate was estimated at 3% for this group of individually prepared medicinal products for 2014 and it was based upon the 2013 consumption of radiopharmaceuticals. The actual costs in 2014, however, were lower than the estimate and, compared to 2013, grew by mere 2.2%.

In the second quarter, general measure 02–14 brought products with short-term interruption in the manufacture thereof in the second half of 2013 and resumed manufacture in 2014 back to the subgroup of individually prepared radiopharmaceuticals. This change did not have any economic impact.

In the fourth quarter, two general measures were issued, to reflect amendment to Act No 235/2004 Coll. on Value-Added Tax, as amended by Act No 262/2014 Coll., introducing another reduced, 10% rate for value-added tax (VAT) on pharmaceuticals, with effective date of 1 January 2015. Changes to reimbursements were proposed and published in OOP 03-14 for radiopharmaceuticals and in OOP 04-14 for parenteral nutrition products for home therapy with effective date as of 1 January 2015. In case of radiopharmaceuticals, a reduction in the costs of this subgroup of individually prepared medicinal products by 3.2% is estimated, i.e. savings amounting to approx. 22 mil. CZK compared to 2014. In case of parenteral nutrition products for home therapy, the reduction in VAT did not cover the costs of mandatory change of production facilities, therefore the

Table 34 Validation of applications for determination/change/cancellation of maximum prices and/or reimbursement amounts and conditions, for abbreviated revision of maximum price or reimbursement system

2014	No. of submitted applications	Suspended due to defective submissions and deficiencies in applications	Discontinued in the validation phase
January	82	21	2
February	45	3	1
March	30	3	1
April	123	19	1
May	81	5	3
June	78	2	1
July	56	1	0
August	37	2	1
September	37	4	0
October	60	0	0
November	31	0	0
December	56	4	2
Total	**716**	**64**	**12**

costs are expected to increase by 1%, i.e. 696 thous. CZK compared to 2014. The conditions of reimbursement of extemporaneous products remain unchanged, as their preparation is based upon starting materials which are not included in the second reduced 10% VAT rate and the costs of preparation are governed by the effective Price Regulation of the Ministry of Health of the Czech Republic 01/2013/FAR. The reduced VAT rate will not be reflected in the costs of transfusion products, either, where the starting material is obtained by draws of human blood or its components, and it does not apply to starting materials, materials and production facilities necessary for the production, either.

Consumption and Costs of Individually Prepared Medicinal Products

In 2014, the costs of individual groups of individually prepared medicinal products were influenced both by the change in the VAT applied also in 2013 and by the change in the €/CZK exchange rate resulting from the intervention of the Czech National Bank at the end of November 2013. The largest impact of these changes was apparent in the individually prepared medicinal product subgroup 13 – radiopharmaceuticals, and 11 – extemporaneous products. The increased costs of subgroup 14 – parenteral nutrition for home therapy result from the increased number of patients in home therapy. Table 35/Figure 20 provide a comparison of costs for the period of 2012 to 2014; Figure 21 illustrates the distribution of costs of individually prepared medicinal products in 2014 by individual subgroups; and Table 36/Figure 32 provides an overview of consumption of individual groups of individually prepared medicinal products in defined units (DU). In addition to the aforementioned subgroups, the costs of individually prepared medicinal products include also the preparation of cytostatic products in pharmaceutical care facilities. As these costs were not included in the extemporaneous product group in the past, Figure 20 shows them as a separate group called Cytostatic dilution (CYT).

Figure 20 Comparison of costs by groups of individually prepared medicinal products for the period of 2012 to 2014 in mil. CZK

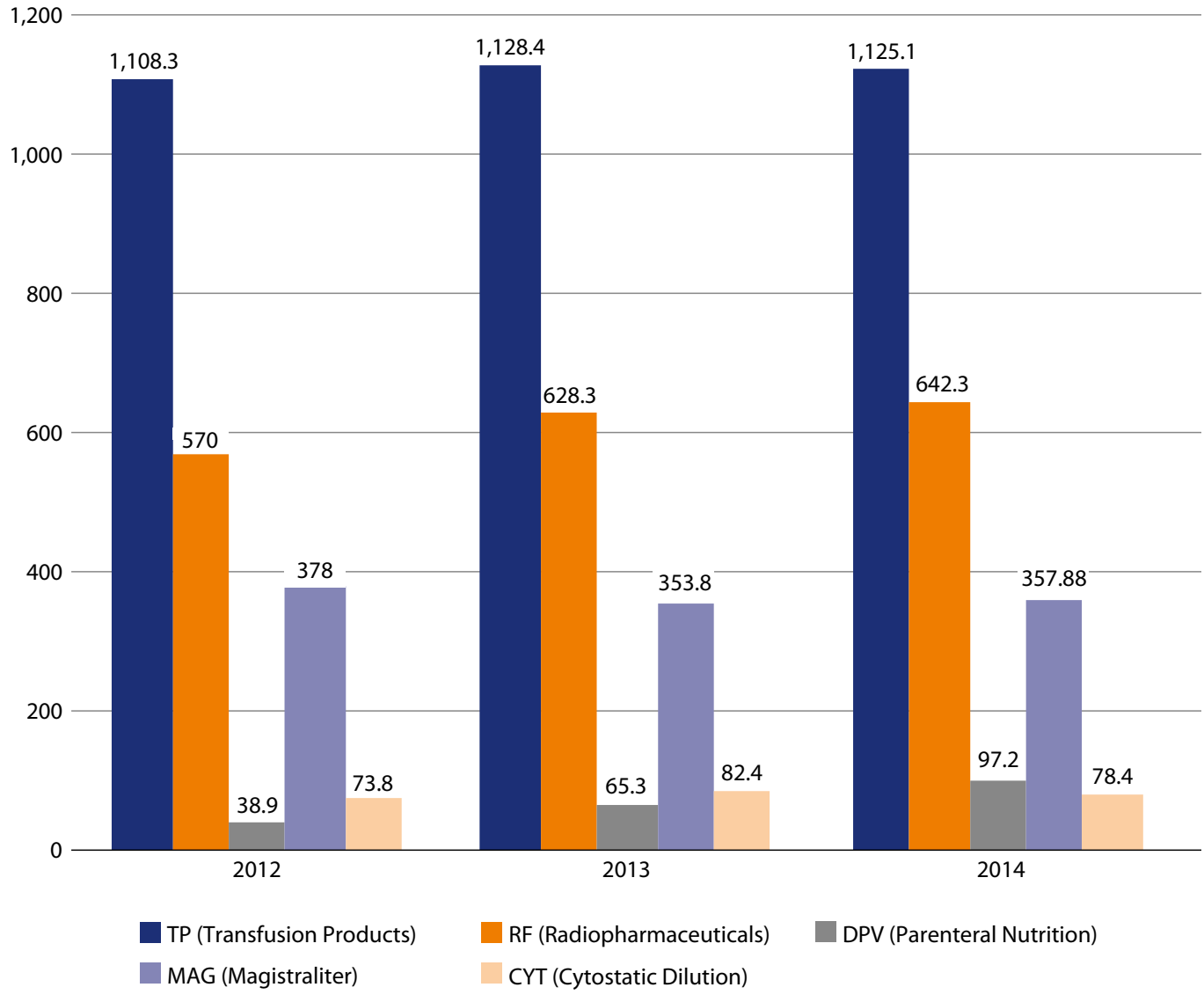
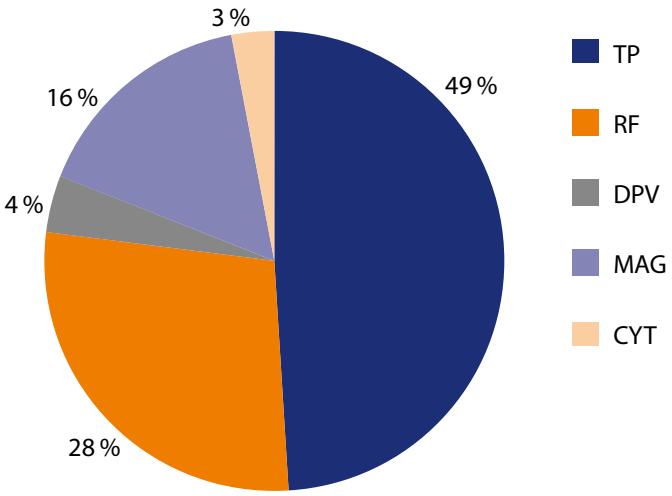


Figure 21 Distribution of overall costs of individually prepared medicinal products in 2014



MEDICAL DEVICES BRANCH

4.16 Department of Clinical Trials and Medical Devices Vigilance

Within the scope of control of clinical trials on medicinal products at providers of healthcare services, 29 inspections were carried out, during which 16 investigated medical devices were inspected. The selection of inspected sites was based upon positive opinions issued by the Institute on the intention to conduct a clinical trial.

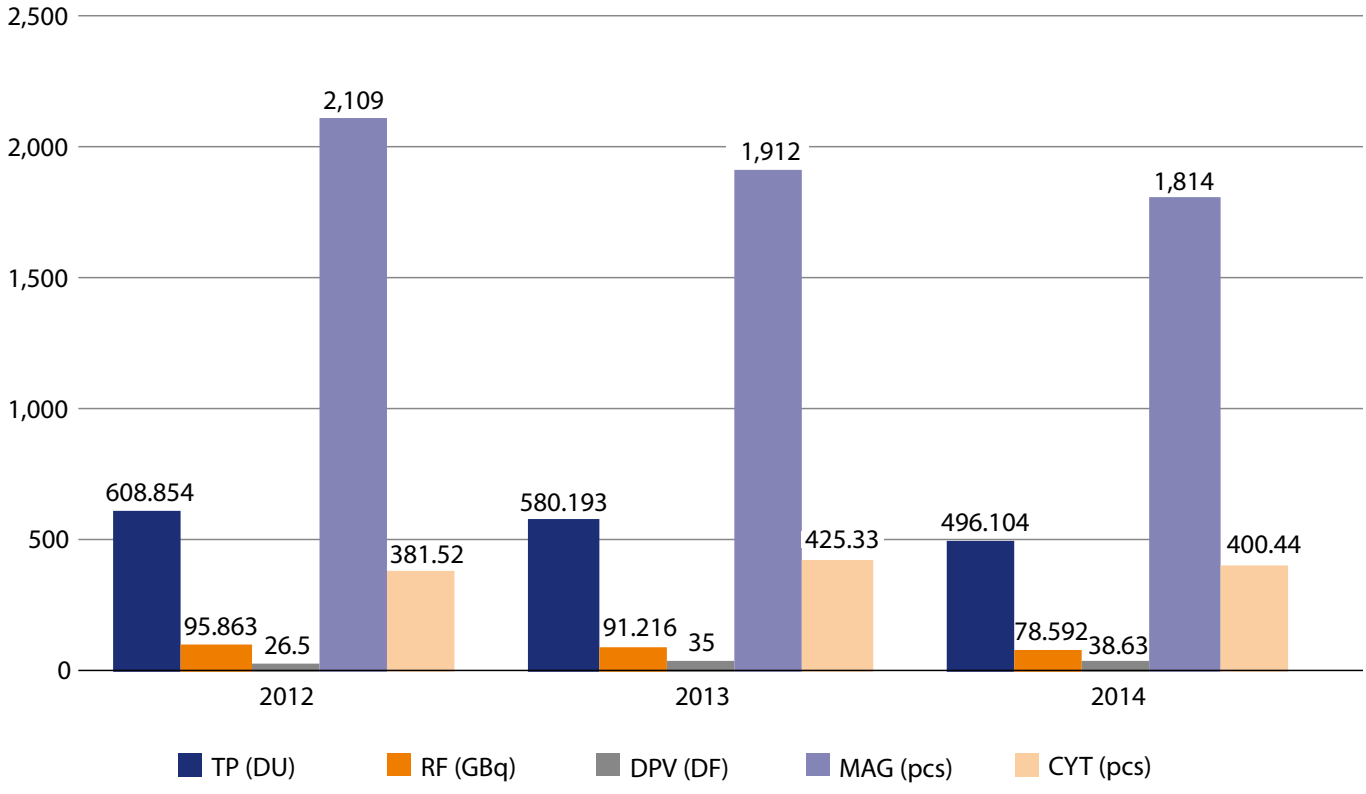
In total, 94 serious adverse events (SAE) were reported from conducted clinical trials on medical devices in the Czech Republic.

In 2014, the intention to conduct a clinical trial was notified to the Institute for 26 medical devices; 20 positive opinions were issued.

Table 35 Overview of consumption for the period of 2012 to 2014 in thous. DU

	TP (DU)	RF (GBq)	DPV (DF)	MAG (pcs)	CYT (pcs)
2012	608.854	95.863	26.5	2,109	381.52
2013	580.193	91.216	35	1,912	425.33
2014	496.104	78.592	38.63	1,814	400.44

Figure 22 Overview of consumption of individually prepared medicinal products 2012 to 2014 in thous. DU



Investigation into adverse events and the monitoring of corrective actions for medical devices

447 adverse events associated with the use of medical devices in the provision of healthcare services were reported to the Institute from the territory of the Czech Republic. Furthermore, 7 adverse events associated with the use of medical devices of Czech manufacturers arising outside the territory of the Czech Republic were reported to the Institute. In all cases, investigation was initiated. Within the scope of investigation into adverse events, 1 inspection at a provider of healthcare services and 1 inspection at a manufacturer of medical devices were conducted.

The total number of received reports on corrective actions regarding medical devices from competent authorities, manufacturers or their authorised representatives, distributors or importers, as applicable, amounted to 1,141. Of the total number of received reports, 510 concerned medical devices distributed to the Czech market (Figure 23 refers).

In 2014, the number of received reports on corrective actions regarding medical devices was 21% higher than in 2013.

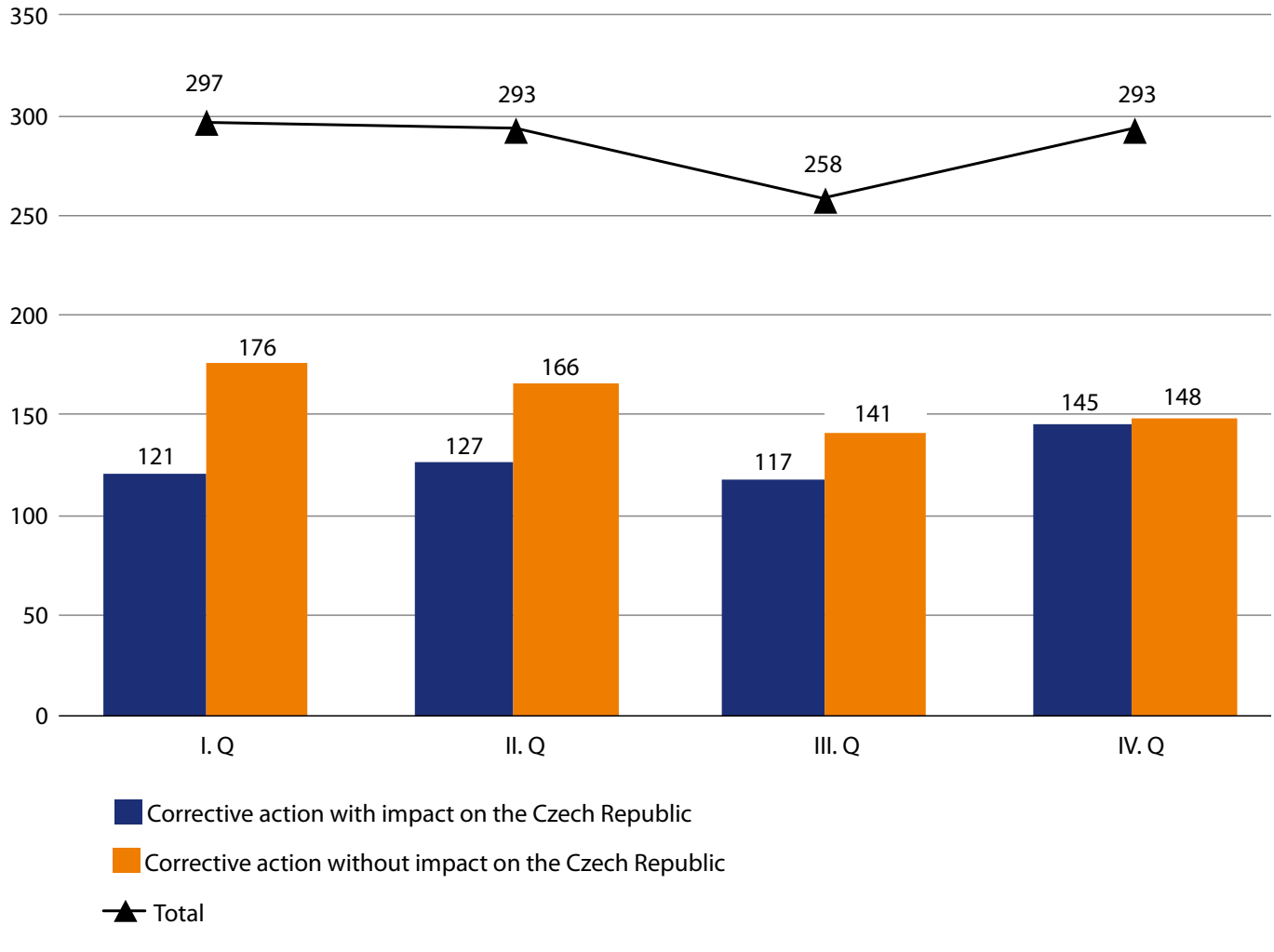
In 2014, the Institute's website published 418 Field Safety Notices (FSN) affecting Czech users, which were sent by the manufacturer, authorised representative or distributor in association with an adopted Field Safety Corrective Action (FSCA), the purpose of which is to minimise the recurrence of an adverse event.

On the basis of the results of investigations into adverse events and inspections of clinical trials on medical devices, 2 fines for administrative offences amounting to 295,000 CZK in total were imposed.

Within the scope of international cooperation in the field of medical device vigilance, in 2014, the inspectors of the Department of Clinical Trials and Vigilance (hereinafter referred to as KHV) participated in 12 teleconferences focused upon exchange of information among the EU Member States concerning current vigilance cases.

Within the scope of national cooperation and their powers, the surveillance bodies for the area of medical devices, the Institute and the

Figure 23 Reports on corrective actions for medical devices adopted in 2014



Czech Trade Inspection mutually shared suggestions for investigation. The KHV Department cooperated with the Czech Office for Standards, Metrology and Testing in the training of notified body representatives in the sphere of vigilance and clinical trials on medical devices.

4.17 Penalties for Breach of Act on Medical Devices

The Institute, as a first-instance authority, initiates administrative procedures regarding administrative offences in case a breach of obligations imposed by the Act on Medical Devices is identified, particularly in relation to inspection activities conducted at providers of healthcare services, within the scope of supervision over the conduct of clinical trials on medical devices, and as part of monitoring of adverse event investigations. The powers of the Institute, moreover, include also powers in the area of fine imposition for failure to comply with notification duties set forth by Section 31 of the aforementioned Act, which, in the last year, represented the highest proportion of the total number of imposed fines.

In 2014, the Institute imposed fines for breach of the Act on Medical Devices amounting to 1,955,000 CZK in total.

STATE AGENCY FOR MEDICAL CANNABIS

In compliance with Act No. 167/1998 Coll., on Dependency-Producing Substances, as amended, the Institute performs the tasks of the State Agency for Cannabis for Medical Use (hereinafter referred to as the "Agency"). The Agency was established on 1 January 2013. Its activities consist of granting licenses to grow cannabis for medical use, 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 towards the Ministry of Health of the Czech Republic and the Police of the Czech Republic.

In 2014, the major task of the Department was to announce a tender for a public contract "Supplies of Cannabis for Medical Use". The timeline for the first round of the tender was established at 1 September 2014; 16 candidates in total entered the tender. 4 candidates meeting the required qualification prerequisites were shortlisted from the first round to the second round, where the major evaluation criterion was the lowest quoted price. The evaluation of price quotations submitted in the second round of the tender was concluded on 16 December 2014.

In November 2014, the Register of Restricted Medicinal Products was put into operation, the purpose of which is to safeguard restricted prescribing and dispensing of medical cannabis in quantities set forth by the Decree. Due to this, medical cannabis was prescribed and dispensed to a patient for the first time in the history of the Czech Republic. Furthermore, the Agency ensures verification of specialised competence of those doctors who apply for access to the Register.

In 2014, close cooperation with the Inspectorate for Narcotic and Psychotropic Substances of the Ministry of Health of the Czech Republic and its relevant specialised sections continued. In addition to cooperation with a regulatory agency in the Netherlands, cooperation with the Israeli state agency for cannabis for medical use was initiated.

In late 2014, the tender dossier for public contract on the safeguarding of storage and distribution of cannabis for medical use was being finalised. Concurrently, intensive works on the new tender dossier for potential future tender for a domestic medical cannabis grower were under way.

Any information relevant to medical cannabis was piecemeal completed on the website of the State Agency for Medical Cannabis www.sakl.cz. This concerns, in particular, information for patients, doctors and pharmacists, as well as for future growers.

Table 36 Penalties imposed for breach of the Act on Medical Devices in 2014

Total number of fines imposed in 2014 for breach of the Act on Medical Devices	31
▪ For failure to comply with notification duty pursuant to Section 31	22
▪ For breach of obligations imposed upon healthcare service providers	7
▪ For breach of obligations imposed upon entities conducting clinical trials and within the scope of vigilance	2
Number of appeals	**5**
▪ Of which granted	5
▪ Of which declined	0

SÚKL STATE INSTITUTE FOR DRUG CONTROL

5. Processing and Provision of Information


5 ml

5.1 Information Technology

The objective of the Information Technology Section (OIT) is to safeguard the provision of quality services to internal and external users in relation to the usage of the information systems of the Institute. OIT primarily safeguards a flawless operation of the IT infrastructure, surveillance over information technologies, and implements infrastructure protection from potential security threats. Furthermore, OIT is involved in projects pertaining to the creation and development of information technologies and systems ensuring support for regulatory branches and security of information.

In the course of 2014, the consolidation of contractual relationships with suppliers continued with the aim to achieve a higher quality and efficiency of the administration of provided IT services. In the said period, OIT managed to conclude a settlement agreement with the vendor of the Register of Restricted Medicinal Products. The agreement resolved the previously existing illegitimate and unclear relationship between both partners, providing a transparent solution of e.g. copyright legal relationship issues, technical support provision issues, or financial claim issues. For the Institute, the agreement also safeguarded an exclusive, unlimited licence for the use of a SW application for the purposes of the Register operation in compliance with currently effective legal regulations. Furthermore, some necessary steps to achieve licence conformity of SW tools used by the Institute were completed.

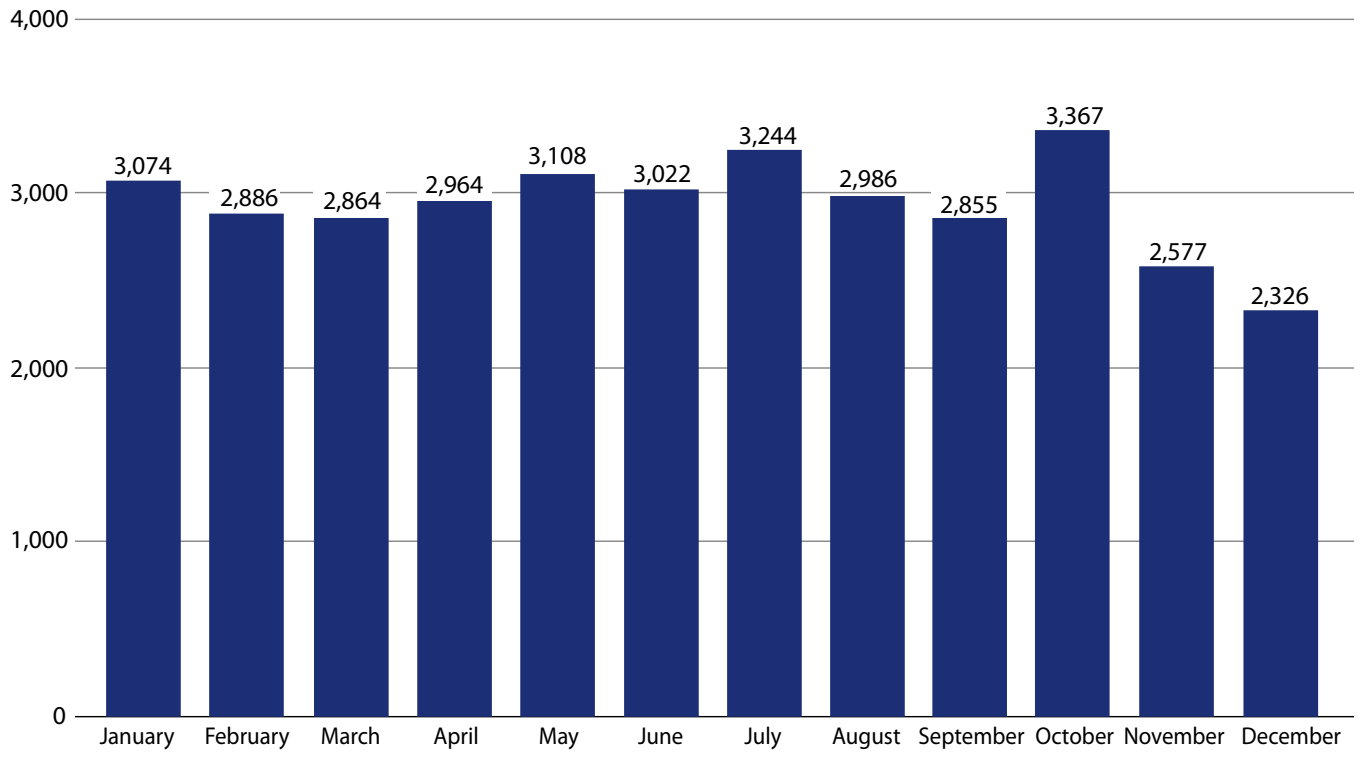
In the course of 2014, the IT Operations Department which safeguards end-user support, administration and support of operated information systems, completed exchange of obsolete end-user stations which allowed for the exchange of the Windows XP operating system in relation to its terminated manufacturer support. This way the security risk implied by operating a system without security updates was reduced. Furthermore, an in-depth inventory of the used SW and HW was conducted, to ensure control of compliance with the licence terms and conditions of individual SW manufacturers. As part of safeguarding a flawless operation of the IT infrastructure, disk repository and back-up tape library equipment were extended, to cover the needs associated with the requirements for an increased volume of data for back-up. Concurrently, an exchange of the existing engine generator for a more efficient one took place, to ensure a higher availability of the operated systems. In 2014, the extension of the existing data centre premises was planned and prepared.

Information Overview of Changes to Reimbursements

In order to increase the provision of information on future changes to reimbursements of medicinal products to the public, the State Institute for Drug Control decided to publish an Information Overview of Changes to Reimbursements of Medicinal Products and Foods for Special Medical Purposes.

On the basis of specification drafted by the Price and Reimbursement Regulation Branch, an application has been developed, the output

Figure 24 Number of views of administrative procedure documentation via website in 2014



of which is an overview of medicinal products and foods for special medical purposes in respect of which a decision within the scope of an in-depth or abbreviated reimbursement revision was issued. The overview is published on an ongoing basis, reflecting currently issued decisions.

Information on changes to reimbursement is published in the Information Overview following the issuance of the respective decision until the enforcement date of the respective decision, i.e. until the time point of publication of the new reimbursement in the List of Prices and Reimbursements of Medicinal Products and Foods for Special Medical Purposes (SCAU).

The Information overview contains, in particular, the original amount of reimbursement for the end user (UHR1), the new amount of reimbursement for the end user (NUHR1), and the enforcement date of the new reimbursement (DAT_VYK).

eRecept

Electronic prescription and the establishment of the Central Repository of Electronic Prescriptions ("CÚ ER") are legislatively set forth by Act No 378/2007 Coll., on Pharmaceuticals, as amended. By means of the Central Repository of Electronic Prescriptions, the doctor issues an electronic prescription (ePrescription) to the patient; on the basis of this prescription the pharmacy dispenses the medicinal product. The Central Repository of Electronic Prescriptions, moreover, collects and stores all ePrescriptions under conditions set forth by effective legislation.

The established electronic prescription system (eRecept) 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. was published in the Collection of Laws, which postponed the obligation to issue electronic prescriptions to 1 January 2018, with effect as of 31 December 2014.

In relation to the requirement for mandatory electronic prescriptions, the process safeguarding support for the Central Repository of Electronic Prescriptions in the coming years and its modernisation commenced in 2014. At the same time, the implementation of the Institute's data centre extension started. All of the activities are aimed at flawless safeguarding of electronic prescriptions in the coming period, when the number of users, and hence also issued electronic prescriptions, is expected to grow, together with the coming timeline for mandatory electronic prescription.

Within the scope of operation of the electronic prescription system, the Institute safeguards support for applicants and users of the given system. One of the most important activities is the operation of a free line which is available to applicants and users during working days from 8:00 a.m. to 5:00 p.m.

In compliance with legislative requirements, the Register of Restricted Medicinal Products ("RLPO") was put into operation in November 2014, in order to restrict the prescription and dispensing of medicinal products to quantities determined by the marketing authorisation pursuant to Section 39 (4c) or Section 39 (5) of Act No 378/200 Coll. and restrictions set forth by Decree No 221/2013.

To comply with the provisions of Section 43a (2b) of Act No 167/1998, on Dependency-Producing Substances, as amended, which set forth the authority of the Czech Police to retrieve data from the Register of restricted Medicinal Products via a predefined contact centre, electronic access to the aforementioned Register was safeguarded 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 CÚ ER 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 are under preparation.

In 2014, 1,099,777 electronic prescriptions were issued. The average monthly number of issued electronic prescriptions in 2014 was 91,648, which, compared to 2013, represents an almost 26% increase. Despite this increase, a major proportion of prescriptions is still issued in the form of paper copies.

In 2014, the total value of reimbursement for dispensed reimbursed medicinal products prescribed through the ePrescription system amounted to 481,365,018 CZK, which is 66,662,608 CZK more than in the previous year.

Since the start of the eRecept system operation to 31 December 2014, the possibility to issue electronic prescriptions was provided to the total number of 3,026 doctors in 483 healthcare facilities, and the possibility to dispense them was given to 4,134 pharmacists in 1,531 pharmacies. Of this, in 2014 the number of doctors with the possibility to issue electronic prescriptions grew by 463 in 135 healthcare facilities and the number of pharmacists with the possibility to dispense electronic prescription grew by 771 in 191 pharmacies.

5.2 Database of Medicinal Products and Monitoring of Supplies to Pharmacies

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

Registry of Active Substances

Currently, the Database of Medicinal Products (DLP) contains 22,686 components (incl. combined components), 338 new components were entered in 2014 and data were updated for 2,078 components.

In 2014, an update of flagging of doping components and of products containing such substances in DLP was carried out pursuant to the 2014 Prohibited List – The World Anti-Doping Code

effective as of 1 January 2014; the latest edition of the European Pharmacopoeia 8.4 and the latest edition of the Japanese Pharmacopoeia J15 (important monographs of therapeutic drugs of so called traditional Chinese medicine) were inserted. The entry of the Czech Pharmacopoeia 2014 Supplement was initiated. Components from lists proposed by INN WHO issued in 2014 were entered and adjustment of components from the recommended INN WHO lists was initiated.

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 were initiated.

Registry of Medicinal Products

In 2014, the Institute granted 446 marketing authorisations (3,691 SÚKL codes). Authorisation was revoked for 566 marketing authorisation numbers, which corresponds to 5,052 codes. The authorisation was revoked either upon request of the marketing authorisation holder (365 authorisation numbers), due to the Sunset Clause (172 authorisation numbers) or due to the fact that the holder did not apply for authorisation renewal (29 authorisation numbers). The validity of 6,916 codes in total expired (the period of final code sale expired or marketing authorisation was revoked).

In the course of 2014, no distribution was reported for 45,899 codes (84%) 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 2,491 various active substances in total.

Regular Outputs from the Database of Medicinal Products

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

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

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

Evaluation of Deliveries of Distributed Medicinal Products

Evaluation of deliveries of distributed medicinal products based upon the mandatory reporting from entities authorised to distribute medicinal products in the Czech Republic was conducted on a monthly basis in 2014. 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 special therapeutic programmes and non-authorised

Table 37 Selected subgroups of authorised medicinal products recorded in the SÚKL database as of 31 December 2014

	Total number of authorisation numbers/marketed authorisation numbers	Total No. of SÚKL codes/marketed SÚKL codes
Medicinal products in total (excl. homeopathic preparations)	15,445/5,826	54,643/8,633
Of which by MA numbers:		
MA numbers granted by the Institute	6,462/4,895	45,642/7,698
MA numbers of products authorised via Community centralised procedure	8,983/931	9,001/935
Of which by content:		
Single-component	12,112	44,863
Multi-component	3,333	9,780
Of which by type of dispensing:		
Prescription-only medicinal products	14,613/5 107	51,336/7,497
OTC medicinal products	874/729	3,264/1,123
Restricted OTC medicinal products	13/7	25/11
Restricted prescription-only medicinal products	4/2	18/2
Homeopathic preparations	269/268	716/327

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 their value over the years, data on financial costs are provided in producer prices, i.e. ex-factory prices excl. VAT (VAT rates were changing over the years), and excl. the profit margin. Since 2008, the regular quarterly evaluation of deliveries of distributed products has been supplemented on the website of the Institute with a table showing deliveries for each active substance (further broken down by route of administration, where applicable). Furthermore, the Institute published summary information from monthly reports of entities authorised to distribute medicinal products in the Czech Republic on its website.

In 2014, 264.229 million packages of medicinal products were distributed, which corresponds to approx. 6,288.580 million defined daily doses. The value of these deliveries was 56.448 billion CZK (based on ex-factory price).

5.3 Information Activities

Keeping the general and professional public informed is the main task of the Press and Information Department (TIO). The most important source of guaranteed data for professionals and for the general public are websites www.sukl.cz, information portal for the public www.olecich.cz, and the website of the campaign Nebezpečné léky (Dangerous Drugs) www.nebezpecneleky.cz. In addition, TIO runs Facebook profiles for the portal for the public and for the Nebezpečné léky campaign.

In 2014, the website for professionals www.sukl.cz had nearly 2.4 million visitors who viewed more than 12 million pages.

The Information portal offers verified and accurate information on medicines to the public, ranging from a database of approved medicines, electronic forms for adverse event reporting and expert consultancy, to current information on the safety of medicines. Information from the www.olecich.cz portal was searched by 339 thousand visitors who viewed more than 1.1 pages.

Furthermore, the Institute administers the website of the Nebezpečné léky (Dangerous Drugs) campaign – www.nebezpecneleky.cz, the website of the ARTHIQS project – www.arthiqs.eu and the website of the State Agency for Medical Cannabis – www.sakl.cz.

In 2014, three issues of the publication for the general public called infoLISTY were published. This publication focuses upon selected topics from the area of health and medicines; in 2014 the following topics were prepared: "Medicines vs. dietary supplements", "The journey of medicines in the human body", and "Original medicines vs. generic products".

Figure 25 Authorised medicinal products in the period 2010–2014

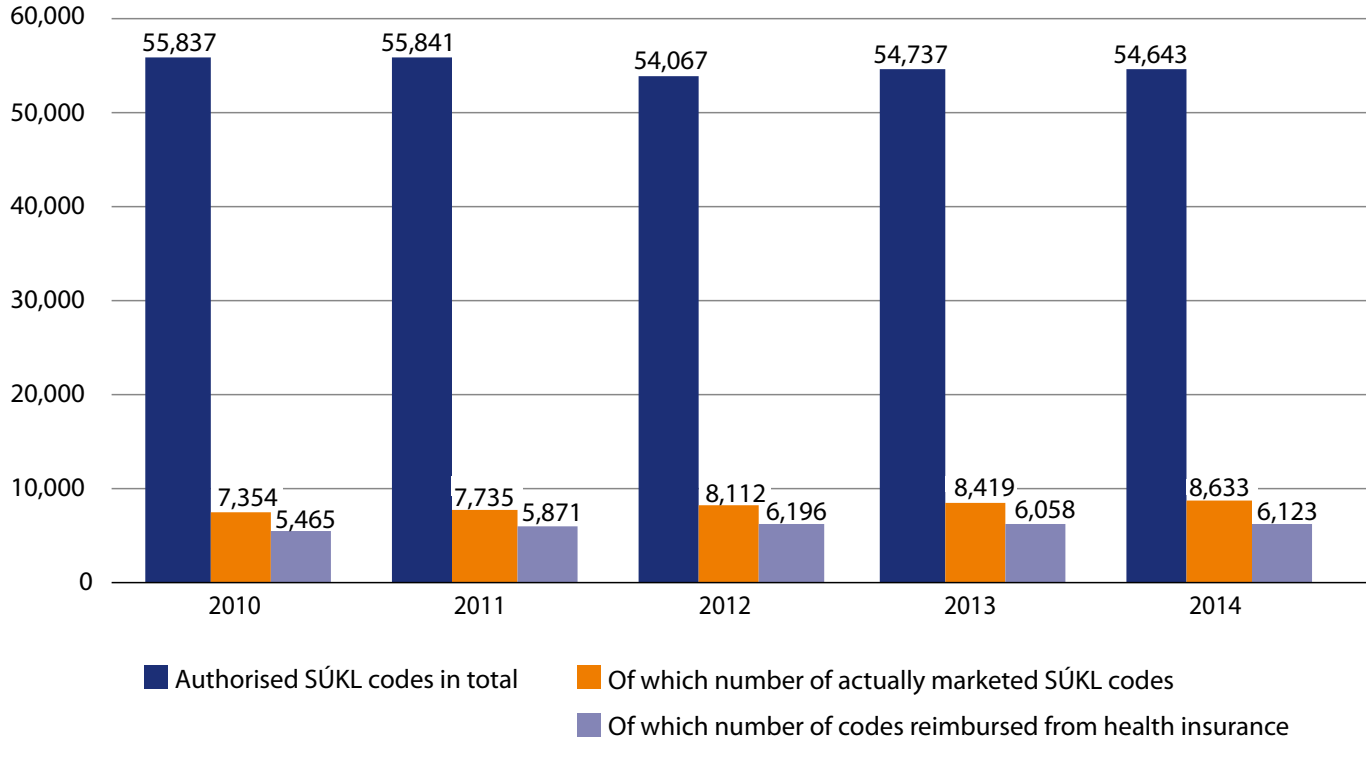


Figure 26 Deliveries of medicinal products in 2010 – 2014

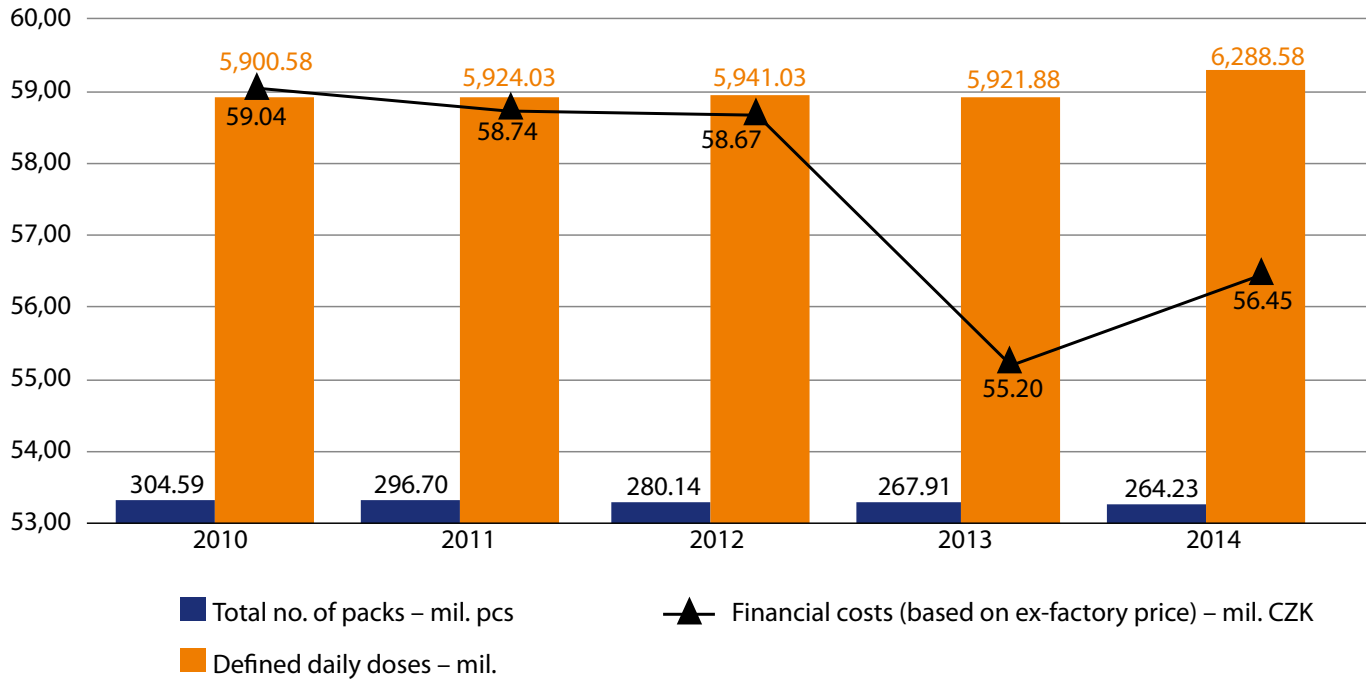


Table 38 Deliveries of distributed medicinal products in 2014

Medicinal products in total	Number
Deliveries to pharmacies and healthcare facilities (mil. packages)	264.229
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	56,448.287
Deliveries to pharmacies and healthcare facilities (mil. DDD)	6,288.580
DDD/1,000 inhabitants/day	1,638.697
Prescription-only medicinal products	**Number**
Deliveries to pharmacies and healthcare facilities (mil. packages)	183.028
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	50,440.162
Deliveries to pharmacies and healthcare facilities (mil. DDD)	5,710.750
DDD/1,000 inhabitants/day	1,488.124
OTC and selected pharmaceuticals	**Number**
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. packages)	80.705
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. CZK based on ex-factory price)	5,939.007
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. DDD)	577.401
DDD/1,000 inhabitants/day	150.461
Restricted OTCs	**Number**
Deliveries to pharmacies and healthcare facilities (mil. packages)	0.496
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	69.118
Deliveries to pharmacies and healthcare facilities (mil. DDD)	0.429
DDD/1,000 inhabitants/day	0.112
Homeopathic preparations	**Number**
Deliveries to pharmacies (mil. packages)	1.645
Deliveries to pharmacies (mil. CZK based on ex-factory price)	143.999

Via the "Ask Us" service, pharmacists and doctors – a general practitioner and a paediatrician, a gynaecologist, a physician specialising in travel medicine, and three pharmacists – answered questions from the public. The service was used by a total of 437 inquirers.

In collaboration with the author of the Stories of Medicines, TIO organised over 18 talks on the topic of safe use of medicinal products for public libraries and senior clubs across the Czech Republic in 2014.

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

Via its information telephone line and e-mail address, TIO handled more than 6,000 inquiries both from the general public and from professionals.

The Department prepared responses to 225 inquiries from journalists and provided a statement for TV or radio broadcasting in 86 instances. On the occasion of the appointment of the new Director of the Institute, a briefing with journalists and two press conferences in cooperation with the Ministry of Health of the Czech Republic took place. The first one was on specific findings from forensic audit, the other focused upon savings generated by abbreviated revisions. 16 press releases and advices were published on the website of the Institute.

In 2014, the Institute handled 73 requests for the provision of information pursuant to Act No 106/1999 Coll., on Free Access to Information, as amended.

Table 39 Number of processed inquiries from journalists and outputs in media in 2012–2014

	Responses to inquiries from journalists	Source materials and outputs for TV or radio broadcasting
2014	225	86
2013	152	60
2012	165	28

SÚKL STATE INSTITUTE FOR DRUG CONTROL

6. Financial and Material Resources of the Institute


5 ml

6.1 Income and Expenditure Account for 2014

Income

In 2014, the Institute had extra-budgetary income in the total amount of 503,744 thous. CZK. The major part of this income was generated by reimbursement for expert activities which were conducted by the Institute upon request from manufacturers, distributors, vendors, and other legal entities and natural persons. The major part of the overall volume was represented by income from applications related to marketing authorisations of medicinal products. Income from conducted expert activities is used piecemeal by the Institute in compliance with Act No 378/2007 Coll., on Pharmaceuticals, as amended, for the funding of expenditures not covered by allocated financial resources from the state budget, namely for the funding of payroll, operating and investment needs. In 2014, a total amount of 412,177 thous. CZK were used in this manner through permissible excess expenditure. Of this amount, 355,909 thous. CZK were used for non-investment expenses and 56,268 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 in the amount of 28,838 thous. CZK, revenues from fines in the amount of 4,645 thous. CZK, income from lease in the amount of 106 thous. CZK, refunds from excess advance payments made, related fully to the previous budgetary years, in the amount of 784 thous. CZK, etc. An overview of the reported budget income as of 31 December 2014 is shown in Table 42.

Expenditure

Data concerning expenditure incurred in 2014 are provided in Table 42.

Total investment expenditure amounted to 56,268 thous. CZK from extra-budgetary resources.

Operating expenditures were drawn in the total amount of 470,816 thous. CZK, of which 114,907 thous. CZK were from the state budget and 355,909 thous. CZK were utilised from extra-budgetary resources. Extra-budgetary resources included resources from abroad provided for the SCOPE project (66,950.95 CZK utilised) and ARTHIQS (137,636.80 CZK utilised).

The Institute participates in two Joint Actions within the scope of the second action programme of the Community in the area of health (2008-2013), one of them being focused upon the area of pharmacovigilance (Strengthening Collaborations for Operating Pharmacovigilance in Europe, SCOPE) and the other upon regulation of human tissues and cells (ART and HSC Improvements for Quality and Safety throughout Europe, ARTHIQS). These joint actions are co-funded by the European Commission and by the Member States; in case of SCOPE, the EC contributes to the costs of the project by 70%, in case of ARTHIQS, the EC involvement is 50%. In the SCOPE project the Institute is a so called associated partner and within the scope of Work Package 4 it cooperates in the development of procedures for adverse drug reaction reporting. The project budget covered the costs of business trips and worked days in the amount of 70%. The SCOPE project was initiated in November 2013, its anticipated duration is 36 months. The ARTHIQS project started on 1 May 2014 and will last until April 2017. The Institute is actively involved in both expert parts and, furthermore, is one of the five Work Package Leaders; specifically, it safeguards communication with the public and hand-over of information about the results of the project.

Assets

The total assets of the Institute as of 31 December 2014 amounted to 478 thous. CZK, of which fixed assets amount to 397,592 thous. CZK and current assets to 2,195,886 thous. CZK. Of the total liabilities of 2,593,478 thous. CZK, equity amounts to 2,511,138 thous. CZK and short-term and long-term liabilities to 82,340 thous. CZK. Selected types of assets and liabilities of the Institute are listed in Table 42.

Other

A total of 4,671 thous. CZK from the budget of the Institute were used for foreign business trips. In 2014, 435 foreign business trips covered by the Institute took place, of which the costs of 63 trips 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 due to membership in relevant bodies. The Institute has its members or alternates in more than 60 working groups across the EU institutions and international organisations. Other business trips were approved with regard to the priorities of the Institute, the topicality and benefits of the discussed topics for the Institute.

Auditing

In February 2014, an audit by the Revenue Authority for the Capital City of Prague initiated by the Ministry of Interior of the Czech Republic took place. The audit identified a breach of budgetary discipline pursuant to the provisions of Section 44a

Table 40 Funds and state budget

	2012	2013	2014
Average converted number of employees	318.57	341	409.44
Funds allocated from the state budget for the operation of SÚKL (in thousands CZK)	39,690	113,241	114,907
Allocation of income in the state budget (in thousands CZK)*	46,986	38,951	36,703

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

(1d), Section 44a (4c) and Section 44a (9) of Act No 218/2000 Coll., on Budgetary Rules, as amended, in the amount of 4,264 CZK, which were paid to the account of the National Fund, and a breach of budgetary discipline pursuant to the provisions of Section 44a (1a), Section 44a (4c) and Section 44a (9) of Act No 218/2000 Coll., as amended, amounting to 753 CZK, which were paid to the account of the Revenue Authority for the Capital City of Prague. Concurrently, the Institute paid a penalty of 2,214 CZK to the account of the Revenue Authority for the Capital City of Prague pursuant to the provisions of Section 44a (8 and 9) of Act No 218/2000 Coll., as amended.

In March 2014, a report from an audit of the Ministry of Interior of the Czech Republic regarding project "Increasing the effectiveness of administrative operation of the State Institute for Drug Control" (project no. CZ.1.04/4.1.00/59.00009) was submitted. The audit revealed extension of average monthly costs determined by the budget by 542.80 CZK, breach of Act No 137/2006 Coll. by concluding amendment 1 to Contract No 78/2011 with suspected discrepancy amounting to 5,473,161.60 CZK and failure to observe the conditions of delivery set forth by a contract with vendor Deloitte Advisory s. r. o.

From February till July 2014, the Ministry of Health of the Czech Republic conducted an on-site public administration inspection pursuant to Section 13 (1) of Act No 320/2001 Coll., which focused upon compliance with legal regulations, in particular Act No 137/2006 Coll., on Public Contracts, internal procedures and standards in public contract awards, small-scale contracts, and contracts awarded in negotiations procedure without publication,

Table 41 Overview of selected types of assets and liabilities of the organisation in thousands of CZK

Name of item	Past period 2013	Present period 2014
ASSETS	**2,438,099**	**2,593,478**
A. Total fixed assets	**329,728**	**397,592**
of which:		
I. Intangible fixed assets – total	92,354	159,448
II. Tangible fixed assets – total	237,374	238,144
Lots	3,984	4,619
Buildings	183,879	187,355
Separate movables and sets of movables	48,802	44,956
Small tangible fixed assets	0	0
Unfinished tangible fixed assets	709	1,214
B. Total current assets	**2,108,371**	**2,195,886**
of which:		
I. Inventory - total	52	63
II. Short-term receivables - total	9,018	2,153
III. Short-term financial assets	2,099,301	2,193,670
LIABILITIES	**2,438,099**	**2,593,478**
C. Equity	**2,410,495**	**2,511,138**
of which:		
I. Assets of the accounting entity and adjustments	219,915	226,709
II. Financial and monetary funds – total	2,073,281	2,165,082
Fund for cultural and social needs	1,194	1,586
Reserve fund	2,072,087	2,163,496
III. Economic result	196,937	-272,933
IV. Income and expenditure account of the budget management	314,236	392,280
D. Total borrowed capital	**27,604**	**82,340**
of which:		
I. Total long-term liabilities	20	20
II. Total short-term liabilities	27,584	82,320

the sphere of inventory and procurement of assets in 2013, transportation, and contractual relationships in the provision of legal services. The summary of results of the inspection included findings from the area of public contracts, transportation, and asset procurement, in respect of which corrective actions were adopted through Director's Order No 581/2014.

In May 2014, an audit of the Ministry of Labour and Social Affairs pursuant to Section 8a of Act No 320/2001 Coll. and Art. 13 of Commission Regulation No 1828/2006 focused upon compliance with the legal act of provision of support, implementation of key activities of the project, fulfilment of project indicators, and a review of project documentation adequacy. The audit revealed an error in claiming personal expenditures of the members of the implementing team in relation to the utilisation of annual leave in 2011 and a suspected breach of Act No 137/2006 Coll. in tender "Process-effectiveness measuring system".

In June 2014, audit by the Revenue Authority for the Capital City of Prague, regional workplace for Prague 1, which focused upon the control of administrative fee administration, was performed. The audit conclusion declared that no shortcomings had been identified and that administrative fees had been collected in compliance with the tariff of Act No 634/2004 Coll., on Administrative Fees.

The Institute paid a fine to the state budget in the total amount of 272,074 CZK, collected through the Labour Office, for breach of the obligation to employ medically handicapped individuals pursuant to Section 81 of Act No 435/2004 Coll., on Employment.

Table 42 Budget income, budget expenditure and financing in thousands of CZK

BUDGET INCOME	Budget for 2014	Real values for 2014	
	Approved budget	Corrected budget	Real values for 2014
Administrative fees	9,000	9,000	28,838
Penalties received	1,000	1,000	4,645
Income from property lease	0	0	106
Non-equity contributions received	0	0	784
Transfers from reserve fund	0	0	412,336
Transfers from other own funds	0	0	680
Operating transfers from the National Fund	0		1,650
TOTAL	**10,000**	**10,000**	**449,039**
EXPENDITURE	**Budget for 2014**	**Real values for 2014**	
	Approved budget	Final budget	Real values in 2014
Employees´ salaries	80,186	221,070	221,069
Other payments for performed work and severance pay	3,330	9,591	9,590
Mandatory premium paid by employer	28,396	76,969	76,967
Contribution to the Fund of Social and Cultural Needs	802	2,210	2,210
Operating acquisitions and related expenditure	799	161,124	160,980
Acquisition of tangible and intangible fixed assets	0	56,278	56,268
TOTAL	**113,513**	**527,242**	**527,084**
of which: operating expenditure	113,513	470,964	470,816
capital expenditure	0	56,278	56,268

6. Financial and Material Resources of the Institute

Table 43 Operating expenditure of individual units of the Institute as of 31 December 2014 in thousands of CZK

	Operating expenditure	Dedicated expenditure
Division of Director*	138	10,734
Director's office **	26	323,788
Service Activities Branch	195	128,431
Surveillance Branch	2,395	4,066
Marketing Authorisation Branch	255	0
Price and Reimbursement Regulation Branch	173	525
Medical Device Branch	90	0
Total expenditure	3,272	467,544

** Director, Deputy Director, CAU and REG coordinator, IAK-internal audit and control, MK, MBI – information security and quality management, OSALK – Dept. of State Agency for Medical Cannabis, TIO – Press and Information Department, PRO – Department of Legal and Legislative Activities*
***Director's office, MEU – manager for European affairs management, MEZ – Department of International Affairs, PVO – Personnel and Education Department*

Table 44 Expenditure statistics in the period 2012–2014

	2012	2013	2014
Total operating expenditure (in thousands of CZK)	346,209	426,815	470,816
Non-investment expenditure (excluding salaries, insurance and fund for cultural and social needs) (in thousands of CZK)	116,869	144,867	160,980
Investment expenditure (in thousands of CZK)	62,629	12,236	56,268
Average converted number of employees	318.57	341	409.44
Expenses per employee (line 1/line 4) in CZK	1,087	1,252	1,150

SÚKL STATE INSTITUTE FOR DRUG CONTROL

7. Focus upon Employees


WHN10X/22
WHN10X/

7.1 Personnel Issues

During 2014, there were several personnel and organisational changes and a new organisational structure was implemented.

In the course of 2014, in relation to the updated organisational structure and in relation to the tasks of the Institute implied by its statutory duties, the Ministry of Health of the Czech Republic approved an increase of the personnel plan by the total of 47.25 FTE to the total of 468 FTEs.

This planned number of FTEs was met at 91.14% which means that 426 FTEs were occupied. The average number of used FTEs on a cumulative basis from the beginning of the year was 409.435 FTEs.

The number of physical employees on payroll as of 31 December 2014 was 444 persons, of which 346 were women (i.e. 77.93%) and 98 men (i.e. 22.07%).

Converted to FTEs worked under non-employment agreements (work agreement and agreement to perform work), a total of 25.2 employees were employed as of 31 December 2014, which is a decrease by 11.3 % compared to 2013.

Age structure of employees

The average age of all employees compared to 2013 decreased by 0.3%, i.e. to 40.78 years of age.

Working Hours Utilisation

Of the total number of 875,791.4 hours worked, 1,600.49 were overtime hours. Overtime work mostly concerned employees from the workers category (drivers).

In 2014, the employees of the Institute were absent for 1,957.5 working days due to sickness leave or nursing a family member (1,211 working days in 2013). Of the total number of employees, absence due to sickness or nursing a family member was observed in case of 151 employees (136 employees in 2013). Absence due to long-term illness concerned: 101 employees (133 employees in 2013), who were absent for up to 2 months; 3 employees (2 employees in 2013), who were absent for up to 3 months; and 5 employees (1 employee in 2013), who were absent for more than 3 months.

Staff Turnover

In 2014, 115 new employees started their jobs in SÚKL (103 in 2013). Employment of 69 employees was terminated (44 in 2013).

Staff turnover is 16.19% (representing a 3.28% increase compared to the previous year).

7.2 Employee Education

Like in the previous years, in the area of employee education emphasis was placed especially on professional and international

Table 45 Age structure of employees in %

YEAR	Employees under 35 years	Employees aged 36 to 55 years	Employees over 55 years
2012	35.7	47.5	16.8
2013	41.2	43.6	15.2
2014	42.3	42.3	15.4

Table 46 Qualification structure of employees by achieved level of education

Primary	Secondary technical	Secondary general	Secondary technical with GCE	Technical colleges	Bachelor's degree	University	University doctorates
2012							
1	3	10	86	4	15	208	12
0.3 %	0.88 %	2.95 %	25.37 %	1.18 %	4.42 %	61.36 %	3.54 %
2013							
1	5	12	86	3	16	264	14
0.25 %	1.25 %	2.99 %	21.45 %	0.75 %	3.99 %	65.83 %	3.49 %
2014							
1	7	8	88	5	19	304	12
0.22 %	1.58 %	1.80 %	19.82 %	1.13 %	4.28 %	68.47 %	2.70 %

education. The total amount of funds spent on education amounted to 4,747,338 CZK. Of this sum, the amount of 1,827,189 CZK was used for professional education, and the amount of 2,138,473 CZK for international education. Due to higher demands on the qualification of the employees and the growing number of employees, the amount spent on education increased by 32.7% compared to 2013.

International education contributes to increasing the qualification and to obtaining the necessary knowledge which may only be learnt abroad. Concurrently, it provides the employees of the Institute with a competitive advantage in the labour market and they become valued workforce for the employer contributing to the enhancement of competitiveness.

Language education helps to maintain and deepen the level of language skills necessary for the everyday work of most employees of the Institute.

Table 47 Overview of employments terminated in 2014 by reason

Reason for termination of employment	In probationary period	Definite-time employment contract expiry	Termination by agreement	Notices given by employees	Termination due to organisational reasons	TOTAL
Number	11	11	17	10	20	69

Table 48 Overview of educational activities in 2014

Type of event	Number of events	Number of hours	Number of attendees	Costs (CZK)
PC training	11	558	42	121,977
Language courses	33	2,015	143	600,579
Specialised courses and training	221	5,350	425	1,827,189
Managerial skills	–	–	–	–
Mandatory training	63	135	82	59,120
Foreign specialised training	46	1,872	74	2,138,473
TOTAL	**374**	**9,930**	**766**	**4,747,338**

SÚKL STATE INSTITUTE FOR DRUG CONTROL

8. Focus upon Quality

The Institute has an established quality management system in compliance with the requirements of the ČSN EN ISO 9001:2008 standards and in 2014 successfully completed a re-certification audit. The functionality of the quality system was regularly checked within the scope of internal audits, in which the Institute's internal auditors were involved.

The Institute also participates in the benchmarking programme of EU drug authorities and in the last year, assessment conducted via benchmarking was completed.

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9. Information Security Management Policy

The Institute strives to maintain security and plausibility of data and information in its information systems and in handling of information. In 2007, the Institute introduced an information security management system (ISMS) and this system and its processes were certified pursuant to the ISO 27001 standard. The Institute continues to comply with and enhance the policy, processes and technical measures for the fulfilment of requirements set forth by the aforementioned standard. In April 2014, the Institute completed another successful re-certification of the ISMS system.

In the second half of the year, the Institute focused also upon the integration of new legislative requirements implied by Act No 181/2014 on Cybernetic Security, into its processes and systems and it is possible to state that the Institute is completely prepared for the coming into force of the Act and the implementing decrees.

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10. Director's Outlook for 2015

Like in the previous years, availability of quality, effective and safe medicinal products is considered the highest priority of the Institute. All activities of the Institute will focus upon the fulfilment of obligations set forth by law in a manner ensuring maximum safety of Czech patients.

Areas where the Institute will operate newly or within an extended scope of powers include, in particular, the area of medical devices. Equal attention will be paid by the Institute to the sphere of medical cannabis. In the course of 2015, a tender for a grower of medical cannabis to be made available to Czech patients will be completed.

Within the scope of price and reimbursement regulation, the Institute will fulfil obligations implied by the law in a manner allowing for the generation of further savings in the public health insurance system. These funds may then be utilised e.g. to cover the high costs of treatment of very severe or rare diseases.

The Institute will continue its intensive cooperation with the Ministry of Health of the Czech Republic. In 2015, cooperation is to focus particularly upon the topic of re-export of pharmaceuticals, which significantly disrupts the Czech medicines market, and upon the amendment to the Act on Pharmaceuticals.

The plan of activities for 2015 includes also development of cooperation and communication with professionals as well as patients. For the general lay public, an information campaign "Medicines Don't Belong in Your Bin", has been prepared; the objective of the campaign is to inform and educate Czech households in issues of handling of medicines, their proper storage and disposal. Another important topic represents illegal and counterfeit products against which the Institute warns the public.

For professionals, the Institute has prepared a number of specialised workshops, such as workshops on the amendment to the Act on Medical Devices or workshops for manufacturers of pharmaceuticals.

Professional entities as well as the patients will be able to obtain the information from several websites administered and regularly updated by the Institute.

I believe that the Institute will manage to accomplish all tasks it faces in 2015. I will strive for the Institute to maintain its image of a respected, highly professional and independent medicines agency.

Zdeněk Blahuta
Director

SÚKL STÁTNÍ ÚSTAV PRO KONTROLU LÉČIV

11. Overview of Essential Contacts for Individual Spheres of Operation of the Institute

11. Overview of Essential Contacts for Individual Spheres of Operation of the Institute

Updated as of 1 May 2015. A detailed updated overview of contacts is available from the website of the Institute; the heads of individual units are specified in the organisational structure of the Institute.

	Prefix	Extension	E-mail
Director of the Institute			
Zdeněk Blahuta	272 185	199	zdenek.blahuta@sukl.cz
Deputy Director			
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Mail and dispatch room	272 185	806 789	posta@sukl.cz
	fax: 271 732	377	
Head of Director's Office			
David Přinesdom	272 185	354	david.prinesdom@sukl.cz
Quality Manager			
Radmila Foretová	272 185	861	radmila.foretova@sukl.cz
Internal Audit and Control			
Kamila Hrušková	272 185	225	kamila.hruskova@sukl.cz
State Agency for Medical Cannabis			
Marcela Škrabalová	272 185	856	marcela.skrabalova@sukl.cz
Press and Information Dept.			
Head of Department and Public Relations Officer			
Lucie Šustková	272 185	756	lucie.sustkova@sukl.cz
Information Centre	272 185	333	infs@sukl.cz
SERVICE ACTIVITIES BRANCH			
Head of Branch			
Vilibald Knob	272 185	873	vilibald.knob@sukl.cz
Economic Division			
Head of Division			
Jana Přerovská	272 185	810	jana.prerovska@sukl.cz
Operations Division			
Head of Division			
Tereza Kotherová	272 185	808	tereza.kotherova@sukl.cz
Information Technology Division			
Head of Division			
Petr Koucký	272 185	898	petr.koucky@sukl.cz
SURVEILLANCE BRANCH			
Head of Branch			
Apolena Jonášová	272 185	706	apolena.jonasova@sukl.cz
MARKETING AUTHORISATION BRANCH			
Head of Branch			
Jana Mladá	272 185	729	jana.mlada@sukl.cz
PRICE AND REIMBURSEMENT REGULATION BRANCH			
Head of Branch			
Helena Skácelová	272 185	403	helena.skacelova@sukl.cz
MEDICAL DEVICE BRANCH			
Head of Branch			
Jakub Machálek	272 185	260	jakub.machalek@sukl.cz

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