SÚKL

STATE INSTITUTE FOR DRUG CONTROL, CZECH REPUBLIC

ANNUAL REPORT 2012

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In 2012, the Institute cooperated with the Ministry of Health, particularly when implementing the tasks performed within the scope of cooperation with the European Union in the field of pharmaceuticals and medical devices, and took part in the preparation and subsequent legislative process of adoption of new legal regulations with significant impact on the scope of the Institute's operation. The legislative process involved primarily the transposition of the European Directive regulating pharmacovigilance and the Directive concerning the prevention of the entry into the legal supply chain of falsified medicinal products. The cooperation in the preparation of a new act regulating the sphere of medical devices made a significant progress at the end of the year.

As in the previous years, the number of received and dispatched documents increased in 2012 and the gradual switch to electronic processing of the Institute's tasks continued.

In the Marketing Authorisation Branch, 622 applications for a new authorisation were successfully validated and forwarded for assessment. Most of them were applications for a marketing authorisation via the Mutual Recognition Procedure or Decentralised Procedure, which confirms the trend from the previous years when the amount of applications for authorisation via the national procedure has been decreasing.

In 2012, the Institute was again involved in the voluntary harmonisation process of joint assessment of clinical trial documentation (Voluntary Harmonisation Procedure, VHP) managed by the EMA working group. The number of assessed applications increased by 43% compared to 2011.

In the Surveillance Branch, the Institute performed all activities related to pharmaceuticals quality control as required by the applicable legislation. The Laboratory Control Section controlled the quality of pharmaceuticals in circulation as per projects prepared in advance and released batches of defined medicinal products and dealt with the solving of quality defects of medicinal products, suspected counterfeit products and illegal pharmaceuticals and adverse reactions. The Institute continued its cooperation with the Official Medicine Control Laboratories network in joint quality control studies. The Laboratory Control Section uses a quality management system in accordance with ČSN EN ISO/IEC 17025. In 2012, a regular check of the implemented quality management system was performed by a group of auditors of the European Directorate for the Quality of Medicines (EDQM).

Based on the facts ascertained during these inspections, the Pharmacy and Distribution Section proposed a fine in 95 cases and issued 4 proposals for commencement of administrative proceedings in relation to fine imposition due to a breach of duties stipulated by the Act on Pharmaceuticals. 282 inspections focused on handling medicinal products in healthcare establishments were carried out.

The Inspections Section performed 288 inspections as part of its surveillance activities in the area of medicinal products manufacturing, of which 102 inspections concerned regulation of tissues and cells. The number of reports received concerning quality defects of pharmaceuticals has been increasing since 2009.

In 2012, active surveillance in the area of illegal handling of medicinal products was focused, in particular, upon the identification, investigation, and penalisation of the cases of distribution and sales by unauthorised persons and upon monitoring of the internet, where illegal sale of medicinal products takes place.

In the area of surveillance over advertising, 11 administrative procedures were finalized in 2012, which resulted in the imposition of fines in the total amount of CZK 2,645,000.

The employees of the Price and Reimbursement Regulation Branch continued to determine maximum prices and amounts and conditions of reimbursements from health insurance in compliance with the internal methodology drafted pursuant to the Act on Public Health Insurance. All procedures aiming at a reduction of the maximum price of medicinal products exceeding the limits stipulated in the amendment to the Act on Public Health Insurance were completed and came into force or are provisionally enforceable. In 2012, 170 appeals were filed against review administrative procedures concerning the amount and conditions of reimbursement finalized in 2011 and 25 administrative procedures were returned for re-assessment. The savings obtained through the revision of the system of reimbursements from the public health insurance funds in 2012 were 1.8 billion CZK.

As in the previous years, the Institute published data about authorised medicinal products, approved specific therapeutic programmes and foods for special medical purposes within the scope of the database of authorised medicinal products to satisfy the needs of professionals and the general public. Since 2008, the Institute has been publishing the List of reimbursed medicinal products and foods for special medical purposes, including its updates, on its website. The Institute publishes quarterly evaluation of supplies of distributed products based on the mandatory reports of the entities authorised to distribute medicinal products in the territory of the Czech Republic.

In the middle of the year, the Institute released a book by Tomáš Cikrt titled Příběhy léků (Stories of Medicines), which is available on the public information portal in various formats – dynamic PDF, the format for e-book readers and tablets and as audio book. The book was presented at a press conference held in cooperation with the Ministry of Health.

In 2012, the Press and Information Department prepared and carried out the regular survey "Issues of Pharmaceutical

1. Director's introduction

Policy", which was this year supplemented with another survey titled "Actual Use of Pharmaceuticals and the Impact on Czech Healthcare System", which is unique in its scope as it processed data from pharmacies, regions and 2000 households from the entire Czech Republic. The survey addressed the question how people dispose of unused pharmaceuticals and what financial losses it means for the Czech healthcare system.

MUDr. Pavel Březovský, MBA
Director of the Institute

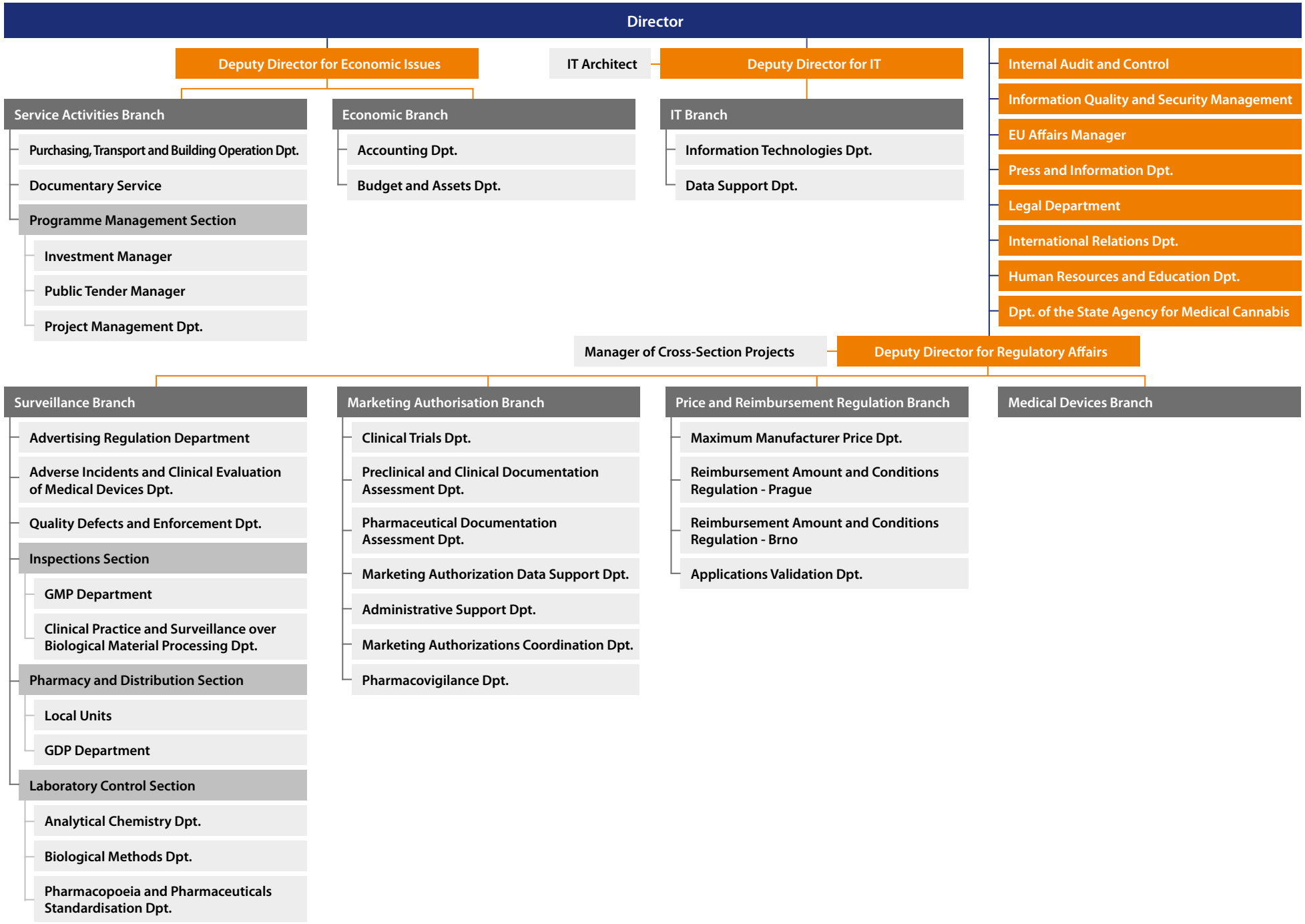
In the course of 2012, the Director's Office was closed down and the Legal Department, International Relations Department and Department of Human Resources and Education will now respond directly to the Institute's Director. As from 1 January 2013, the EU Affairs Manager and the Department of the State Agency for Medical Cannabis also respond directly to the Institute's Director. Project Management was transferred from the Director's Office to the Service Activities Branch.

The Division of the Deputy Director for IT and Economic Issues was divided, giving place to the Division of the Deputy Director for Economic Issues, which comprises the Service Activities Branch and Economic Branch, and to the Division of the Deputy Director for IT, which comprises the IT Branch and the new position of IT Architect. The Validation Department was transferred from the IT Branch partly to the Price and Reimbursement Regulation Branch and partly to the Marketing Authorisation Branch. A new Programme Management Section was created in the Service Activities Branch, which includes the new positions of Investment Manager and Manager for Public Tenders.

The Division of the Deputy Director for Regulatory Affairs includes the Surveillance Branch, Marketing Authorisation Branch, Price and Reimbursement Regulation Branch and newly also the Medical Devices Branch. The Consumer Protection Branch was closed down. The Quality Defects and Enforcement Department, the Advertising Regulation Department and the Adverse Incidents and Clinical Evaluation of Medical Devices Department were transferred back to the Surveillance Branch, the Pharmacovigilance Department now belongs to the Marketing Authorisation Branch. A new Department of Applications Validation was created in the Price and Reimbursement Regulation Branch and the Department of Statistics and Analyses was renamed to Reimbursement Amount and Conditions Department – Brno.

The position of the Regulatory and EU Procedures Manager in the Division of the Deputy Director for Regulatory Affairs was cancelled and the position of the Manager of Cross-Section Projects was created.

The Organisational structure of SÚKL effective as of January 01 2013 forms part of this Report (p. 10). The Organisational structure indicating the names of managerial staff is provided on the website of the Institute.


Director
Deputy Director for Economic Issues
IT Architect
Deputy Director for IT
Internal Audit and Control
Information Quality and Security Management
EU Affairs Manager
Press and Information Dpt.
Legal Department
International Relations Dpt.
Human Resources and Education Dpt.
Dpt. of the State Agency for Medical Cannabis
Service Activities Branch
Purchasing, Transport and Building Operation Dpt.
Documentary Service
Programme Management Section
Investment Manager
Public Tender Manager
Project Management Dpt.
Economic Branch
Accounting Dpt.
Budget and Assets Dpt.
IT Branch
Information Technologies Dpt.
Data Support Dpt.
Manager of Cross-Section Projects
Deputy Director for Regulatory Affairs
Surveillance Branch
Advertising Regulation Department
Adverse Incidents and Clinical Evaluation of Medical Devices Dpt.
Quality Defects and Enforcement Dpt.
Inspections Section
GMP Department
Clinical Practice and Surveillance over Biological Material Processing Dpt.
Pharmacy and Distribution Section
Local Units
GDP Department
Laboratory Control Section
Analytical Chemistry Dpt.
Biological Methods Dpt.
Pharmacopoeia and Pharmaceuticals Standardisation Dpt.
Marketing Authorisation Branch
Clinical Trials Dpt.
Preclinical and Clinical Documentation Assessment Dpt.
Pharmaceutical Documentation Assessment Dpt.
Marketing Authorization Data Support Dpt.
Administrative Support Dpt.
Marketing Authorizations Coordination Dpt.
Pharmacovigilance Dpt.
Price and Reimbursement Regulation Branch
Maximum Manufacturer Price Dpt.
Reimbursement Amount and Conditions Regulation - Prague
Reimbursement Amount and Conditions Regulation - Brno
Applications Validation Dpt.
Medical Devices Branch

3.1 Cooperation with the Ministry of Health and other state institutions in the Czech Republic

In 2012, the Institute 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 on the scope of operation of the Institute.

A close cooperation continued in the legislative process concerning the transposition of Directive 2010/84/EU and Directive 2012/26/EU, both these directives amending Directive 2001/83/EU as regards pharmacovigilance. The Institute also participated in the transposition of Directive 2011/62/EU, which amends the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products. The Institute also cooperated with the Ministry of Health in the legislative work on the Parliament's draft amendments to the Act on Pharmaceuticals and Act on Dependence-Producing Substances, which will permit the use of cannabis for medicinal purposes. These amendments will significantly influence the scope of the Institute's competence.

The work on amendments to the Act on Pharmaceuticals also involved the preparation of amendments to the implementing regulations, namely amendment to Decree No. 228/2008 Sb., Decree No. 54/2008 Sb., and Decree No. 84/2008 Sb.

Other legislative work was related to the draft amendment to the Act on Advertising Regulation. This draft amendment is currently being discussed by the Chamber of Deputies of the Parliament.

At the end of the year, progress was made in the cooperation in the preparation of a new act regulating the area of medical devices. The preparation phase should result in the submission of a draft of the new Act to the Government's Legislative Board followed by further legislative process.

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

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 informed the public about the guidance 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 continued in the preparation of opinions of the Czech Republic on preliminary questions raised by the European Court of Justice regarding the sphere of competence of the Institute.

Cooperation with the Institute for the State Control of Veterinary Biologicals and Medicaments in Brno and with the State Office for Nuclear Safety continued also in 2012. 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 in the preparation of standards governing the area of medical devices with the Czech Office for Standards, Metrology, and Testing was going on.

3.2 Cooperation with EU institutions and other foreign partners

The Institute is actively involved in more than 70 working groups and committees. These concern the working groups of the EU Council, European Commission and its agency – the European Medicines Agency (EMA), but also the bodies of the World Health Organisation, Council of Europe and its European Directorate for the Quality of Medicines and Healthcare (EDQM), and the Organisation for Economic Cooperation and Development. Last but not least, the Institute also participates in informal groups of experts from various countries specialized in the sphere of pharmaceuticals, medical devices or tissues and cells. The Institute also actively participates in the cooperation within the network of the Heads of Medicines Agencies, which is one of informal groups with voluntary participation.

The constant priorities of the Institute include, in particular, its representation in the EMA scientific committees. At the EU level, the Institute participates in the discussions of the review of the legal regulations governing clinical trials and medical devices.

The Institute's employees went for 335 international business trips to 40 countries in 2012. Out of these business trips, 109 were fully reimbursed, 48 partially reimbursed, and 178 fully financed by the Institute. The Institute also participates in the organisation of international activities. In 2012 two international events were held in Prague. On 19 and 20 April 2012, the Institute organised the EU Assessors Training on Efficient and Effective Quality Assessment 2012, and on 29 and 30 November 2012, the Clinical Trial Quality Assessors Meeting was held.

3.3 Projects

In 2012, two projects co-financed by the European Social Funds within the framework of the Human Resources and Employment Operational Programme (HREOP) were carried through to the implementation phase. The HREOP is focused on minimizing unemployment by means of active policy on the labour market,

3. Involvement in the national, EU and other international institutions network

professional education, reintegration of socially excluded citizens into society, improvement of public administration quality and international cooperation in the said areas. Both projects focus on increasing the effectiveness of the Institute's operation and extending staff qualifications. Their essential aim is to enhance the effectiveness of the administrative tasks which the Institute is obliged to fulfil under the law, and, at the same time, to contribute to increasing the effectiveness of work processes and achieving of objectives.

The first project, entitled "Increasing the Effectiveness of the Administrative Agenda of the State Institute for Drug Control" registration number CZ1.04/4.1.00/59.00009, launched on April 01 2011, aims at fulfilling two basic objectives: elaborate and implement a unified concept of computerisation of the administrative agenda and to introduce effective project management in the Institute. The implementation of the project's results will increase the effectiveness of the Institute's performance, ensure greater transparency of individual administrative tasks and cut the red tape for regulated entities. A positive impact will also reflect itself in the development of the employees' knowledge, primarily in the area of information systems architecture and project management. The innovative influence of the project will contribute to reducing the administrative load and to the effective development of information and communication technologies of the Institute.

In 2012, both projects continued after their analytical phase. Within the project phase focused on the implementation of the project management in the Institute, the contractor's works were carried out in cooperation with the Institute's employees consisting in defining project management with respect to the organisational structure and nature of the projects implemented by the Institute. The outcome is a project management methodology based on the principles of internationally recognized methodologies. In the outcome of the Computerisation of Administrative Agenda the contractor created analyses for tasks defined by the Institute that are being introduced or have been introduced already but require further development in order to increase user comfort.

Given the possibility to use up the funds that were allocated to the Institute based on the application for co-financing, the Institute decided to further expand the project. The expansion consisted in the analysis and optimization of the Institute's support processes and creation of a strategy to reduce the workload related to regulatory affairs in relation to the computerization of the area of healthcare. In both cases, the project was delivered by contractors and the outcomes are strategic documents.

The other project co-financed by the European Structural Funds was the "System for Measuring Process Effectiveness" registration number CZ.1.04/4.1.00/59.00023, launched on May 01 2011. Its main aim was the creation and step-by step implementation of the system for measuring the efficiency of the Institute's processes.

Under the guidance of the sponsor, the real situation in SÚKL was analysed. Subsequently, the efficiency measuring system was piloted in two selected departments. The pilot operation and the organisational changes that are under way showed that the timing of the project is not appropriate and therefore the Institute's management decided to terminate the project. Despite of this early termination, a methodology for an efficiency measuring system was created and the Institute received a software tool to be used for this purpose.

At the same time, a Steering and Monitoring Committee was created in the Institute (based on the Institute's new Guideline), introducing standard project management procedures in the project portfolio. The Committee is composed of competent managers of the Institute and meets once a month. Its main task is systematic management of selected projects (including projects funded from structural funds), their monitoring and inspection in terms of adherence to the time schedule, use of funds and achievement of the required quality of project outcomes (including monitoring and management in the sustainability period).

4.1 Office work in total

In 2012, the electronic record system of the Institute registered 61,868 delivered documents and 57,607 sent documents (see Table 1). The priority of official document delivery is delivery to data mailboxes; the Institute has been gradually moving towards the electronic processing of individual areas of its office work (see Table 2).

MARKETING AUTHORISATION BRANCH

Each proprietary medicinal product is subject to a marketing authorisation prior to placing on the Czech market. Within the scope of the marketing authorisation procedure, the Marketing Authorisation Branch assesses dossiers, in which the future marketing authorisation holder evidences the safety, efficacy and quality of the product. Indications, contraindications, product posology, classification for supply, as well as package leaflets for patients and proposed labelling of the medicinal product are also subject to assessment. The marketing authorisation includes both the package leaflet and the summary of the product characteristics, which serves doctors and healthcare professionals as a key source of information about the medicinal product.

The Institute issues its opinions/decisions where doubts arise as to whether a product is a medicinal product subject to marketing authorisation or an active substance or another product or a homeopathic product, where applicable, either upon request or on its own initiative. SÚKL's decision is essential for the regulatory regimen of the assessed product and for the subsequent process the applicant has to employ prior to the placement of the product on the Czech market.

Moreover, the Institute issues opinions on applications for specific therapeutic programmes for 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 under certain conditions.

Table 1. Registration of documents going through the Institute in 2010–2012

Mail room	2010	2011	2012
Received documents	57 100	59 355	61 868
Dispatch room	**2010**	**2011**	**2012**
Sent documents	47 726	46 840	57 607

Table 2. Overview of communication channels in 2012

YEAR 2012	Mail room, dispatch room	Data messages	E-mail messages	Electronic notice board	Total
Received documents	48 734	5 678	7 456	–	61 868
Sent documents	14 131	35 826	1 516	6 134	57 607

Table 3. Marketing authorisation applications

	Forwarded in 2012	Decided in total in 2012	Pending applications as of 31/12/2012
Applications for marketing authorisation	622	911	871
of which national	43	53	96
of which MRP RMS	23	15	29
of which DCP RMS	41	46	59
of which CMS (MRP and DCP)	538	811	716
Switch from national to the MRP/DCP	0	0	3
Renewals of marketing authorisation	1 320	837	2 370
of which national	799	449	1 687
of which RMS	49	37	37
of which CMS	472	362	646
National variations to marketing authorisation	5 695	5 666	1 300
of which IA	2 331	2 382	52
of which IB	1 278	1 312	124
of which II	1 735	1 543	1 089
of which PI and labelling	351	429	35
MRP variations to marketing authorisation	4 842	5 613	2 252
of which IA	16	50	31
of which IB	161	236	31
of which II	46	272	54
of which PI and labelling	156	151	40
of which bulk MRP variations to marketing authorisation	4 463	4 904	2 096
MA revocations	690	660	6
Parallel import	34	54	23
Variation to parallel import	28	29	0

The table does not reflect the numbers of pending applications from the previous period.
Explanatory notes: RMS – Reference Member State, CMS – Concerned Member State, MRP – marketing authorisation via mutual recognition procedure, DCP marketing authorisation via decentralised procedure

Table 4. Applications for exemption from the sunset clause

	Procedures conducted in 2012
Administrative proceedings on granting an exemption from the sunset clause	104
▪ of which initiated based on an application	93
▪ of which ex officio initiated administrative procedures	11
granted	41
declined	34
rejected as undue	12
stopped for failure to supplement	17

The Department of Clinical Trials assesses applications for authorisation/notifications of clinical trials, performs surveillance over the conduct of clinical trials, issues opinions for project assessment when trials are not regulated by the Institute, and maintains records on use of non-authorised medicinal products.

From 2012, the Pharmacovigilance Department forms part of the Marketing Authorisation Branch, which is responsible for the surveillance over the risks related to the administration of medicinal products. This surveillance includes particularly the collection and evaluation of information from the reports on suspected adverse effects reported by healthcare professionals and patients as well as information obtained in non-interventional post-marketing studies.

4.2 Marketing authorisation of medicinal products

Applications for new marketing authorisation

In September 2012, the Applications Validation Department was transferred to this Branch. A total of 622 applications were submitted for assessment after successful validation. The applications for marketing authorisation via the Mutual Recognition Procedure (MRP) and Decentralised Procedure (DCP) represented a major proportion, which confirms the trend from the previous year – the number of applications for marketing authorisations via national procedure has been gradually decreasing.

In the area of DCP procedures there is a key number of applications where the Czech Republic is involved as the Reference Member State. In 2012, 64 applications were filed for the conduction of MRP/DCP with the Czech Republic as the Reference Member State.

Variations to marketing authorisation

In this year, the total number of received applications for variations to marketing authorisations increased once more, both in MRP variations and national variations.

Parallel import

In 2012, 54 parallel imports were authorised.

Revocation of marketing authorisation

In 2012, 690 applications for revocation of marketing authorisation were decided.

Expiry / non-expiry of marketing authorisations

In 2012, the Institute held 104 administrative proceedings on granting of exemptions from the sunset clause.

The Institute received 9 repeals from the issued decisions – 1 was addressed by error coramnobis, in 4 cases the Institute's decision was confirmed, in 3 cases the Institute's decision was revoked (the exemption was granted), none repeal was submitted late, 1 is still pending.

During the year 2012, in 197 marketing authorisation numbers the sunset clause was applied under Section 34, paragraph 3 of the Act on Pharmaceuticals, and the

Table 5. Applications for distinguishing borderline products submitted by legal and natural persons in addition to state administration bodies

Pending from the previous period	Applications received in 2012	Number of issued decisions	Number of issued opinions	Of which number of rejections	Of which suspended/ withdrawn	Brought forward to the next year
7	18	13	5	0	2	5

marketing authorisation of these medicinal products expired.

4.3 Borderline products assessment, use of non-authorised products, issuance of opinions on specific therapeutic programmes

The assessment of borderline products and issuance of decisions and opinions on product classification were carried out under similar conditions as in 2011. The number of applications for assessment in 2012 was slightly higher than in the previous year (13 applications were received in 2011). For state administration bodies the Institute issued opinions on 7 products in total. Furthermore, the Institute dealt with reports from natural or legal persons for 93 products, potentially illegally marketed in respect of regulation set forth by the Act on Pharmaceuticals.

Out of the 13 decisions and 5 opinions issued, in 5 cases the Institute classified the products as medicinal products, in 13 cases the products were not classified as medicinal products. Three repeals from the decisions issued upon request were filed, in 2 cases the Czech Ministry of Health confirmed the Institute's decision. Furthermore, consultations on 3 products were carried out in the sphere of borderline products.

4.4 Clinical trials on pharmaceuticals

In 2012, the Institute continued 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 scope of VHP, 43 clinical trials were submitted and assessed in the Czech Republic in this year, which is 43% more than in 2011, when 30 applications were

Table 6. Clinical trials (CT)

	Pending from the previous period	Applications received in 2012	Number of decisions issued in 2012	Of which number of rejections	Of which withdrawn
Application for CT authorisation	17	100	104	–	4
CT notification	74	314	287	–	30
Notification of CT amendment	–	2 052	2 458	–	–

Fig. 1. Number of applications assessed in 2012 by clinical trial phase

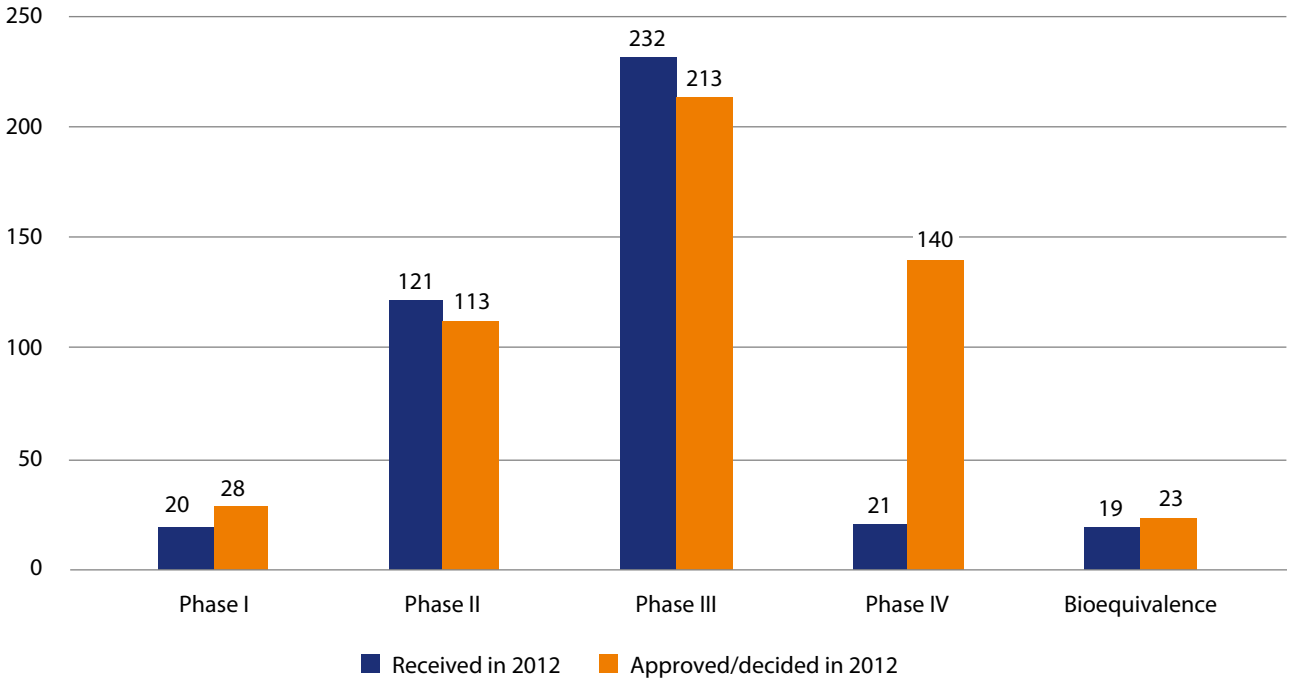


Table 7. Therapeutic areas of clinical trials assessed in 2012

Therapeutic area	No.
Oncology	92
Respiratory + Allergology	17
Healthy volunters	33
Neurology	32
Cardiovascular system	27
Reumatology	376
Other	18
Psychiatry	13
Diabetology	23
Infectious	6
Urogenital disease	13
Gastrointestinal disease	21
Hematology	7
Methabolism disorders + Endocrinology	1
Dermatology	11
Transplantation	1
Ophtalmology	8
Gynecology	7
Otolaryngology	4
Anaesthesiology and Resuscitation	0
Pain	13
Examination procedures	1
Internal medicine	6

filed within this process. The Institute has never refused to participate in the VHP procedure so far; we will keep trying to participate in all joint assessments which include the Czech Republic, however, due to the capacity of our staff, we do not participate as a Reference Member State.

The total number of applications for authorisation/ /notifications of clinical trials submitted in 2012 slightly increased in comparison with the previous year 2011 – in total by 41 applications, which is more than 11% increase. Most of the applications are for Phase III studies: international, multicentric, randomised, blinded, placebo or active-substance controlled clinical trials conducted by foreign sponsors. Of the total number of 414 applications for authorisation/notifications of clinical trials, 14 clinical trials were submitted by non-commercial entities (academic research); 7 applications involved orphan drugs and there were 22 clinical trials that included children or that were directly designed for paediatric population.

In 2012, 11 ethics committees for multicentric clinical trials were active. Four working meetings of the representatives of the Working Group for Multicentric Ethics Committees and of the representatives of the Institute's Department of Clinical Trials took place.

In 2012, 73 applications for project (grant projects in particular) assessment were assessed to determine whether a clinical trial regulated by the Institute was concerned or not.

Specific Therapeutic Programmes

49 applications for opinion on proposed specific therapeutic programmes were submitted, which is 9 applications more than in 2011. Opinions were issued for 45 applications; 4 were pending and brought forward to the next year.

Non-authorised medicinal products

In 2012, 2,207 notifications of the use of non-authorised medicinal products were received, which is 13 % of notifications less than in 2011.

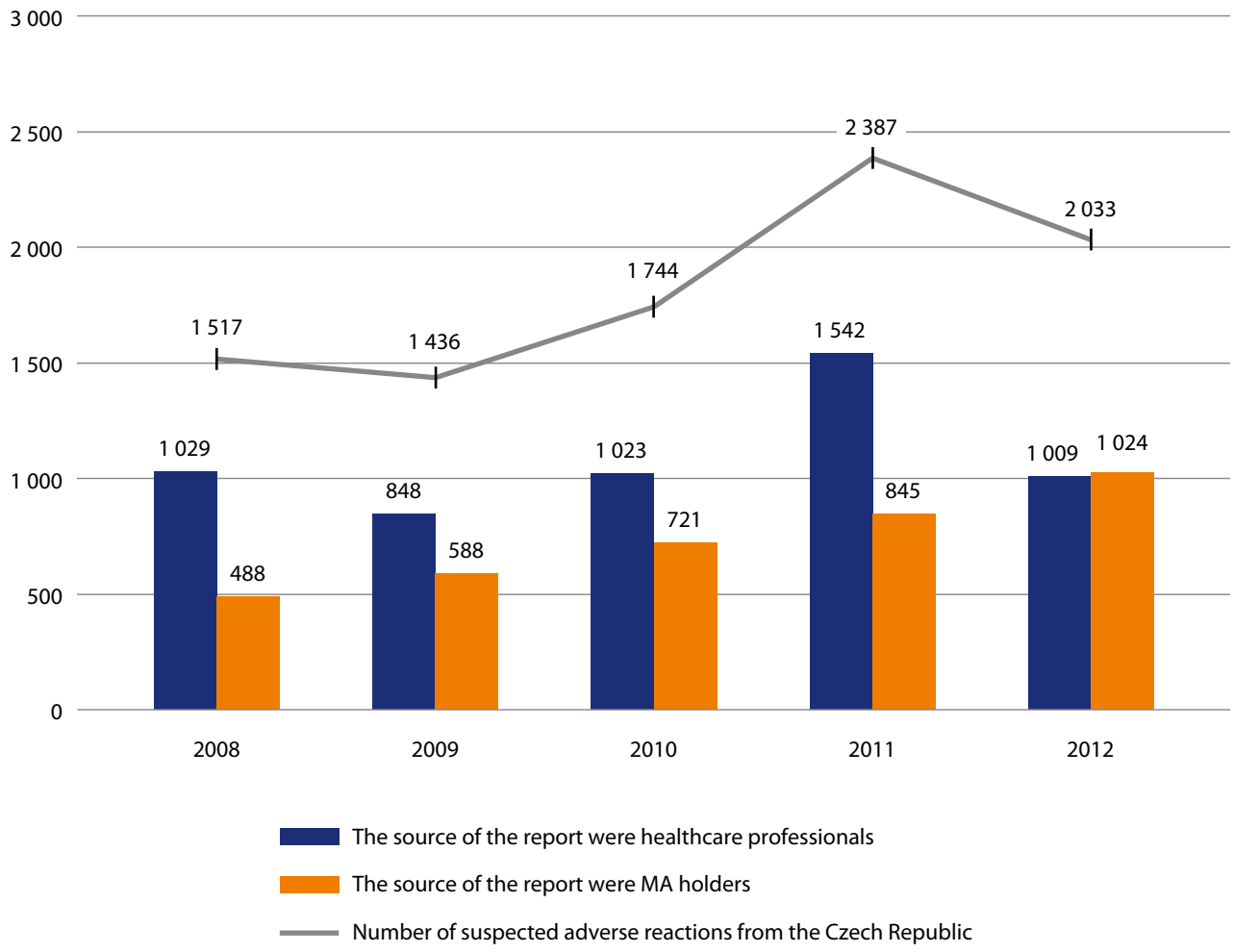
In 2012, we gave 24 consultations and issued 2 written opinions on issues covered by our department.

4.5 Pharmacovigilance

In 2012, the Institute received 2,033 primary reports of suspected adverse reactions from the Czech Republic, and 651 follow-up reports relevant thereto were made (verification or obtaining of additional information with/from the reporter).

Periodic Safety Update Reports (PSUR) for individual products were, like in the previous year, evaluated only for products where a safety risk was identified or where it was necessary to review data of the medicinal product in respect of the EU regulatory procedures or where marketing authorisation was to be renewed. In 2012, 2,405 reports were submitted. The conclusions of CHMP and of the CHMP Pharmacovigilance Working Party and the Pharmacovigilance Risk Assessment Committee (PRAC) were being transposed to the Czech clinical practice in cooperation with the Marketing Authorisation Department on an ongoing basis. 50 times the Institute published information intended for healthcare professionals or for the general public on the safety of medicinal products on its website, in Farmakoterapeutické informace (Pharmacotherapeutic Information, FI) or in other media. In cooperation with the marketing authorisation holders, the Institute published 32 letters for healthcare professionals regarding updated information on the safe use of medicinal products as well as 77 educational materials targeted at increasing the safety of the use of newly authorised medicinal products in particular.

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



The Institute published 4 editions of the Adverse Reactions Information Bulletin which provided current information on the safe use of pharmaceuticals.

The pharmacovigilance systems of market authorisation holders were inspected 18 times.

SURVEILLANCE BRANCH

The Laboratory Control Section performs analyses of pharmaceuticals required by law (e.g. random controls of pharmaceuticals on the market, batch release), requested by other SÚKL units, or by state administration bodies and within the scope of international cooperation. Laboratories are part of the international General Network of Official Medicines Control Laboratories. Laboratories do not conduct analyses upon request from any commercial entities (except for batch release pursuant to the Act on Pharmaceuticals). The Department of Pharmacopoeia is involved in the publication of the Czech Pharmacopoeia and in the preparation of the European Pharmacopoeia.

The Section of Pharmacy and Distribution provides for the control over compliance with legislative requirements in the sphere of distribution of pharmaceuticals, focusing upon the principles of good distribution practice and issuance of authorisation of distribution activities, as well as requests for dispensing, sale and preparation of pharmaceuticals. The controlled entities are distributors, pharmacies, vendors of selected pharmaceuticals, and specialised workplaces of healthcare facilities. Controls of medicinal product handling are also performed in all healthcare facilities. The controls are performed by the relevant regional offices of SÚKL.

The Inspection section provides for surveillance activities in the sphere of manufacture of pharmaceuticals, good clinical practice and good laboratory practice, issuance of binding opinions on import and export of medicinal products, including

cooperation with customs authorities. Furthermore, the section carries out surveillance over donations, procurement, examination, processing, storing, and distribution of human tissues and cells, aimed at safeguarding their quality and safety. These activities include also the issuance of authorisation to engage in the activities of tissue centres, donation centres or diagnostic laboratories, the performance of inspections, monitoring of occurring or suspected serious adverse events and reactions, and, where doubts arise, decision-making to establish whether tissues and cells subject to regulation by the relevant law are concerned.

The Department of Quality Defects and Enforcement involves the solution of quality defects of pharmaceuticals and excipients available on the Czech market. The department is, moreover, in charge of detection and penalisation of illicit activities as well as enforcement of law in those cases where an illegal situation has been disclosed, i.e. unauthorised handling of pharmaceuticals. In the sphere of enforcement, the Institute cooperates also with other institutions both in the Czech Republic and abroad (in particular with the Czech Police, Customs Administration, CAFIA, and surveillance authorities of the EU Member States).

The performance of surveillance over compliance with the Act on Advertising Regulation in the sphere of advertising for human medicinal products and sponsoring within this sphere (except for TV and radio broadcasting) is covered by the Advertising Regulation department. It investigates reports of objectionable advertising for human medicinal products, issuance of expert opinions on advertising materials and on advertising regulation issues.

Furthermore, the Institute provides for activities which are implied by legislation governing the safety of medical devices placed on the market in the Czech Republic. It investigates adverse incidents of medical devices and evaluates the incidents, it controls the conduct of clinical trials or clinical evaluations of medical devices. It inspects medical devices at providers of health care, focusing primarily upon the maintenance and storage of files, records and documents of the medical devices.

Table 8. Surveillance over the quality of marketed pharmaceuticals by means of laboratory analyses as per projects prepared in advance (Projects concluded in 2012)

Project title	Number of analysed products	Number of analysed samples	Number of compliant samples	Number of out-of--specification samples	Number of comments on MA dossier
1/2011 Endotoxin assay in selected vaccines	17	42	42	0	0
2/2011 Endotoxin and sterility assays in selected solutions for infusion	6	6	6	0	0
3/2011 – Pharmacy samples *	62	276	260	11 5 analyses not performed	2
4/2011- Verification of microbiological quality of herbal medicinal products	17	17	17	0	0
1c/2010 Bisoprolol + 10 cardiac therapy medicinal products with the highest consumption	11	27	27	0	0
1e/2010 Antiepileptics	20	33	33	0	1
2/2010 Counterfeit products*	174	174	–	–	–
Total	**71**	**125**	**125**	**0**	**3**

**/samples of these projects included in 2011 statistics*

Table 9. Batch release for defined medicinal products

Product type	Number of reported medicinal products	Number of reported batches	Released on the basis of a certificate	Number of samples subjected to laboratory verification	Total number of released batches	Unreleased
Blood derivatives	41	483	455	25	553	0
CZ vaccines	1	10	–	10	10	0
Imported vaccines	64	214	214	0	214	0

Table 10. Laboratory control of pharmaceuticals and excipients requested by other sections of the Institue, by other state administration bodies or by EDQM

	Number of samples	Of which compliant	Of which non-compliant
Suspected quality defect of a pharmaceutical	64	61	3
IPLP	96	95	1
Suspected counterfeit products, illegal pharmaceuticals *	72	–	–
Pharmacy samples	223	221	2
International studies within the scope of OMCL*	22	–	–
Purified water internal quality control	126	126	0
Verification of pharmacopoieal monograph drafts	1	1	0
Other analyses**	8	8	0
Total	**612**	**512**	**6**

** Cannot be assessed if sample is compliant or not*
*** E.g. LAL tests, other requested analyses etc.*

4.6 Laboratory control

Laboratory control is conducted by the Laboratory Control Section, both within the scope of requirements stipulated by the Act on Pharmaceuticals, i.e. the section controls the quality of pharmaceuticals in circulation as per projects prepared in advance and releases batches of defined medicinal products and on the basis of requirements raised by internal parties (other SÚKL units). This includes, in particular, the solving of quality defects of medicinal products, analyses of pharmacy samples, suspected counterfeit products and illegal pharmaceuticals, adverse reactions, etc.

The results of sample analyses carried out in 2012 by both laboratory departments of the Laboratory Control Section are summarised in tables above.

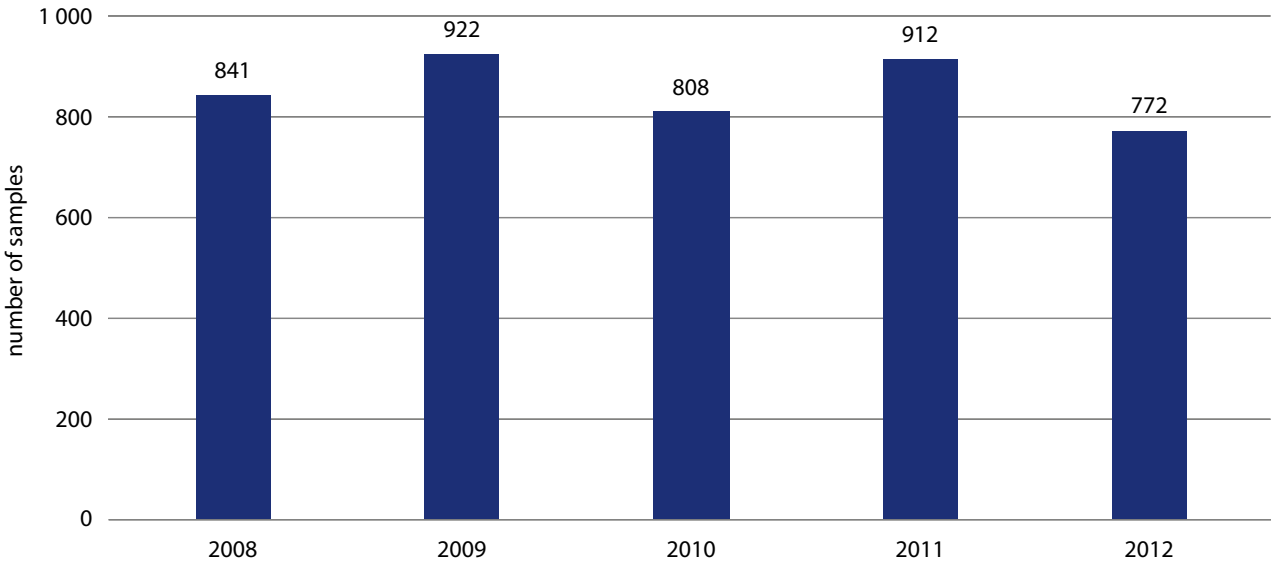
The projects are prepared on the basis of "risk based" analysis. The criterion is, in particular, a high consumption of the controlled products, less common pharmaceutical forms or routes of administration, the target patient group, or eventually frequent complaints by patients or professionals such as physicians or pharmacists. The reports on concluded projects have to be approved by the SÚKL Quality Team. The work on 2012 projects has commenced. These include in particular the

Table 11. Involvement in international studies

Study	Study title	Ratings
PTS124	Bacterial Endotoxins	satisfactory
PTS129	Loss on Drying	good
PTS131	UV-VIS Spectrophotometry	good
PTS132	Thin Layer Chromatography	good
CAP33/2012	Rilutek	good

Explanation of 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.

Fig. 3. Number of sample analyses in 2008–2012



control of generic medicinal products (products containing nimesulid, glimepirid, furosemid and donepezil), control of eye drops and products with prolonged release of active substance, attention will be focused also on products for child patients with regard to their chemical as well as microbiological compositions. Controls of pharmacy samples will continue.

As indicated in the above provided tables, 772 sample analyses were carried out in the Laboratory Control Section. Lower number of analysed samples in comparison with previous years is due to the refurbishment of laboratories of the Analytical Chemistry Department as well as reduction of the number of staff of laboratory departments. Of importance are analyses of samples analysed as suspected counterfeit or illicit products (cooperation with the Quality Defects and Enforcement Department and, through this department, with the Czech Police and Customs Administration). The number of analysis of suspected quality defects increased compared to previous years, this fact is due to more frequent complaints of patients and doctors. However, the number of incompliant samples did not increase. On the contrary, the number of samples evaluated as non-compliant (excluding counterfeits and illicit products and international studies) decreased and amounted to 0.9% (3.7% in 2011). Defects of pharmaceuticals were associated mainly with the content of active substances and purity thereof.

Within the scope of the Institute's statutory task of batch release, all reported batches were released onto the market in time, i.e. within the timelines established by the Act.

International cooperation in the area of laboratory control

In addition to other international cooperation within the framework of the EDQM OCML network, the section is involved in joint studies in quality control of marketed pharmaceuticals, comparative studies, quality control of reference substances for the European Pharmacopoeia, as well as in the joint EMA/EDQM study in laboratory quality control of centrally authorised products (joint EMA and EDQM activity – the CAP programme). In 2012, laboratory control of 21 samples was performed for foreign applicants from the OMCL network.

In 2012, the Laboratory Control Section participated in collaborative international studies listed in Table 11.

4.7. Surveillance in the area of preparation, dispensing, sale and distribution of pharmaceuticals

In late 2012, SÚKL had a list of 2,513 pharmacies in total, of which 4 fell within the scope of operation of the Ministry of Defence of the Czech Republic; moreover, the Institute registered 241 detached pharmaceutical and medical devices dispensing units (hereinafter referred to as OOVL), 362 approved medical device dispensaries, 316 vendors of selected medicinal products, 44 nuclear medicine departments of healthcare facilities and 407 distributors of medicinal products. The trend of past years of slightly growing number of pharmacies continued and compared to 2011, the total number of pharmacies increased by 65 entities, with a parallel drop by 2 OOVLs (Fig. 4).

In 2012, the inspectors of the Pharmacy and Distribution Section conducted 804 pharmacy inspections in total; in 15 cases they concerned hospital pharmacies and in 2 cases they concerned university hospital pharmacies. Of the total number of inspected pharmacies, 32 inspections were targeted inspections, carried out on the basis of reports.

Independent inspections aimed at handling of dependency--producing substances were carried out in 308 pharmacies, of which 300 were planned inspections and 8 targeted inspections. Price control focusing upon compliance with the Act on Prices and rules of price regulation was conducted in 101 pharmacies and at 14 distributors of pharmaceuticals.

On the basis of the facts identified during the inspections, fine was proposed in 95 cases in total and proposal to initiate administrative proceedings to impose a fine for breach of duties stipulated by the Act on Pharmaceuticals was submitted in 4 cases, in 5 cases the preparation of medicinal products was suspended in the pharmacy, and in 3 cases the operation of the entire pharmacy or OOVL was suspended.

Fig. 4. Number of pharmacies and OOVLs in the last 10 years (situation as of January 2, 2013)

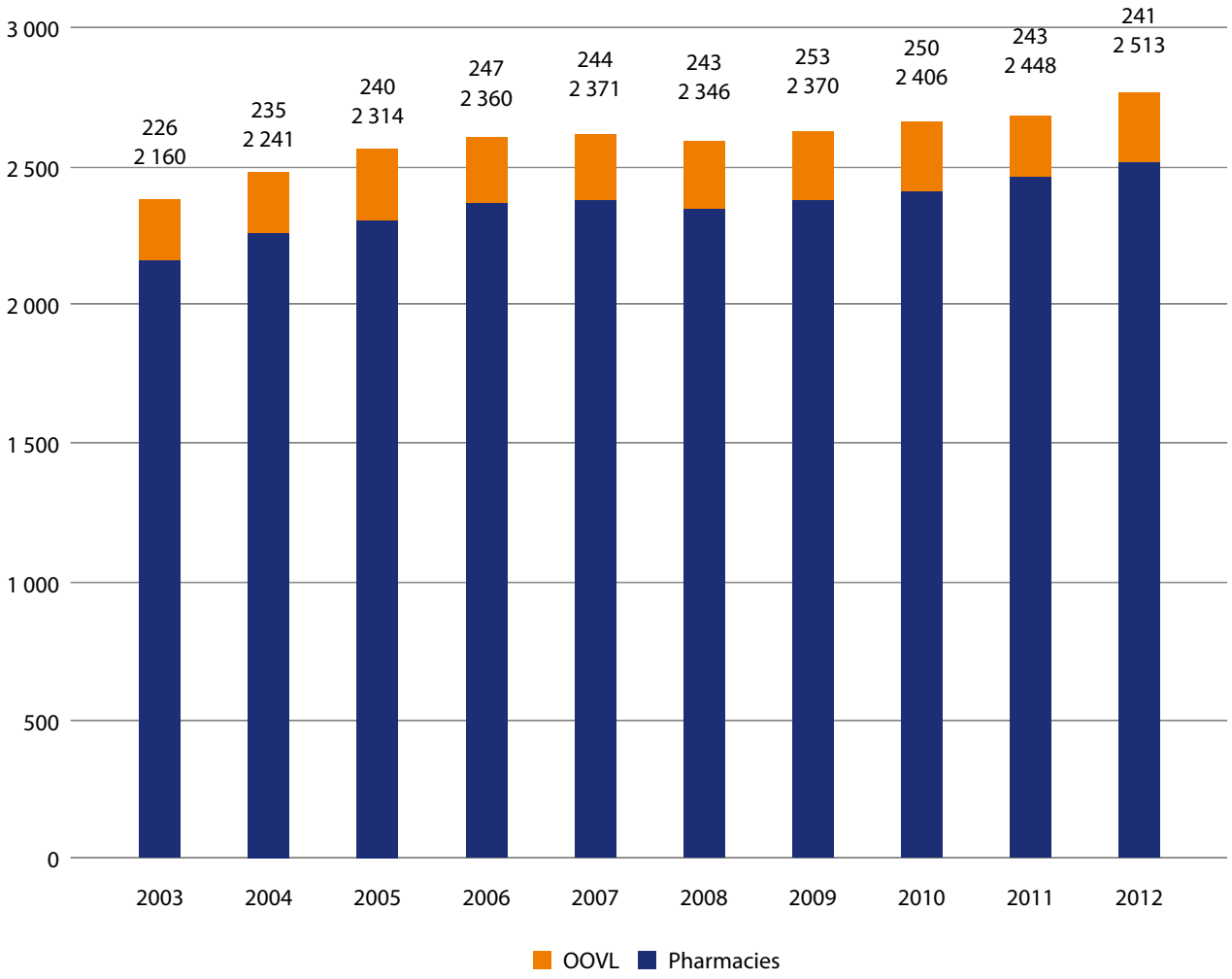


Table 12. Inspection surveillance over pharmacies, nuclear medicine departments, healthcare facilities, and vendors of selected medicinal products in 2012

Inspected entity			Classification of shortcomings							Penalties	
	Inspection type	Number	1	%	2	%	3	%	A	B	C
Pharmacies	Regular inspections	804	570	70,9	161	20,0	73	9,1	5	3	99
	Price inspections	101	Not rated by classification of shortcomings						–	–	–
	Inspections of dependency--producing substances	308	226	73,4	62	20,1	20	6,5	–	–	15
ONM		11	5	45,4	3	27,3	3	27,3	–	–	1
HAV		2	2	100,0	–	–	–	–	–	–	–
Healthcare facilities		282	203	72,0	62	22,0	17	6,0	–	–	2
Vendors of selected pharmaceuticals		24	17	70,8	5	20,8	2	8,4	–	–	–

Classification of shortcomings
1 – no or minor shortcoming identified
2 – major or repeated shortcomings
3 – critical shortcoming or serious breach of law (administrative procedure)

Penalties
A – suspended preparation
B – suspended operation
C – proposed fine

The main reasons for imposing fines or proposing the commencement of administrative proceedings were failure to provide data on medicinal products in the form of reports – 77 orders (85 pharmacies), dispensing of defective quality medicinal products, preparation from uncertified raw materials, dispensing medicinal products without prescription, incorrect records of the number of pieces, dispensing products to distributors, transfers of medicinal products among pharmacies outside the scope permitted by the law, incomplete or incorrect operational and record-keeping documents and other.

Within the scope of inspections focused upon handling dependency-producing substances in pharmacies, serious breaches of the Act on Dependency-Producing Substances were identified in 15 pharmacies, which resulted in imposing a fine. In 12 cases it was the failure to submit annual report on the status and movement of dependency--producing substances and products and in 3 cases it was a serious breach of the Act on Dependency-Producing Substances pertaining to record-keeping and documentation or entering incorrect data in annual reports. Inspections focusing upon the compliance with price regulation rules did not identify any breaches of the Act on Prices and the related price regulations.

Table 13. Occurrence of monitored types of shortcomings in %

Type of shortcoming	2008	2009	2010	2011	2012
Out-of-specification content of active substance	64,1	72,7	51,9	50,0	40,0
Out-of-specification total weight	25,6	18,2	29,6	30,0	40,0
Out-of-specification purified water Microbiological compliance	–	9,1	–	–	–
Out-of-specification galenic processing	–	–	7,4	–	–
Out-of-specification microbiological compliance	–	–	–	10,0	20,0
Active substance and excipient identity confusion	10,3	–	11,1	10,0	–

4. Regulatory activities of the Institute

Table 14. Other activities of the Distribution and Pharmacy Section

Initial pharmacy inspection	Establishment of a new pharmacy/OOVL	Defunct pharmacies/OOVLs
153	122/12	57/14
Initial OOVL inspection	**Initial inspection of medical device dispensaries**	**Consultations**
16	17	144

Table 15. Distribution of pharmaceuticals in 2012

	Received applications	Issued decisions
Application for distribution authorisation	40	40
Application for change to distribution authorisation	80	72
Application for distribution authorisation revocation	14	14

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

In 2012, 282 inspections focused upon handling of medicinal products in healthcare facilities were carried out. The inspections took place in 24 inpatient hospital departments and in 258 independent outpatient offices of general practitioners, specialists and in other healthcare facilities. On the basis of reports on the operation of healthcare facilities where health care is delivered, received by SÚKL, 32 targeted inspections took place in total. The identified breaches of the Act on Pharmaceuticals resulted in the imposition of one fine, in one case, procedural fine for obstructing the control was imposed on the inspected person.

In other healthcare facilities authorised to prepare medicinal products (Nuclear Medicine Departments – ONM and workplaces preparing autogenous vaccines for human use – HAV) 13 inspections in total were carried out; only one sanction for failure to fulfil the notification duty in case of termination of activities of the workplace was imposed.

The summary results of inspections carried out in 2012 are provided in Table 12.

In 2012, during inspections in pharmacies the inspectors from the Pharmacy and Distribution Section took 227 samples of medicinal products in total, of which 124 samples were samples of medicinal products intended for extemporaneous preparation in pharmacies. Out of the 103 pharmacy samples (medicinal products prepared in pharmacies), a total of 5 were out-of-specification, the shortcoming being out-of-specification total weight or content of active substance in the medicinal product and unsatisfactory result of the sterility assay. A lower number of samples taken corresponds to the long-term trend of decreasing preparation of medicinal products in pharmacies.

Comparison of occurrence of monitored shortcomings in out-of-specification pharmacy samples in the last years is provided in Table 13.

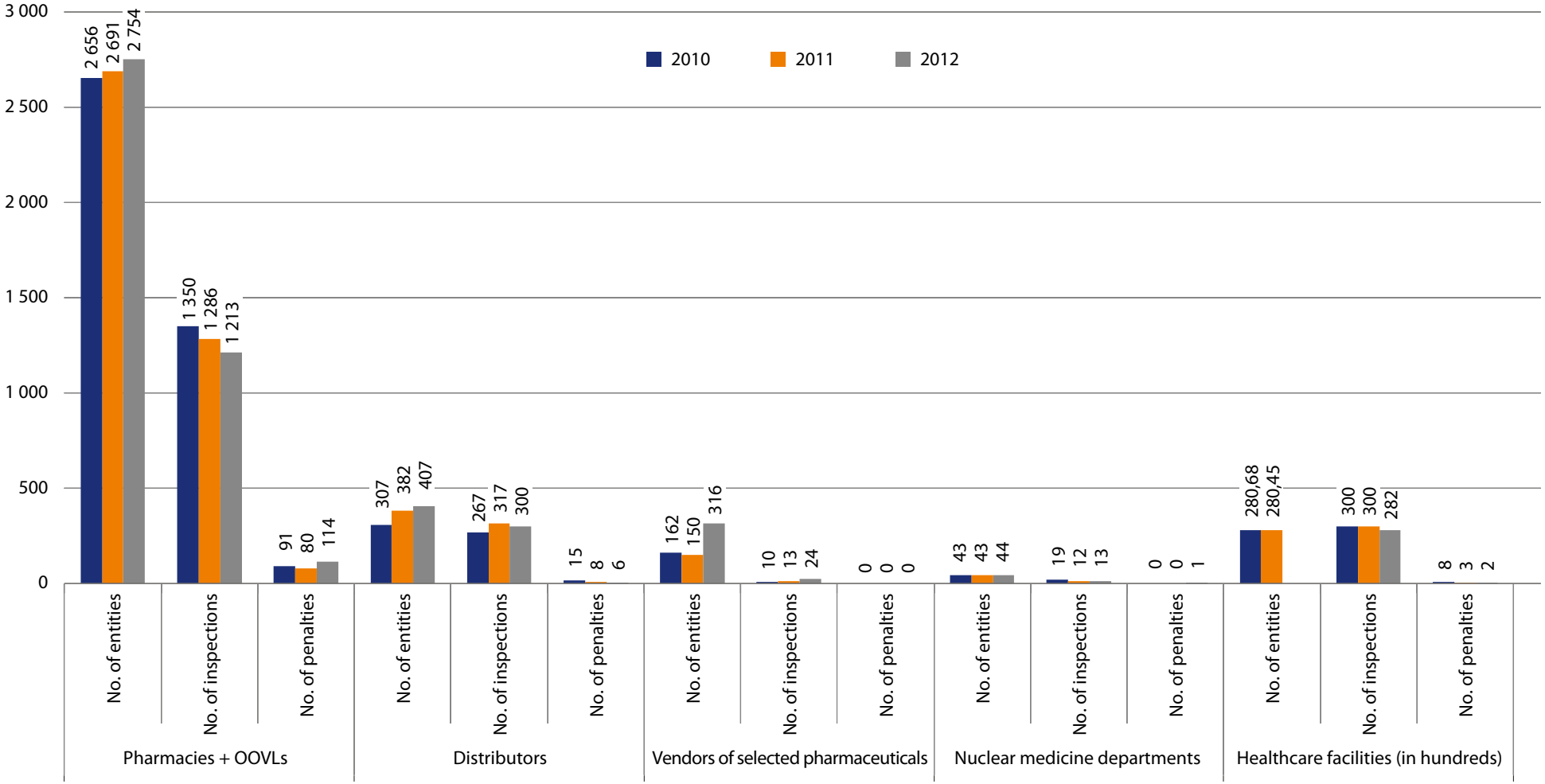
Other activities of the Pharmacy and Distribution Section include issuance of binding opinions on the material and technical equipment of pharmacies and medical device dispensaries (until April, 1, 2012 certificates on the material and technical equipment of pharmacies and approval of operation of medical device dispensaries). In 2012, a total of 475 applications of pharmacy operators for the issue of certificate/ /opinion were received and 124 certificates and 325 opinions

Table 16. Inspection surveillance over distributors

Number of inspections					Rating from the inspection			Action	
Total	Initial	Follow-up	Targeted	Variation	1	2	3	Breach of law	Fine proposed
300	48	219	7	26	181	38	7	40	6

Rating from inspections
On the basis of the identified shortcomings and their severity the inspection is rated and according to the achieved point score, the overall level of compliance with the principles of good distribution practice is expressed by the following rating: 1 – good , 2 – satisfactory, 3 - not satisfactory

Fig. 5. Comparison of the number of regulated entities, conducted inspections and imposed penalties over the last 3 years



were issued, none of the applications was dismissed. 23 operators in total applied for approval of/opinion on operation of medical device dispensaries and 7 approvals and 14 opinions were issued.

In 153 cases the issue of the certificate or opinion was preceded by the inspection of the pharmacy (on-the-spot check of the technical and material equipment), in 16 cases by the inspection of the OOVL (Table 14). Furthermore, initial inspections of medical device dispensaries and 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

Table 17. Applications in the sphere of manufacture of pharmaceuticals and in the sphere of human tissues and cells

Application type		2010		2011		2012	
		Received applications	Issued decisions	Received applications	Issued decisions	Received applications	Issued decisions
Application for manufacturing authorisation	Manufacturer of medicinal products	3	6	7	7	4	2
	Control laboratory	2	1	4	4	3	3
	Blood centre	1	1	1	1	0	0
Application for variation to manufacturing authorisation	Manufacturer of medicinal products	47	48	45	41	58	55
	Control laboratory	1	1	2	1	1	2
	Blood centre	22	20	19	17	28	27
Application for revocation of manufacturing authorisation	Manufacturer of medicinal products	3	3	5	5	1	1
	Control laboratory	–	–	–	–	2	2
	Blood centre	–	–	–	–	3	3
Application for authorisation to engage in the activities of:	A tissue centre	3	34	18	12	4	9
	A donation centre	2	2	2	0	3	1
	A diagnostic laboratory	10	23	5	4	2	5
Application for variation to activities of:	A tissue centre	5	1	16	15	28	24
	A donation centre	1	0	2	2	0	0
	A diagnostic laboratory	5	3	7	7	12	10
Total		**105**	**143**	**133**	**116**	**149**	**145**

Act on Pharmaceuticals or Act of Dependency-Producing Substances took place. Table 14 also provides data on newly established/defunct pharmacies/OOVLs.

Distribution

In 2012, the number of distributors increased by 25 entities to the total number of 407 medicinal product distribution authorisation holders. Of the total number of approved distributors, 168 entities already are those where the pharmacy operator is also a distribution authorisation holder.

Table 15 provides an overview of received applications and issued decisions in respect of distribution authorisation, variations thereto or revocation thereof.

The validity of the distribution authorisation of one distributor expired in compliance with Section 76, paragraph 4, of Act No. 378/2007 Coll., on Pharmaceuticals, as amended.

300 inspections of distributors were conducted in total, which, compared to 2011, represents an increase in inspections conducted as part of planned follow-up distributor controls. The number of such controls grew by 65 due to higher number of new distributors in recent years.

Of the total number of 226 rated inspections of distributors, 80% were rated with grade 1 (good), 17% with grade 2 (satisfactory) and 3% with grade 3 (not satisfactory). On the basis of the identified facts, the commencement of administrative procedure for fine imposition was proposed in 6 cases in total.

For the failure to comply with the distributors' and manufacturers' duty to report to the Institute on supplies of medicinal products for human use under the SÚKL DIS-13 guideline, the Pharmacy and Distribution Section issued a total of 79 orders to impose a fine. In case of 18 distributors, inspections to check if the data contained in the distributors' reports are correct and complete, by comparing the data reported to the Institute with the data in the supply records of the distributor were carried out. In total, 192 randomly chosen medicinal products were checked, 3.7% of data in the reports did not correspond with the distributor's records.

The results of inspections of distributors in 2012 are provided in Table 16.

Rating from inspections

On the basis of the identified shortcomings and their severity the inspection is rated and according to the achieved point score, the overall level of compliance with the principles of good distribution practice is expressed by the following rating:

1 – good
2 – satisfactory
3 – not satisfactory

Fig. 6. Numbers of manufacturers of medicinal products, active substances and control laboratories and overview of completed inspections

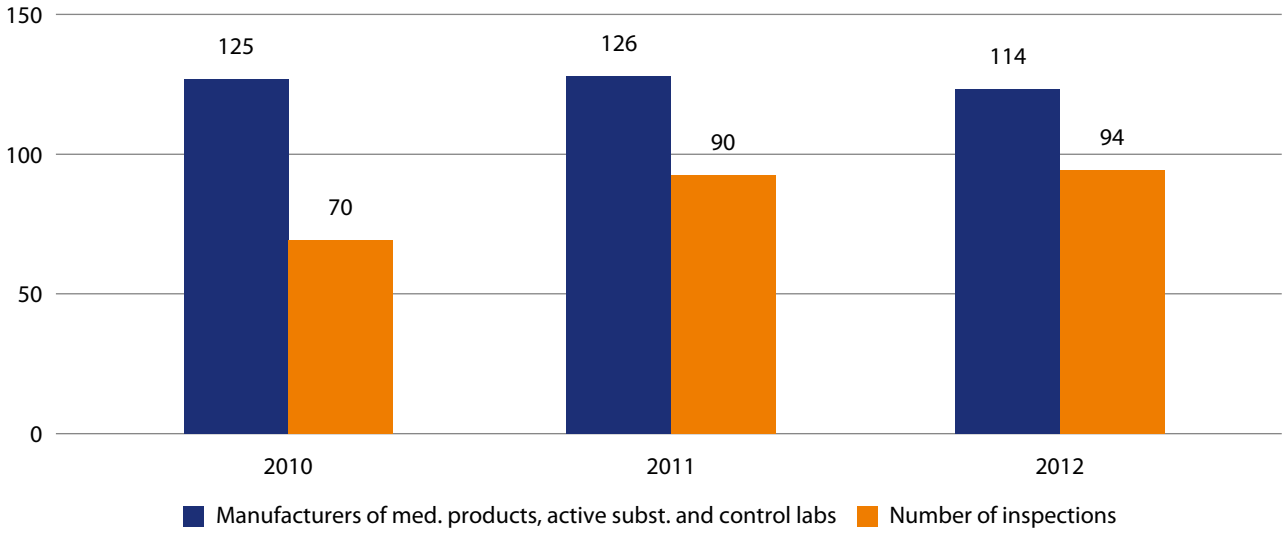


Table 18. Inspections conducted in 2012 and their outcomes

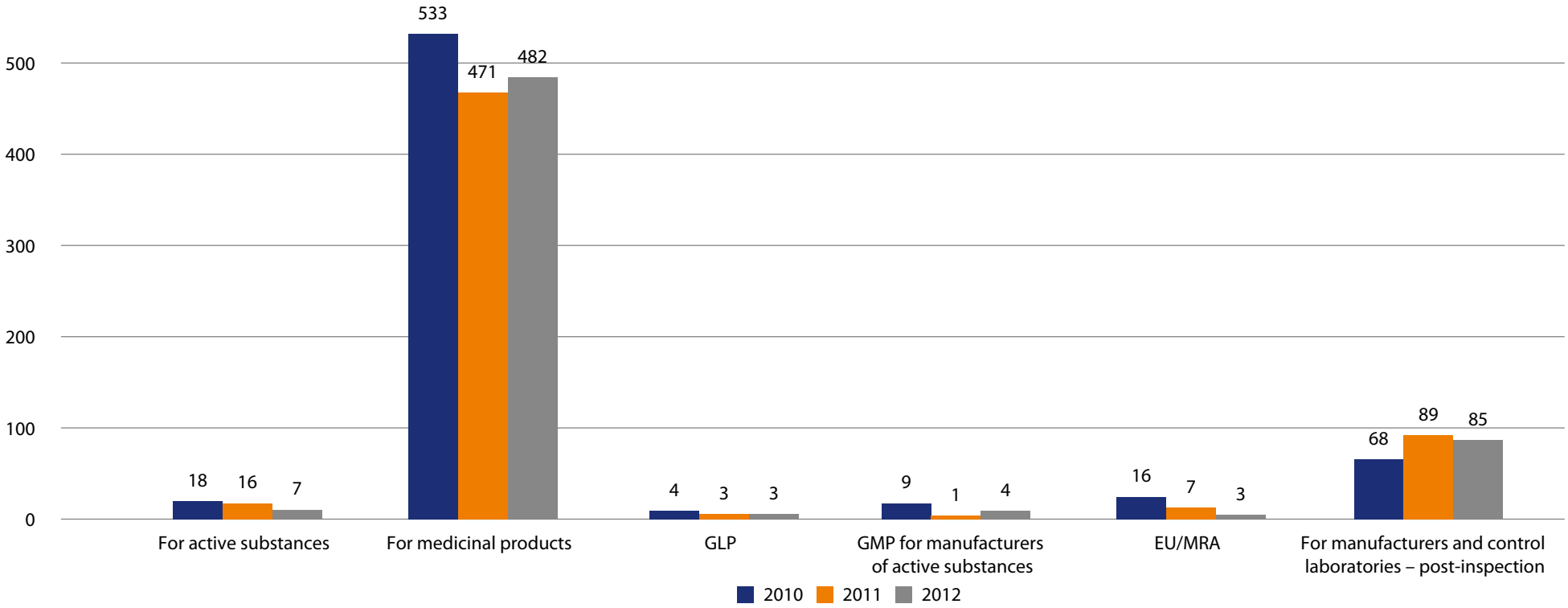
	Number of inspections					Rating from inspections			
	Total	Initial	Follow-up	Targeted	Variation	Compliant	Non-compliant	Breach of law	Fine/order
Manufacturers of medicinal products	57	4	42	1	10	57	0	1	1
Manufacturers of active substances	25	2	12	1	10	25	0	0	0
Control laboratories	12	3	8	0	1	12	0	0	0
Blood centres	44	0	39	0	5	44	0	0	0
Blood banks	22	9	13	0	0	22	0	1	0
GCP inspections – Ethics Committees	17	10	7	0	0	0	0	0	0
GCP inspections – other	9	9	0	0	0	0	0	0	0
TC, DC, DL inspections	102	54	33	8	7	0	0	12	12

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

Table 19. Inspections conducted in 2010–2012

	2010		2011		2012	
	No. of inspections	Breach of law	No. of inspections	Breach of law	No. of inspections	Breach of law
Manufacturers of medicinal products	43	1	64	0	57	1
Manufacturers of active substances	18	0	13	0	25	0
Control laboratories	9	0	13	0	12	0
Blood centres	44	0	51	0	44	0
Blood banks	1	0	4	0	22	0
GCP inspections +ethics committees	25	4	29	0	26	0
Tissue centres, donation centres, diagnostic laboratories	88	0	102	0	102	12
Celkem	**228**	**5**	**276**	**0**	**288**	**15**

Fig. 7. Issued certificates



4.8 Surveillance in the area of manufacture of pharmaceuticals, human tissues and cells, good laboratory practice and good clinical practice

Manufacture of pharmaceuticals

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

In the sphere of manufacturers (incl. blood centres) the total of 94 applications for manufacturing authorisation or variations thereto was received (Tab. 17). The number of cases transferred between years corresponds to the period of application processing. The number of decisions issued for variation to manufacturing authorisation increased compared to 2011. The number of applications for revocation of the manufacturing authorisation grew as well.

Human tissues and cells

This is a sphere regulated by the Institute pursuant to Act No 296/2008 Coll., on Human Tissues and Cells. In 2012, 49 applications for authorisation for variations to authorisation were received.

In 2012, the Institute carried out 288 inspections in total, of which 102 inspections were associated with the

regulated sphere of tissues and cells. Their nature and results of evaluation are provided in Table 18. 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 the period from 2010 to 2012 is provided in Table 19 and Fig. 6.

Initial inspections were conducted in respect of applications for authorisation to engage in an activity pursuant to Section 63, paragraph 4 of Act No. 378/2007 Coll. Follow-up inspections were conducted at the manufacturer of medicinal products, active substances, a control laboratory or a blood centre in intervals stipulated by Decree No. 229/2008 Coll., and for blood centres pursuant to Decree No. 143/2008 Coll. Inspections relating to variations are performed in case of change in the conditions under which the activity was permitted. 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 94 inspections at the manufacturers of medicinal products, active substances, and control laboratories, three cases were rated as not satisfactory, and one order on fine imposition was issued. The plan of follow-up inspections was fulfilled for all regulated entities and the inspection interval stipulated by the relevant decrees was complied with.

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 use in man.

Good laboratory practice (GLP)

In 2012, 9 holders of Good Laboratory Practice Certificates issued by the Institute were registered in total, with prevailing scope of activities in toxicological studies; these were included in the National GLP Programme. In the same year, 5 follow-up and 2 targeted inspections of holders of GLP certificates and one preliminary inspection of applicant for the GLP Certificate were conducted.

Good clinical practice (GCP)

In the course of the year, the Institute carried out 2 targeted joint inspections with foreign agencies at trial sites in the Czech Republic for two marketing authorisation of medicinal products applications in other EU member states, 2 systemic follow-up inspections of contractual research organisations (CRO) carrying out BA/BE studies for an application for GCP Certificate, 1 systemic follow-up inspection CRO with inpatient unit, 2 targeted initial inspections at investigators' based on report, 13 initial systemic inspections of local ethical committees (EC), 2 systemic follow-up inspections of EC for application for redefinition of multicentric ECs, 1 systemic follow-up inspection of multicentric EC (23 inspections in total). In case of GCP no decision on permission of activities of the inspected entities is issued.

Actions and penalties

In 2012, one breach of the Act on Pharmaceuticals was identified and one order was issued. The Act on Tissues and Cells was breached in 12 cases and 12 orders on fine impositions were issued.

Certification

584 various certificates were issued in total (587 in 2011), of which, like in the previous years, the highest number was the number of certificates issued for medicinal products (482), see Fig. 7. Post-inspection good manufacturing certificates are entered in the EudraGMP database maintained by EMA. All certificates of medicinal products were issued within the 30-day period and of good manufacturing practice in the 90-day period.

Table 21. Actions taken in 2012

Actions taken	Number
Recalls from distributor level	3
Recalls from healthcare facility level	80
Recalls from patient level	1
Suspended distribution, dispensing and therapeutic use	6

Table 20. Number of received reports

Quality defects	2008	2009	2010	2011	2012
Received reports in total	201	235	248	357	416
▪ Reports from the Czech Rep.	107	141	150	203	294
▪ Reports from abroad	98	94	98	124	122
Resulted in recalls	34	19	47	129	84
Issued RWs *	4	5	5	2	4
Issued RAs **	1	2	1	5	7

** RW – Rapid Warning, ** RA – Rapid Alert*

Assessment of GMP compliance within the scope of marketing authorisation procedure

2,188 cases in total were received (a 29.3% increase compared to 2011), all of which were dealt with within the time limit.

4.9 Quality defects

In the sphere of quality defects of pharmaceuticals, the number of reports received is still increasing; it has been growing since 2009. The comparison of the numbers of received reports for the period from 2008 to 2012 is provided in Table 20.

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

Exchange of information with the Slovak State Institute for Drug Control (ŠÚKL) in Bratislava still continues and in 2012, the Institute received a number of reports from ŠÚKL.

Received reports also include reports on non-compliance of the manufacturing site of a medicinal product or an active substance with the GMP principles. The department addressed a total of 27 such reports in 2012.

Within the scope of the solution of quality defects of pharmaceuticals, effective actions have been taken to reduce

Fig. 8. Enforcement control activities 2008–2012

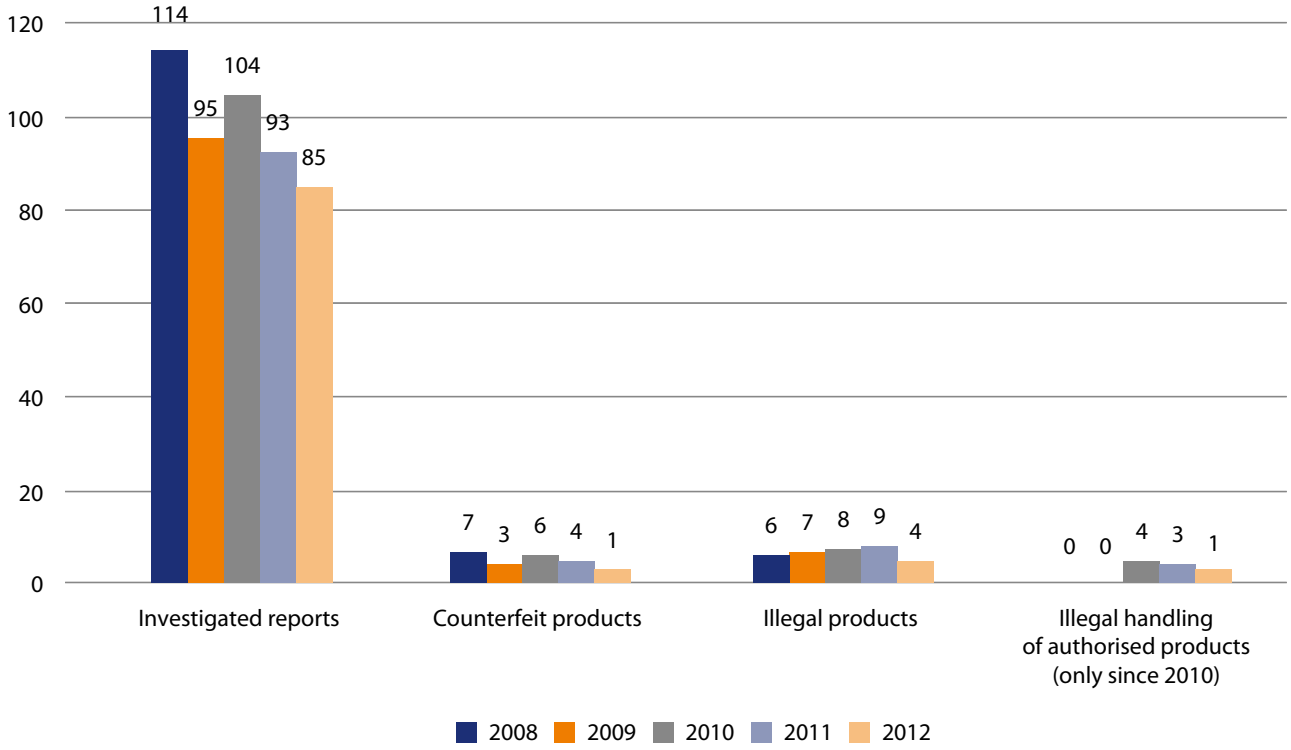


Table 22. Results of investigated cases

Cases concluded by:	2010	2011	2012
administrative procedure with proposed fines	10	2	2
reports of crime	8	6	2
cases forwarded to other authorities (CAFIA, etc.)	2	3	4

the impact of the quality defect on patient health. Table 21 gives an overview of actions taken as part of solving the quality defects in individual medicinal products (SÚKL codes) in 2012.

Products were recalled from patient level only in one case. The medicinal product was Euthyrox 50 microgramma, por. tbl. nob. 100x50 rg, batch No. 148799, expiry date 04/2015 due to packs with information in the Chinese language.

The Quality Defects and Enforcement Department was also involved in the control of the compliance of the notification duty by the marketing authorisation holder laid down in Section 33, paragraph 2 of Act No. 378/2007 Coll., on Pharmaceuticals and on Amendments to Some Related Acts (Act on Pharmaceuticals).

4.10 Enforcement

In 2012, active surveillance in the area of illegal handling of medicinal products focused, in particular, upon the

Fig. 9. Overview of investigated reports of suspected breach of the Act on Advertising Regulation (2008–2012) in %

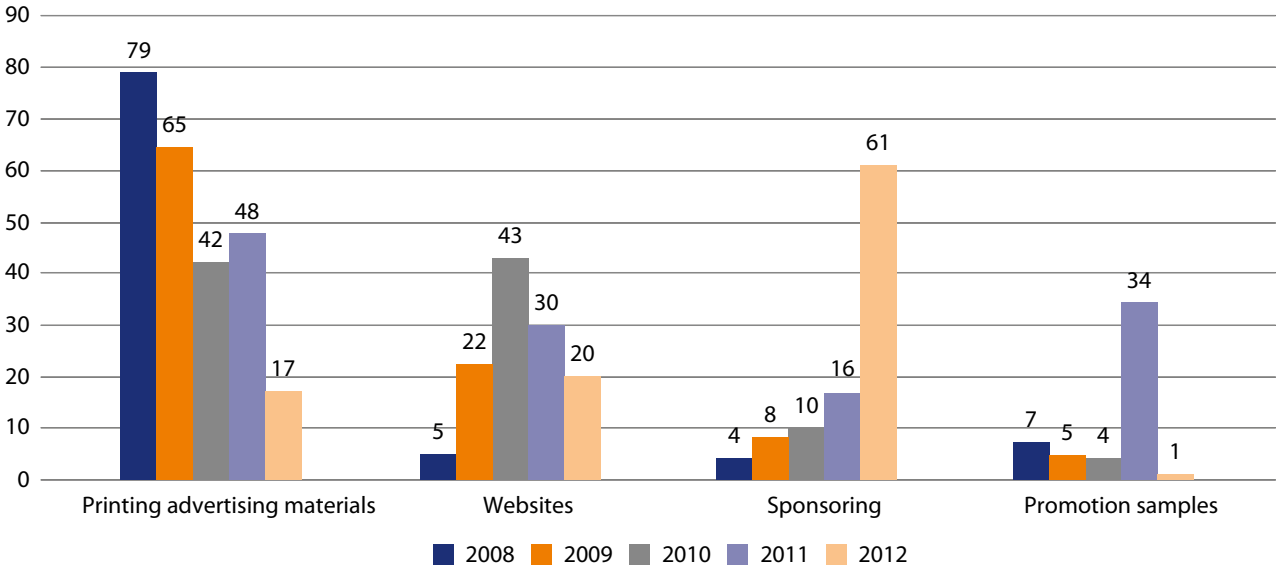


Table 23. Overview of investigated reports of suspected breaches of the Act on Advertising Regulation

	Reports brought forward from 2011	Newly received reports in 2012	Total
Number of reports	15	249	264
Completed investigation	13	240	253
Forwarded for commencement of administrative procedure	2	9	11
Pending	0	0	0
Completed administrative procedure	2	9	11
Number of final decisions on fines	2	13	15

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 (ŽÚ). 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 2012, the total of 85 reports were investigated, either received ones or the Institute's own motions. During control actions on the Internet the employees of the Institute identified and investigated 4 cases of non-authorised medicinal products, 1 case of counterfeit products, and 1 case of unauthorised handling of authorised medicinal products.

In 2012, the Institute prepared the total of 786 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 have been authorised neither in the Czech Republic, nor in any other EU Member State, haven't been properly labelled and their import violated the applicable legislation. For the Czech Police the Institute prepared 13 expert opinions for the purposes of identification of medicinal products and for clarification of legislation governing the supply, distribution, import, and export of medicinal products.

4.11 Surveillance in the area of regulation of advertising for medicinal products

In 2012, the Institute investigated the total of 264 reports of suspected breaches of Act No. 40/1995 Coll., on Advertising

Table 24. Inspections of medical devices carried out at providers of health care in 2012

Nature of the inspection		General rating						Penalisation (proposed fines)
Total	Of which initiated by report	1	%	2	%	3	%	
91	10	67	73,6	17	18,7	7	7,7	1

Classification

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

Fig. 10. Number of inspections in 2008–2012

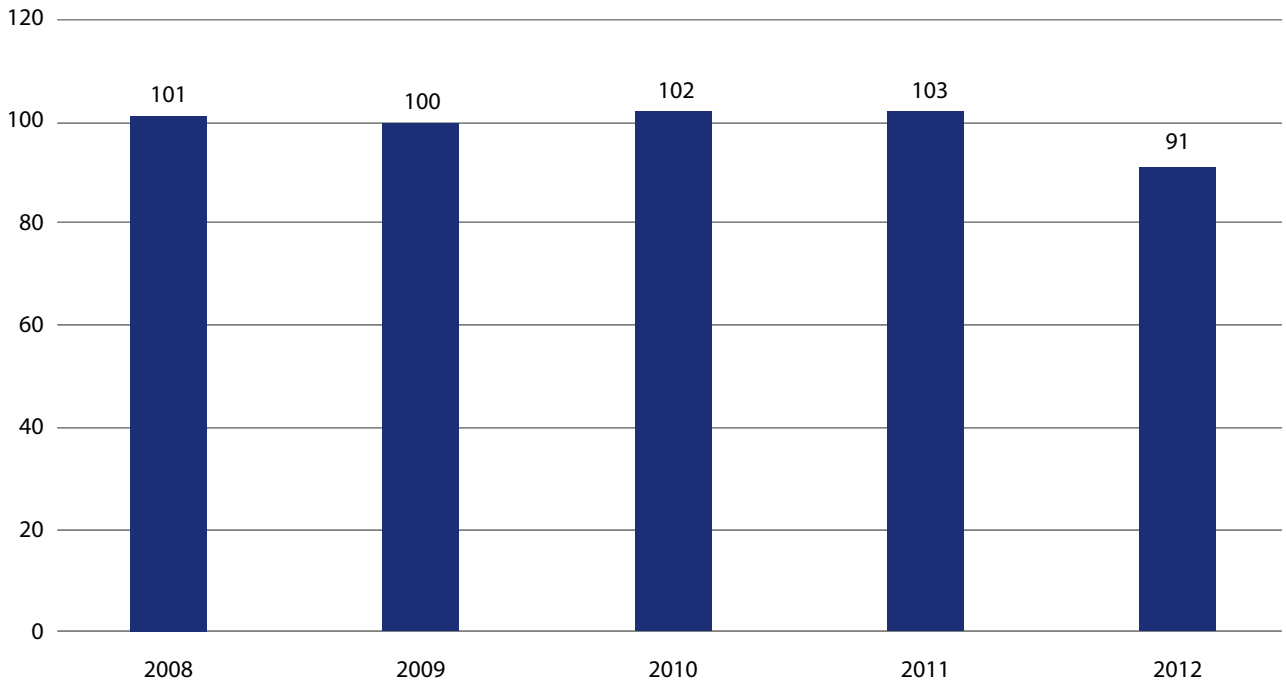


Fig. 11. Percentage of defects in inspected medical devices

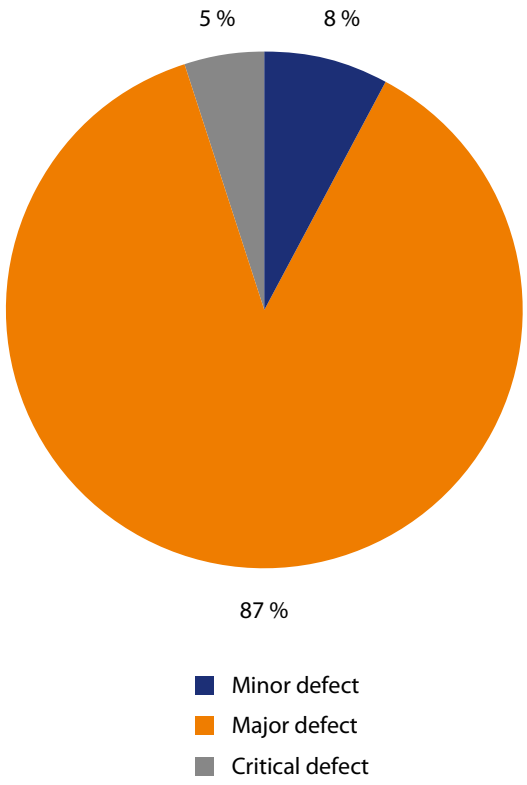
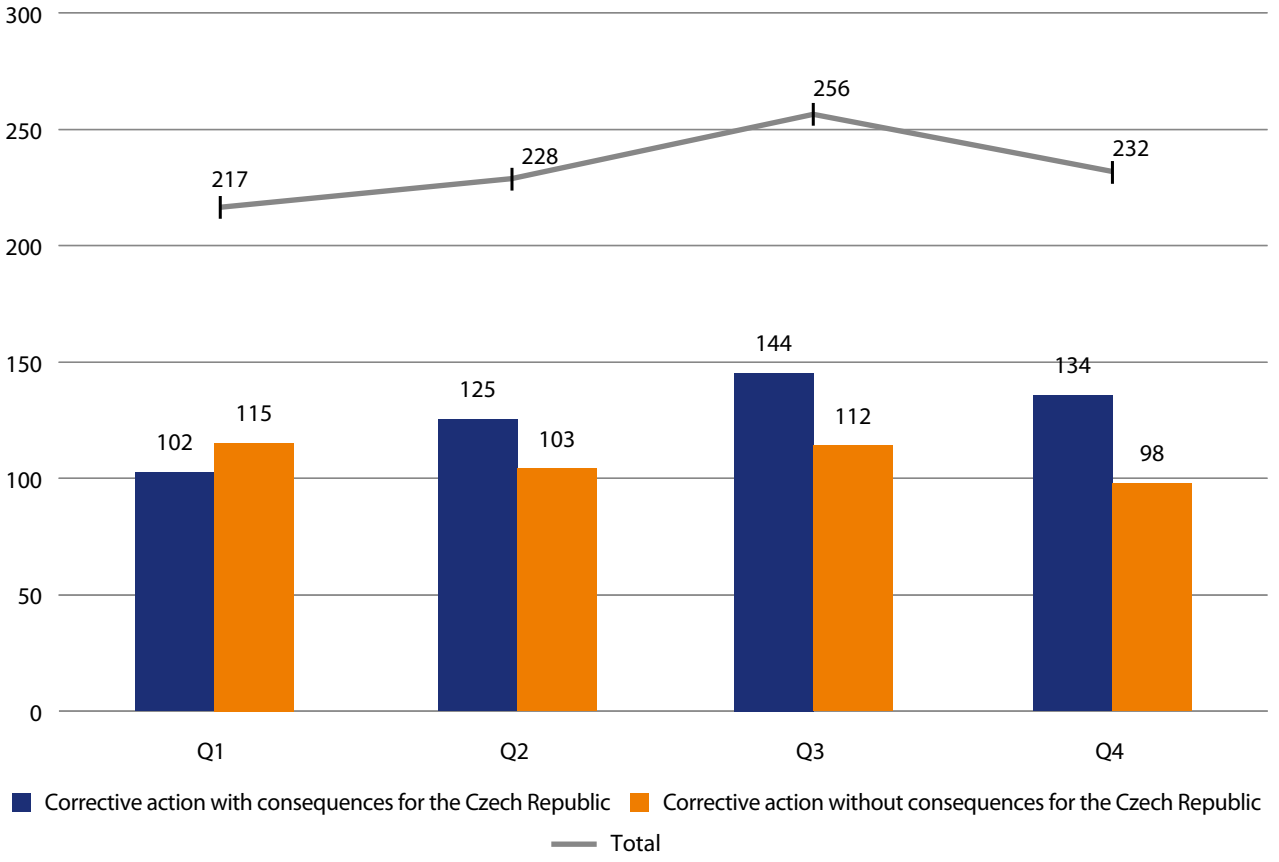


Fig. 12 Corrective action reports in respect of medical devices received in 2012



Regulation, as amended (Act on Advertising Regulation), see Table 23. In 2012 it received by 78 new reports more compared to 2011 (171 newly accepted reports in 2010). In 012, 11 administrative procedures were completed that resulted in imposition of 15 fines in the aggregate amount of 2,645 000, CZK.

Advertising for prescription-only medicines represented 78% of investigated cases; advertising for OTC medicines represented 20% of cases; 2% of reports were forwarded to

competent authorities, as they did not concern advertising for medicinal products for human use.

Pharmaceutical companies or their legal representatives filed 8% of reports on suspected breach of law, 2% of reports were filed by professional societies, 1% was anonymous, 67% were lodged by private individuals, 2% by state administration bodies and 20% by the employees of the Institute.

The Institute issued 71 expert opinions on the issues of intended advertising upon request.

Surveillance in the sphere of decisions regarding the nature of the product

In 2012, the Institute commenced investigations of 57 cases involving various products, most often dietary supplements and cosmetic products, for suspicion that the product concerned might be a medicinal product. In 1 case it was decided in administrative proceedings that the product was a medicinal product referred to in the Act on Pharmaceuticals.

4.12 Medical devices

In 2012, the inspectors from the Pharmacy and Distribution Section carried out in total 91 inspections of healthcare providers (both state and non-state healthcare establishments), during which 639 medical devices were inspected (hereinafter referred to as "MD").

Table 24 provides the numbers of completed inspections and their total rating using the 1 to 3 scale for the occurrence and severity of identified shortcomings.

In total, 186 devices, which were put into operation before the end of 1999, were inspected. 111 devices were found flawless, in 75 devices 129 defects were identified (6 minor defects, 114 major defects and 9 critical ones); while 41 devices were classified according to the degree of risk for users as Class IIb. For all of the 186 devices, documents on compliance with the conditions of use of medical devices in the delivery of health care were inspected.

The total number of inspected medical devices, which were put into operation after 2000, was 453 devices, of which 290 devices were found to be flawless. In 163 devices 372 defects in total were identified (35 minor defects, 320 major defects and 17 critical defects); in terms of the degree of risks for users, 83 of these devices were classified as Class IIb. For all of the 453 devices, documents on compliance with the conditions of use of medical devices in the delivery of health care were inspected.

Furthermore, inspection of 98 established measuring devices (7 of them without verification) was conducted.

Within the scope of inspections of the conduct of clinical trials on medical devices at healthcare providers' 11 inspections were carried out, during which 11 tested medical devices were inspected. The selection of workplaces to be inspected was based upon positive opinions issued by the Institute in respect of the intention to carry out a clinical trial.

66 serious adverse incidents (SAE) were reported to the Institute in respect of the ongoing clinical trials on medical devices in the Czech Republic. The intention to carry out a clinical trial was reported to the Institute for 23 MD in 2012, 25 positive opinions were issued.

Investigation of adverse incidents and monitoring of corrective action for medical devices

213 adverse incidents with expected causality with the use of a medical device in the provision of healthcare within the territory of the Czech Republic were reported to the Institute. Furthermore, 8 adverse incidents occurring outside the territory of the Czech Republic involving medical devices of Czech manufacturers were reported. In all cases investigation was launched. Within the scope of adverse incident investigations, 5 inspections at healthcare providers´ and 4 inspections of the manufacturer, importer and distributor were carried out.

The total number of reports on corrective action in respect of medical devices received from competent authorities, manufacturers or their authorised representatives, distributors or importers, where applicable, was 933. Of the total number of received reports, 505 concerned medical devices distributed within the Czech market, see Fig. 12.

In 2012, the number of received reports on corrective action for medical devices was 25% higher compared to 2011.

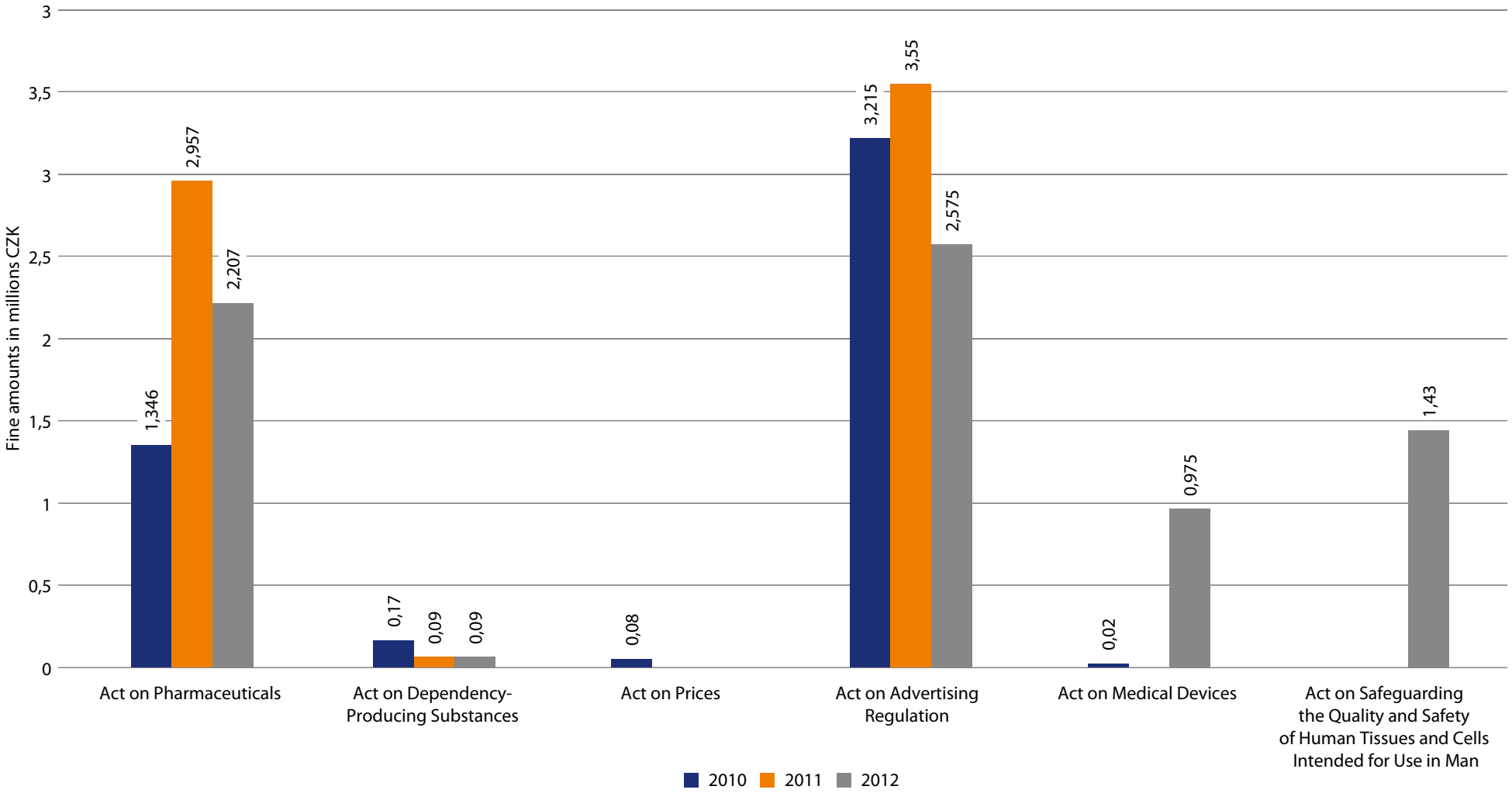
In 2012, the Institute published on its website 359 Field Safety Notices (FSN) pertaining to Czech users, which are distributed by the producer, authorised representative or distributor in connection with the Field Safety Corrective Action (FSCA) in order to minimise possible recurrence of an adverse event.

On the basis of results of adverse incident investigation and MD clinical trial inspections 4 fines for administrative delicts were imposed in the total amount of 775,000 CZK.

Table 25. Czech Pharmacopoeia 2009 – Supplement 2013

	General articles, tables	Articles	Total
European part	38	334	372
National part	9	39	48
Total	**47**	**373**	**420**

Fig. 13. Overall amount of penalties that came into force in 2010–2012



Explanation to Fig. 13:
- *Act No. 378/2007 Coll., on Pharmaceuticals, as amended*
- *Act No. 167/1998 Coll., on Dependency-Producing Substances, as amended*
- *Act No. 526/1990 Coll., on Prices, as amended*
- *Act No. 40/1995 Coll., on Advertising Regulation, as amended*
- *Act No. 123/2000 Coll., on Medical Devices, as amended*
- *Act No. 296/2008 Coll., on Safeguarding the Quality and Safety of Human Tissues and Cells Intended for Use in Man and on Amendments to Related Acts, as amended*

In the framework of international cooperation in the area of medical device vigilance the inspectors of Adverse Incident and Clinical Trial Department participated in 12 teleconferences in 2012 focused in particular on the issue of PIP breast implants and metal-on-metal hip implants.

Within their cooperation and competences the Institute and the Czech Trade Inspection, supervisory authorities in the area of medical devices, were mutually exchanging motions to initiate investigations in the sphere of medical devices.

4.13 Standardisation and pharmacopoeial activities

The employees of the Department of Pharmacopoeia and Pharmaceutical Standardisation prepared a draft of Czech Pharmacopoeia 2009 – Supplement 2013 (hereinafter referred to as Ph.Cz. 2009 – Suppl. 2013). This edition contains, in its European section, translations of the texts of three supplements to the seventh edition of the European Pharmacopoeia, i.e. Ph.Eur.- Suppl. 7.6, Ph. Eur. / Suppl. 7.7 and Ph. Eur. – Supl. 7.8, which represents 372 texts in total, of which 47 are new articles and 227 are review articles;

The general section of the National part of Ph.Cz. 2009 – Suppl. 2013 newly contains Table XVI: Storage and expiry of products prepared in pharmacies, which was prepared in cooperation with the analytical department of the Institute and selected hospital pharmacies. Full versions of those revised tables which were supplemented with information on newly included substances are provided in the general section of the National part. The Special section of the National part newly includes 4 articles and 35 medicinal product articles with data acquired while monitoring their stability; these texts were submitted for public review (notified) and 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, as amended by Directive 98/48/EC, were notified under no. 2013/0008/CZ, 2013/0009/CZ, 2013/0011/CZ and 2013/0014/CZ.

In coordination with the Department of Pharmacopoeia, other expert employees of the Institute were also participated in the preparation of Ph.Cz. 2009 – Suppl. 2013. Czech Pharmacopoeia – Supplement 2013 will be binding as of September 1, 2013.

Cooperation with the European Pharmacopoeial Commission (hereinafter referred to as EPC) in the preparation of another edition of Ph. Eur. and in the preparation of translation and revision of the "Standard Terms" database continued. The Department of Pharmacopoeia informs about the binding nature of the Ph. Eur. editions in SÚKL's information media. The employees of the department regularly took part in the EPC meetings and national secretariat staff meetings.

In 2012, 10 draft translations of Czech technical standards for medical devices were commented on within the scope of standardisation activities.

4.14 Penalties imposed by the institute

On the basis of identified breaches of legislative requirements in the course of inspections, the Institute initiates administrative proceedings within which penalties referred to in the Acts are imposed according to the severity of the identified problem. Since August 2011 the Institute started to take advantage also of the option to impose sanctions on the basis of the so-called administrative order, under the Administrative Procedure Code. An overview of penalties imposed since 2010 pursuant to individual acts is provided in Fig. 13.

PRICE AND REIMBURSEMENT REGULATION BRANCH

The Branch issues decisions on maximum prices of medicinal products and on reimbursement amounts and conditions for medicinal products. The process of maximum price and reimbursement amount and conditions determination is individual and may be reviewed; it is carried out in the form of administrative procedures with fixed timelines, fully reflecting the European Transparency Directive. Applications and reports are evaluated especially on the basis of efficacy, safety, and cost efficiency assessments. By law, the parties to the administrative procedure are health insurance companies and marketing authorisation holders, and in case of foods for special medical purposes domestic producers or importers. Motions may be filed also by patient organisations or professional associations.

4.15 Determination of prices and reimbursement

In the course of 2012, the employees of the Institute continued to determine maximum prices and amounts and conditions of reimbursements from health insurance in compliance with the internal methodology drafted pursuant to Act No 48/1997 Coll., on Public Health Insurance and

Table 26. Overview of administrative proceedings in 2012

Applications for maximum ex-factory price determination	No. of SÚKL codes
Pending	149
Decided	149
Appeal filed	1
Came into force	148
Came into force	
Pending	170
Decided	166
Appeal filed	0
Came into force	154
Applications for maximum ex-factory price cancellation	
Pending	16
Decided	16
Appeal filed	0
Came into force	16
Ex officio procedures on cancellation of maximum price	
Pending	3 072
Decided	3 072
Appeal filed (enforcement before final and conclusive decision)	250
Came into force	2 822

on Amendments to Some Related Acts, and related legal regulations.

Maximum ex-factory prices

Even in 2012, the Institute worked on the completion of administrative proceedings regarding maximum ex-factory prices initiated ex officio in 2008.The administrative proceedings dealt with in 2012 concerned in particular medicinal products, in case of which parties to the proceedings repeatedly lodged an appeal and the Ministry of Health of the Czech Republic subsequently decided on reconsideration of these cases. As of December 31, 2011 a total of 1 administrative proceeding concerning 1 medicinal product in the aggregate has not been completed. Final and conclusive decision was issued in 2012.

Pursuant to transitional provisions of Act No. 298/2011 Coll. the Institute started 308 proceedings on reducing maximum price of medicinal products that exceeded the limits set by the provision of § 39a(2) of Act on Public Health Insurance (extension of reference basket to 21 EU countries, later in the course of 2012 amended to 18). Final and conclusive decisions or enforcement before final and conclusive decisions were issued in all of the above administrative proceedings in 2012.

The Institute also concluded the remaining of 185 ex officio proceedings on cancellation of maximum price and the amount and conditions of reimbursement in respect of products that have not been marketed in the long term, which had been initiated in 2011.

Furthermore, proceedings on determination and change of maximum prices within the scope of individual administrative proceedings upon request of the marketing authorisation holder continued.

In 2012, no proceedings on granting exception from reducing maximum ex-factory price were conducted. The Institute did not conduct any proceedings on price competition in 2012. The price competition was replaced by reimbursement competition in compliance with Act No. 298/2011 Coll. with the effect as of December 1, 2011. The Institute has not received any legally compliant applications for reimbursement competition tender.

Reductions pursuant to Šnajdr's package

In connection with Act No 76/2011 Coll., on temporary reduction of prices and reimbursement of medicinal products (the so-called Šnajdr's package), a 7% reduction

Table 27. Overview of the number of codes of medicinal products/foods for special medical purposes in maximum ex-factory price zones as per the List of Prices and Reimbursements by month

Up to 20 CZK inclusive	28	23	24	23	24	23	15	16	24	22	27	36
More than 20 CZK–50 CZK inclusive	367	355	356	338	338	336	320	321	316	318	335	346
More than 50 CZK–100 CZK inclusive	619	597	581	568	579	586	531	547	548	565	560	557
More than 100 CZK–200 CZK inclusive	660	649	634	653	666	693	652	665	666	670	677	690
More than 200 CZK–300 CZK inclusive	357	342	347	356	358	369	362	362	370	373	368	368
More than 300 CZK–500 CZK inclusive	495	482	485	501	499	517	506	520	535	549	546	534
More than 500 CZK–1000 CZK inclusive	555	546	536	543	554	562	577	591	616	624	646	662
More than 1000 CZK–2000 CZK inclusive	538	523	539	577	598	633	640	657	671	682	674	671
More than 2000 CZK–3000 CZK inclusive	244	230	235	240	235	236	240	253	268	276	270	276
More than 3000 CZK–5000 CZK inclusive	276	262	263	282	287	293	304	322	328	322	328	321
More than 5000 CZK–10000 CZK inclusive	231	224	212	215	216	219	217	223	224	222	230	231
More than 10000 CZK–20000 CZK inclusive	172	150	142	149	149	150	152	168	170	169	168	167
More than 20000 CZK–30000 CZK inclusive	74	59	53	54	53	54	54	56	61	61	63	60
More than 30000 CZK–50000 CZK inclusive	50	46	44	46	46	47	46	49	48	50	51	42
More than 50000 CZK–100000 CZK inclusive	37	31	28	28	28	30	32	32	35	34	34	34
More than 100000 CZK	17	16	14	16	16	16	15	15	14	14	17	17
Number of codes	**4 720**	**4 535**	**4 493**	**4 589**	**4 646**	**4 764**	**4 663**	**4 797**	**4 894**	**4 951**	**4 994**	**5 012**

Table 28. Overview of reimbursed and actually marketed medicinal products with increase of reduced price as of April, 1, 2012

Medicinal products	Number of SÚKL codes
Reimbursed and actually marketed – total	**5 621**
Of which returned back to original price as of April 1, 2012 - total	**1 615**

of determined maximum ex-factory prices and notified producer prices was implemented as of April 1, 2011.

The effect of the provision ended as at April 1, 2012 and an increase of the reduced price was performed in case of all medicinal products for which the above revision of reimbursement amount and conditions had not come into force yet to that date (Table 28).

On the year-on-year basis till 1 January 2012 a decrease in the share of medicinal products regulated only by the maximum profit margin (OP) continued and on the other hand the share of medicinal products regulated by the maximum ex-factory price (MCV) increased. The situation changed as of January 1, 2012, when the FAR pricing decision that deregulates medicinal products containing one of 133 active substances took effect (Figure 14).

Development of average prices for end users

In case of medicinal products regulated by the maximum ex-factory price (the medicinal products are regulated also by the maximum profit margin), in general the average

price increased. The total increase amounted to 6.67%, which in percentage is higher than the increase between 4 Q 2010 and 4 Q 2011, which amounted to 4.85%. The increase was mainly due the VAT increase (approx. 3.6%) and the change of maximum profit margins (less than 1%). The total net increase was then only 2%, which was less than in the previous period. The increase was caused in particular by the change of structure/portfolio of supplied medicinal products. The total number of the supplied packages dropped by 7.31% in all price zones against the compared period, while 95% of the decrease was due to the decrease in the first price zone (0 – 150 CZK) and the second price zone (150 – 300 CZK) (Fig. 15). The lacking packages were not transferred to the other price zones and/or different type of regulation. The decrease in the number of packages of relatively cheap products translated into a relative increase of package weight in higher price zones, which finally contributed to the increase of total average price per package.

In the case of medicinal products regulated only by maximum profit margin the overall average price increased significantly, by 18.67%, compared to the previous period. The increase of the average price has been caused also by the decrease in

Fig. 14. Structure of reimbursed products per type of price regulation

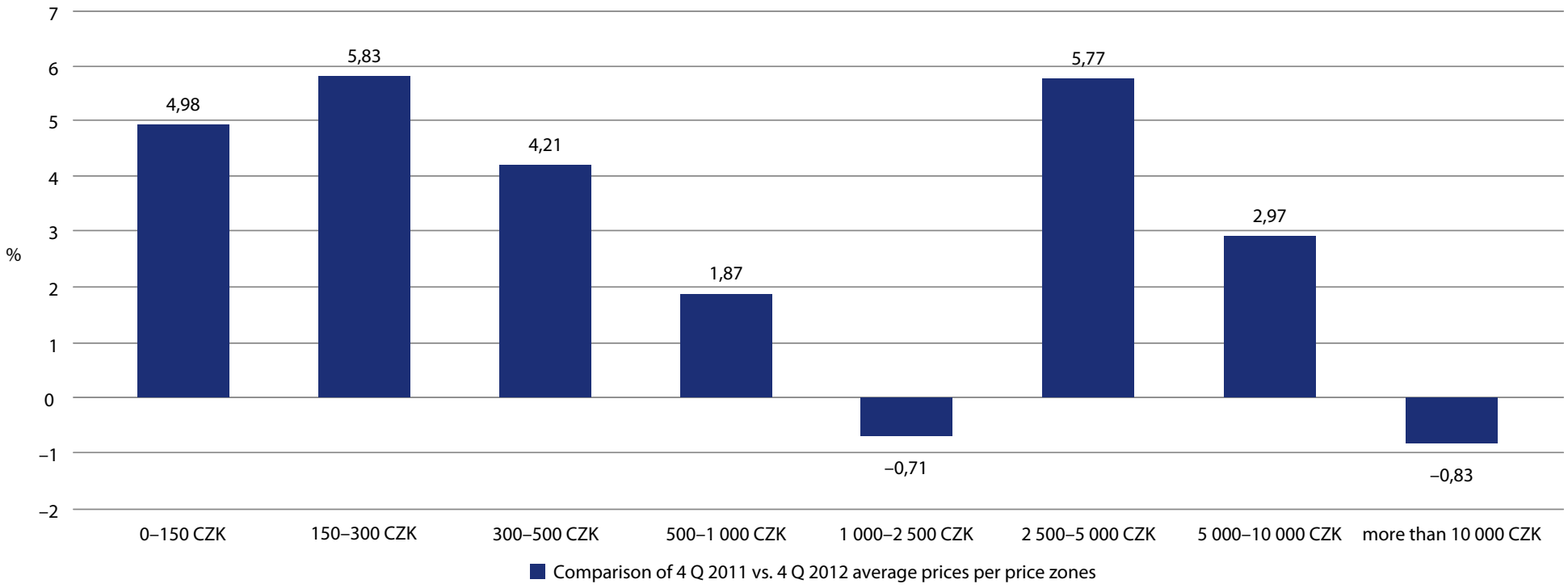
the supply of relatively cheap packages of the first zone, and, on the contrary, the increase in the supply of packages of all other price zones, while the total price of supplied packages remained more or less the same.

The source of previous data are distributors' reports pursuant to the provisions of Act No 378/2007 Coll., on Pharmaceuticals and on Amendments to Some Related Acts (Act on Pharmaceuticals), as amended.

Overview of the most often distributed products for which the maximum ex-factory price was changed

On the basis of the mandatory periodical distributor reports on realised supplies of medicinal products (DIS-13) an overview was compiled of ten most often distributed medicinal products, along with ten medicinal products with the highest financial volume according to ex-factory price, for which the maximum ex-factory price was changed (Table 29). The segment of ten most frequently distributed medicinal products is characterised by a relatively low price and quite high heterogeneous volatility. On the contrary,

Fig. 15. End user prices of pharmaceuticals regulated by maximum ex-factory price



medicinal products essential in terms of financial volume show overall decrease in price across almost all listed products (Table 30).

Amounts and conditions of reimbursements from health insurance

In 2012, the Institute continued the previously initiated revision of amounts and conditions of reimbursement of medicinal products and foods for special medical purposes, which are covered by health insurance. In compliance with effective legislation, the amounts of reimbursement in these procedures are amended as per the current price references and conditions of reimbursements in a manner allowing to meet the expected results and reasons for pharmacotherapy. Within the scope of a revision procedure, the amounts and conditions of reimbursements may not only be changed, but also cancelled for those products which cannot be administered as part of outpatient care and/or for which no effect has been evidenced or the administration of which is not, from the expert point of view, suitable.

Revision procedures are also joined with administrative procedures initiated upon request. The reason for this

Fig. 16. End user prices of pharmaceuticals regulated by maximum profit margin

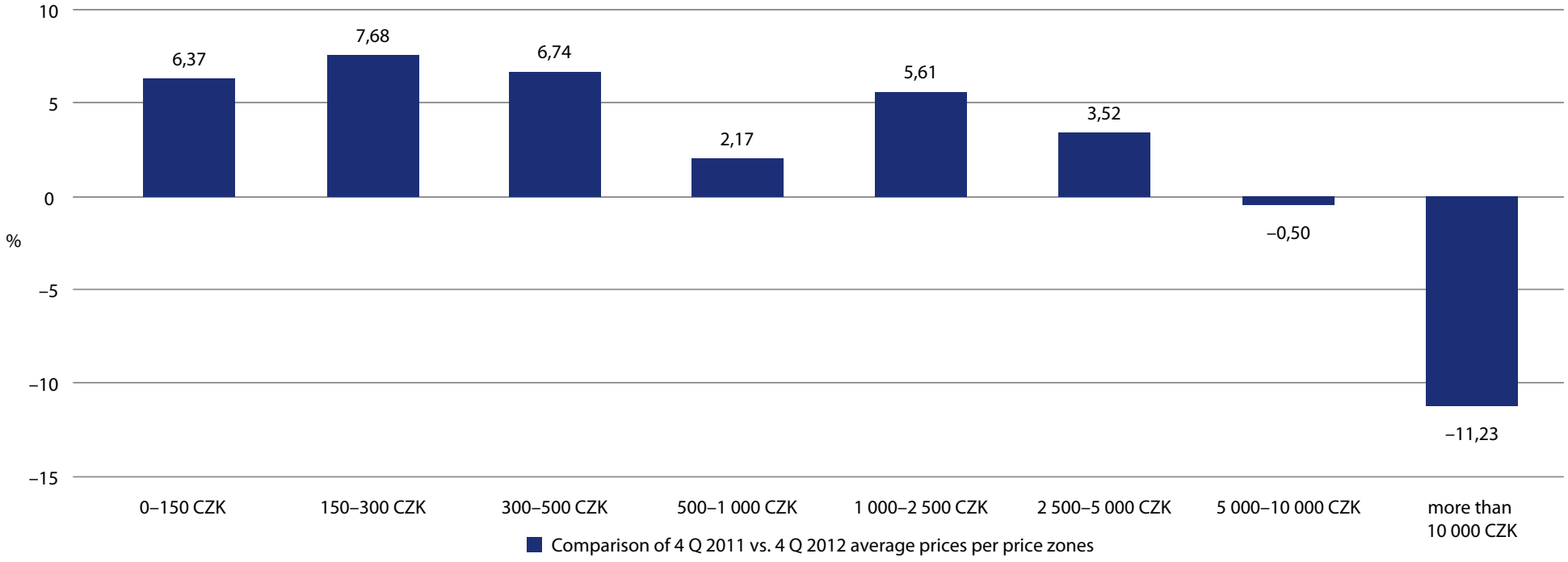


Table 29. 10 most often distributed medicinal products by number of packages reported in compliance with DIS-13 for which the maximum ex-factory price was changed

Code	ATC	Name	Name supplement	No. of packages (A)	Original price (CZK)	New price (CZK)	No. of packages (B)	*/
0002592	M04AA01	MILURIT 100	POR TBL NOB 50X100MG	308 705	37,52	52,34	432 909	*/
0069189	H03AA01	EUTHYROX 50 MIKROGRAMŮ	POR TBL NOB 100X50RG	93 622	35,63	57,08	113 355	*/
0016462	D02AE01	EXCIPIAL U LIPOLOTIO	DRM EML 1X200ML	248 207	137,64	79,07	136 037	
0001710	M04AA01	MILURIT 300	POR TBL NOB 30X300MG	100 971	52,91	56,33	114 068	*/
0093724	M01AB01	INDOMETACIN 100 BERLIN-CHEMIE	RCT SUP 10X100MG	187 235	64,13	63,00	173 113	
0097186	H03AA01	EUTHYROX 100 MIKROGRAMŮ	POR TBL NOB 100X100RG	68 862	51,10	80,02	85 932	*/
0014958	N03AE01	RIVOTRIL 2 MG	POR TBL NOB 30X2MG	62 141	48,58	33,08	66 113	*/
0002684	N01BB	MESOCAIN	URT GEL 1X20GM/200MG	145 771	22,46	38,05	99 712	
0097402	B03AE10	SORBIFER DURULES	POR TBL FLM 50X100MG	123 098	76,12	98,95	106 491	
0076921	G03DA04	UTROGESTAN	POR CPS MOL 30X100MG	50 516	122,81	120,84	55 598	*/

*A – number of packages distributed during 6 months before change, B – number of packages distributed during 6 months after change, */ - the period of one quarter.*

Table 30. 10 most often distributed medicinal products by financial volume in ex-factory price 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 %
0026252	L03AB07	AVONEX	INJ SOL 4X30RG/DÁV+4JEH	383 628 167	20 571,58	17 967,49	–12,7
0149868	J07AL02	PREVENAR 13	INJ SUS 1X0.5ML+SJ	276 002 523	1 425,81	1 112,30	–22,0
0027905	L04AB01	ENBREL 50 MG	INJ SOL 4X1ML/50MG-PS	231 653 219	24 976,03	20 696,60	–17,1
0125287	B01AB05	CLEXANE	INJ SOL 50X0.4ML/4KU	224 205 606	4 299,49	4 365,78	1,5
0027192	L01XE04	SUTENT 50 MG	POR CPS DUR 30X50MG	207 836 846	130 474,10	113 482,44	–13,0
0028217	N03AX16	LYRICA 75 MG	POR CPS DUR 56X75MG	182 949 854	932,12	810,05	–13,1
0027259	L03AB07	REBIF 22 MCG	INJ SOL 12X0.5ML	164 579 837	20 906,16	18 300,88	–12,5
0028223	N03AX16	LYRICA 150 MG	POR CPS DUR 56X150MG	159 002 256	1 405,80	1 207,19	–14,1
0027262	L03AB07	REBIF 44 MCG	INJ SOL 12X0.5ML	140 902 926	26 717,17	21 019,32	–21,3
0026042	J06BA02	KIOVIG 100MG/ML	INF SOL 1X10GM/100ML	137 291 698	12 223,12	11 909,78	–2,6

A – total cost in end user prices for 2012.

Table 31. Overview of administrative procedures in 2012

Applications for determination or change of the reimbursement amount and conditions	No. of SÚKL codes
Pending	156
Decided	163
Appeal filed	230
Came into force	221
Applications for determination or change of maximum prices and reimbursement amount and conditions	
Pending	257
Decided	572
Appeal filed	360
Came into force	607
Applications for reimbursement cancellation	
Pending	126
Decided	107
Appeal filed	0
Came into force	119
Applications for maximum price and reimbursement cancellation	
Pending	127
Decided	93
Appeal filed	0
Came into force	111
Procedures initiated ex officio	
Pending	2 177
Decided	870
Appeal filed	560
Came into force	3 228
Procedures on similar products	
Pending	841
Decided	879
Appeal filed	109
Came into force	988

Table 32. Overview of legitimate decisions on the revision of reimbursements and savings in health insurance

Effective date	No. of SÚKL codes	No. of administrative procedures	Savings in health insurance
1/2012	284	28	67 261 768
2/2012	140	11	100 380 774
3/2012	131	23	133 821 365
4/2012	258	16	268 668 678
5/2012	513	15	215 336 776
6/2012	394	26	178 208 001
7/2012	74	10	–19 923 979
8/2012	162	15	–8 350 226
9/2012	314	13	425 877 839
10/2012	463	14	290 499 614
11/2012	311	30	50 997 095
12/2012	88	10	59 005 312

Note: positive number shows the savings in health insurance, negative number the increase of impact on the budget.

is the provision of the law on conducting the revision procedure jointly for all therapeutically interchangeable products. This way the amount and conditions of reimbursement may be set up for all therapeutically interchangeable products in the same manner.

In parallel with the conduct of reimbursement revisions, the Institute handles submitted applications for the determination, change or cancellation of maximum prices and conditions of reimbursement.

Table 33. Overview of the number of codes of medicinal products/foods for special medical purposes in reimbursement amount price zones as per the List of Prices and Reimbursements by month

Price zones	2012/01	2012/02	2012/03	2012/04	2012/05	2012/06	2012/07	2012/08	2012/09	2012/10	2012/11	2012/12
Up to 20 CZK inclusive	341	245	233	217	217	213	155	156	155	148	145	156
More than 20 CZK–50 CZK inclusive	961	945	903	880	889	878	764	752	754	746	747	745
More than 50 CZK–100 CZK inclusive	1 281	1 222	1 201	1 210	1 213	1 222	1 080	1 097	1 093	1 122	1 157	1 176
More than 100 CZK–200 CZK inclusive	1 752	1 710	1 687	1 681	1 683	1 710	1 624	1 613	1 598	1 603	1 625	1 640
More than 200 CZK–300 CZK inclusive	844	801	762	769	780	802	788	787	785	852	873	860
More than 300 CZK–500 CZK inclusive	1 080	1 011	966	988	1 001	1 038	1 024	1 045	1 060	1 003	1 033	1 025
More than 500 CZK–1000 CZK inclusive	1 169	1 144	1 140	1 190	1 210	1 301	1 330	1 340	1 354	1 365	1 354	1 368
More than 1000 CZK–2000 CZK inclusive	864	813	814	831	844	820	841	863	884	866	958	967
More than 2000 CZK–3000 CZK inclusive	414	412	406	411	426	440	454	455	453	474	413	417
More than 3000 CZK–5000 CZK inclusive	385	360	329	344	338	327	337	352	350	364	368	372
More than 5000 CZK–10000 CZK inclusive	370	361	344	376	383	383	386	408	421	422	424	424
More than 10000 CZK–20000 CZK inclusive	258	234	218	223	226	227	222	232	234	233	241	238
More than 20000 CZK–30000 CZK inclusive	87	74	66	70	69	71	73	81	86	88	90	90
More than 30000 CZK–50000 CZK inclusive	57	51	46	47	46	45	46	46	45	47	48	47
More than 50000 CZK–100000 CZK inclusive	39	33	32	33	33	35	37	37	40	40	40	39
More than 100000 CZK	20	17	15	14	14	13	12	12	11	11	14	15
Number of codes	**9 922**	**9 433**	**9 162**	**9 284**	**9 372**	**9 525**	**9 173**	**9 276**	**9 323**	**9 384**	**9 530**	**9 579**

As a new feature, under the amendment to Act No 48/1997 Coll., on Public Health Insurance, effective as of December 1, 2011, the Institute also conducts a new type of administrative proceedings regarding similar products that enables, if the statutory conditions are met, marketing of the products within 30 days after the application is filed.

By the end of 2011, the Institute had issued decisions on all procedures pertaining to the revision of the system of reimbursements. With regard to revision administrative procedures, in 2012, 170 appeals to 119 administrative proceedings were filed and 25 administrative proceedings were referred back for reconsideration.

The savings obtained through the revision of the system of reimbursements from the public health insurance funds in 2012 were 1.8 billion CZK.

Table 34. Overview of reimbursed and actually marketed medicinal products with increasing the price to 100% original price (previous 7% price reduction)

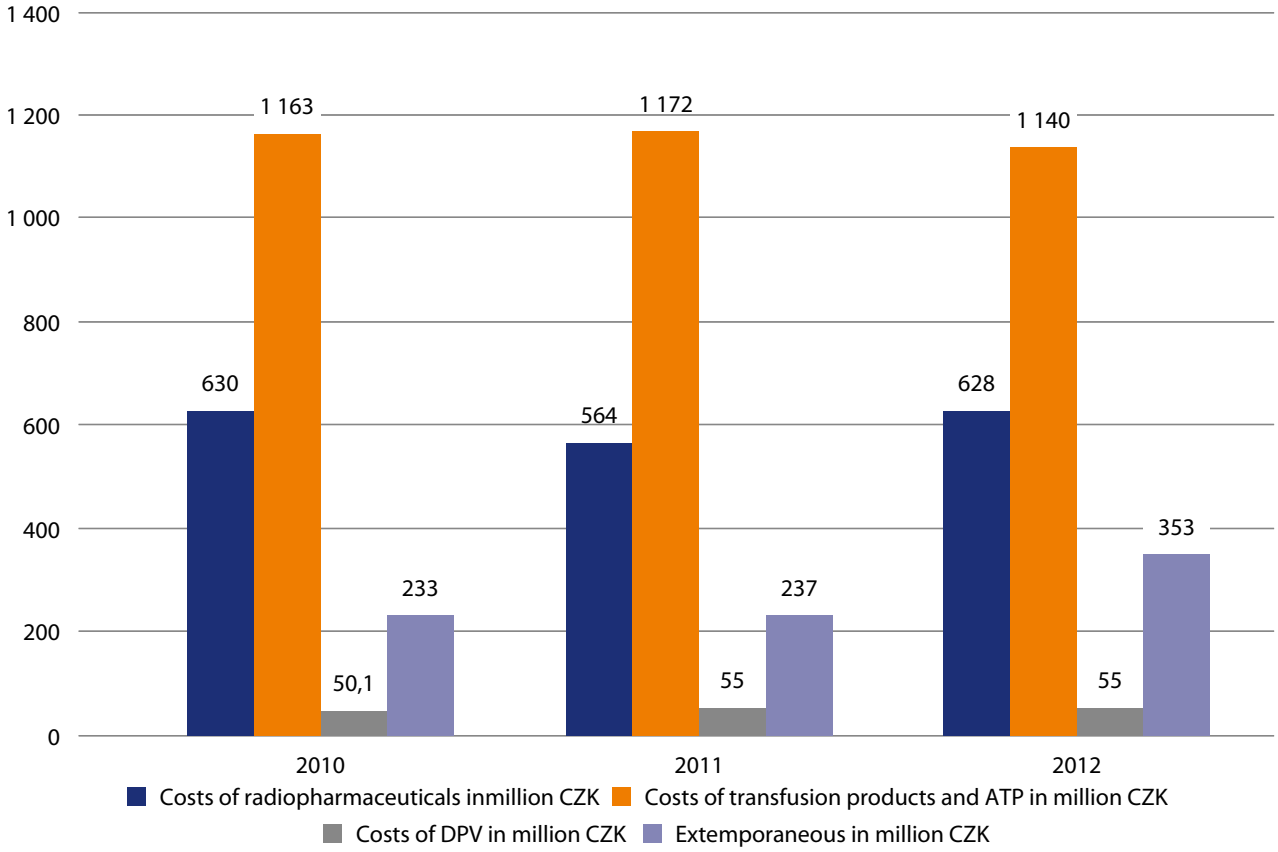
Medicinal products	No. of SÚKL codes
Reimbursed and actually marketed – total	5 405
Of which back to original price as of April 1, 2012 – total	**1 443**

Reductions pursuant to Šnajdr's package

In connection with Act No 76/2011 Coll. on temporary reduction of prices and reimbursement of medicinal products (the so-called Šnajdr's package), a 7% reduction was implemented as of April 1, 2011.

As of April 1, 2012 the above measure expired and the prices were increased back in case of all medicinal products, in which the revision of reimbursement amount and conditions had not been effective at that date.

Fig. 17. Overview of costs of IPLP groups for the period between 2010 and 2012



Overview of the most often distributed products for which reimbursement from health insurance was changed

The overview indicates for which products reimbursement changed in the course of 2012, both in terms of most often distributed products and products with the highest originator's price (Tab. 35 and 36).

Validation of applications

As of 1 September, 2012, the Applications Validation Department became part of the Price and Reimbursement Regulation Branch within the reorganisation and it conducts the entry check-in in respect of applications related to setting the price and reimbursement. Apart from formal assessment of completeness of applications with the objective of positive validation the department administers web forms and enters basic data from the applications into the systems, which allows for subsequent integrated processing in expert evaluation.

In 2012 the number of applications submitted increased by 14.9% compared to the previous year (in total by 98 administrative procedures). There was a high increase in particular in January due to Price Regulation 1/2012/FAR of the Ministry of Health of December 12, 2011 which placed an obligation on originators to submit applications for determination of maximum price for price regulated medicinal products for which the maximum price has not been set by the Institute, within 30 days from the regulation coming into effect (Tab. 37).

Individually prepared medicinal products (IPLP)

Legislative change

As of January 1, 2012 an amendment to Act No. 235/2004 Coll., on value added tax (hereinafter the VAT), came into force, which increased the VAT from 10 to 14%. As of the above date three general proceedings were finished in summary proceedings, which in compliance with the VAT change

Table 35. 10 most often distributed medicinal products by the number of packages reported in compliance with DIS-13, for which reimbursement from health insurance was changed

Code	ATC	Name	Name supplement	No. of packages (A)	Original reimb. (CZK)	New reimb. (CZK)	No. of packages (B)	*/
0107295	B05BB01	0.9% SODIUM CHLORIDE IN WATER FOR INJECTION FRESENIUS	INF SOL 1X100ML-PE	1 200 256	13,97	3,75	1 342 890	
0014075	C05CA53	DETRALEX	POR TBL FLM 60	719 071	111,08	137,41	692 650	
0098219	C03CA01	FURON 40 MG	POR TBL NOB 50X40MG	588 776	41,08	57,72	617 937	
0097682	B05BB01	CHLORID SODNÝ 0,9% BRAUN	INF SOL 1X250ML-PE	631 699	15,68	9,37	543 466	
0107298	B05BB01	0.9% SODIUM CHLORIDE IN WATER FOR INJECTION FRESENIUS	INF SOL 1X250ML-PE	448 417	16,90	9,37	502 842	
0091788	N05BA12	NEUROL 0,25	POR TBL NOB 30X0.25MG	459 464	5,22	7,92	422 795	
0107291	B05BB01	0.9% SODIUM CHLORIDE IN WATER FOR INJECTION FRESENIUS	INF SOL 1X500ML-PE	394 687	15,81	18,74	445 589	
0050335	A03DA02	ALGIFEN NEO	POR GTT SOL 1X25ML	425 949	52,26	56,20	399 808	
0026578	C09DA07	MICARDISPLUS 80/12,5 MG	POR TBL NOB 28	172 844	208,22	128,82	181 110	*/
0020132	N06AB10	CIPRALEX 10 MG	POR TBL FLM 28X10MG I	149 531	291,81	200,00	176 298	*/

*A – No. of packages distributed during 6 months before change, B – number of packages distributed during 6 months after change, */ - the period of one quarter.*

adjusted reimbursements of individually prepared medicinal products of the group of prepared radiopharmaceuticals, prepared parenteral nutrition products for home therapy and transfusion products. As of the above date a new Price Regulation 1/2012/FAR came into force amending e.g. Annex 1 of Price regulation and newly defining extemporaneous preparation fee groups including the highest possible reimbursement for special products as well as their cost.

In the first half of 2012, the Institute carried out two revisions focused on verifying the validity of issued methodologies for the determination of reimbursement amounts for two IPLP subgroups, namely transfusion products and prepared radiopharmaceuticlas. Revised IPLP cost items in CZK according to the data from health insurance companies were applied in statistics. In the course of the year updated methodologies for individual IPLP groups were issued pertaining to the procedure and conditions of reimbursement and adoption of general measures due to legislative change and in compliance with the results of the revisions.

General Measures

A total of 8 proceedings on general measures (hereinafter referred to as OOP) were initiated and duly completed in the course of 2012. In the first quarter of 2012 the OOP 01-12 was initiated at the motion of expert society for clinical nutrition to change the reimbursement amount for children's packages of parenteral nutrition for home therapy (hereinafter referred to as DPV). A new basic component of Peditrace allowing for suitable combination of electrolytes for prematurely born or small children up to 4 years of age with low weight up to 15 kg whose use in child nutrition was stipulated by approved specific programme and ensures improvement of nutritional properties of DPV for child patients was included in the reimbursement. When calculated with regard to the volume of prepared child DPV in 2011 the measure provided savings of 0.1% of total DPV cost, which corresponds to approx. 5682 CZK/year. At the motion of the health insurance company the proceedings OOP 02-12 were initiated in the first half of 2012 for the group of prepared radiopharmaceuticals, which reflected also the results of conducted revision and new price background documents. The changes represent an increase of reimbursement by 1% on average, which does not exceed the permitted year-on-year limit determined by the effective price regulation and represents an annual increase by 5.9 mil. CZK for

this IPLP group. When dealing with comments pertaining to the reimbursement conditions for prepared radiopharmaceuticals and transfusion products at specialized workplaces the Institute used the possibility provided for by Act No. 500/2004 Coll., Administrative Procedure Code, as amended, i.e. public consultations, the conclusions of which are part of OOP 03-12 for radiopharmaceuticals and OOP 04-12 for transfusion products. In the second half of 2012 preparatory negotiations related to the amendment of reimbursement conditions for individually prepared (extemporaneous) medicinal products were carried out. The amendment extended the list of codes representing individual cost groups in the IPLP (extemporaneous) list connected to the changes of extemporaneous preparation fee. Other changes for this group of medicinal products are unification of conditions for IPLP reimbursement with authorised human medicinal products reimbursement with a view to reduce cost for this group of medicinal products. The conclusions are part of OOP 05-12, which came into force as of December, 1, 2013.

At the end of 2012, in connection with the amendment to Act No. 235/2004 Coll. on Value Added Tax (hereinafter referred to as VAT), as amended (No 500/2012 Coll.), adjustments of reimbursement for all IPLP subgroups were proposed. The procedure regarding these changes was carried out, due to time constraints and in accordance with the provision of Section 172, paragraph 3 of Act No. 500/2004 Coll., the Administrative Procedure Code, as amended, only in the form of summary procedure. Proposals for general measures 06-12, 07-11 and 08-11 adjust the amount of reimbursement only in case of items subject to Value Added Tax, by increasing the original 14% VAT to 15% VAT. This change means increasing the reimbursement of individual IPLPs ranging from 1 to 2% and does not exceed the permitted 3% annual limit stipulated by the effective price regulation. Own OOP was in compliance with the provision of

Table 36. 10 most often distributed medicinal products by financial volume in end user prices reported in compliance with DIS-13, for which reimbursement from health insurance was changed

Code	ATC	Name	Name supplement	Financial volume in end user prices (CZK)	Original reimb. (CZK)	New reimb. (CZK)	Change in reimb. in %
0014075	C05CA53	DETRALEX	POR TBL FLM 60	591 584 173	111,08	137,41	23,7
0028028	L01XE01	GLIVEC 400 MG	POR TBL FLM 30X400MG	339 565 192	69 593,17	58 579,62	–15,8
0027184	L04AA23	TYSABRI 300 MG	INF CNC SOL 1X15ML (20MG/ML)	329 446 935	41 910,71	39 592,46	–5,5
0028026	L01XE01	GLIVEC 100 MG	POR TBL FLM 60X100MG	279 814 355	34 764,39	29 289,81	–15,7
0014498	G04CA02	OMNIC TOCAS 0,4	POR TBL PRO 100X0.4MG	233 458 075	1 060,88	840,73	–20,8
0026578	C09DA07	MICARDISPLUS 80/12,5 MG	POR TBL NOB 28	211 835 919	208,22	128,82	–38,1
0149308	A10BX07	VICTOZA 6 MG/ML	INJ SOL 2X3ML	188 568 670	1 209,58	1 278,21	5,7
0018279	G04BD08	VESICARE 5 MG	POR TBL FLM 100X5MG	183 553 637	2 212,42	1 475,58	–33,3
0072972	J01CR02	AMOKSIKLAV 1,2 G	INJ PLV SOL 5X1.2GM	181 725 005	594,22	376,45	–36,6
0020132	N06AB10	CIPRALEX 10 MG	POR TBL FLM 28X10MG I	177 943 608	291,81	200,00	–31,5

A – total cost in end user prices for 2012.

Table 37. Validation of applications for determination/ change/cancellation of maximum prices and reimbursement amounts and conditions, for summary revision of system of maximum prices or reimbursement

Year 2012 – month	No. of applications submitted	Suspended for defective submission and deficiencies in application	Discontinued in the validation phase
January	112	25	11
February	88	27	13
March	85	10	2
April	53	3	1
May	54	10	2
June	52	1	2
July	52	3	1
August	48	6	1
September	62	13	3
October	73	10	1
November	44	5	1
December	32	0	0
Total	**755**	**88**	**38**

Section 173, paragraph 1 of the Administrative Procedure Code issued in the summary proceedings as of January 1, 2013.

IPLP costs

Costs of individual IPLP groups in 2012 were assessed with regard to price development and against the previous year. In case of the group of transfusion products, no adjustments of reimbursement amounts were carried out in the course of 2012, therefore there was no increase in cost related to VAT increase compensated for by regulation and adjustment of reimbursement at the end of 2011. The drop in total cost of transfusion products group is related to the decrease in their total use, from 608855 DJ in 2011 to 580173 DJ in 2012. The group of individually prepared radiopharmaceuticals in spite of average 1% increase of reimbursement shows only mild increase of cost compared to 2011. The 11% increase is caused by the extension of the range of products of positron radiopharmaceuticals and work places with PET diagnostics and has been compensated for by a 5% decrease of use of radiopharmaceuticals containing 99mTc. The increase of cost of the DPV group by 13% in 2012 compared to 2011 indicates further transfer of inpatients to outpatients and in particular to care in own social care facility. Compared to 2011 the number of DPV patients increased by 29%. The highest increase, by 49%, was detected in case of individually prepared (extemporaneous) medicinal devices, where the increase reflects the change implemented by the effective price regulation and new system of extemporaneous preparation fee.

5.1 Information technology

The IT Branch is responsible for flawless operation of the whole IT infrastructure, information technology supervision and IT infrastructure security against the outside attacks. The objective is to provide high quality service to users in the Institute as well as cooperating entities.
The IT Branch actively participates in projects pertaining to the development of information technology and data safety.

A consolidation was initiated in the IT Branch with regard to contractual relations as well as improving quality of IT administration. An analysis of current IT status was carried out with a view to improve the quality of IT management and financing processes including the control of external IT service providers. Work related to the enhancement of role of IT Branch in monitoring of IT operational and security parameters started. In the area of data analyses a high performance BI tool was deployed, which will speed up significantly and improve the quality of statistical outputs for the needs of the Institute management, units of expert activities branch, supervisory bodies and the public.

In order to improve the above services and to reflect the IT trends a number of technology measures was adopted. In the area of HW they were the following:
- increasing capacity of disk field
- purchase of new notebooks for inspectors
- expansion of data centre by 2 pcs. of Blade servers

In the area of SW and system measures they were the following:
- upgrade of servers from MS Windows server 2003 to 2008 version
- upgrade of MS Exchange mail system to 2010 version
- upgrade of MS Office to 2010 version
- upgrade of email archiving system
- optimisation of DMS and document service communication

Fig. 1. Document viewing via verso website service in 2012

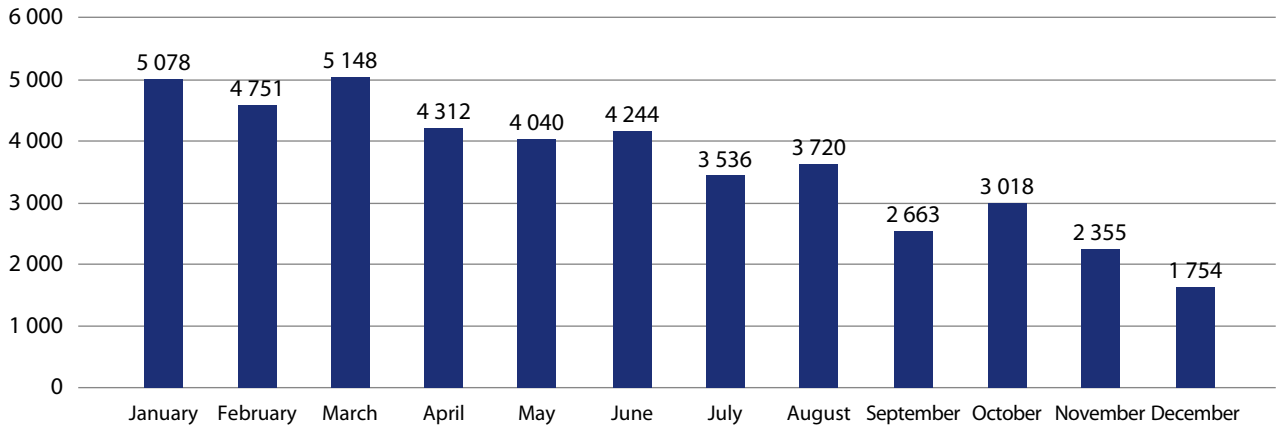


Fig. 2. Number of entities connected to the Database of Administrative Proceedings interface in 2012

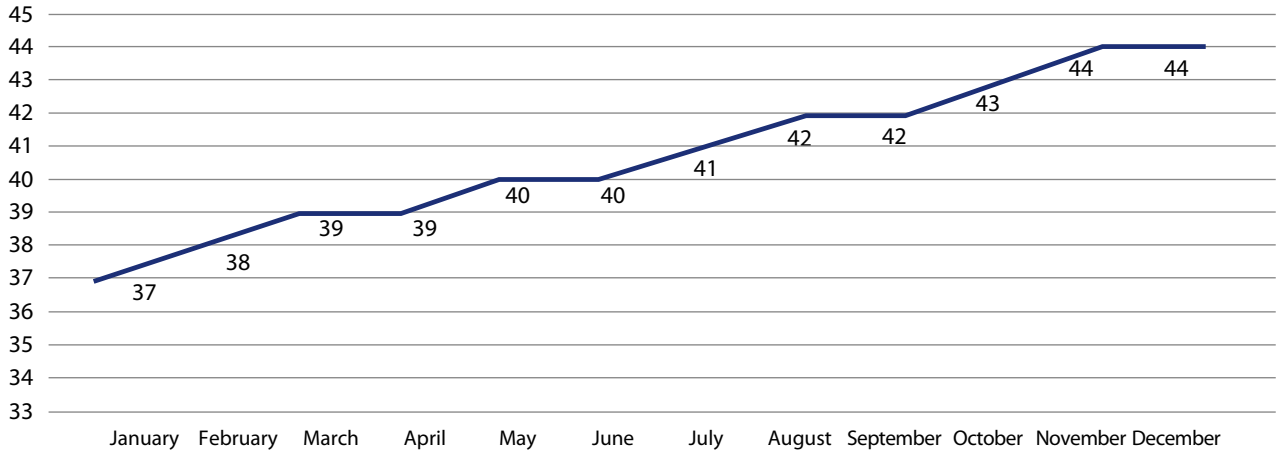
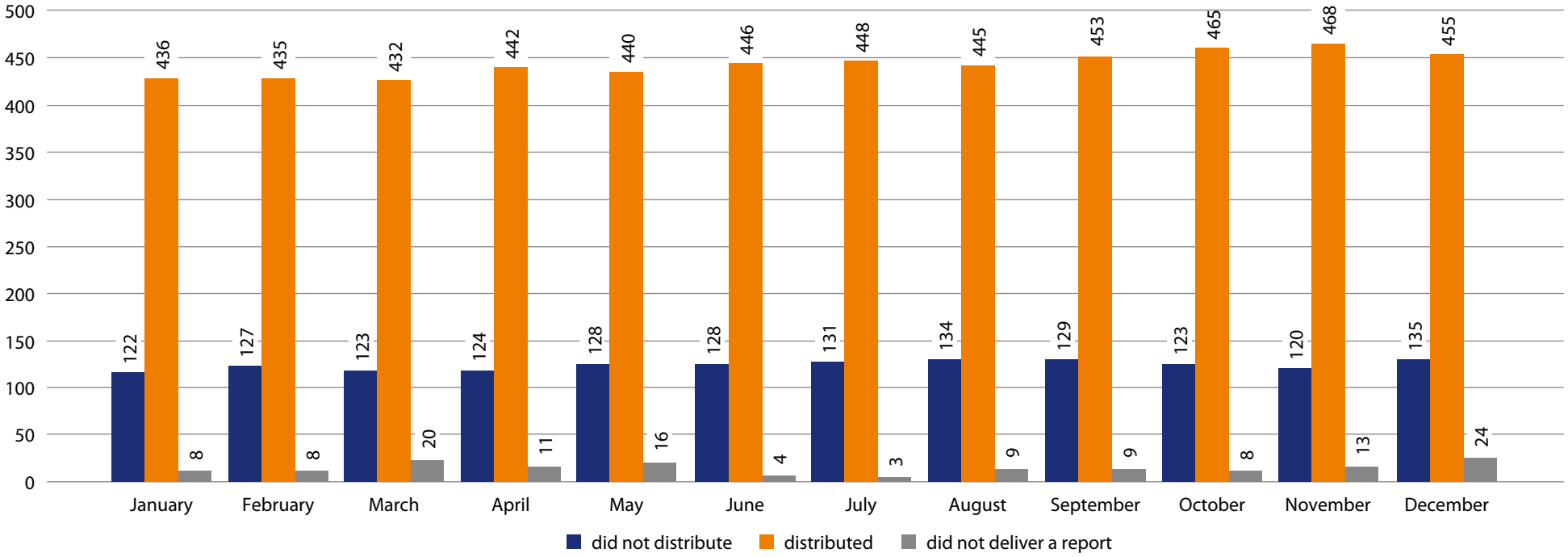


Fig. 3. Overview of distributors' reports within the DIS13 system in 2012



- start of implementation of new monitoring tools Actional Intermediary

The IT Branch puts high emphasis on increasing the level of information security. Therefore the encryption SW was updated and the related reinstallation and reencryption of PCs and notebooks was carried out.

Agreements on service support of key IT areas of the Institute were concluded in order to improve the services of IT Branch. These are in particular the following:

- ORACLE systems service support
- infrastructure service support
- integration infrastructure systems service support
- application software operation support
- ICT end user devices outsourcing
- ePrescription application software operation support
- LEK13 and DIS13 application software operation support
- web portal operation support

In 2012, the IT Branch put emphasis on providing high quality service to cooperating entities. At the end of 2012, a total of 89 % of pharmacies participated in the system of data collection and 95% of distributors submitted reports on their activities within the deadline.

5.2 Database of medicinal products and monitoring of supplies to pharmacies

With regard to the obligation stipulated by the Act on Pharmaceuticals, the Institute maintains a registry of authorised medicinal products and provides for the

publication of selected information in its information media. For the purposes of this registry, the Institute uses an internal database of medicinal products (DLP) which is updated on an on-going basis.

Registry of active substances

Currently, the Database of Medicinal Products (DLP) contains 21,954 substances, in 2012, 386 new components were entered and data was updated for 10,358 components.

In 2012, update of flagging of doping components and of products containing such substances in DLP was carried out pursuant to The 2012 Prohibited List – The World Anti-Doping Code effective as of January 1, 2012.

Supplements of latest version of European Pharmacopoeia 7.0 continued to be entered in the database, The Czech Pharmacopoeia 2009 – Supplement 2012 was entered in the database.

Registry of Medicinal Products

In 2012, the Institute issued 703 decisions on marketing authorisation (5,543 SÚKL codes). Authorisation was revoked for 1,865 marketing authorisation numbers, which corresponds to 12,419 codes. The authorisation was cancelled either at the request of the marketing authorisation holder (654 authorisation numbers), due to the Sunset Clause (197 authorisation numbers) or due to the fact that the holder did not apply for authorisation renewal (1,014 authorisation numbers). In 2012, the validity of 13,938 codes in total expired (the period of final code sale expired or marketing authorisation was revoked).

In the course of 2012, the distribution of 45,678 SÚKL codes of medicinal products in total (84.48%) excl. homeopathic products was not reported. Hence despite having a valid marketing authorisation, these products were not marketed.

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

Table 1. Selected subgroups of authorised medicinal products recorded in the SÚKL database as of December 31, 2012

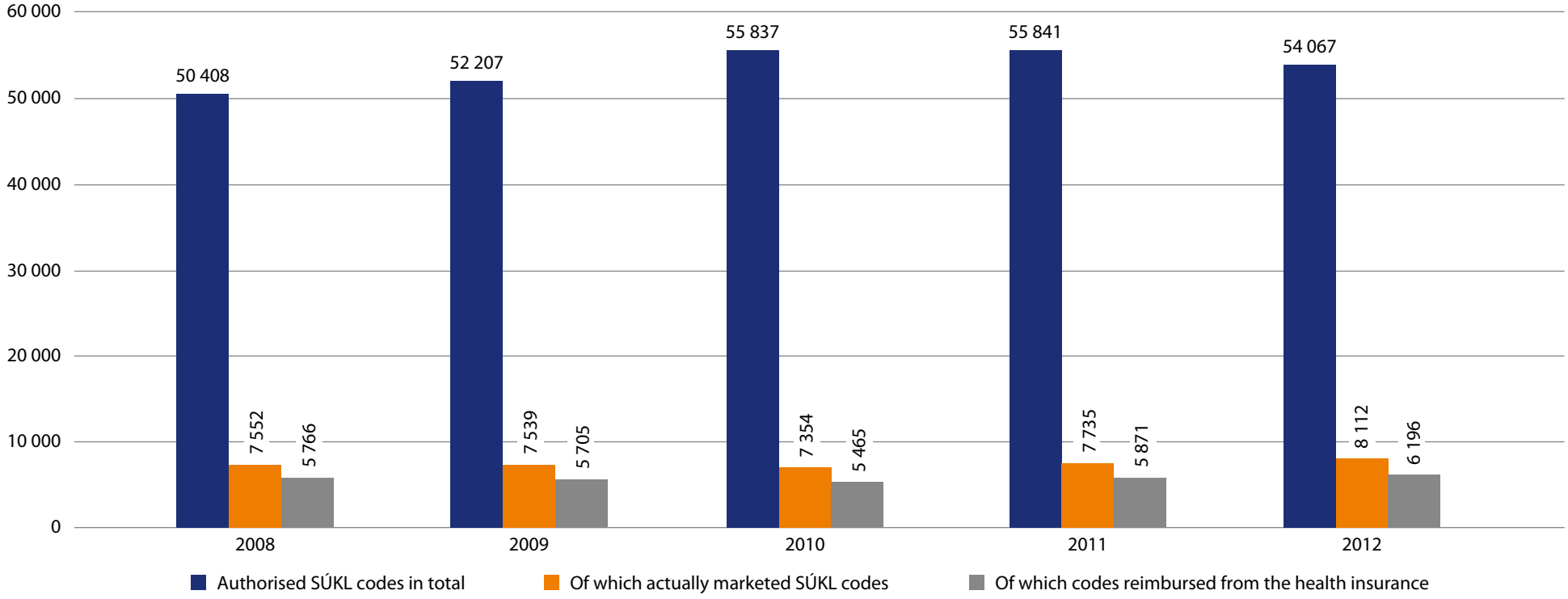
	Total no. of authorised MA numbers/marketed MA numbers	Total no. of SÚKL codes/marketed SÚKL codes
Medicinal products in total (excl. homeopathic products)	**14 555/5 570**	**54 067/8 112**
Of which by MA numbers:		
MA numbers granted by the Institute	6 647/4 753	46 065/7 256
MA numbers of products authorised via Community centralised procedure	7 908/817	7 927/819
Of which by content:		
Single-component	11 544	45 303
Multi-component	3 011	8 764
Of which by type of dispensing:		
Prescription-only medicinal products	13 751/4 862	50 975/7 051
Sale OTC	863/723	3065/1048
Restricted Sale OTC	12/8	27/13
Homeopathic products	**268/257**	**714/347**

within the scope of the database of authorised medicinal products.

Since 2008, the Institute has been publishing the List of reimbursed medicinal products and foods for special medical purposes, including its updates, on its website. In 2010, the system of so-called Control List publishing was established, which notifies health professionals in advance of possible changes to maximum prices and reimbursements implied by completed decisions which came into force. In 2011, in accordance with Act No. 298/2011 Coll. the name Control List was changed to the 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 on the market, in the overview of variations to marketing authorisations or in the overview of non-interventional post-marketing studies.

Fig. 4. Authorised medicinal products in the period 2008–2012



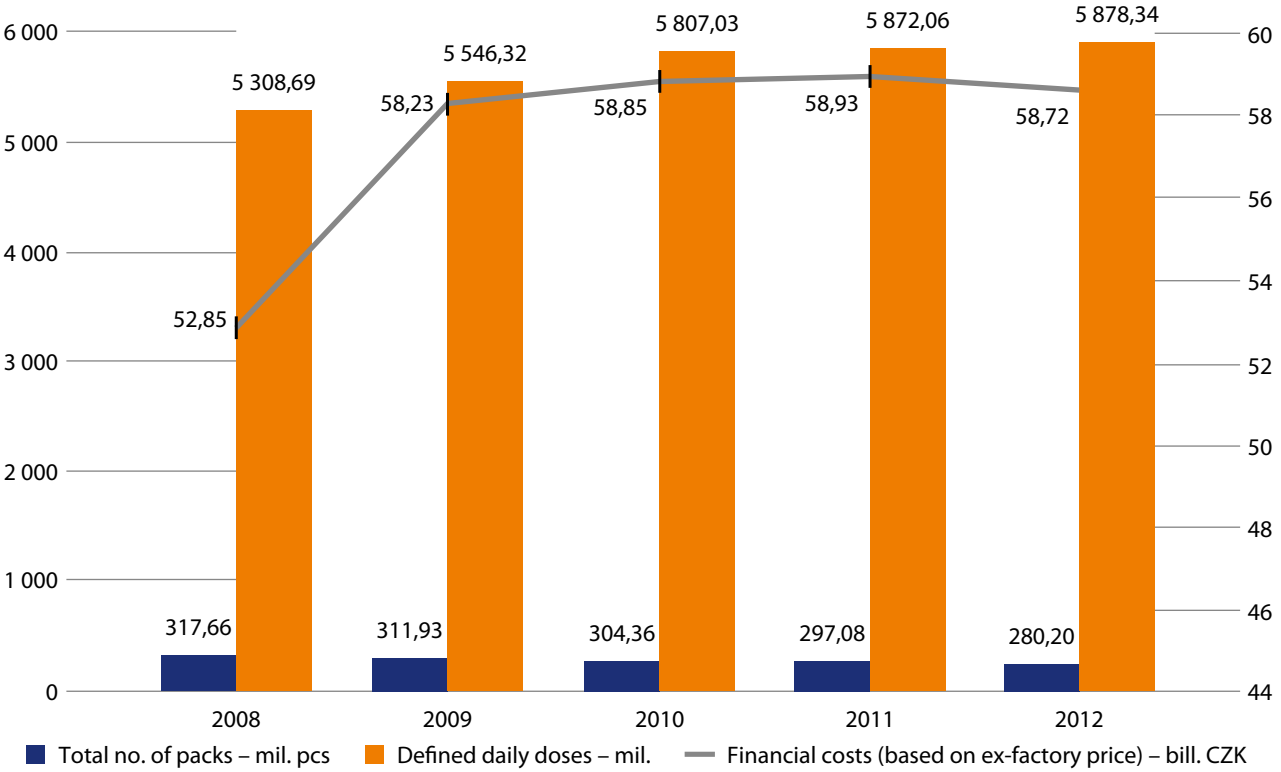
Evaluation of deliveries of distributed medicinal products

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 2012. The subject-matter of the reports concerned the deliveries of medicinal products to pharmacies, other healthcare establishments in the Czech Republic and abroad. In addition to the authorised medicinal products, also products used in special therapeutic programmes

Table 2. Deliveries of distributed medicinal products in 2012

Medicinal products in total	No.
Deliveries to pharmacies and healthcare establishments (mil. packages)	280,195
Deliveries to pharmacies and healthcare establishments (mil. CZK based on ex-factory price)	58 720,589
Deliveries to pharmacies and healthcare establishments (mil. DDD)	5 878,337
DDD/1000 inhabitants/day	1 526,757
Prescription-only medicinal products	**No.**
Deliveries to pharmacies and healthcare establishments (mil. packages)	191,991
Deliveries to pharmacies and healthcare establishments (mil. CZK based on ex-factory price)	52 794,063
Deliveries to pharmacies and healthcare establishments (mil. DDD)	5 366,726
DDD/1000 inhabitants/day	1 393,878
OTC and selected pharmaceuticals	**No.**
Deliveries to pharmacies, healthcare establishments, and vendors of selected pharmaceuticals (mil. packages)	87,558
Deliveries to pharmacies, healthcare establishments, and vendors of selected pharmaceuticals (mil. CZK based on ex-factory price)	5 852,283
Deliveries to pharmacies, healthcare establishments, and vendors of selected pharmaceuticals (mil. DDD)	511,031
DDD/1000 inhabitants/day	132,728
Restricted OTCs	**No.**
Deliveries to pharmacies and healthcare establishments (mil. packages)	0,646
Deliveries to pharmacies and healthcare establishments (mil. CZK based on ex-factory price)	73,949
Deliveries to pharmacies and healthcare establishments (mil. DDD)	0,580
DDD/1000 inhabitants/day	0,151
Homeopathic products	**No.**
Deliveries to pharmacies (mil. packages)	1,628
Deliveries to pharmacies (mil. CZK based on ex-factory price)	133,617

Fig. 5. Deliveries of medicinal products in the period 2008 – 2012



and non-authorised products supplied on medical prescription to a specific patient were included in the evaluation.

Data on the volumes of distributed medicinal products in number of packages, in financial volumes (in CZK), and in DDD were evaluated. With a view to the need to compare their value over the years, data on financial costs are provided in originator prices, i.e. ex-factory prices excl. VAT (VAT rates were changing over the years), and excl. profit margin. The regular quarterly evaluation of supplies of distributed products has been, since 2008, 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).

In 2012, the Institute in evaluating supplies of distributed medicinal products each quarter newly focused upon a selected group of medicinal products and evaluated the long-term development within the concerned group in detail. In the 1st quarter it was the group of antihistaminic products, in the 2nd quarter the N06D group – Alzheimer's Disease therapy; in the 3rd quarter treatment of acidity disorder related diseases; and in the 4th quarter influenza vaccines.

In 2012, 280.195 mil. packages of medicinal products were distributed, which corresponds to approx. 5878.337 mil. defined daily doses. The value of these deliveries was 58.72 billion CZK (based on ex-factory price).

5.3 Information activities

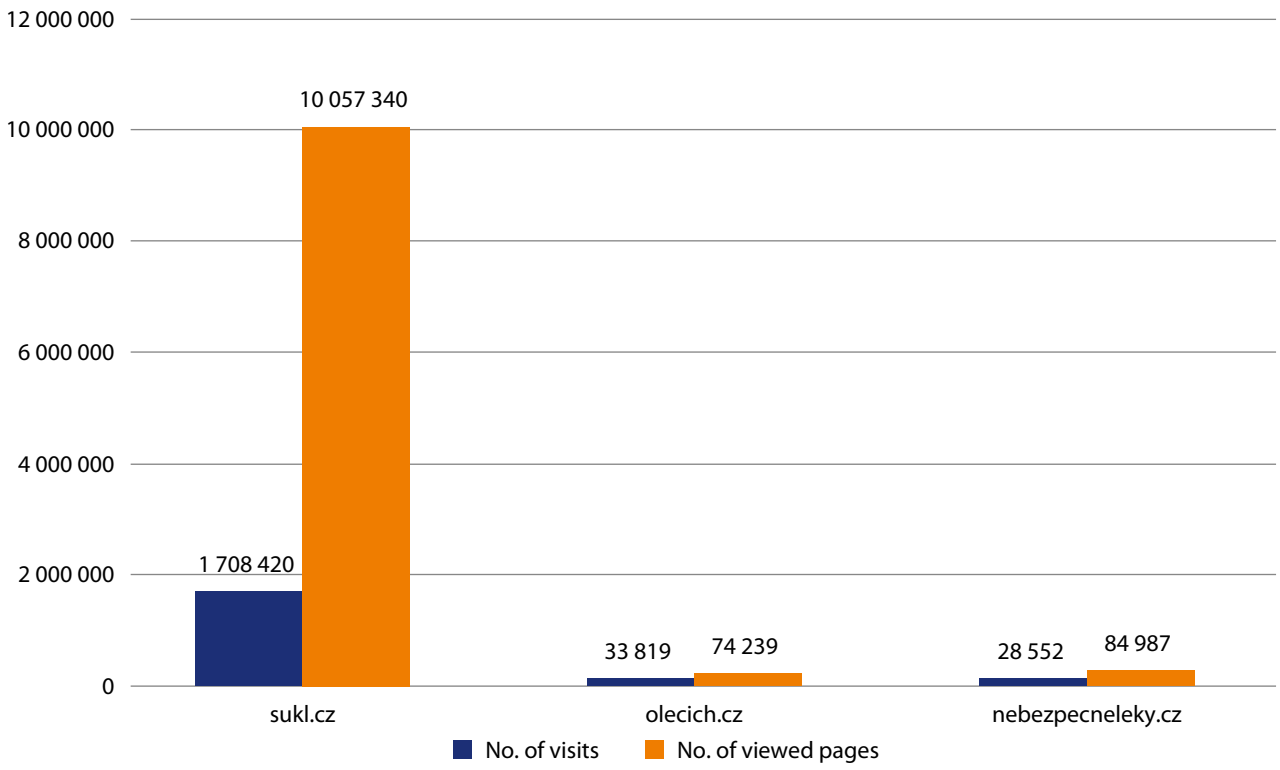
The Press and Information Department (TIO) provides information to the expert as well as general public.

TIO provides for the operation and administration of SÚKL's website www.sukl.cz, the Public Information Portal located at www.olecich.cz and the website of the hazardous medicines campaign www.nebezpecneleky.cz.

In 2012, the webpage for professionals www.sukl.cz had 1.7 mil. visitors who viewed more than 10 million pages.

The address of the Public Information Portal www.olecich.cz was entered into the web browser by 33 thousand of visitors who viewed over 74 thousand pages. The aim of the portal is to educate and protect the public against unverified and inaccurate information in the area of pharmaceuticals. In 2012, there were published 10 new issues of the infoLISTY publication, which focuses on selected topic of the area of health and medicines every month.

Fig. 6. Number of visits and viewed pages on the Institute's information portals



As part of the "Ask-an-Expert" service pharmacists and doctors – general practitioner and paediatrician, gynaecologist, a physician specialising in travel medicine, paediatric pulmonologist and a physician specialising in sports medicine answered questions from the public. The service was used by a total of 500 enquirers.

Part of the www.olecich.cz portal and www.nebezpecneleky.cz webpage are also Facebook profiles where TIO regularly publishes important warnings, information and curiosities.

TIO also maintains the professional library of the Institute and is responsible for the publishing activities of SÚKL, which involves the preparation and publication of SÚKL Bulletin, and the drug bulletin Farmakoterapeutické informace (Pharmacotherapeutic Information), a member of the International Society of Drug Bulletins (ISDB) and the electronic Adverse Drug Reactions bulletin. All publications are available from SÚKL's website at www.sukl.cz.

In 2012, TIO processed 29 requests for information pursuant of Act No. 106/1999 Coll., on Free Access to Information, as amended, and via its information phone line and e-mail address infs@sukl.cz it answered 6,050 enquiries. TIO issued 10 SÚKL press releases or advices and answered 169 journalists´ questions and provided 30 opinions to the media (TV and radio). Together with the Ministry of Health, a press conference was held at the occasion of the publication of the Stories of Medicines.

In the mid-2012 the Institute published the Stories of Medicines by Tomáš Cikrt, which is accessible from the portal in various electronic formats; from dynamic PDF, the format for e-book readers and tablets and an audio version. The printed version is designated mainly for organisations representing people with difficult or limited access to the Internet, i.e. patients' organisations and organisations of the elderly in particular. The Institute distributed the book to public municipal libraries all over the Czech Republic.

In 2012, TIO prepared and carried out two surveys. One of them was a regular annual survey Pharmaceutical Policy Issues focused on doctors, pharmacists and the general public. The other survey Actual Use of Pharmaceuticals and its Financial Impact on the Czech Healthcare System was a unique project in terms of its scope, since apart from the data gathered from pharmacies and regions it collected information from 2,000 households in the Czech Republic. The results of the survey show that every year medicines in the amount of approx. 1 billion CZK are returned to pharmacies for disposal, which

means unbelievable 245 tons of disposed pharmaceuticals. Other medicines in the amount of hundreds of million are thrown to municipal waste.

In September 2012, TIO acquired a new responsibility for internal communication within SÚKL. TIO is responsible for internal communication system management in order to provide for early, accessible and correct information necessary for due performance at work of the Institute staff. At the end of 2012 TIO started to carry out adjustments and development of the intranet portal for employees, which is an essential tool for the Institute's communication.

TIO also intensively cooperated and communicated with patients' organisations, especially via the olecich.cz portal. There was an intensive cooperation with the Czech organisation of blind and visually impaired (SONS), thanks to which the information portal was adjusted in order to meet the requirements of the "blind friendly web" and be accessible to blind and visually impaired patients.

Income

In 2012, a total off-budget income of 620,952 thous. CZK was generated. The major part of this income was generated by reimbursement for expert activities which, pursuant to Act No 378/2007 Coll., on Pharmaceuticals, as amended, 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 218/2000 Coll., on Budgetary Rules, as last 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 2012, a total amount of 373,193 thous. CZK were thus used through permissible excess expenditure. Of this amount, 310,564 thous. CZK were used for operating purposes whereas 62,629 thous. CZK were used to cover investment needs.

In addition to income from reimbursement of costs for expert activities, another part of income was obtained from the state budget, e.g. through the collected administrative fees for submitted applications amounting to 35,643 thous. CZK, income generated from imposed fines amounting to 2,578 thous. CZK, income generated from the interest on funds on deposit accounts with the Czech National Bank, etc. An overview of recorded budgetary income as of 31/12/2012 is shown in Table 3.

Expenditure

Data concerning expenditure incurred in 2012 are provided in Tables 3 to 5, broken down by individual categories.

Total investment expenditure amounted to 62,629 thous. CZK. Investment resources were utilised to complete the renovation of buildings in Brno (20,802 thous. CZK) and in Prague (6,501 thous. CZK), a renovation of laboratories was carried out (11,079 thous. CZK) and laboratory devices were purchased (3,938 thous. CZK). Further investment expenditure was incurred primarily in the IT area: the reporting and analysis platform upgrade (10,571 thous. CZK), e-learning (4,486 thous. CZK), disk array upgrade (2,373 thous. CZK), Internal Identity Software, Medicinal Products Database Management System, modification of the Economic Information System (RIS) in accordance with the Treasury, adjustments made to the Athena record system, etc.

Operating expenditure amounting to the total of 346,209 thous. CZK was related to the activities of regulatory units fulfilling the tasks of the Institute. Of the total volume, the extra budgetary funds used to cover operating expenditure amounted to 310,564 thous. CZK and state budget funds to 35,645 thous. CZK.

Assets

The total assets of the Institute as of December 31, 2011 were 2,179,946 thous. CZK, of which the volume of fixed assets is 361,611 thous. CZK and the volume of current assets is 1,818,335 thous. CZK. Of the total liabilities amounting to 2,179,946 thous. CZK, 2,154,163 thous. CZK are own capital and 25,783 thous. CZK are borrowed capital. Selected types of assets and liabilities of the Institute are specified in Table 2.

Other

2,700 thous. CZK from the budget of the Institute were paid for business trips abroad. Most of these business trips were related to regular meetings of different committees and working groups in relation to the membership in respective bodies. The Institute has members or alternates in more than 60 groups across the EU institutions and international organisations. Other business trips were approved taking into account the priorities of the Institute, the relevance and the benefits for the Institute of the topics covered.

Table 1. Funds and the state budget

	2010 (Average headcount – 333)	2011 (Average headcount – 313)	2012 (Average recalculated headcount – 318,57)
Funds allocated from the state budget for the operation of SÚKL (thous. CZK)	45 182	26 000	39 690
Payments to the state budget (thous. CZK)	40 151	42 705	46 986

6. Financial and material resources of the Institute

Table 2. Overview of the Institute's selected assets and liabilities in thousands of CZK

Name of item	Previous period 2011	Current period 2012
ASSETS	**1 957 109**	**2 179 946**
A. Total fixed assets	**381 294**	**361 611**
including:		
I. Total intangible fixed assets	118 530	109 227
II. Total tangible fixed assets	262 764	252 384
Land	3 984	3 984
Buildings	144 805	185 910
Separate movables and sets of movables	71 255	62 424
Low-value fixed assets	35 641	0
Tangible fixed assets in the course of construction	7 079	66
B. Total current assets	**1 575 815**	**1 818 335**
including:		
I. Total inventories	54	54
II. Total receivables	4 790	3 394
III. Current liquid assets	1 570 971	1 814 887
LIABILITIES	**1 957 109**	**2 179 946**
C. Equity	**1 933 877**	**2 154 163**
including:		
I. Accounting entity assets including adjustments	263 023	220 799
II. Total financial and money funds	1 547 361	1 794 659
Fund of cultural and social needs	1 275	824
Reserve fund	1 546 085	1 793 835
III. Economic result	18 984	–17 084
IV. Revenue and expenditure account of budgetary operations	104 510	155 789
D. Total borrowed capital	**23 231**	**25 783**
including:		
I. Total long-term liabilities	0	40
II. Total short-term liabilities	23 231	25 743

Table 3. Budget income, budget expenditure and financing in thousands of CZK

Budget Income	Budget for 2012		2012 reality
	Approved budget	Corrected budget	
Administrative fees	9 000	9 000	35 643
Penalties received	1 000	1 000	2 578
Income from property lease	0	0	44
Non-equity contributions received	0	0	666
Interest income	0	0	1 990
Other income	0	0	4
Transfers from reserve fund	0	0	310 572
Transfers from other own funds	0	0	2 388
Operating transfers from the National Fund	12 257	12 257	3 607
TOTAL	**22 257**	**22 257**	**357 558**

Expenditure	Budget for 2012		2012 reality
	Approved budget	Final budget	
Employees' salaries	79 386	221 511	161 806
Other personnel expenditure	3 265	11 939	9 490
Mandatory premium paid by employer	28 102	77 557	56 424
Contribution to the Fund of Social and Cultural Needs	794	2 220	1 620
Operating acquisitions and related expenditure	14 377	120 919	116 869
Acquisition of tangible and intangible fixed assets	0	62 630	62 629
TOTAL	**125 924**	**496 776**	**408 838**
including: Current expenditure	125 924	434 146	346 209
Capital expenditure	0	62 630	62 629

Table 4. Operating expenditures of the Institute's individual departments and branches as of December 31, 2012 (thous. CZK)

Units	Operating expenditure	Dedicated expenditure
Division of Director, internal audit, quality management department	380	30 867
Division of Deputy Director for Economic Issues	69	0
Division of Deputy Director for IT	14	300
Division of Deputy Director for Regulatory Affairs	206	2
Total	***669***	***31 169***
Service Activities Branch	167	25 067
Economic Issues Branch	42	4 008
IT Branch	375	52 109
Surveillance Branch	2 942	3 317
Marketing Authorisation Branch	843	0
Price and Reimbursement Regulation Branch	366	297
Cost reduction on an accrual basis	*0*	*–4 502*
Total expenditure	**5 404**	**111 465**

6. Financial and material resources of the Institute

Auditing

In 2012, the Ministry of Health of the Czech Republic conducted an on spot inspection pursuant to Section 13 paragraph 1 of the Act No 320/2001 Coll. focused on the compliance with legislation, especially the Act No 137/2006 Coll. on Public Contracts, internal procedures and standards in public procurement, procurement of small scale contracts and contracts awarded within a negotiated procedure without publication. The summary of the inspection outcome revealed misconduct in the area of internal regulation, of the Public Contracts Act in general as well as in individual contracts subject to the inspection. Already in the course of the inspection, the Institute reacted to the misconducts revealed and took corrective measures.

In relation with the utilisation of EU funding for the project called Establishment of an Evaluation System of Process Efficiency of the Institute and its Branches, an inspection was carried out by the Ministry of Interior of the Czech Republic following the public service inspection rules in accordance with Sections 12 to 21 of Act No 320/2001 Coll. The inspection summary did not reveal any errors of neither factual nor financial nature, no influence was noted on the selection of the best provider, and the procedures adopted for the project in question were found to be in accordance with Act No 137/2006 Coll.

A fine amounting to a total of 240,819 CZK was paid into the state budget through the employment office imposed for not having fulfilled the obligation to employ disabled persons in compliance with Act No 435/2004 Coll.

Furthermore, two inspections by the VZP health insurance company and the Prague Social Security Administration were conducted in 2012. No corrective measures were required.

Table 5. Expenditure statistics in the period 2010–2012

	2010	2011	2012
Total operating expenditure (thous. CZK)	320 698	310 377	346 209
Operating expenditure (excl. wages, insurance and the Fund of Cultural and Social Needs) (thous. CZK)	82 044	86 586	116 869
Capital assets expenditure (thous. CZK)	61 003	56 025	62 629
Average converted number of employees	333	313	318,57
Expenses per employee (line 1/line 4)	963	992	1 087

7.1 Personnel issues

Some personnel changes were made in the Institute management and a new organisational structure was implemented mid-2012. Related to establishment of the new organisational structure and to the Institute's tasks arising from its legal obligations, the Ministry of Health of the Czech Republic approved in the course of 2012 an increase of the planned headcount by 14 FTEs to a total of 325.073 FTEs. This planned number of FTEs was used as of 31/12/2012 at 98.2% which means that 319.2 FTEs were occupied. The average number of used FTEs on a cumulative basis, since the beginning of the year was 316.68 FTEs.

The number of physical employees on payroll as of December 31, 2012 was 339 persons, of which 281 were women (i.e. 82.89%) and 58 men (i.e. 17.11%). Converted to FTEs worked under contracts of work and contracts of services a total number of 22.43 persons were employed as of December 31, 2012, i.e. an increase by 27.4% compared to 2011.

Age structure of employees

The average age of all employees compared to 2011 has increased by 0,2%, i.e. 42.2 years.

Working hours utilisation

Of the total number of 570,149 hours worked, 663 were overtime hours. Overtime work mostly concerned employees from the workers category (drivers).

Table 1. Age structure of employees (%)

Year	Employees under 35 years (incl.)	Employees aged 36 to 55 years	Employees over 55 years
2010	37,46	46,40	16,44
2011	37,00	48,38	14,68
2012	35,70	47,50	16,80

In 2012, the employees of the Institute were absent for 1,959 working days (2,424 in 2011) due to sickness leave or nursing a family member. Of the total number of employees, absence due to sickness or nursing a family member was observed in case of 94 employees (102 in 2011). Absence due to long-term sickness concerned 10 employees (12 in 2011) absent for less than 2 months, 2 employees (5 in 2011) absent for less than 3 months and 3 employees (12 in 2011) absent for more than 3 months.

Staff turnover

In 2012, 55 new employees started their jobs in SÚKL (2009 = 72; 2010 = 67; 2011 = 64). 40 employees left (2009 = 61; 2010 = 67; 2011 = 64).

Staff turnover was lower compared to 2011 decreasing from 20.64 % to 12.82 %.

Wage policy

- In 2012, total wage and salary bill amounted to 170,057,187 CZK including gross salaries and remuneration of work done outside employment.
- Net paid salaries amounted to 128,971,733 CZK, which corresponds to the net employees' revenues excluding the tax bonus.

Employee benefits

The Institute provides for employee catering contracted out with other legal entities. In compliance with the Decree of the Ministry of Finance No 430/2001 and in compliance with the Agreement concluded between the employer and the trade union organization, "Principles and rules for drawing down the resources from the Fund of Cultural and Social Needs" the employer contributes to the reimbursement of costs per one main meal. In addition to this reimbursement of costs, the employer

Table 2. 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
			2010				
0	4	11	93	10	9	213	7
0 %	1,15 %	3,17 %	26,80 %	2,88 %	2,59 %	61,38 %	2,03 %
			2011				
1	4	10	87	3	13	195	14
0,30 %	1,12 %	3,06 %	26,60 %	0,92 %	3,98 %	59,63 %	4,28 %
			2012				
1	3	10	86	4	15	208	12
0,30 %	0,88 %	2,95 %	25,37 %	1,18 %	4,42 %	61,36 %	3,54 %

contributes to one main meal from the resources of the Fund of Cultural and Social Needs (FKSP) by 10 CZK (in 2011 employer's contribution was 6.65 CZK). In compliance with the above Agreement, the employer supports, by means of FKSP resources, also sports and cultural activities of employees, and motivates employees to take care of their health. Resources for these activities are taken either from the common part of the Fund, which provides for the operation of sports equipment hire service, employee library, sauna, or from the so-called personal employee account, which supports individually focused employee activities. As part of the Support of Employment for Parents with Young Children Programme, the Institute employs a flexible working hours schedule and allows employees to work part-time or from home. This option helps effectively reconcile family life and work of employees and is used in particular in those positions where it is feasible and efficient with a view to the particular work. In 2012, 13 employees (6 in 2011) took advantage of the option to regularly work from home and an average of 24 employees per month do so on a one-off basis. This benefit is used by an increasing number of employees, there was a 20 % increase compared to 2011.

7.2 Employee education

In the area of employee education, similarly as in previous years, emphasis was placed especially on professional training. The overall costs related to employee education amounted in 2012 to 2,641,808 CZK, from which 850,774 CZK were used to cover professional trainings.

The aim of employee education is to permanently guarantee a high level of expertise of employees of the Institute, which can be further deepened also through participation in educational events and expert conferences abroad.

In 2012, 62 applicants among employees of the Institute could benefit from language teaching. The cost of language teaching was 228,634 CZK.

Table 3. Overview of employments terminated in 2012 by reason

Reason of termination of employment	In probationary period	Definite-time employment contract expiry	Termination by agreement	Notices given by employees	Notices for organisational reasons	Total
Total	6	9	5	13	7	40

Table 4. Overview of educational activities in 2012

Type of event	Number of events	Number of hours	Number of attendees	Costs in CZK
PC training	3	48	3	17 550
Language courses	22	1 140	62	228 634
Specialised courses and training	108	2 831	429	850 774
Managerial skills	6	48	38	61 200
Mandatory training	66	161	113	23 350
Foreign specialised training	36	900	45	1 460 300
Total	**241**	**5 128**	**690**	**2 641 808**

The quality management system of the Institute is certified in compliance with the requirements of the ČSN EN ISO 9001:2008 standard and applies to all performed activities. The regular external supervisory audit did not reveal any non-compliances.

The quality management system of the Laboratory Control Department has been put into place in compliance with the ČSN EN ISO/IEC 17025 standard. In 2012, a regular check of the system in place was performed by a group of EDQM auditors. The corresponding certificate will be issued at the beginning of 2013. International recognition of the quality management system is a condition of participation in international studies of centrally authorised medicinal product organised by EMA/EDQM, in the process of recognition of results of MRP/DCP product analysis and of international recognition of batch release of selected medicinal product (OCABR) within the EU.

Information security management policy

The Institute pays attention to ensuring the security and trustworthiness of data and information in its information systems. In 2007 the Institute established the information security management system (ISMS) and this system and its processes were certified pursuant to the ISO 27001 standard. The certificate of the ISMS system of the Institute was renewed in December 2010. The regular supervisory audit by a certification authority is performed on an annual basis. In these supervisory audits, the auditing body did not reveal any non-compliance of the system in place.

The certification authority is CQS – a Quality System Certification Association.

9. Outlook for 2013

As the main task, the Institute will be taking all the necessary measures to implement the requirements of amended regulations, in particular those of the Act on Pharmaceuticals, the upcoming Act on Medical Devices or the Advertising Regulation Act. The new legislative requirements will also be reflected in the modifications of the Institute's organisational structure. The State Agency for Medicinal Cannabis will be created and developed within the Institute. Moreover, the creation of the Medical Devices Branch will help to achieve a smooth take-over and management of competencies in the area of medical devices.

As in previous years, the Institute will be one of important actors in the process of computerisation of the Czech health system. It is managing the Central Repository of Electronic Prescriptions, which has already been accessed by thousands of doctors and pharmacies throughout the Czech Republic. At the same time, a Registry of medicinal products subject to sales restriction will be established. All activities in the area of information technologies aim to allow a smooth introduction of the electronic prescription in the years to come.

One of the main objectives in 2013 will be to increase the support provided to the information and communication activities of the Institute focusing on experts as well as on the lay public. In case of expected fundamental changes in legislation, seminars will be organised for experts including doctors, pharmacists, pharmaceutical associations and companies. Entities concerned will be informed by all means available in order to avoid informational deficit which could give rise to misunderstandings.

As during the last twelve months, the Institute will put emphasis on cooperation in 2013 with patient organisations. Awareness-raising and information activities directed towards the lay public will continue through infosheet publishing as well as through series of talks on safe use of medicinal products based on the book "Stories of Medicines" published last year. With the number of visitors steadily growing from one year to another, the website of the Institute will continue to be the main means of maximising the reach of the information published.

In the upcoming year 2013, the Institute will again focus on all its tasks and obligations in order to provide for accessible, up-to-date, high quality, efficient and safe pharmaceuticals, medical devices as well as human tissues and cells.

MUDr. Pavel Březovský, MBA
Director of the Institute

10. Overview of essential contacts for individual spheres of operation of the Institute

10. Overview of essential contacts for individual spheres of operation of the Institute

Updated as of April 1, 2013. 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.

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