SÚKL

ANNUAL REPORT **2019**

STATE INSTITUTE FOR DRUG CONTROL

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CONTENT

1 INTRODUCTION

In 2019, the State Institute for Drug Control (hereinafter referred to as the "Institute") continued its intensive cooperation with the Ministry of Health of the Czech Republic. This cooperation concerned, in particular, the implementation of tasks within the scope of collaboration with the EU, namely in the sphere of pharmaceuticals and medical devices, and also in the preparation and subsequent legislative process of adoption of new legal regulations, highly relevant for the areas of Institute's operation. In addition to activities associated with these major tasks, the Institute also paid due attention to cooperation in the sphere of drafting other legal regulations governing other areas of relevance for its operation. The Institute continued to explain the statutory requirements in individual areas of its expert activities via its published guidelines. In these guidelines, the Institute also informed the public about guidance published by the European Commission and by the European Medicines Agency (hereinafter referred to as "EMA").

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

In total, 522 applications for new marketing authorisation and 315 applications for marketing authorisation renewal were submitted for expert assessment; furthermore, 333 applications for marketing authorisation revocation were processed.

In 2019, the Institute received 369 applications for clinical trial authorisation/notification, which was three more applications than in the previous year. Most of the applications concerned phase III studies; international, multicentric, randomised, placebo- or active- controlled clinical trials conducted by foreign sponsors. In 2019, the Institute continued its activities in the sphere of Development Safety Update Report (DSUR) assessment and Suspected Unexpected Serious Adverse Reaction (SUSAR) control; 509 DSURs were submitted.

The Laboratory Control Department completed 738 sample analyses. The number of samples rated as non-compliant slightly decreased. These concerned primarily pharmacy samples and samples queried by doctors and patients.

Since 2015, the Quality Defects Department has noted a major increase in the number of instigations regarding the occurrence of counterfeit medicinal products in the legal distribution chain or product theft. In 2019, the Quality Defects Department addressed 41 such cases in total, of which seven were cases of theft of medicinal products from the legal distribution chain.

In the course of 2019, the Section of Pricing and Reimbursement Regulation continued to commence in-depth reimbursement revisions as planned; within the scope of these revisions, it was assessed whether the established amounts and conditions of reimbursement were consistent with the conditions set forth by the Act on Public Health Insurance. In 2019, 28 in-depth revisions (concerning 276 SÚKL codes) were commenced.

Savings in public health insurance funds were generated both through in-depth and abbreviated reimbursement revisions. The total savings generated by abbreviated revisions and by in-depth revisions completed in 2019 is estimated at 1,738,546,822 CZK and at 3,175,635,750 CZK, respectively.

The Institute, as the supervisory authority, also conducts inspections of manufacturers, importers, distributors, servicing organisations, vendors, and dispensaries of medical devices, as well as activities in the field of assessments of proper placement of medical devices onto the market.

In 2019, the Unit of the State Agency for Medical Cannabis (OSALK) was involved in the safeguarding of processes and activities aimed at ensuring availability of the medical cannabis active substance from a Czech grower for Czech patients. In 2019, the Institute took over and placed into distribution 24.7 kg of medical cannabis from the winner of the public contract for medical cannabis supply, Elkoplast Slušovice s.r.o. In its third and fourth order of medical cannabis, the Institute ordered 16 kg of medical cannabis from the contract winner, which ensured continuity of medical cannabis supply onto the Czech market.

With regard to the requirements for mandatory electronic prescription and the establishment of the Central Repository of Electronic Prescriptions, legislatively based in the Act on Pharmaceuticals, the process of modernisation of the entire system was commenced as early as in 2015, having regard also to its incorporation in the eHealth – National Strategy of Electronic Health and the Strategic eGovernment Development Framework 2014+. The IS ePrescription project implementation followed the current schedule and the project was completed in December 2017. Since 1 January 2018, the system has been in operation in the mandatory electronic prescription mode. Throughout 2019, the system has functioned without any major problems and with a significant performance reserve. In total, 71.5 million ePrescriptions were issued. Almost 11 million ePrescription identifiers were sent via SMS messages and more than 700 thousand via e-mail messages. In 2019, the website www.epreskripce.cz that was put into live operation in 2018, was complemented with information regarding so called shared medication record the launch of which is expected on 01 June 2020.

As part of its obligation to inform both the professionals and the general public, the Institute administered the following websites: www.sukl.cz, www.olecich.cz, and www. nebezpecneleky.cz. It also administered the OSALK website at www.sakl.cz.

2 SÚKL'S ORGANISATIONAL STRUCTURE

SÚKL's organisational structure effective as of 31 December 2019 is provided below.

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

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

In 2019, the Institute intensively cooperated with the Ministry of Health of the Czech Republic, particularly in the implementation of tasks within the scope of cooperation with the EU in the sphere of pharmaceuticals and medical devices, as well as in the preparation and subsequent legislative process of adoption of new legal regulations with significant impact upon areas of the Institute's operation.

In 2019, cooperation in the course of the legislative process of adopting several proposed amendments to Act No 378/2007 Coll., on Pharmaceuticals, as amended, and its implementing regulations continued.

This involved continued cooperation that started in 2017 and concerned the implementation of Commission Delegated Regulation (EU) 2016/161 of 2 October 2015 supplementing Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use.

In association with Regulation (EU) 536/2014 that was implemented into the Czech legislation in the form of an amendment implemented by Act No 66/2017 Coll., other EU legal regulations were published:

- Commission Implementing Regulation (EU) 2017/556 of 24 March 2017 on the detailed arrangements for the good clinical practice inspection procedures pursuant to Regulation (EU) No 536/2014 of the European Parliament and of the Council (hereinafter referred to as "Regulation 2017/556");
- Commission Delegated Regulation (EU) 2017/1569 of 23 May 2017 supplementing Regulation (EU) No 536/2014 of the European Parliament and of the Council by specifying principles of and guidelines for good manufacturing practice for investigational medicinal products for human use and arrangements for inspections (hereinafter referred to as "Regulation 2017/1569"),
- Commission Directive (EU) 2017/1572 of 15 September 2017 supplementing Directive 2001/83/EC of the European Parliament and of the Council as regards the principles and guidelines of good manufacturing practice for medicinal products for human use (hereinafter referred to as "Directive 2017/1572").

Regulation (EU) No 536/2014 sets the legal framework for the conduct of clinical trials on medicinal products for human use in the European Union in order to ensure that the rights, safety, and well-being of trial subjects and data obtained from clinical trials be robust and reliable. The sponsor of the clinical trial and the investigator should, in particular, ensure that the clinical trial is conducted in compliance with the respective protocol and the principles of Good Clinical Practice. Compliance with effective legal requirements, the protocol, and Good Clinical Practice principles, including standards governing data integrity and the ethical conduct of the clinical trial should be verified by inspections the execution of which is the responsibility of the Member State in which the inspection is carried out with a view to these provisions, the EU established (in the form of an implementing regulation) uniform detailed rules for the conduct of Good Clinical Practice inspection procedures compliant with Regulation (EU) No 536/2014 of the European Parliament and of the Council. By means of a regulation supplementing Regulation No 535/2014, the EU has amended the principles and guidance for Good Manufacturing Practice of investigational medicinal products for human use and the rules for conducting inspections of manufacture. As the to-date governing legislation was a common one, it was necessary to supplement the newly defined principles and guidance for Good Manufacturing Practice of investigational medicinal products for human use also with a separate amendment of the principles and guidance for Good Manufacturing Practice of investigational medicinal products for human use, which was done by Directive 2017/1572, supplementing Directive 2001/83/EC (so called Drug Code).

These changes called for the need to implement all of these aforementioned three EU legal regulations into the Act on Pharmaceuticals.

In the drafting of the amendment to the Act on Pharmaceuticals reflecting these changes, the preparation of this amendment to the Act on Pharmaceuticals and the amendment reflecting Regulation 2016/161 (safety features) was merged into a single process.

The legislative process was completed in early 2019 by the publication of Act No 44/2019 Coll. in the Collection of Acts (entry into force: 15 February 2019, coming into effect: 02 March 2019).

Furthermore, the Institute intensively cooperated with the Ministry of Health of the Czech Republic in the drafting of other legislative proposals pertaining to healthcare and medicines computerisation. This concerned the drafting of an amendment to the Act on Pharmaceuticals specifying the legislation governing the electronic prescription system and adding the rules of so called "medication record" into the law. The medication record will allow the treating doctor or the dispensing pharmacist to view information on the patient's pharmacotherapy. The aforementioned amendment also included a proposed amendment to the Act on General Health Insurance allowing for the reimbursement of magistral formulas containing medical cannabis from the public health insurance funds. These amendments were complemented with the amendment to the Act on Healthcare Services defining the National Point of Contact in association with the planned cross-border electronic prescription exchange. In 2019, the Act containing the aforementioned amendments passed the legislative process and on 18 October 2019 was published in the Collection of Acts under No. 262/2019 Coll. with the date of coming into effect of 01 December 2019 (except for some provisions with deferred effective date).

The Institute was also significantly involved in the drafting of amendment to the Act on Pharmaceuticals allowing for better availability of medicinal products to patients, so called emergency system. This draft is currently under discussion by the Chamber of Deputies of the Parliament as Chamber Document No. 581.

In the course of 2019, the adopted as well as drafted amendments to the Act on Pharmaceuticals were followed by cooperation in the incorporation of the amendments to the Act on Pharmaceuticals into implementing legal regulations. This concerned, specifically, drafting of a new Decree on the Prescribing of Medicinal Products for Human Use reflecting the new legislation governing electronic prescription and the introduction of medication record. This Decree was published in the Collection of Acts on 05 December 2019 with effective date of 01 January 2020. The new Decree supersedes and, concurrently, repeals the existing Decree No 54/2008 Coll. and Decree No 415/2018 Coll. Furthermore, the process included preparation of amendment to Decree No 84/2008 Coll., again in association with the changes in the area of electronic prescription. This Decree is still in the legislative process which is to be completed only in early 2020.

In the sphere of medical devices, the Institute and the Ministry of Health intensively cooperated in the legislative process of adapting Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/ EEC, and Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU. In the course of 2019, a draft of a new Act on Medical Devices was prepared as a complement to the aforementioned Medical Devices Regulation in those areas where permissible by the Regulation. As a result of this change, it was also necessary to commence works on the preparation of a draft of the act currently governing the area of in vitro diagnostic medical devices. In association with the adaptation of the law to reflect the Medical Devices Regulation, proposals of amendments to other legal regulations were also drafted, specifically to Act No 40/1995 Coll., on Advertising Regulation, and Act No 634/2004 Coll., on Administrative Fees. At the end of 2019, this suite of bills was forwarded to the Legislative Council of the Government for assessment and subsequently was approved by the Government. The bills are now to be subjected to discussion in the Chamber of Deputies of the Czech Parliament as Chamber Documents Nos. 696 and 697.

In addition to the activities associated with these major legislative tasks, the Institute was also involved in the comments procedure regarding other draft legal regulations governing other areas of relevance for the Institute's operation, inter alia those in the sphere of healthcare computerisation.

The statutory requirements governing individual areas of expert activities were further explained by the Institute in the guidelines published thereby. In these guidelines, the Institute was also informing the public about the guidance published by the European Commission and by the European Medicines Agency.

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

The Institute continued its cooperation with the Institute for State Control of Veterinary Biologicals and Medicines in Brno. In the sphere of market surveillance, the Institute's partners were particularly the Czech Agriculture and Food Inspection Authority (CAFIA) and the Customs Administration of the Czech Republic; the Institute also communicated with the Czech Trade Inspection.

In the last year, the Institute also cooperated with the Czech Police, courts of justice, and public prosecution offices, providing expert opinions on questions raised by these institutions in areas within the remit of the Institute.

In total, this involved 145 queries, of which 124 were raised by the Czech Police, four by courts of justice, one by a public prosecution office, five by the Customs Administration, six by tax authorities, three by insolvency practitioners, one by the Industrial Property Office, and one by the Fire Department.

3.2 Cooperation with EU Institutions and Other Foreign Partners

The Institute has been actively involved in international cooperation in more than 70 working groups and committees. These represent, in particular, bodies of the EU Council, the European Commission, and the European Medicines Agency, as well as the working bodies of the World Health Organisation (WHO), the Council of Europe and its European Directorate for the Quality of Medicines (EDQM), or the Organisation for Economic Co-operation and Development (OECD). Constant priorities of the Institute include namely representation in EMA scientific committees that address e.g. issues associated with medicinal product safety on the EU market or the approval of new pharmaceuticals. Last but not least, the Institute has been actively involved in informal groups that bring together experts from various countries specialised in the area of regulation of pharmaceuticals and medical devices, pricing and health technology assessment, or the regulation of human tissues and cells. Of these informal groups, the main one is the network of the Heads of Medicines Agencies (HMA) that, along with the EMA, forms the European medicines regulatory network. The Institute regularly participates in its activities not only via the membership of

the Institute's director, but also through direct involvement in the team for executive support of the steering group of the entire network and the development of regulatory strategy, including implementation thereof. It is a member of HMA working groups and management structures and it is involved in the coordination of priorities of a joint HMA/EMA strategy working plan for several years. In 2019, the Institute was actively involved in the initiated preparation of a new joint HMA/EMA strategy for 2020–2025 and together with Germany is to be responsible for the drafting of the strategy in one of its six defined areas of priority. The Institute has been regularly delegating its representatives, including top management members, senior staff as well as external experts, to attend the meetings of the aforementioned working bodies.

Relevant strategic information from international meetings is forwarded via membership in cross-sectoral and sectoral bodies also down to the national level. One of the key problems addressed on the global international level is the area of antimicrobial resistance (AMR). The issue of AMR, in which the Institute has been planning, in the long term, its more active involvement through membership in the respective HMA working group upon its extension to human medicinal products, has remained one of the 11 key priorities after the 2018 revision of the existing HMA action plan for several years. Following the European review of one of the major groups of antibiotics – fluoroquinolones – the Institute continued the information campaign lead thereby as the rapporteur for this European procedure, and intensively participated in the review of the risk/benefit ratio of antibiotics containing phosphomycin; in 2019, it commenced the preparation of an extensive information campaign focusing upon the topic of AMR and prudent use of anti-infectives. In the interest of public health, the Institute strives to be a respected partner in this area on both national and international level also in the coming period.

The Institute's international activities on the EU level include also involvement in the EU Council process of adoption of new European legislation and discussions on non-legislative proposals falling under the Institute's responsibility. In 2019, the Institute participated in a continued debate on draft Health Technology Assessment (so called HTA) Regulation. The Regulation establishes a framework to support cooperation, the procedures for cooperation among Member States in the sphere of HTA, and common rules governing clinical assessments of healthcare technologies, with particular focus upon medicinal products authorised via the centralised procedure and selected medical devices. Cooperation should be carried out in four areas, specifically: a) joint clinical assessments; b) joint scientific consultations; c) identification of emerging health technology suitable for joint assessment; and d) voluntary cooperation among Member States.

The Institute continues to be an active member of the EMA/HMA steering group of the EU-NTC European training centre, serving for the purposes of harmonisation of the scientific as well as regulatory practice across the EU and enhanced qualification of the employees of medicines agencies of the EU Member States. Through this activity, it has been involved in the preparation of educational strategy for the entire medicines regulatory network of the European Union and of the EEA and in the development of cooperation with other stakeholders in this area, particularly with the academia.

In 2019, the Institute hosted three international events within its premises. The first one took place in March and it concerned an educational event within the scope of the EU NTC programme called "QWP Seminar – Learn to Develop and Draft Regulatory Documents on Quality". The event was attended by 57 participants in total and interested staff of the Institute had a chance to attend the lectures as well. In June, a meeting of the working group of quality managers from the medicines agencies (HMA WGQM) took place. The Institute took the organisation of this regular event over from its Romanian colleagues within the scope of their Presidency of the EU Council. In November, the Institute organised a meeting of EMA's Committee on Herbal Medicinal Products – a Strategic Review and Learning Meeting at the time of the Finnish Presidency of the EU Council.

In the second half of 2022, the Czech Republic will, for the second time, take over the Presidency of the EU Council, and preparation works on the successful accomplishment of this demanding task started as early as in 2019. The Institute took part in these initiatives as well, particularly in activities focused upon the planning of international events to be organised by the Institute within the scope of the Czech Presidency 2022.

4 REGULATORY ACTIVITIES OF SÚKL

4.1 Record System

In 2019, the electronic record system of the Institute, incl. its regional workplaces, registered 112,034 delivered documents and 78,902 dispatched documents (Tab. 1, 2). The increase in the number of received documents was associated with new activities in the sphere of medical device reimbursement notifications in the Medical Device Department. The reduced number of dispatched documents was thanks to the completion of a substantial part of activities in the area of electronic prescriptions in the previous years. The priority channel for official document delivery are data mailboxes.

Tab. 1 **Registration of documents in 2017–2019**

	2017	2018	2019
Received documents	145 986	103 833	112 034
Dispatched documents	84 288	101 229	78 902

Tab. 2 **Overview of communication channels in 2019**

	Mailroom	E-mail messages	Data messages	Medical device reimbursement notifications	Total
Received documents	32 536	49 088	9 992	20 418	112 034

	Dispatch room	E-mail messages	Data messages	Electronic notice board	Total
Dispatched documents	9 830	1 213	53 296	14 563	78 902

■ MARKETING AUTHORISATION SECTION

Prior to its placement onto the market in the Czech Republic, each proprietary medicinal product is subject to marketing authorisation. Within the scope of the marketing authorisation procedure, the Marketing Authorisation Section assesses dossiers, through which the future marketing authorisation holder evidences the safety, efficacy, and quality of the product. Indications, contraindications, product posology, classification for dispensing, name of the medicinal product as well as the package leaflet and proposed labelling of the medicinal product are assessed. Upon the issuance of the marketing authorisation, the Institute sends the following to the marketing authorisation holder: the approved Summary of the Product Characteristics, which serves doctors and healthcare professionals as a key source of information about the medicinal product, approved package leaflet, approved labelling of the medicinal product, and the identification sheet with the allocated medicinal product codes allowing for the identification of each presentation of the medicinal product. Furthermore, the Marketing Authorisation Section assesses submitted applications for variations to marketing authorisation, marketing authorisation renewals as well as applications for the authorisation of parallel import and variations to, renewals of or revocations of parallel import authorisations. Concurrently, the Section is responsible for the implementation of the results of European assessments into the marketing authorisations of individual products (e.g. referrals, uniform PSUR assessments, PRAC recommendations on pharmacovigilance signals or paediatric work-sharing), for the development of lists of medicinal products jeopardized or extinct due to the sunset clause application, and for the conduct of administrative procedures regarding exceptions from the sunset clause application.

The Clinical Trials of Medicinal Products Department assesses applications for authorisation/notifications of clinical trials, supervision over the conduct of clinical trials, and assessment of applications for hospital exemptions; furthermore, it assesses non-interventional efficacy studies and projects of studies to decide whether a clinical trial on pharmaceuticals is concerned or not.

The Department of Pharmacovigilance is responsible for safeguarding the safety of medicinal products and the evaluation of their risk/benefit ratios. The pharmacovigilance activity comprises of the collection of data about potential risks of pharmaceuticals (from the system of spontaneous suspected adverse drug reaction reporting, from post-marketing studies of various types, scientific literature, etc.); the evaluation of any available data on potential risks; introduction of regulatory measures that may minimise risks; and the provision of new information both to professionals and to the general public.

4.2 Marketing Authorisation of Medicinal Products

Applications for New Marketing Authorisation

In 2019, 522 applications in total were forwarded for expert assessment following successful validation. Most of them were applications for MRP/DCP marketing authorisations. In the area of DCP/MRP marketing authorisations, the number of procedures where the Czech Republic acts as the Reference Member State is essential. In 2019, the number of received applications for MRP marketing authorisation with the Czech Republic as the Reference Member State significantly increased – from 16 applications in 2018 to 33 applications in 2019.

Marketing Authorisation Renewals

In 2019, 315 applications in total were forwarded for expert assessment following successful validation. The number of submitted applications for MRP/DCP marketing authorisation renewal with the Czech Republic as the Reference Member State increased from 38 applications in 2018 to 44 applications in 2019.

Variations to Marketing Authorisation

In 2019, the number of received applications for variations to national marketing authorisations as well as applications for variations to MRP/DCP marketing authorisations substantially increased. The number of submitted applications for variations to MRP/DCP marketing authorisations with the Czech Republic acting as the Reference Member State increased from 506 applications in 2018 to 725 applications in 2019. The number of submitted applications for variations to national marketing authorisations increased from 1,960 applications in 2018 to 2,274 applications in 2019. The number of submitted applications for variations to MRP/DCP marketing authorisations with the Czech Republic acting as the Concerned Member State increased from 3,698 applications in 2018 to 4,087 applications in 2019.

Parallel Import

In 2019, the number of submitted applications for parallel import authorisation grew; the number of these applications increased from eight applications in 2018 to 58 applications in 2019. At the same time, the number of submitted applications for variations to parallel import authorisations increased from 89 applications in 2018 to 121 applications in 2019.

Marketing Authorisation Revocations

In 2019, 333 applications for revocation of marketing authorisation were decided.

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

Process of marketing authorisation of medicinal products	Submitted in 2019	Decided in total in 2019	Pending as of 31 December 2019
New marketing authorisations	**539**	**626**	**701**
- of which national	48	42	74
- of which MRP-RMS	33	15	42
- of which DCP-RMS	69	113	106
- of which CMS (MRP and DCP)	389	456	479
MA renewals	**329**	**346**	**376**
- of which national	23	32	95
- of which RMS	44	49	21
- of which CMS	262	265	260
National variations to MAs	**2,511**	**2,492**	**463**
- of which MA transfers	103	140	0
- of which PIL and labelling	134	188	8
- of which bulk NAT variations	2 274	2 164	455
MRP-RMS variations	**794**	**804**	**150**
- of which MA transfers	25	39	1
- of which PIL and labelling	44	52	2
- of which bulk MRP-RMS variations	725	713	147
MRP-CMS variations	**4,657**	**4,656**	**1,325**
- of which MA transfers	304	348	13
- of which PIL and labelling	266	380	27
- of which bulk MRP-CMS variations	4,087	3,928	1,285
MA revocations	**306**	**333**	**4**
Parallel import	**58**	**29**	**40**
Parallel import variations	**121**	**77**	**86**
Parallel import renewals	**33**	**45**	**8**
Parallel import revocations	**8**	**8**	**0**

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

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

Applications for exemption from the sunset clause

In 2019, the Institute conducted 109 administrative procedures concerning the granting of an exemption from the sunset clause.

In the course of 2019, the sunset clause as referred to under Section 34a of the Act on Pharmaceuticals applied to 101 MA numbers and the marketing authorisation of these medicinal products was terminated.

Tab. 4 **Applications for exemption from the sunset clause**

Administrative procedures for exemption from the sunset clause	**109**
- of which: submitted applications	**109**
- of which: ex officio initiated administrative procedures	**0**
- granted	91
- declined	6
- suspended as undue	12
- suspended as unjustified	0
- suspended for failure to provide amendment	0
- withdrawal of application	0

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

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

In 2019, the Institute gave seven oral consultations and issued 20 written opinions on process-regulation and expert requests for consultations.

In June 2019, the Institute held two full-day seminars for companies regarding news in the area of marketing authorisation of medicinal products.

4.3 Cooperation with the European Medicines Agency and CHMP

In 2019, within the scope of cooperation with the European Medicines Agency (EMA) and the Committee for Medicinal Products for Human Use (CHMP), the Institute was involved in the assessment of centralised marketing authorisations as follows:

- Seven times as the rapporteur/co-rapporteur;
- Twice as the peer reviewer,
- Seventeen times it assessed type I and II variations to centralised marketing authorisations;
- Twice it assessed a referral;
- Twice it assessed documentation for MA renewal.

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

4.4 Clinical Trials

In 2019, the total of 369 applications for clinical trial authorisation/notifications were submitted, which was three more applications than in the previous year. In total, 351 decisions were issued. Most applications concerned phase III studies, international, multicentric, randomized, blinded, placebo- or active substance-controlled clinical trials conducted by foreign sponsors. Of the total number of 351 decided applications for clinical trial authorisation/notification, 18 were for clinical trials submitted by non-commercial entities (academic research), 28 applications concerned orphan drugs, 45 were applications for clinical trial enrolling also children or intended directly for the paediatric population (paediatric clinical trials), ten concerned clinical trials on advanced therapy products (six somatic cell therapies; two gene therapies; and two tissue engineering therapies), three applications were for first-in-human (FIH) trials. In the course of the assessment process, 31 applications in total were withdrawn (seven applications for clinical trial authorisation and 24 applications concerning clinical trial notifications); one application was declined.

Tab. 5 **Clinical trials in 2019**

	Pending from the previous period	Applications received in 2019	Number of decisions issued in 2019	Of which declined	Of which withdrawn
Applications for CT authorisation	18	107	93	1	7
CT notifications	51	262	258	---	24
Notifications of amendments to CTs	---	3,729	3,378	---	---

Tab. 6 **Numbers of applications in 2019 by clinical trial phase**

	Applications received in 2019	Applications assessed in 2019
Phase I	29	31
Phase II	107	92
Phase III	202	198
Phase IV	12	13
Bioequivalence studies	19	17

Tab. 7 **Indication groups of clinical trials assessed in 2019**

Indication group	Number
Oncology	79
Metabolic disorders + endocrinology	2
Healthy volunteers	24
Neurology	37
Cardiovascular system	16
Respiratory + allergology	19
Infectious	4
Dermatology	26
Rheumatology	27
Haematology	5
Psychiatry	11
GIT	22
Urogenital diseases	11
ENT	4
Gynaecology	8
Ophthalmology	13
Paediatric	2
Internal medicine	11
Transplantations	2
Anaesthesiology and resuscitation	2
Investigations	0
Diabetology	13
Other	1
Pain	3
Vaccination	1
Pharmacokinetics	8

In 2019, Development Safety Update Report (DSUR) assessment and control of SUSAR reports continued to be carried out. During the year, 509 DSURs in total were submitted. In 2019, the Assessment Safety Report Worksharing (ASR-WS) project continued, i.e. the assessment and drafting of Assessment Reports (AR) on DSURs; other Member States were also involved in the project. The activities of the ASR-WS project continues to be coordinated by the Czech Republic. In 2019, 12 Member States were involved and 67 assessment reports were drafted, which is 83 less than in 2018. The reason for the decrease is a pronounced drop in the number of assessors in the EU, the largest of which has been seen in Ireland. The Czech Republic drafted 20 ARs, of which 16 DSURs were newly assessed and four DSURs were updated. DSUR assessment and assessment report drafting will continue also in the next year. Within the scope of the ASR-WS project, our assessors took part in ten teleconferences of the CTFG – Safety Group and in four teleconferences on UAT9 Champions (creation of a section of the EU portal pertaining to pharmacovigilance reports from clinical trials).

The Institute continues its involvement in the Voluntary Harmonisation Procedure (VHP), which is a voluntary harmonisation process of joint assessment of clinical trial dossiers managed by the EMA Clinical Trial Facilitation Group (CTFG). Within the scope of the VHP, 204 applications for clinical trial authorisation/notifications were submitted in the EU, of which the Czech Republic was asked to participate in 79 assessments, and it accepted participation in all of the 79 VHPs. In respect of 28 VHPs, the Czech Republic was asked to act as the Reference Member State (RMS), the Member State conducting the procedure; in 26 VHPs, the Czech Republic conducted the assessment process as the RMS; in six cases, it acted as the RMS for newly accessing countries in previously approved procedures (second wave). In 2019, 695 substantial amendments were submitted within the scope of VHPs, of which 363 were in the Czech Republic, and in 104 cases, the Czech Republic conducted the assessment procedure as the RMS. In 2019, the Czech Republic continued to participate in the VHP-plus project (involvement of multicentric ethics committees in the common assessment within the scope of VHPs). The Czech Republic accepted involvement in 18 VHP-plus procedures and in four cases, it acted as the RMS.

Also in this year, the preparatory activities regarding the adaptation of Regulation No 536/2014, on clinical trials, represented a large proportion of work. The largest part of these works concerned the involvement of two coordinators in the Clinical Trials Information System (CTIS) activities in the role of rapporteurs, involved in the comments procedure and testing of the EU portal functionality. They took part in 36 teleconferences, three meetings in EMA (two weekly in-site testing and one working meeting) and one off-site testing. Due to the delay in the development of the EU portal and persistent unclarities regarding the future connection of SÚKL's database to this portal, the preparation of SÚKL's project of a new database of clinical trials was postponed; tender documentation has been prepared. The Institute continues its active involvement in the activities of the EMA working group for the development of the EU portal and the new EU database of clinical trials, via participation in the experts' group, Member States' group, and stakeholders' group. We attended four meetings in EMA and 91 teleconferences. Preparations for the adaptation of the Regulation are to continue also in 2020.

We have continued our active involvement in international expert working groups. Within the scope of the Clinical Trials Facilitation Group (CTFG), we participated in six meetings and two teleconferences

on complex designs. The working group addresses current issues of the adaptation of Regulation No 536/2014 (how to resolve disputable issues; how to speed up assessment of resubmitted clinical trial applications as per the Regulation; how to address the conditions of Member States in the decision, etc.). Furthermore, the group discussed the possibilities of providing Scientific Advice by the CTFG, cooperation between CTFG and other EMA groups (CAT, PDCO, CHMP, etc.). Our representative has been involved in the select group that prepares recommendations for all countries in addressing the issue of complex protocol designs. Since autumn, the impact of Brexit, VHPs and RMS takeover for procedures conducted by the United Kingdom have been addressed. Our assessors attended one international workshop for sponsors organised by the CTFG. We took part in four meetings of the CTEG (Clinical Trials Expert Group – the former ad hoc group for the adaption of Regulation No 536/2014) held in Brussels.

Newly, we have been involved in the activities of the Paediatric Committee (PDCO); our representative in this Committee attended five meetings out of 11 and actively participated in five procedures as the peer reviewer.

We resumed our involvement in the activities of the Committee for Advanced Therapies (CAT), taking part in five meetings in EMA and one joint meeting with the CTFG in Budapest. Our assessor prepared the clinical part of an application for product classification to decide whether the product is an advanced therapy product (ATP).

Our assessors were actively involved in international workshops organised by the EU NTC for CT assessors in Bonn and in Bratislava.

In the area of ethics committees, in 2019, we took active part in two meetings of the Ethics Committee Forum. We organised two working groups with the representatives of multicentric ethics committees and summoned one meeting with the representatives of regulated entities and stakeholders (AIFP, ČAFF, ACRO, AFM, multicentric ethics committees). And as mentioned above, we organised coordination of multicentric ethics committee involvement in the VHP-plus project.

In total, we organised one seminar for sponsors, contract research organisations and monitors, investigators, and members of ethics committees, and four seminars for the submitters of academic studies. In cooperation with other SÚKL units, we held two seminars for researchers ("From the Molecule to Clinical Trial on Pharmaceuticals" and "Advanced Therapy Medicinal Products – from Research to First-in-Man Administration"), and one seminar on radiopharmaceuticals, intended for sponsors, manufacturers, distributors, and doctors-radiologists.

In 2019, we gave 16 consultations for seven pharmaceutical companies and nine non-commercial entities (academicians, researchers, and representatives of healthcare service providers).

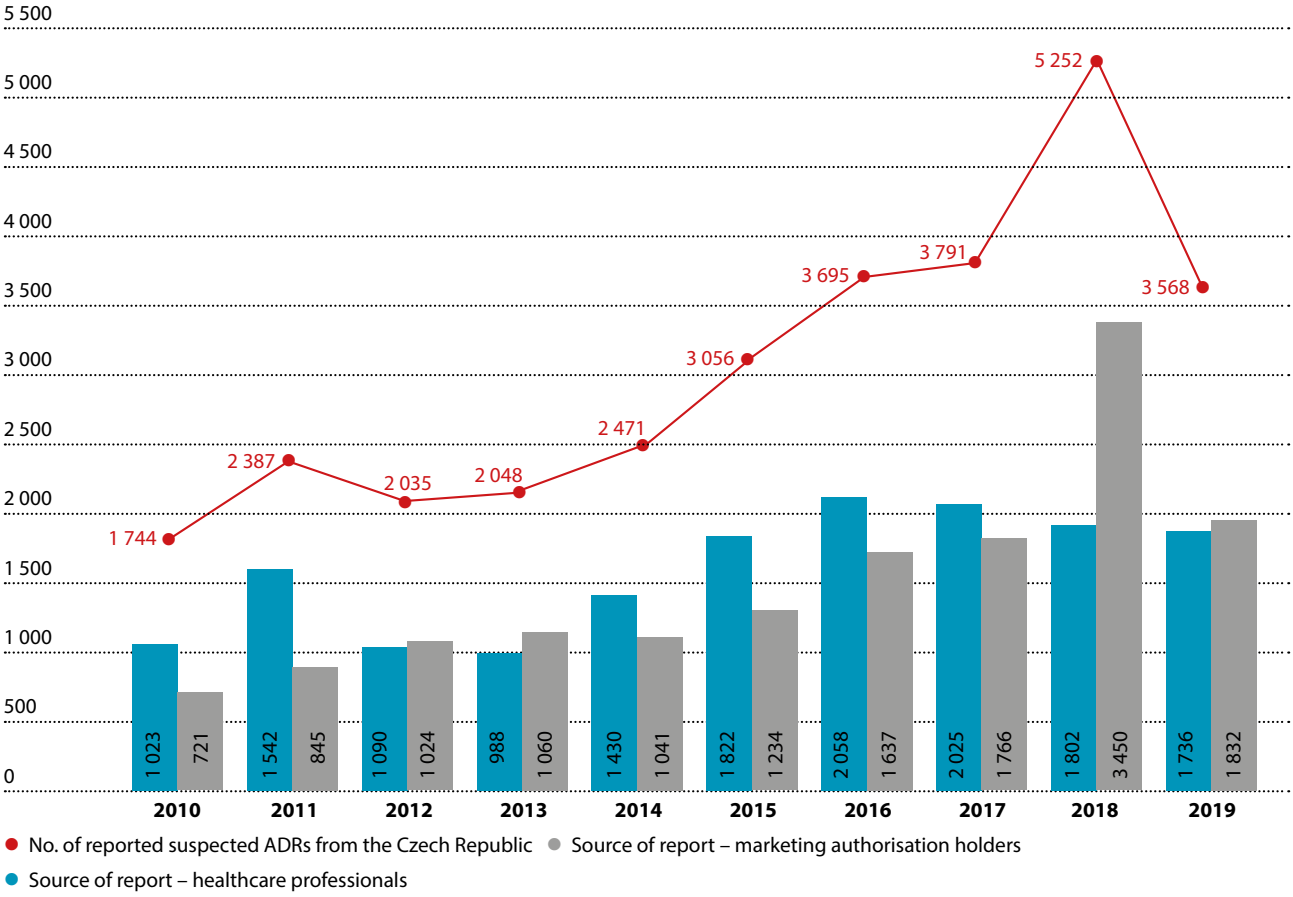
With regard to organisational changes, in 2019, we gradually handed over the activities in the sphere of non-authorised medicinal product use reporting, authorisation of non-authorised medicinal product import from third countries, and issuance of opinions on applications for specific therapeutic programmes to the Expert Activity Coordination Unit that has been newly responsible for these activities.

4.5 Pharmacovigilance

On 01 January 2019, the original Pharmacovigilance Unit was transferred to the Pharmacovigilance Department that comprises of two Units – the Pharmacovigilance Assessment Unit, and the Pharmacovigilance Inspection and Data Support Unit. This change of structure allows for better and more targeted management of individual activities that the Pharmacovigilance Department is in charge of.

In 2019, SÚKL received 3,568 primary suspected adverse drug reaction (ADR) reports from the territory of the Czech Republic, of which 1,832 were reports filed by medicinal product marketing authorisation holders (pharmaceutical companies), and 1,736 were reports sent to SÚKL directly by healthcare professionals and patients (of which 764 were reports from patients).

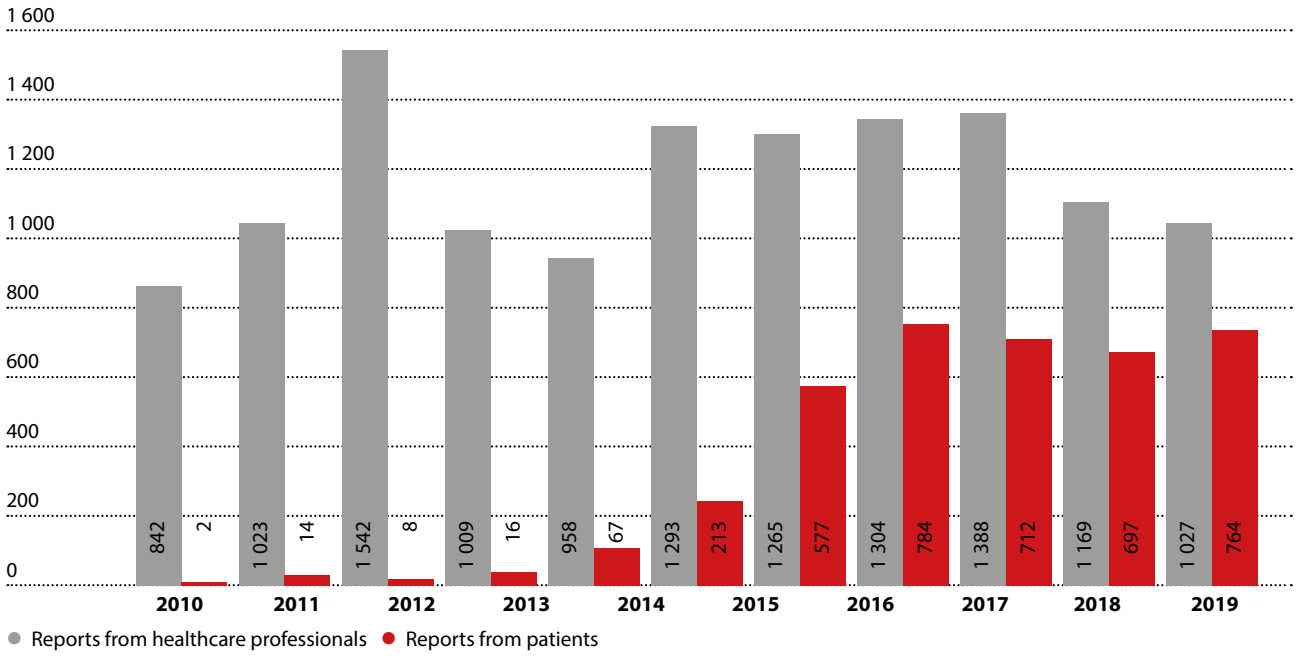
Fig. 1 **Number of reported suspected adverse drug reactions from the Czech Republic in 2010–2019**



The chart illustrates that until 2016, over 3,500 suspected ADRs were reported annually in the Czech Republic. The only exception is the number of reports from 2018, which is significantly higher than in the previous years and than in the following year. The high number of reports in 2018 is incomparable with other years, as only in that year, different rules of report receipt to SÚKL were transiently set up with regard to the commencement of operation of the new EudraVigilance European database. On a temporary basis, the Institute was receiving also reports of non-serious ADRs from pharmaceutical companies that had never been submitted thereto before and have not been submitted to it thereafter, either. As a standard, SÚKL receives all suspected (serious as well as non-serious) ADR reports from healthcare professionals and from patients and all suspected serious ADR reports from pharmaceutical companies. The reporting of non-serious ADRs that pharmaceutical companies gain knowledge of remain in the company databases and in the EudraVigilance European database, and hence are available also to SÚKL and remain part of any subsequent assessments as relevant.

The number of spontaneous suspected ADR reports sent directly to SÚKL in 2019 slightly decreased as a result of the slight decrease in the number of reports from healthcare professionals. On the contrary, the number of reports submitted to SÚKL by patients slightly increased.

Fig. 2 **ADR reports submitted to SÚKL by healthcare professionals and patients**



Each individual spontaneous report delivered to the Institute is processed, individually assessed, entered into the database of adverse drug reactions from the Czech Republic (CDNÚ), and, concurrently, sent to the EudraVigilance pan-European database as well as the WHO global database. Records in ADR databases are regularly checked and evaluated using statistical as well as qualitative methods for the purposes of new pharmacovigilance signal identification. In addition to thorough continuous assessment of all reported adverse drug reactions from the Czech Republic, pharmacovigilance assessors are responsible for the evaluation of signals regarding 77 active substances on the pan-European level. In 2019, the Pharmacovigilance Assessment Unit assessed 871 monthly ADR reports from the EudraVigilance database regarding substances for which the Czech Republic acts as a pharmacovigilance signal rapporteur for the EU.

The Pharmacovigilance Assessment Unit keeps increasing its involvement in international pharmacovigilance procedures. In the sphere of Periodic Safety Update Reports (PSURs) for individual products, the Institute assessed the total of 16 PSUSA procedures (i.e. PSUR single assessment for a particular substance) from the position of so called PSUSA - Lead Member State in the course of 2019. SÚKL is responsible for PSUSA of 46 substances in total, for which the respective PSUR reports are submitted in regular intervals of various duration. As the EU PRAC rapporteur (the chief pharmacovigilance assessor) for centrally authorised medicinal products Blincyto, Namuscla, Venclyxto, Doxorubicin Tilomed, Xenleta, and Posdox, we assessed 12 procedures in total during 2019.

We actively participated in 11 meetings of the Pharmacovigilance Risk Assessment Committee (PRAC) in the European Medicines Agency (EMA) and in ten teleconference meetings of the PRAC Committee. Furthermore, we were actively involved in the European group of pharmacovigilance inspectors (PhV IWG), an expert group for the EudraVigilance system (EV EWG), the PhV Business Team, and an EMA group focusing upon big data. We also actively took part in and gave presentations during the extraordinary meeting of the PRAC Committee in Bucharest and Helsinki, during the Romanian and Finish EU presidency.

In the course of 2019, as the PRAC rapporteur, we lead the pan-European risk/benefit review of high-strength estradiol creams (100 micrograms/gram – 0.01 %), an Art. 31 EU referral. In October 2019, the conclusion of our assessment was unanimously accepted by the PRAC Committee and approved also by the EMA CMDh coordination group (Co-ordination Group for Mutual Recognition and Decentralised Procedures – human). We were actively involved in the creation of several EMA documents – GVP Product - or populations-specific considerations III – Pregnant and breastfeeding women, revision of GVP module VI and of document Detailed guide regarding EV data management activities by EMA.

In cooperation with other units of the Marketing Authorisation Section, the conclusions of CHMP (Committee for Medicinal Products for Human Use) and the PRAC pharmacovigilance committee were being transposed to the Czech clinical practice on a continuous basis. On its website, the Institute published 24 communications on the safety of medicinal products addressed to healthcare professionals or to the general public. In cooperation with marketing authorisation holders, the Institute published 152 educational materials on 61 medicinal products and 35 letters to healthcare professionals focused upon increased safety of medicinal product use.

Assessors from the Pharmacovigilance Assessment Unit were involved in the assessment of marketing authorisation dossiers where they evaluated the pharmacovigilance part; in 2019, they prepared 820 reports of pharmacovigilance documentation in total.

The Pharmacovigilance Department continues to issue the Adverse Drug Reactions Bulletin. In 2019, we published three issues (of which one was a double issue) containing 35 articles in total. The Bulletin provides up-to-date information on suspected adverse drug reactions reported in the Czech Republic in the course of the previous year, other pharmacovigilance news, a regular column "You Reported to Us" which gives specific cases of adverse drug reactions reported from the Czech Republic, as well as quarterly reviews of various pharmacovigilance outputs.

Thirty-one notifications (of commencement, termination, or update) of post-marketing safety studies conducted in the Czech Republic were processed.

Along with their colleagues, pharmacovigilance inspectors carried out the total of five inspections of the pharmacovigilance system of marketing authorisation holders in 2019, of which one was an international inspection requested as part of the EMA inspection programme.

The Pharmacovigilance Department communicates with the public, it answers questions from healthcare professionals, the general public as well as pharmaceutical companies. In 2019, more than 600 questions were answered in writing or by phone.

As part of dissemination of information on the safety of pharmaceuticals and also to increase suspected adverse drug reaction reporting, the employees of the Pharmacovigilance Department gave 12 presentations within the scope of professional congresses or seminars for doctors and pharmacists or courses of the Institute for Postgraduate Medical Education (IPVZ). Some of these presentations focused upon the dissemination of information on the conclusions of the European review of fluoroquinolone antibiotics conducted in 2018, which brought the recommendation to significantly restrict the use of these antibiotics in clinical practice and in which SÚKL acted as the main rapporteur

The Institute also focuses upon the education of pharmaceutical companies in the proper conduct of pharmacovigilance. In 2019, we continued the tradition of organising two one-day seminars for companies on news in pharmacovigilance from the previous year as well as one one-day seminar called the Essentials of Pharmacovigilance. We contributed to the organisation of a two-day international training in MedDRA terminology coding and in MedDRA SMQ analysis.

By the end of 2019, the Pharmacovigilance Department began to prepare conditions for the implementation of a new project – inclusion of important information on the safety of pharmaceuticals in the electronic prescription system. The technical aspects of the project have been addressed and the project should be functional in the course of 2020. As a result, an alert of important new information on the safety of certain medicinal products will be available to doctors during their electronic prescription, for pharmacists during dispensing, and for patients on the patient ePrescription web or mobile application.

SURVEILLANCE SECTION

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

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

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

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

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

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

4.6 Laboratory Control

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

The Department has an established quality management system compliant with the ČSN EN ISO/IEC 17025 standard. In 2016, a regular verification of the established quality system by a group of EDQM auditors took place. International recognition of the quality management system is a precondition for participation in international studies of control of centrally authorised medicinal products organised by EMA/EDQM, recognition of the results of MRP/DCP product analyses, and international recognition of batch release certificates for selected medicinal products (OCABR - Official Control Authority Batch Release) within the EU.

The results of sample analyses conducted in 2019 by both Laboratory Units of the Laboratory Control Department are summarised in the tables below.

Tab. 8 **Surveillance over the quality of pharmaceuticals on the market by means of laboratory analyses by predefined projects – projects concluded in 2019**

Project name	Number of analysed products	Number of analysed samples	Number of compliant samples	Number of non-compliant samples	Number of comments on MA dossier
1/2017 – Control of Braille on medicinal product labelling	53	59	57	2	0
3/2018 – Pharmacy samples	109	242	222	20	1
4/2018 – Medicinal products containing diclofenac	16	31	31	0	0
2/2018 – Medicinal products containing azithromycin	8	15	15	0	0
BIO/1/2018 – Influenza vaccines	3	7	7	0	0
BIO/2/2018 – Herbal products	18	27	27	0	0
Total	**207**	**381**	**359**	**22**	**1**

Projects are prepared on the basis of a "risk-based" analysis. The criteria include, in particular, high consumption of the controlled products, less common pharmaceutical forms or routes of administration, target patient groups, or frequent complaints of patients or medical and pharmaceutical professionals. Proposed projects and reports on completed projects are approved by the Institute's Quality Team. In 2020, works on the following projects have been under way: control of paediatric syrups with dispenser; Control of medicinal products containing omeprazole, enalapril-maleate, and ibuprofen. On an ongoing basis, samples for the following projects are being taken: Control of medicinal products containing pregabalin, desloratadin, and losartan; and Control of selected cardiac and diuretic products. The following projects of the Biological Methods Unit approach their completion: Microbiological control of purified water and Control of selected nasal medicinal products. Pharmaceutical samples and Braille on the labelling of medicinal products continue to be controlled and analyses of identified counterfeit and illegal samples carried out, particularly upon request of the Czech Police

Tab. 9 **Batch release of defined medicinal products**

Product type	No. of reported medicinal products	No. of reported batches	Released on the basis of certificate	No. of laboratory-verified samples	Total number of released batches*	Not released
Blood derivatives	54	827	819	8	827	0
Vaccines	29	290	290	0	290	0

* *Some batches were released repeatedly.*

Tab. 10 **Laboratory control of pharmaceuticals and excipients requested by other units of the Institute, other state administration organisations or EDQM**

	Number of samples	Of which compliant	Of which non-compliant
Suspected quality defect of a pharmaceutical	35	34	1
Suspected counterfeit, illegal samples*	148	-	-
International studies withinOMCL*	7	-	-
Internal quality control of purified water	140	134	6
Verification of quality of a reference substance for Ph. Eur.	1	1	0
Other analyses**	18	16	2
Total	**349**	**185**	**9**

* *Sample compliance cannot be evaluated.*

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

The tables above indicate that in the Laboratory Control Department, 738 sample analyses were completed. Compared to the last year, the number of samples rated as non-compliant (ex. counterfeit products and samples from international studies) slightly decreased to 4.2 % (5.8 % in 2018; 3.9 % in 2017; 6.3% in 2016; 5.3% in 2015). Quality defects were confirmed particularly for pharmacy samples (incl. adjusting defects). The quality of proprietary medicinal products available on the Czech market has been very good. Only in respect of one sample examined for suspected quality defect the defect was confirmed.

Within the scope of the statutory task of batch release, all the reported batches were released onto the market in time, i.e. within timelines stipulated by the law. Fig. 5 illustrates the number of released batches of blood derivatives and vaccines; for some blood derivatives, an internationally recognised certificate (OCABR) was issued after the laboratory testing. Although the number of released vaccine batches has been slightly dropping, the batch volumes are larger, and hence the number of released vaccines is greater than in the past few years.

Fig. 3 **Number of sample analyses in 2013–2019**

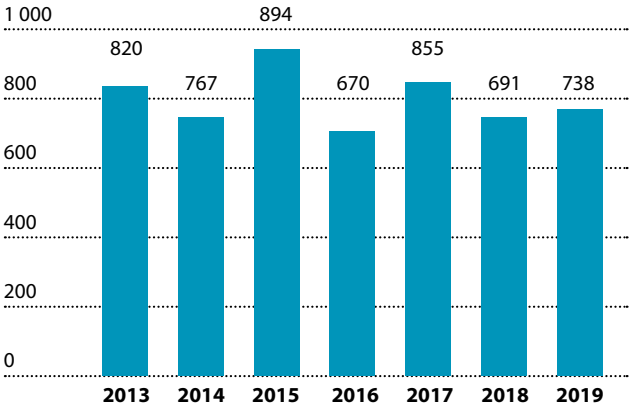


Fig. 4 **Development in the number of non-compliant samples in 2013–2019 (%)**

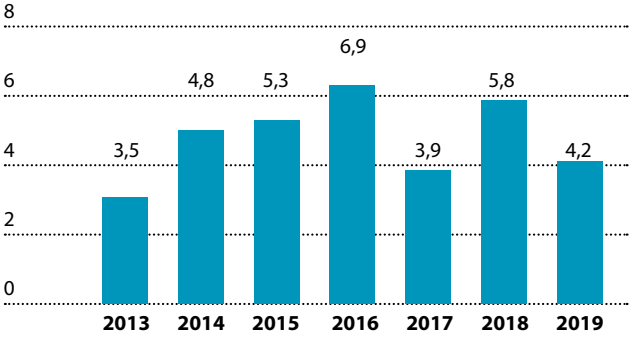
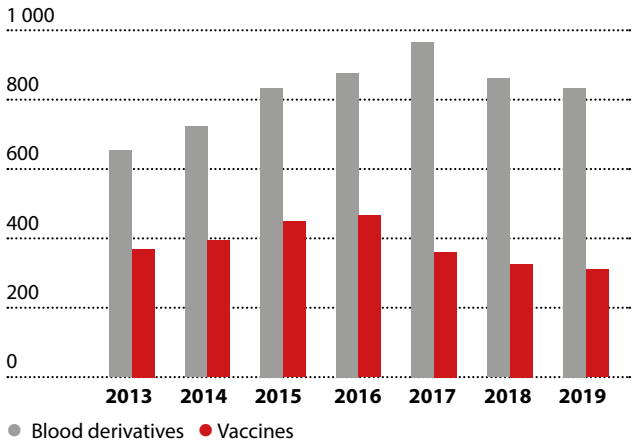


Fig. 5 **Number of released batches**



International Cooperation in the Sphere of Laboratory Control

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

In 2019, the Laboratory Control Department participated in collaborative international studies listed in Table 11.

Tab. 11 **Participation in international studies**

Study	Study name	Rating
PTS 190	Melting Point	good
PTS 194	Optical Rotation	good
PTS 195	Infrared Absorption Spectrophotometry	good
PTS 196	Dissolution Test	good
PTS 201	Immunoglobulin Protein Composition	good
CAP 2019/15	Foscan	good
CRS	Calcium Folinate	good

Legend to abbreviations:

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

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

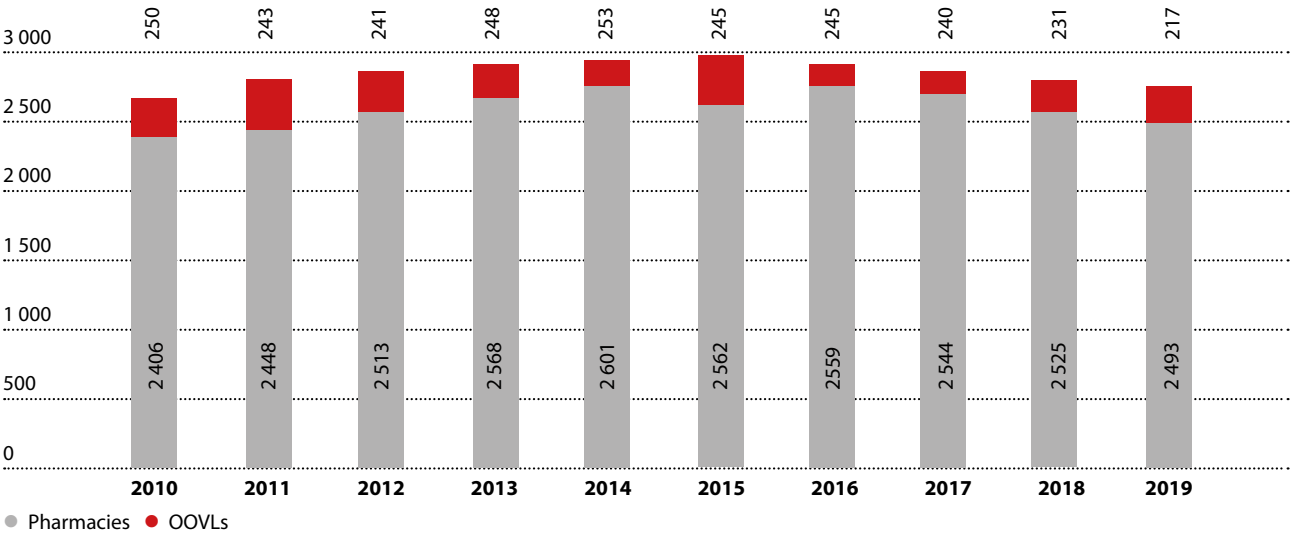
CRS – Verification of the quality of the reference substance for EDQM/Chemical Reference Substance.

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

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

By the end of 2019, the Institute kept a record on 2,493 pharmacies in total, of which five were within the scope of powers of the Ministry of Defence of the Czech Republic; moreover, the Institute kept a record on 217 detached pharmaceuticals and medical device dispensing units (hereinafter referred to as "OOVL"), 380 medical device dispensaries, 2,825 vendors of selected medicinal products for human use, 43 nuclear medicine departments of healthcare facilities, and 410 wholesale distributors of medicinal products. Compared to 2018, the total number of pharmacies decreased by 32 entities and the number of OOVLs by 14 units (Fig. 6).

Fig. 6 **Number of pharmacies and OOVLs in the last 10 years (as of 31 December 2019)**



In 2019, the inspectors of the Pharmacy and Distribution Department conducted the total of 830 inspections in pharmaceutical care facilities – pharmacies, of which 30 were hospital pharmacies of inpatient care providers. Of the total number of completed inspections, 28 were targeted inspections, conducted on the basis of reports or complaints. Separate inspections aimed at handling of dependency-producing substances and precursors were carried out in 430 pharmacies.

Price control focusing upon compliance with the Act on Prices and rules of price regulation was conducted in 110 pharmacies and 14 wholesale distributors.

On the basis of facts identified during the conducted inspections, the total of 13 admonitions and 59 final decisions on imposition of a fine for breach of obligations stipulated by the Act on Pharmaceuticals in the total amount of 13,228,000 CZK, incl. aggregate fines (see below), and on finalised administrative procedures based on inspections carried out in the previous period were adopted in respect of pharmacy operators. In total, three fines in the total amount of 310,000 CZK were imposed for failure to cooperate during the inspection. In four cases, the preparation of medicinal products was suspended for a pharmacy; in three cases, the operation of the pharmacy was suspended.

The main reasons for the issuance of a decision imposing a fine included dispensing of medicinal products without medical prescription or on invalid prescription; dispensing by unauthorised staff; serious shortcomings in the record-keeping of the number of pieces received, stocked, dispensed, and stored; dispensing of medicinal products which should have been withdrawn from the market based on a decision of the marketing authorisation holder; and illegal distribution and export of medicinal products abroad, as well as failure to comply with the principles of good pharmaceutical practice in the preparation of medicinal products, in particular the use of expired active substances and excipients for preparation.

Within the scope of inspections of the handling of dependency-producing substances in pharmacies, in 2019, identification of major breaches of the Act on Dependency-Producing Substances resulted in the total of 13 final decisions on fine imposition to pharmacy operators, of which five were fines only for offences referred to under this Act in the total amount of 263,000 CZK. In other cases, pharmacy operators committed offences referred to also by other acts, and for this reason, an aggregate fine was imposed thereupon.

In the case of breaches of the Act on Precursors, four final decisions on fine imposition were issued in total; in all cases, an aggregate fine was imposed. Aggregate fines are included under the aforementioned fines imposed in compliance with the Act on Pharmaceuticals.

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

Inspections focusing on compliance with price regulation rules in pharmacies identified a breach of price regulations in 46 cases. Pharmaceutical care providers were issued 15 final decisions on fine imposition pursuant to the Act on Prices in the total amount of 637,000 CZK (incl. finalised administrative procedures based on inspections from the previous period) for price offences regarding failure to comply with the binding procedure for pricing of individually prepared medicinal products and proprietary medicinal products treated prior to dispensing; failure to keep or store evidentiary price records; failure to observe officially fixed maximum prices during sales; and failure to observe the conditions and procedures for their application.

In 2019, a breach of the ban on the offering and provision of advantageous sale in respect of reimbursed medicinal products dispensing was identified in five cases. On the basis of the inspection findings, two admonitions and one final decision on fine imposition were issued pursuant to the Act on Public Health Insurance, with the fines amounting to the total of 50,000 CZK.

Furthermore, in 2019, 297 inspections of the handling of medicinal products in healthcare facilities were carried out. The inspections took place in 35 inpatient departments of healthcare service providers and in 262 separate outpatient offices of general practitioners and medical specialists and in other healthcare facilities. On the basis of reports received by the Institute in connection with the operation of healthcare facilities, where health care is provided, a total of 14 targeted inspections were performed. In total, one admonition and 12 final decisions on fine imposition in the total amount of 1,015,000 CZK were issued for the identified breaches of the Act on Pharmaceuticals (this includes also finalised administrative procedures based on inspections conducted in the previous period).

The major reasons for the issue of the decision on fine imposition included, in particular, procedures contrary to the summary of the product characteristics; failure to meet the medicinal product storage conditions; use or storage of expired medicinal products or recalled medicinal products; and other serious breaches of the obligations governing the handling of medicinal products set forth by implementing regulations.

In 2019, inspections of vendors of selected medicinal products involved 110 outlets in total, of which two were targeted inspections. In one case, the vendor's operation was suspended; in total, two final decisions on fine imposition in the total amount of 55,000 CZK for breach of the obligations implied by the Act on Pharmaceuticals were issued.
In other healthcare facilities authorised to prepare medicinal products (Nuclear Medicine Departments [ONM] and workplaces preparing autogenous vaccines for human use [HAV]), a total of 17 inspections were carried out; the findings from the inspections did not result in the need for the imposition of any penalty.

Summary results from inspections completed in 2019 are provided in Table 12.

Tab. 12 **Inspection surveillance over pharmacies, nuclear medicine departments, healthcare facilities, and vendors of selected medicinal products in 2019**

			Classification of defects						Penalties		
Inspected entity	**Inspection type**	**Number**	**1**	**%**	**2**	**%**	**3**	**%**	**A**	**B**	**C**
Pharmacies	Regular inspections	830	517	62.3	195	23.5	118	14.2	4	3	62
	Price controls	110	Not rated by classification of defects						-	-	15
	Inspections of dependency-producing substances and precursors	430	319	74,2	89	20,7	22	5,1	-	-	17
ONMs		14	12	85.8	1	7.1	1	7.1	-	-	-
HAVs		3	1	33.3	2	66.7	-	-	-	-	-
Healthcare facilities		297	196	66.0	74	24.9	27	9.1	-	-	12
Vendors of selected medicinal products		110	74	67.3	14	12.7	22	20.0	-	-	2

Classification of defects

1 – None or minor defects identified

2 – Major or repeated defects

3 – Critical defect or serious breach of law

Penalties

A – Suspended preparation

B – Suspended operation

C – Fine imposed (final decision)

In 2019, inspectors from the Pharmacy and Distribution Department took a total of 232 samples of medicinal products during inspections in pharmacies, of which 97 were samples of pharmaceutical products intended for the preparation of magistral formulas in the pharmacy. Out of 135 pharmacy samples (medicinal products prepared in pharmacies), only one was out-of-specification, the defect being out-of-specification content of active substances. In four samples intended for dispensing, defects in their labelling were identified.

A comparison of the occurrence of monitored defects in out-of-specification pharmacy samples in the last years is provided in Table 13.

Tab. 13 **Occurrence of monitored types of defects (% of the total number of out-of-specification samples)**

Type of defect	2012	2013	2014	2015	2016	2017	2018	2019
Out-of-specification content of active substance	40.0	63.6	50.0	42.9	25.0	57.1	100.0	100.0
Out-of-specification total weight	40.0	9.1	37.5	42.9	50.0	14.3	40.0	-
Out-of-specification purified water								
Microbiological compliance	-	-	-	-	-	-	-	-
Out-of-specification galenic processing	-	18.2	12.5	-	25.0	28.6	-	-
Out-of-specification microbiological compliance	20.0	9.1	-	14.2	-	-	-	-
Active substance and excipient identity confusion	-	-	-	-	-	-	-	-

Other activities of the Pharmacy and Distribution Department include issuance of binding opinions on the technical and material equipment of pharmacies and medical device dispensaries. In 2019, a total of 271 applications for issuance of an opinion were received from pharmacy operators and 260 favourable binding opinions were issued. In case of medical device dispensaries, a total of 35 operators applied for a binding opinion and 31 favourable binding opinions were issued.

In 122 cases, the issuance of the binding opinion was associated with an inspection in the pharmacy (on-the-spot check of technical and material equipment) and in three cases, with an inspection of the OOVL (Table 14 refers). Furthermore, in this context, 21 initial inspections of medical device dispensaries and 133 consultations on the technical equipment of existing pharmacies or the construction of new pharmacies, and 293 consultations regarding the obligations of inspected entities implied by the Act on Pharmaceuticals, Act on Dependency-Producing Substances and on Precursors, their implementing regulations, and SÚKL guidelines took place. Table 14 also provides data on newly established and defunct pharmacies/OOVLs.

Tab. 14 **Další činnost Odboru lékárenství a distribuce**

Initial pharmacy inspection	Establishment of a new pharmacy/OOVL	Defunct pharmacies/OOVLs
122	57/9	89/23
Initial OOVL inspection	**Initial medical device dispensary inspections**	**Total no. of consultations**
3	21	426

Distribution of Medicinal Products

In 2019, the number of distributors exhibited a year-to-year decrease by 36 entities to the total of 410 medicinal products distribution authorisation holders. Of the total number of authorised distributors, 125 entities were both a distribution authorisation holder and a pharmacy operator.

In 2019, 18 new distribution authorisations and 147 decisions on variations to distribution authorisations were issued, and 49 authorisations were revoked upon request of their holders. In three cases, the distribution authorisation expired in compliance with Section 76(4) of the Act on Pharmaceuticals and in respect of two entities, the authorisation was revoked by the decision of the Institute pursuant to Section 76(3) of the Act on Pharmaceuticals.

The total of 11 entities applied for entry into, variation to entry in, or deletion from the Registry of Brokers of Human Medicinal Products in 2019; as of 31 December 2019, the Registry included 44 entities in total. Table 15 provides an overview of received applications and issued decisions in respect of distribution authorisation, variations thereto or revocation thereof, and the registration of brokers of medicinal products.

Tab. 15 **Distribution and brokerage of pharmaceuticals in 2019**

	Received applications	Authorisations issued/Registry entries made
Application for distribution authorisation	21	18
Application for variation to distribution authorisation	160	147
Application for revocation of distribution authorisation	53	49
Application for entry in the Registry /variation to entry in the Registry /deletion from the Registry	11	11

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

In 2019, the total of 290 inspections of distributors and four inspections of brokers were conducted, of which 18 were targeted inspections carried out on the basis of internal and external reports. In total, 32 reports on the operation of distributors were received; in two cases, a declaration of non-conformity with the rules of Good Distribution Practice (GDP) were issued and in three cases, an administrative procedure regarding fine imposition was proposed on the basis thereof. The top priorities of the surveillance activities included a complex control of the medicinal product distribution chain and associated compliance with GDP principles, of the quality assurance system and analysis of risks associated with the distribution activities, conditions of storage and transport of medicinal products, including control of records kept on the distribution activities carried out, controls of proper and complete provision of data on the volume of distributed medicinal products, and control of compliance with the distributor's obligations associated with the checks of safety features in respect of those medicinal products that bear such features.

Of the total number of 235 rated inspections of distributors (follow-up and targeted inspections), 77 % were rated with grade 1 (good), 15.3 % with grade 2 (satisfactory), and 7.7 % with grade 3 (not satisfactory). On the basis of identified facts, in 15 cases in total it was proposed to initiate an administrative procedure regarding fine imposition for major breaches of obligations implied by the Act on Pharmaceuticals and its implementing regulations and related GDP guidance.

Following the completed inspections, the total of 182 post-inspection good distribution practice certificates were issued, of which 10 certificates were of limited validity (for one year in one case; for two years in six cases; and in respect of three certificates, the inspection findings resulted in limited scope of the distributor's certified activities). Just like distribution authorisations and variations thereto, all of the issued certificates have been regularly entered into the EudraGMDP European Database.

The Good Distribution Practice Unit was also involved in one investigation of suspected quality defect of a medicinal product and suspected presence of a counterfeit product in the distribution chain, and, with the authorisation of the Strasbourg EDQM inspectorate and the Institute's Laboratory Control Department, the Unit performed sampling of authorised medicinal products in the distribution chain for the purposes of laboratory control of the product quality.

Within the scope of consultation activities, the Unit gave the total of 37 consultations regarding the application of GDP principles and, on an ongoing basis, has been providing opinions and source materials upon request from other bodies and organisations, including those from abroad (the Czech Ministry of Health, revenue authorities, courts of justice, the Czech Police, MHRA or EMA).

In 2019, 14 price controls of distributors focusing upon control of compliance with the Act on Prices and with the rules of pricing regulation governing medicinal products were conducted. A breach of pricing regulations was identified in two cases and they consisted of inadequate price record-keeping and failure to comply with the procedure set forth by material conditions, rules or procedures governing the establishment of official prices, changes thereto, and the method of their negotiation, application, and accounting as required by the pricing authority pursuant to Section 5(5) of the Act on Prices. Three fines amounting to the total of 3,750,000 CZK were finally imposed for the price offences in 2019.

On the basis of facts identified during the completed inspections, distributors were imposed one admonition and the total of 12 final decisions on fine for breach of obligations set forth by the Act on Pharmaceuticals and its implementing regulations amounting to 5,860,000 CZK in total (incl. also finalised administrative procedures based on inspections conducted in the previous period). One fine in the amount of 100,000 CZK was imposed for failure to provide cooperation during the inspection.

The main reasons for the proposed fine imposition included failure to comply with GDP rules; failure to file an application for variation to the distribution authorisation in case of changes concerning the distributor; failure to safeguard the services of a qualified person; distribution of medicinal products purchased from the position of a pharmacy operator; distribution outside the territory of the Czech Republic contrary to the issued measure of the Ministry of Health of the Czech Republic; and serious shortcomings in the keeping of regulatory and record documentation of the distributor.

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

The results of inspections at distributors in 2019 are available in Table 16.

Tab. 16 **Inspection surveillance over distributors**

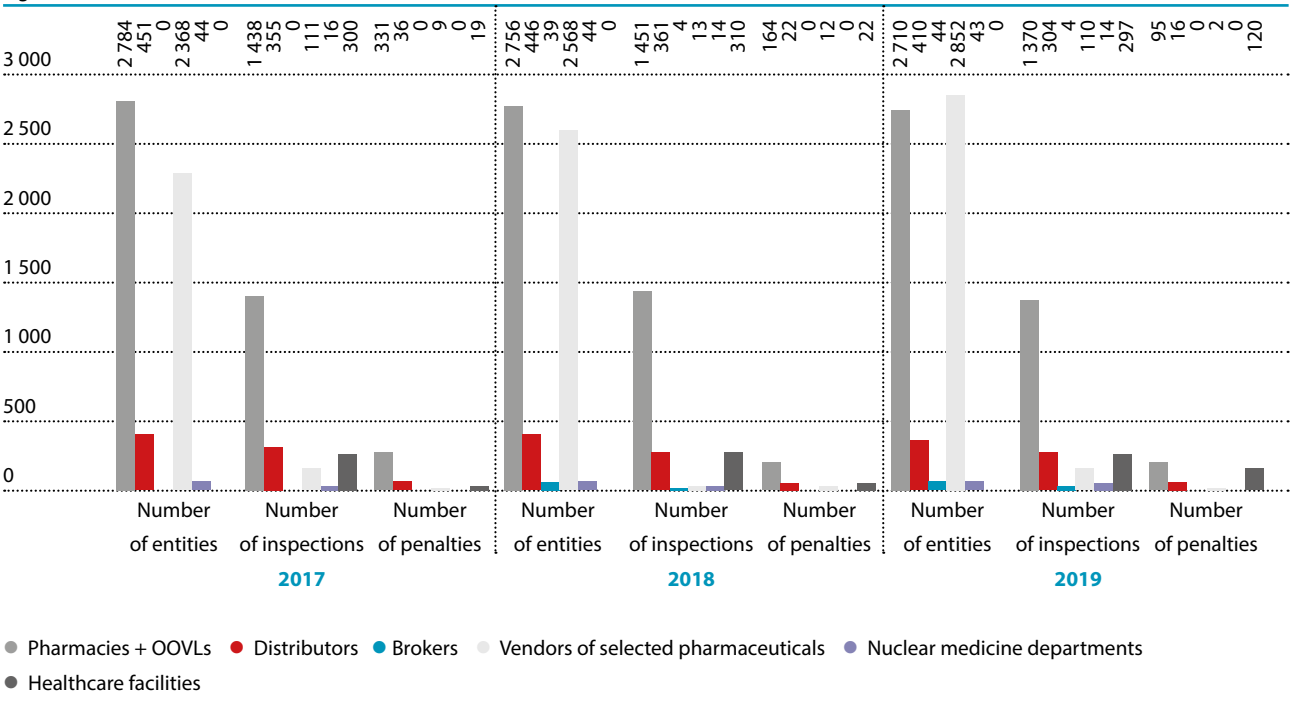
	Number of inspections				Inspection rating			Measures	
Total	Initial	Follow-up	Targeted	Variation	1	2	3	NCR	Proposed fine
290	19	217	18	36	181	36	18	2	15

Inspection Rating

Inspections are rated on the basis of the identified shortcomings and their severity, 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.

A comparison of the number of regulated entities, conducted inspections, and imposed penalties for the last four years is illustrated by Fig. 7.

Fig. 7 **Information on surveillance activities in 2016–2019**



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

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

Manufacture of Pharmaceuticals

The updated lists of supervised operators in the sphere of manufacture and research of pharmaceuticals are available from the Institute's website.

In the area of manufacturers (incl. blood centres), the total of 111 applications for manufacturing authorisation or variations thereto were received (Tab. 17). The number of cases brought forward from one year to another corresponds to the intervals for application processing.

Human Tissues and Cells

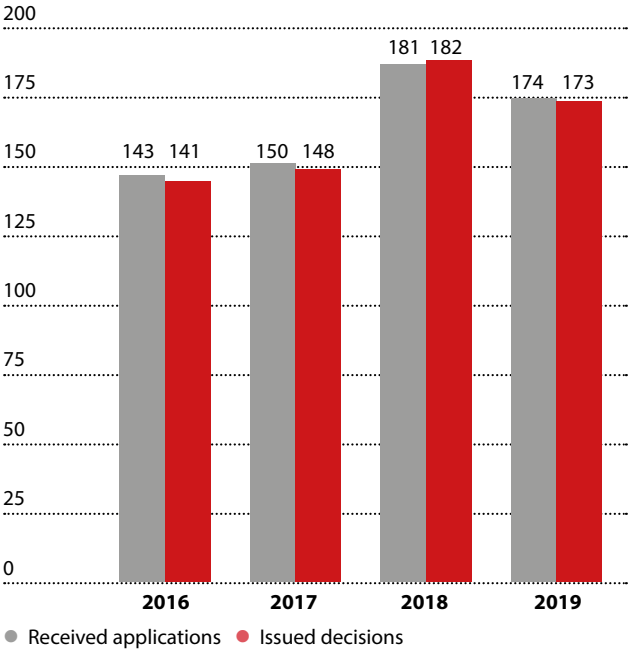
This is an area regulated by the Institute pursuant to Act No 296/2008 Coll., on Human Tissues and Cells.

In 2019, 55 applications for operating authorisation and applications for variations to operating authorisations were received.

Tab. 17 **Activities associated with applications in the sphere of manufacture of pharmaceuticals and in the sphere of human tissues and cells**

Application type		2016		2017		2018		2019	
		Received applications	Issued decisions	Received applications	Issued decisions	Received applications	Issued decisions	Received applications	Issued decisions
Application for manufacturing authorisation	Manufacturers of medicinal products	3	2	4	4	2	1	2	2
	Control laboratories	2	1	1	1	2	0	1	3
	Blood centres	1	0	2	3	1	1	3	3
Application for variation to manufacturing authorisation	Manufacturers of medicinal products	55	55	56	53	58	57	59	60
	Control laboratories	5	4	2	3	3	3	1	1
	Blood centres	23	26	27	26	39	40	45	44
Application for manufacturing authorisation revocation	Manufacturers of medicinal products	2	3	0	1	5	5	4	5
	Control laboratories	0	2	2	2	3	3	1	1
	Blood centres	0	0	1	1	1	1	0	0
Application for operating authorisation for:	Tissue centre	1	1	3	2	4	5	1	1
	Distribution of tissues and cells	-	-	1	0	3	4	1	1
	Donation centre	0	0	0	0	0	0	0	0
	Diagnostic laboratory	0	0	3	2	1	1	1	0
Application for variation to operation of:	Tissue centre	41	37	40	39	44	48	43	38
	Distribution of tissues and cells	-	-	-	-	1	0	0	1
	Donation centre	0	0	1	1	0	0	0	0
	Diagnostic laboratory	8	8	4	6	4	4	9	9
Application for revocation of operation of:	Tissue centre	2	2	1	1	7	6	0	1
	Distribution of tissues and cells	-	-	-	-	-	-	0	0
	Donation centre	0	0	0	0	0	0	2	2
	Diagnostic laboratory	0	0	2	2	3	3	1	1
Total		**143**	**141**	**150**	**148**	**181**	**182**	**174**	**173**

Fig. 8 **Numbers of received and concluded applications**



In 2019, 271 inspections in total were completed, of which 59 inspections were associated with the regulated area of tissues and cells. Their character and resulting ratings 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 2016 to 2019 is provided in Table 19 and in Fig. 9 and 10.

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

Of the total number of 103 inspections at manufacturers of medicinal products and active substances or in control laboratories, a breach of the Act on Pharmaceuticals was identified in nine cases. The GMP standard in blood centres was rated mostly as good; no breach of law was identified. The plan of follow-up inspections was fulfilled for all regulated entities and the inspection interval stipulated by the Decree was observed.

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

Tab. 18 **Inspections conducted in 2019 and their outcomes**

	Number of inspections						Inspection rating		
	Total	Initial	Follow-up	Targeted	Variation	Compliant[1]	Non -compliant	Breach of law	Fine/ Order
Manufacturers of medicinal products	59	2	42	3	12	42	2	2	2
Manufacturers of active substances	23	2	18	1	2	20	0	3	3
Control laboratories	17	1	15	0	1	16	0	0	0
Active substance importers	4	3	1	0	0	4	0	0	0
Blood centres	64	3	48	1	12	51	0	0	0
Blood banks	11	1	9	1	0	10	0	0	0
GCP inspections – Ethics Committees	1	0	0	1	0	0	0	0	0
GCP inspections – others	32	0	0	32	0	0	0	1	0
TC, DC, DL, DIS inspections	59	6	45	3	5	51	0	0	0

Explanatory notes: TC – tissue centre; DC – donation centre; DL – diagnostic laboratory; DIS – distributor of tissues and cells

[1] *Rated only in case of initial and follow-up inspections.*

Tab. 19 **Inspections conducted in 2016–2019**

	2016		2017		2018		2019	
	No. of inspections	Breaches of law	No. of inspections	Breaches of law	No. of inspections	Breaches of law	No. of inspections	Breaches of law
Manufacturers of medicinal products	71	3	57	8	58	9	59	2
Manufacturers of active substances	18	2	20	1	14	0	23	3
Control laboratories	9	0	22	0	8	0	17	0
Active substance importers	4	0	5	0	2	0	4	0
Blood centres	47	0	57	0	51	0	64	0
Blood banks	22	0	22	0	19	0	11	
GCP inspections + ethics committees	16	7	25	0	34	1	33	1
Tissue centres, donation centres, diagnostic laboratories	104	1	84	0	101	0	59	0
Total	**295**	**13**	**292**	**9**	**286**	**10**	**270**	**6**

Fig. 9 **Number of manufacturers of medicinal products, active substances and control laboratories and an overview of completed inspections**

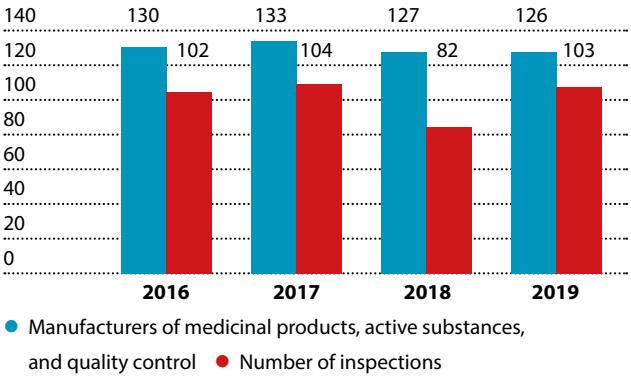
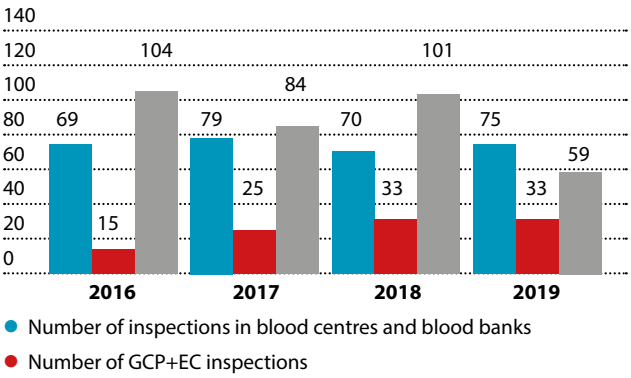


Fig. 10 **Overview of completed inspections in the area of blood centres + blood banks, GCP + EC, and HTC (tissue centres, diagnostic laboratories, donation centres) in the period of 2016–2019**



Haemovigilance

In 2019, 32 reports of suspected serious adverse reactions (hereinafter referred to as "SAR") experienced by donors of blood and blood components or recipients of transfusion products were received, of which two reports are still pending and in eight cases, the suspected SAR was not confirmed. Of confirmed serious adverse reactions, ten SARs involved blood or blood component donors and 12 SARs concerned post-transfusion reactions in transfusion product recipients (five haemolytic reactions arising from AB0 system incompatibility; six cases of anaphylaxis; and one case of a transfusion-related acute lung injury (TRALI)). In all cases, transfusion product recipients fully recovered from the SARs associated with post-administration reaction to the transfusion product (i.e. from the post-transfusion reaction). In the aforementioned ten cases of blood or blood component donor SARs, the donors also fully recovered.

Furthermore, 24 reports of suspected serious adverse events (hereinafter referred to as SAE) associated with blood donation, testing, processing, storage, and distribution of transfusion products or raw materials for further manufacture or transfusion product dispensing were reported. Seven cases did not constitute a SAE; four suspected SAEs are still pending. Of this number, nine cases constituted suspected product confusion; two cases involved manufacturing equipment failure; two cases out-of-specification sterility tests. Each report that the Institute received was processed, evaluated, and entered in the database of SARs and SAEs and, concurrently, processed to be incorporated in the Annual SAE and SAR Report for the Czech Republic for the European Commission. Educational activities to raise the awareness of regulated entities regarding the importance of suspected SAR and SAE reporting continue to be carried out. Within the scope of its involvement in the European Rapid Alert System for Blood and Blood Components (RAB), the Institute in 2019 received 18 reports from nine countries. Sixteen cases involved an epidemiological situation (in 14 cases associated with

the occurrence of the West Nile virus; in two cases with the occurrence of the dengue fever); two cases constituted a warning regarding the quality and safety of medical devices used by transfusion product manufacturers.

Good Laboratory Practice (GLP)

In 2019, a total of nine holders of Good Laboratory Practice Certificates issued by the Institute were listed, with prevailing scope of activities in toxicological studies; these are included in the National GLP Programme. In the same year, eight follow-up inspections were completed.

Good Clinical Practice (GCP)

In the course of 2019, the total of 32 inspections of good clinical practice were conducted. Of the said number, 30 concerned a targeted inspection of a trial site (a GCP inspection at the investigator's), of which one was an inspection conducted on behalf of the European Medicines Agency as part of the abbreviated centralised procedure assessment concerning application for marketing authorisation of an orphan medicinal product; the inspection was carried out in cooperation with inspectors from another EU Member State; the other two were a targeted inspection of a clinical trial sponsor and a targeted inspection of an ethics committee.

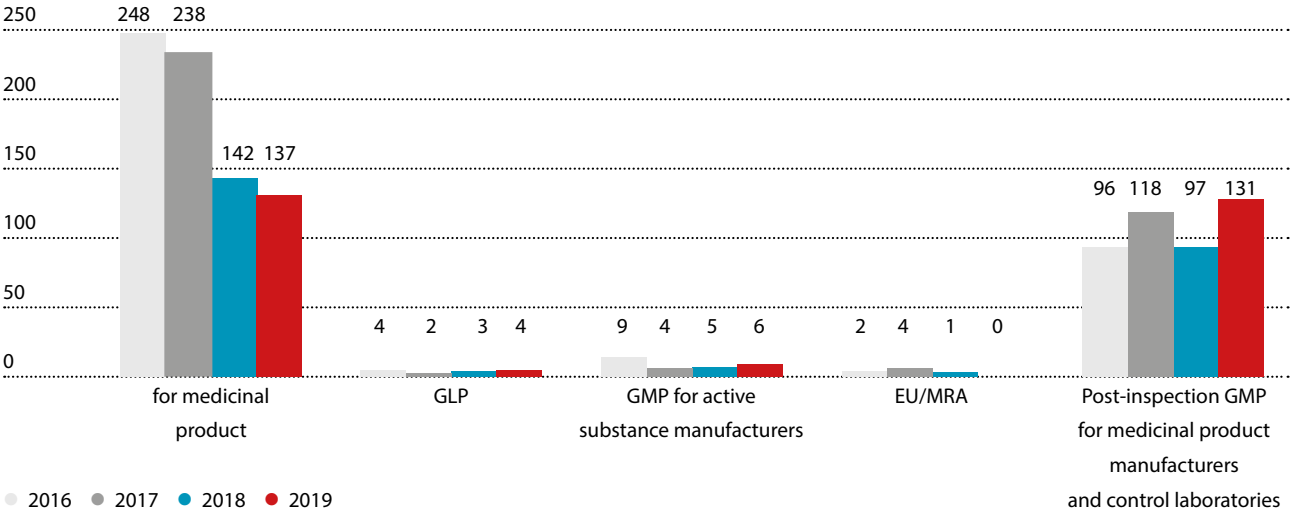
Actions and Penalties

In 2019, six breaches of the Act on Pharmaceuticals were identified.

Certification

In total, 278 various certificates were issued. Post-inspection good manufacturing practice certificates are subsequently entered in the EudraGMP database kept by EMA. All of the certificates for medicinal products were issued within the prescribed 30-day timeline and all post-inspection good manufacturing practice certificates within the 90-day timeline.

Fig. 11 **Issued certificates**



Assessment of GMP Compliance within the Scope of Marketing Authorisation Activities

A total of 1,341 cases were received (a 6.6% increase compared to 2018); all of them were processed within predefined timelines.

Foreign Inspections

In 2019, five good manufacturing practice inspections at foreign entities were conducted.

In 2019, the inspectors from the Clinical Practices Unit (OKP) participated in two international inspections in Germany, a clinical trial sponsor inspection and a contract research organisation inspection, within the scope of the PIC/S – JVP programme.

Tab. 20 **Foreign inspections**

	2016	2017	2018	2019
Number of inspections	3	8	4	7
Certificate issuance	3	3	1	4
Issued non-compliance	1	0	0	1

4.9 Quality Defects of Pharmaceuticals and Counterfeit Products in the Legal Distribution Chain

Since 2016, a major increase in the number of reports in the area of quality defects of pharmaceuticals has been observed. In 2019, the number of received reports was the highest since the establishment of the Quality Defects Unit (Tab. 21 refers).

Tab. 21 **Number of received reports in the period of 2014-2019**

Quality defects	2014	2015	2016	2017	2018	2019
Reports received in total	345	333	420	443	496	**497**
Reports from the Czech Republic	181	181	243	277	286	**284**
Reports from abroad	164	152	177	166	210	**213**
Resulted in recall (in SÚKL codes)	60	79	72	79	89	**59**
Administrative procedure (since 04/2017)	-	-	-	20	33	**81**
Rapid alert	6	11	17	22	6	**15**

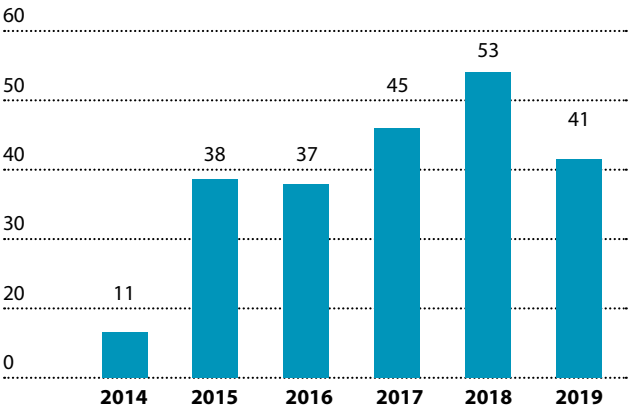
Explanatory notes: Rapid alert = a rapid alert notification sent by the Institute within the scope of the international Rapid Alert system

Within the scope of addressing quality defects, effective actions have been taken to reduce the impact of the quality defects of pharmaceuticals upon patient health. In 2019, the reports concerned not only authorised medicinal products and individually prepared medicinal products, but also non-authorised or investigational medicinal products as well as substances intended for the preparation of medicinal products in pharmacies and for the manufacture of medicinal products. Through the international Rapid Alert System involving the EU, MRA, and PIC/S Member States, the Institute received and evaluated the total of 138 reports on quality defects of pharmaceuticals.

Compared to the previous years, in 2019, there was a significant increase in the number of reports for the commencement of administrative procedures regarding the possibility to distribute, dispense, place on the market, or use in the provision of healthcare services such pharmaceuticals or individual batches thereof that exhibit a quality defect not constituting a jeopardy to the life or health of people. Where the quality defect concerns more than one batch of the medicinal product, each batch must be subjected to inspection. In 2019, 76 administrative procedures were commenced and 81 final decisions were issued; these concerned 165 medicinal products (in SÚKL codes) and 289 batches of medicinal products.

Since 2015, a major increase in the number of reports concerning the occurrence of counterfeit medicinal products in the legal distribution chain or their theft has been seen compared to the previous years (Fig. 12 refers). In 2019, the Quality Defects Unit addressed 41 such cases in total, of which seven cases concerned theft of medicinal products from the legal distribution chain.

Fig. 12 **Counterfeit medicinal products in the legal distribution chain and stolen medicinal products**



The reports received from foreign countries include also reports on GMP non-compliance on the part of the manufacturer of a medicinal product or active substance. In 2019, the Unit received and evaluated 35 such reports in total. Furthermore, the Quality Defects Unit monitored the recall of five medicinal products (in SÚKL codes) for marketing authorisation reasons (e.g. reduced shelf-life, changed method of dispensing, etc.).

An overview of measures taken in this year for individual medicinal products (in SÚKL codes) is provided in Table 22. All of these measures were actions taken and implemented by the marketing authorisation holders or operators themselves; the Institute was only monitoring or adjusting their measures.

Tab. 22 **Actions taken in 2019 (related to SÚKL codes)**

Actions taken	Number
Recall from distributor level	0
Recall from healthcare facility level	52
Recall from patient level	7
Suspended distribution, dispensing and/or use	12
Released distribution, dispensing, and use	0
Permitted distribution, dispensing, marketing, and use in the provision of healthcare services through an administrative procedure (number of batches: 289)	165

Mutual exchange of information and cooperation with the Slovak authority, ŠÚKL in Bratislava, continued and in 2019, the Quality Defects Unit cooperated with ŠÚKL in several cases.

The Quality Defects Unit was involved in the preparation of adaptation of Commission Delegated Regulation (EU) 2016/161 supplementing Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use (hereinafter referred to as the "Safety Feature Regulation"). In the course of 2019, working

meetings aimed at the preparation of a web interface and an electronic form for the reporting of unsuccessful verification of safety features by the concerned entities took place. The representatives of the Institute regularly participated in the meetings of the expert group for safety features and in international teleconferences.

In the period from 09 February 2019 to 31 December 2019, the Institute filed the total of 923,390 reports on unsuccessful safety feature verification. In the course of this year, the Quality Defects Unit communicated with 21 marketing authorisation holders in respect of whose products a high number of such reports was identified. At the same time, meetings with 11 marketing authorisation holders were held in the Institute. In the course of 2019, the Unit issued favourable recommendations for the total of 61 medicinal products and 86 batches, on the basis of which a temporary measure as referred to under Section 11(r) of the Act on Pharmaceuticals was issued by the Ministry of Health so as to safeguard the availability of medicinal products in the Czech Republic. The Quality Defects Unit also conducted investigations into 48 reports concerning suspected broken anti-tamper devices (ATDs).

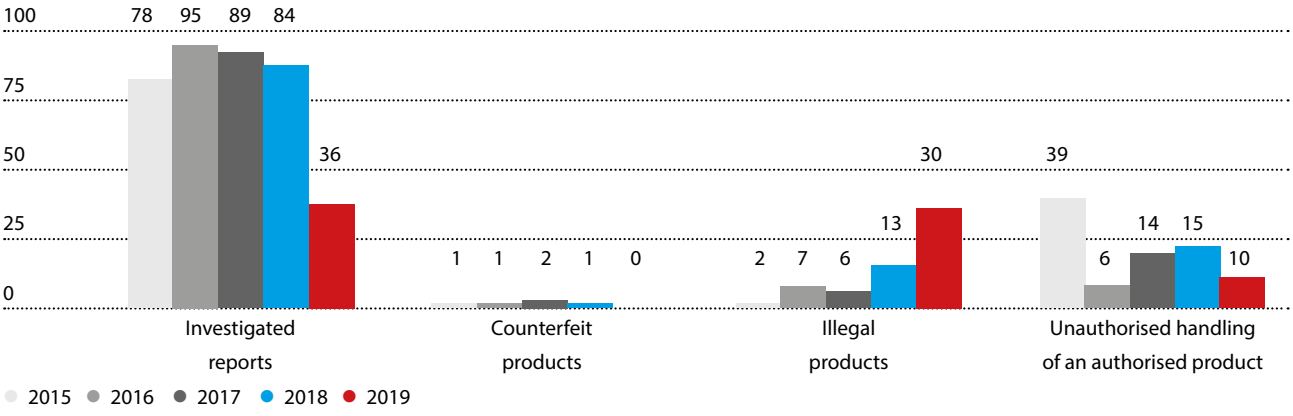
As in previous years, the Institute focused upon surveillance over compliance with the obligation of marketing authorisation holders stipulated under the provisions of Section 33(2) of Act No. 378/2007 Coll., on Pharmaceuticals and on Amendments to Some Related Acts (Act on Pharmaceuticals), as amended. In the first quarter of 2019, the Institute addressed 33 such reports in total, of which four were forwarded for the issuance of an order for breach of the aforementioned obligation.

4.10 Enforcement

In 2019, active surveillance in the area of illegal handling of medicinal products focused, in particular, upon the identification, investigation, and penalisation of cases of distribution and sales by unauthorised persons and upon monitoring of the internet environment, where illegal sale of medicinal products is being carried out. In the sphere of enforcement, the Institute closely cooperates with the Czech Customs Administration, Czech Police, Czech Trade Inspection, and the Czech Agriculture and Food Inspection Authority (CAFIA). Cooperation has been extended also to foreign partners, not only in the exchange of information, but also in the investigation of specific cases with potentially international impact.

In 2019, a total of 36 reports (either the Institute's own or received reports) were investigated. In 2019, the Institute was monitoring and detecting illegal offers of medicinal products in the internet environment and executed 14 control purchases. Thirty cases of handling of unauthorised medicinal products and ten cases of unauthorised handling of authorised medicinal products were identified.

Fig. 13 **Control activities in the period of 2015–2019**



In 2019, the Institute prepared a total of 152 opinions on shipments from third countries for the customs authorities for the purposes of release/non-release of medicinal products imported from third countries. The Institute assessed whether products that were the subject of non-commercial import in mail shipments, express shipments, and other types of shipment, were medicinal products as defined by the provision of Section 2 of Act No 378/2007 Coll., on Pharmaceuticals and on Amendments to Some Related Acts (the Act on Pharmaceuticals).

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

In 2019, the Institute investigated a total of 139 reports of suspected breaches of Act No. 40/1995 Coll., on Advertising Regulation, as amended (hereinafter referred to as the "Act on Advertising Regulation"). In 2019, the Institute received ten new reports less than in 2018 (134 newly received reports in 2018). In 2019, 15 administrative procedures were completed which resulted in the imposition of 14 fines in the aggregate amount of 4,715,000 CZK.

The subject of investigation into advertising was printed advertising matter (61 %), websites (15 %), and promotional samples (24 %).

Advertising for prescription-only medicines accounted for 28 % of the investigated cases, advertising for over-the-counter medicines represented 72 % of cases.

Pharmaceutical companies or their legal representatives filed 6 % of reports on suspected breaches of law, 1 % of reports was filed anonymously, 10 % were lodged by private individuals, 1 % by state administration bodies, and 82 % by the employees of the Institute.

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

	Reports brought forward from 2018	Newly received reports in 2019	Total
Number of reports	15	124	139
Investigation completed	15	121	136
Forwarded for commencement of administrative procedure	0	2	2
Completed administrative procedures	0	0	0
Number of finally imposed fines	0	0	0

Fig. 14 **Overview of investigated reports of suspected breaches of the Act on Advertising Regulation (2015–2019)**

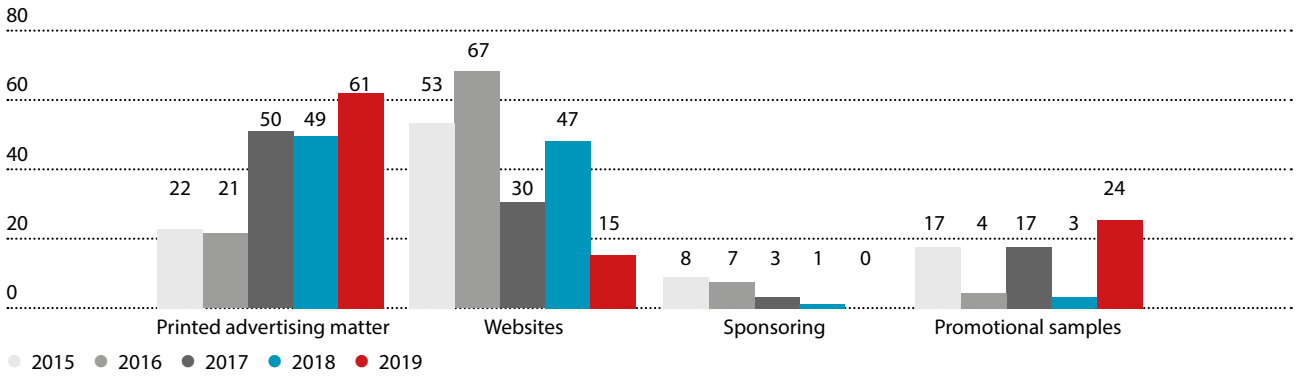
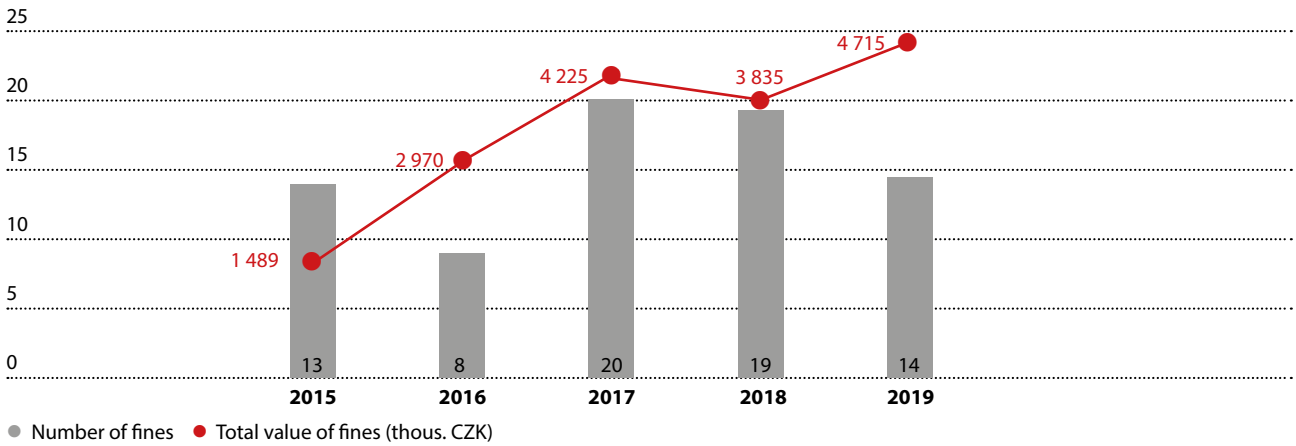


Fig. 15 **Overview of fines imposed for breaches of the Act on Advertising Regulation (2015–2019)**



Upon request, the Institute issued/provided 54 expert opinions/consultations on the issue of proposed advertising for medicinal products for human use.

The inspectors of the Advertising Surveillance Unit completed 25 inspections of compliance with the Act on Advertising Regulation and the Act on Pharmaceuticals.

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

In 2019, the Institute commenced investigation into 94 cases of various products, most often dietary supplements and cosmetic products, for suspected classification as a medicinal product. In 16 cases, an administrative procedure regarding the nature of the product was initiated ex officio or upon request. In 2019, the Institute reclassified the total of 18 products to the group of medicinal products. Upon request, it provided six expert opinions/consultations on issues regarding product classification as a medicinal product or another product.

4.12 Standardisation and Pharmacopoeial Activities

In the first half of 2019, the Pharmacopoeia employees prepared for print second supplement to the Czech Pharmacopoeia 2017 – Supplement 2019 (hereinafter referred to as "CP 2017 – Suppl. 2019"). In its European part, it contains the translations of the sixth to eighth supplement of the European Pharmacopoeia (Suppl. 9.6–9.8).

The European part contains the total of 364 texts, of which the General Part includes 50 general texts (of which four are new ones), six general articles (of which one is new), and three revised general articles concerning pharmaceutical forms. The Special Part contains texts for 43 vaccines for human use (of which one is new), and two revised monographs on vaccines for veterinary use, six monographs on radiopharmaceuticals (of which two are new), 37 herbal drug monographs (of which seven are new), two monographs on homeopathic products (of which one is new), and three monographs of surgical sutures for use in animals (of which one is new). The number of chemical and biological monographs on active substances amounted to 212 (of which 27 were new).

The National Part of the CP 2017 – Suppl. 2019 contains the total of 12 texts. Its General Part includes the full version of Tables I, II, III, IV, V, VI, and XII that contain active substances included in CP 2017, CP 2017 – Suppl. 2018 as well as in Suppl. 2019. Revised Table X, listing the valid standard names of pharmaceutical forms, methods of administration, and packaging, is also provided in its full version. Furthermore, the General Part contains an overview of updated testing agents used in national monographs.
The Special Part of the National Part contains two revised monographs – Ethacridini lactatis solutio and Ichthammoli unguentum. The Ichthammoli unguentum monograph was presented for public investigation (notified) under ID number 2019/109/CZ. National monograph Cacao oleum was deleted and replaced with European monograph Theobromatis oleum (2607), published in Ph. Eur. 10.0 as binding from 01 January 2020.

Czech Pharmacopoeia 2017 – Suppl. 2019 is available also in electronic format that is on sale also separately, independently of the book publication, and contains all unrevised CP 2017 texts together with new and revised texts of CP 2017 – Suppl. 2018 and CP 2017 – Suppl. 2019.

CP 2017 – Suppl. 2019 was published in cooperation with the Grada Publishing house as a single volume that is binding as of 01 December 2019.

Tab. 24 **Number of texts in the European Part of CP 2017 – Suppl. 2019**

European Part	General Part	Special Part	Total
New	5	39	44
Revised	54	266	320
Total	**59**	**305**	**364**

Concurrently with the proof-reading and print preparation of CP 2017 – Suppl. 2019, translations and revisions of monographs from European Pharmacopoeia, 10th edition (10.0) and, subsequently, two further European Pharmacopoeia supplements (10.1 and 10.2) were under way. The three European editions (10.0 to 10.2) will form part of Czech Pharmacopoeia 2017 – Supplement 2020 (hereinafter referred to as "CP 2017 – Suppl. 2020"). Due to the high amount of adjusted articles (over 500) in the European Part, this concerns approximately 780 texts.

In the second half of 2019, works on the National Part of CP 2017 – Suppl. 2020 began; also in this case, updated tables and revisions of national monographs will be included. Another revision of national monograph Butamirati citras and the inclusion of a new monograph Adeps suillus stabilisatus are under preparation.

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

The employees of the Pharmacopoeia and Pharmaceuticals Standardisation Unit informed about the binding nature of individual Ph. Eur. editions in SÚKL's information media.
The employees of the Unit regularly attended the EPC meetings and meetings of secretariats of national pharmacopoeial commissions.

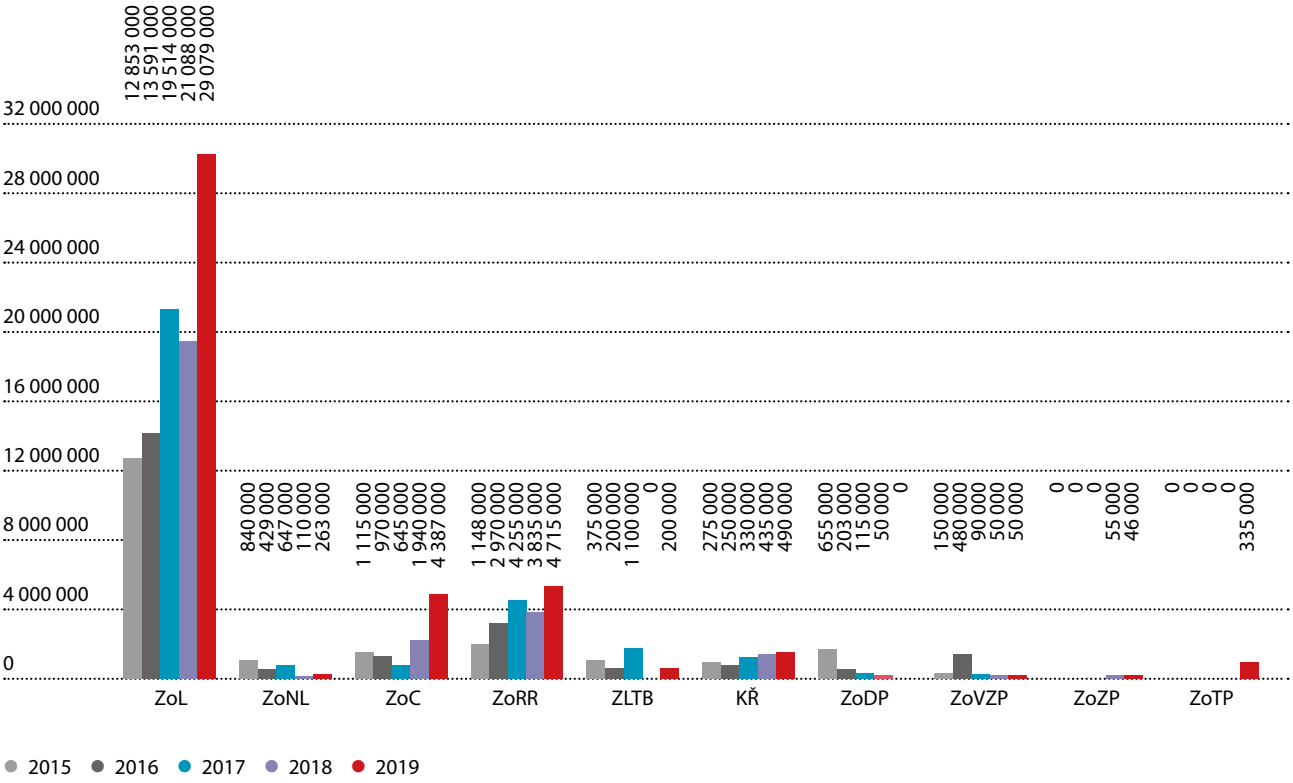
In May, the "Shelf-Life of Magistral Formulas" project was launched in cooperation with the laboratories and the Pharmacy Section of the Pharmacopeia Commission and it concerned the following products: Solutio Jarisch (sine parabenis), Solutio Jarisch (cum parabenis), Aqua conservans, Ethacridini lactatis solutio 0.1%, Methylrosanilinii chloridi solutio 0.5%, Methylrosanilinii chloridi solutio 1%. Testing is being conducted pursuant to the individual national monographs and national monograph Table XVI: Storage and shelf-life of products prepared in pharmacies. The verified shelf-lives will be provided in Table XVI (and probably published in Suppl. 2020). This project is still ongoing.

The Pharmacopoeia employees were involved in the revision of Guideline LEK-5, regarding the inclusion of requirements for quality testing of purified water prepared in pharmacies.

4.13 Imposed Penalties

Based on its ex-officio findings and breaches of legislative requirements identified in the course of inspections in the area of medicinal products and human tissues and cells or in the surveillance of advertising and based on reports, the Institute initiates administrative procedures on administrative offences within which penalties referred to in the applicable laws are imposed according to the severity of the identified breach. Since August 2011, the Institute has been availing also of the option to impose penalties on the basis of so-called administrative order referred to under the Code of Administrative Procedure. The Institute observed this practice also in 2019. Since January 2015, the Institute has been imposing also penalties for committing an administrative offence referred to by the Act on Public Health Insurance regarding the provision of unauthorised bonuses in the dispensing of prescription-only medicinal products. In 2019, the Institute continued also the imposition of penalties in the form of so-called aggregate fines for committed administrative offences governed by several laws within the powers of the Institute in the sphere of medicinal products. As of 1 July 2017, the Institute has been applying Act No 250/2016 Coll., on Liability for Offences and Procedures Pertaining Thereto, in its practice of administrative penalisation. Furthermore, as a form of penalisation, the Institute avails also of the new option to impose admonitions as referred to under Act No 250/2016 Coll., on Liability for Offences and Procedures Pertaining Thereto, as amended.

Fig. 16 Imposed penalties which became final in 2015–2019 (in mil. CZK)



- *ZoL = Act on Pharmaceuticals*
- *ZoNL = Act on Dependency-Producing Substances*
- *ZoC = Act on Prices*
- *ZoRR = Act on Advertising Regulation*
- *ZLTB = Act on Safeguarding the Quality and Safety of Human Tissues and Cells Intended for Use in Man*
- *KŘ = Code of Control Procedure*
- *ZoPD = Act on Drug Precursors*
- *ZoVZP = Act on Public Health Insurance*
- *ZoZP = Act on Medical Devices*
- *ZoTP = Act on Technical Requirements for Products*

4. 14 Medical Device Control and Expert Opinion Unit

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

The objective of both scheduled and unscheduled SÚKL inspections is to ensure that medical devices supplied onto the market in the Czech Republic were safe and functional and that health care was provided using adequate, safe, and effective medical devices so that the health of users or patients was not compromised during the proper use of the medical devices for the intended purpose. In 2019, the inspectors of the Medical Device Control Unit conducted 102 inspections in total, of which 20 were inspections at healthcare service providers (both state and non-state healthcare facilities) and 82 were inspections at medical device manufacturers, importers, distributors, vendors, dispensaries, and servicing organisations. During these inspections, 495 medical devices were checked. For a more detailed statistics regarding the total number of inspected medical devices and inspected persons, please refer to Tables 25 and 26.

Twenty inspections were conducted at healthcare service providers; within the scope of these inspections, documentation evidencing compliance with the condition of use of the medical device in the provision of health care was checked for 148 medical devices. Furthermore, 82 inspections were carried out as part of market surveillance, within the scope of which 347 medical devices were checked for compliance with the requirements of medical device supply onto the market. The number of shortcomings identified at persons subjected to market surveillance amounted to 266.

The Medical Device Control Unit forwarded 118 reports in total for further procedure to the Legal Support Units (Medical Devices and Surveillance Section).

Tab. 25 **Overview of medical device inspections**

Number of inspections (several roles may be inspected during a single inspection)	102
Number of inspected roles (price control, distributor, importer, provider, vendor, servicing, dispensary, manufacturer)	180
Number of inspected medical devices	495
Number of inspected established meters (of the total number of inspected medical devices)	6
Number of class IIb and III medical devices (of the total number of inspected medical devices)	150
Number of inspected medical devices without shortcomings (of the total number of inspected medical devices)	*364
Number of inspected medical devices without shortcomings (of the total number of inspected medical devices)	*131
Number of shortcomings	*266
Number of shortcomings in class IIb and III medical devices (of the total number of inspected medical devices with shortcomings)	*70
Number of reports (proposals for initiation of an administrative procedure) forwarded to the Legal Support Units (Medical Devices and Surveillance Section)	118

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

Tab. 26 **Rating of medical device inspections**

Entity	Number of inspections	1	2	3
POS – providers	20	10	9	1
CEN – price control	2	2	0	0
DIS – distributors	52	28	17	7
DOV – importers	32	25	3	4
PRO – vendors	18	13	5	0
SER – servicing organisations	26	20	3	3
VYD – dispensaries	16	14	2	0
VYR – manufacturers	14	7	0	7

Inspections are rated pursuant to an internal classification of shortcomings; the inspector rates and classifies the shortcoming (DN – minor or no shortcoming – 1; VN – major shortcoming – 2; KN – critical shortcoming – 3). The inspection is rated by attributing the value of the most severe shortcoming to the inspection.

■ SECTION OF PRICING AND REIMBURSEMENT REGULATION

In compliance with the provisions of Act No 48/1997 Coll., on Public Health Insurance and Amendments to Some Related Acts (hereinafter referred to as the "Act on Public Health Insurance"), the Section of Pricing and Reimbursement Regulation decides on maximum prices and reimbursement of medicinal products and foods for special medical purposes. For proprietary medicinal products, this is done in administrative procedures that fully comply with the transparent procedures set forth by the European legislation. Administrative procedures are conducted in cases specified by law either ex officio (typically so called in-depth and abbreviated revisions) or upon request of persons authorised by law (marketing authorisation holders in the case of authorised medicinal products; importers or domestic manufacturers of medicinal products if the medicinal product imported or produced thereby is used in the territory of the Czech Republic within a specific therapeutic programme or other persons applying for a specific therapeutic programme; importers or domestic manufacturers of foods for special medical purposes; health insurance companies). A request for the ex officio initiation of an administrative procedure may be submitted by any person.

Tab. 27 **Overview of administrative procedures in 2019**

Applications for maximum ex-factory price determination	**Number of SÚKL codes**
Initiated	746
Decided	742
Appeal procedure pending	4
Became final	738
Applications for maximum ex-factory price change	
Initiated	75
Decided	66
Appeal procedure pending	0
Became final	64
Applications for maximum ex-factory price r eduction – abbreviated procedure	
Initiated	1
Decided	1
Appeal procedure pending	0
Became final	1
Applications for maximum ex-factory price revocation	
Initiated	0
Decided	0
Appeal procedure pending	0
Became final	0

4.15 Pricing and Reimbursements

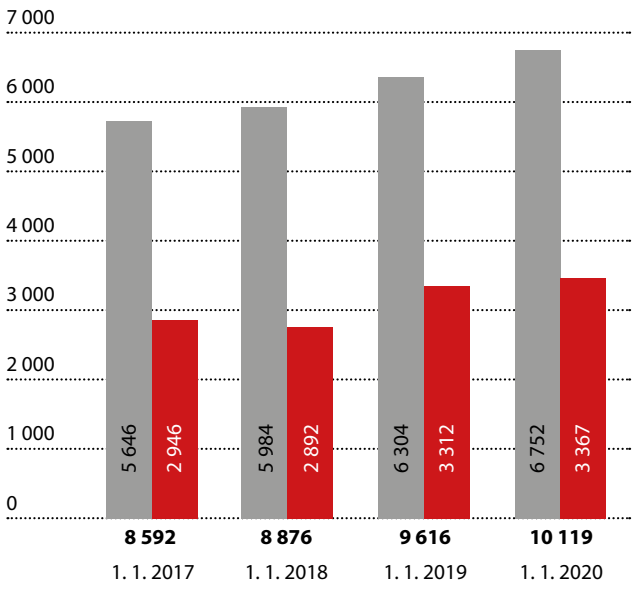
In the course of 2019, the Section continued in the initiation of in-depth reimbursement revisions in accordance with the schedule. For 2019, the initiation of 38 in-depth revisions was scheduled, of which 28 in-depth revisions (276 SÚKL codes) were actually commenced. The difference in the number of scheduled and initiated in-depth revisions reflects process and organisational & technical facts at the time of in-depth revision initiation (pending previous in-depth revision, termination of marketing authorisation or cancellation of reimbursement of medicinal products containing a particular active substance, etc.). In-depth revisions that were initiated above the scope of the schedule reflected current requirements of professionals asking for changes of inadequate conditions of medicinal product reimbursement or were initiated on the basis of reports from marketing authorisation holders, e.g. due to the existence of new clinical evidence relevant in respect of review of the therapeutic replaceability and the position of the therapy in the clinical settings in the Czech Republic.

The principal legislation governing the area of price regulation for 2019 was the Price Regulation of the Ministry of Health of the Czech Republic 1/2019/FAR on the regulation of prices of medicinal products and foods for special medical purposes (hereinafter referred to as the "Price Regulation") and the Price Decision of the Ministry of Health of the Czech Republic 1/19-FAR laying down a list of ATC groups that are not subject to price regulation by setting a maximum price in the specified pharmaceutical form (hereinafter referred to as the "Price Decision"); both regulations stipulate the method of price regulation with effect from 01 January 2019 and due to the change in the Price Decision, the number of applications for maximum price determination increased in 2019 from 29 codes (in 2018) to 746 codes (in 2019).

In 2019, 47 administrative procedures regarding the maximum ex-factory price change were commenced (compared to 29 administrative procedures in 2018); applications filed by marketing authorisation holders prevailed (20 applications were filed by health insurance companies and 27 applications were filed by marketing authorisation holders).

With a view to the stability of the price regulation, the share of medicinal products regulated by the profit margin only remained almost unchanged compared to 2018 (Fig. 17).

Fig. 17 **Structure of reimbursed products by the type of price regulation (no. of codes of medicinal products/foods for special medical purposes)**



With a view to the structure of medicinal products (Tab. 28), it may be stated that in 2019, the numbers of medicinal products in the below-mentioned maximum price zones were mostly growing, continuously throughout the year. The most pronounced increase was seen in the Over 50 CZK to 100 CZK zone and in the Over 100 CZK to 200 CZK incl. zone. A less pronounced increase was seen in the Over 20 CZK to 50 CZK incl. zone. A mild drop in the number of medicinal products was observed in the Over 500 CZK to 1,000 CZK incl. zone and in the Over 1,000 CZK to 2,000 CZK incl. zone.

Development of Average End-User Prices

In 2019, there was no change to the profit margins or to the VAT, the rate of which for medicinal products was 10 %. In respect of medicinal products regulated by the determined maximum price (maximum price determined by an administrative procedure and profit margin as per the Price Regulation), the average end-user price decreased by 0.7 %. The average price increase was not caused by the growth of unit prices of medicinal products compared to the previous period, but was influenced particularly by an increase in the deliveries of relatively expensive medicinal products (expensive care increase). Average prices in the highest price zone remained unchanged. In respect of medicinal products regulated by notified price and profit margin (as per the Price Regulation and the Price Decision), the average end-user price increased by 35 %. The situation in ex-factory price levels (ex. profit margin and VAT) focusing upon a more detailed comparison of the latest quarters of 2018 and 2019 is illustrated by Fig. 18 and 19.

Tab. 28 **Overview of the number of codes of medicinal products/foods for special medical purposes in the maximum price zones as per the List of Prices and Reimbursements (SCAU) by month**

Price regulation zone	01	02	03	04	05	06	07	08	09	10	11	12
Up to 20 CZK incl.	26	26	25	26	18	18	20	20	21	21	21	21
Over 20 CZK to 50 CZK incl.	372	364	360	371	368	370	377	383	397	394	406	413
Over 50 CZK to 100 CZK incl.	792	799	794	807	808	822	839	859	869	865	880	888
Over 100 CZK to 200 CZK incl.	999	999	968	988	992	1,034	1,045	1,064	1,074	1,082	1,085	1,086
Over 200 CZK to 300 CZK incl.	517	519	512	520	522	529	518	519	527	530	532	540
Over 300 CZK to 500 CZK incl.	643	646	621	627	627	602	602	611	615	620	628	632
Over 500 CZK to 1,000 CZK incl.	779	780	766	797	801	802	780	765	762	765	787	795
Over 1,000 CZK to 2,000 CZK incl.	654	656	643	663	663	666	687	698	698	705	714	717
Over 2,000 CZK to 3,000 CZK incl.	270	273	271	287	290	295	283	284	283	285	287	289
Over 3,000 CZK to 5,000 CZK incl.	355	353	348	360	364	363	362	365	364	364	365	366
Over 5,000 CZK to 10,000 CZK incl.	333	336	320	335	335	326	326	326	329	331	334	336
Over 10,000 CZK to 20,000 CZK incl.	235	236	229	234	233	236	234	238	234	235	237	240
Over 20,000 CZK to 30,000 CZK incl.	100	101	101	101	102	100	102	103	98	98	101	100
Over 30,000 CZK to 50,000 CZK incl.	76	78	79	79	80	82	81	85	77	77	77	78
Over 50,000 CZK to 100,000 CZK incl.	86	95	96	97	100	100	100	105	101	104	104	105
Over 100,000 CZK	67	70	74	78	80	80	80	81	79	81	82	77
Number of codes	**6,304**	**6,331**	**6,207**	**6,370**	**6,383**	**6,425**	**6,436**	**6,506**	**6,528**	**6,557**	**6,640**	**6,683**

Fig. 18 **Prices of pharmaceuticals regulated by maximum price – comparison of average prices in Q4 2018 and Q4 2019 by price zones**

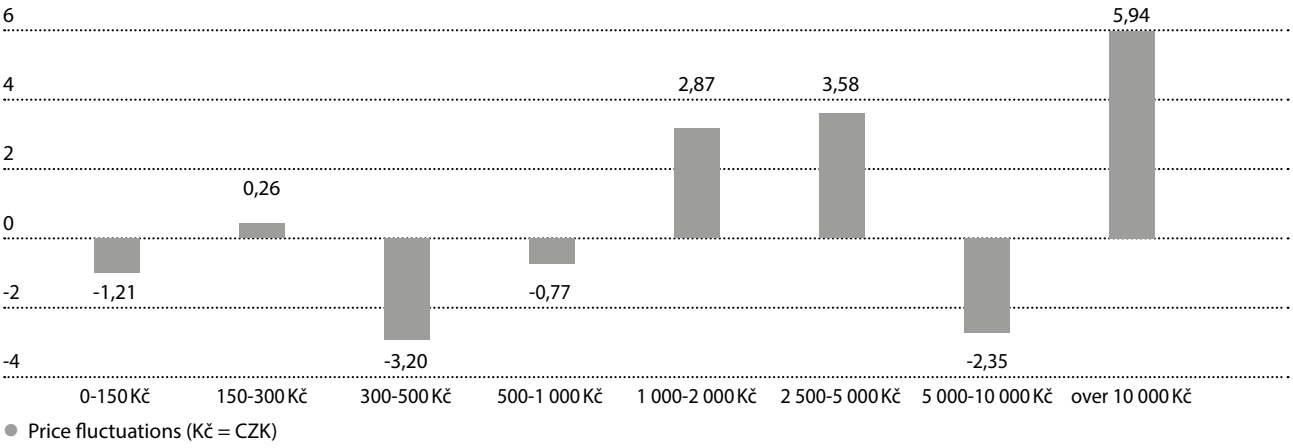
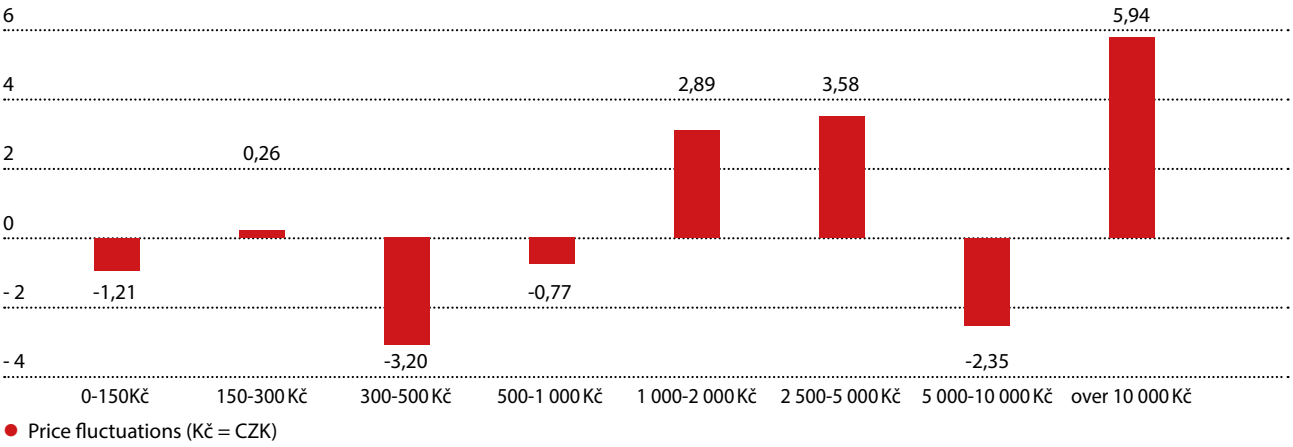


Fig. 19 **Prices of pharmaceuticals regulated by profit margin – comparison of average prices in Q4 2018 and Q4 2019 by price zones**



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

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

In 2019, the maximum prices both increased and decreased in the group of the most commonly distributed medicinal products in respect of which the maximum price was changed. Nevertheless, where the price increased, this happened in the case of medicinal products that may be classified as relatively cheap ones. The biggest price increase was that of medicinal product SUMATRIPTAN, where the original price increased due to changes on the markets in the reference basket countries and change of the reference product for maximum price determination (Tab. 29).

Tab. 29 **Ten most commonly distributed medicinal products by number of packages reported in compliance with DIS-13 for which the maximum price was changed**

Code	ATC	Name	Name supplement	No. of packages	Original maximum price (CZK)	New maximum price (CZK)	Change to maximum price (%)
0119672	M01AB05	DICLOFENAC DUO PHARMASWISS	75MG CPS RDR 30 I	483 238	110,00	81,84	-25,6
0191922	A10BA02	SIOFOR	1000MG TBL FLM 60	449 493	96,39	62,82	-34,8
0003801	C07AB07	CONCOR COR	2,5MG TBL FLM 28	445 158	59,75	38,62	-35,4
0119115	N02CC01	SUMATRIPTAN ACTAVIS	50MG TBL OBD 6 I	320 620	64,06	93,93	+46,6
0148070	C10AA07	ROSUCARD	10MG TBL FLM 90	307 481	1 608,20	186,55	-88,4
0019577	A10BA02	STADAMET	1000MG TBL FLM 60 I	292 863	127,77	54,38	-57,4
0100101	A10BA02	STADAMET	500MG TBL FLM 60	284 130	104,56	28,67	-72,6
0148074	C10AA07	ROSUCARD	20MG TBL FLM 90	281 000	2 643,17	289,44	-89,1
0096087	A10BA02	METFORMIN TEVA	500MG TBL FLM 60	273 814	54,85	61,22	+11,6
0000502	N01BB	MESOCAIN 1%	10MG/ML INJ SOL 10X10ML	260 861	212,73	240,00	+12,8

Medicinal products with the highest financial volume are distributed across a broad range of price zones. For all of the mentioned medicinal products, however, the maximum price was reduced (Tab. 30).

Tab. 30 **en most commonly distributed medicinal products by financial volume in end-user prices reported in compliance with DIS-13 for which the maximum price was changed**

Code	ATC	Name	Name supplement	Financial volume in end-user price	Original maximum price (CZK)	New maximum price (CZK)	Change to maximum price (%)
0210935	L04AB04	HUMIRA	40MG INJ SOL 2X0,4ML I	599 090 725	22 646,93	14 513,61	-35,9
0214739	L03AX13	COPAXONE	40MG/ML INJ SOL ISP 12X1ML	536 702 814	25 622,04	14 822,34	-42,2
0193696	S01LA05	EYLEA	40MG/ML INJ SOL 1X0,1ML	447 688 821	15 599,69	15 274,18	-2,1
0209097	L04AB04	HUMIRA	40MG INJ SOL 2X0,4ML	431 514 900	22 646,93	14 513,61	-35,9
0194569	S01LA04	LUCENTIS	10MG/ML INJ SOL 1X0,165ML	390 010 656	16 470,33	15 277,36	-7,2
0168373	B01AE07	PRADAXA	150MG CPS DUR 60X1 I	336 430 108	1 565,40	1 312,80	-16,1
0222682	L04AA36	OCREVUS	300MG INF CNC SOL 1X10ML	312 451 536	129 786,95	137 084,65	+5,6
0029328	B01AE07	PRADAXA	110MG CPS DUR 60X1 I	276 371 743	1 565,40	1 315,50	-16,0
0209429	J05AP54	ZEPATIER	50MG/100MG TBL FLM 28	244 347 985	373 138,20	167 851,60	-55,0
0210026	A10BK03	JARDIANCE	10MG TBL FLM 90X1	144 596 558	3 379,49	2 813,41	-16,8

Amounts and Conditions of Reimbursements from Health Insurance

Tab. 31 **Overview of administrative procedures in 2019**

Applications for determination or change conditions of reimbursement	Number of SÚKL codes
Zahájeno	338
Initiated	338
Decided	149
Appeal procedure pending	34
Became final	86
Applications for determination or change of maximum price and the amount and conditions of reimbursement	
Initiated	433
Decided	211
Appeal procedure pending	26
Became final	170
Applications for reimbursement revocation	
Initiated	86
Decided	83
Appeal procedure pending	0
Became final	75
Applications for maximum price and reimbursement revocation	
Initiated	90
Decided	86
Appeal procedure pending	0
Became final	82
Ex officio initiated procedures	
Initiated	1,566
Decided	261
Appeal procedure pending	105
Became final	173
Procedures concerning similar products	
Initiated	1,287
Decided	1,204
Appeal procedure pending	30
Became final	1,154

In 2019, 21 applications for determination of reimbursement of highly innovative products were submitted.

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

In 2019, savings of public health insurance funds were generated both by in-depth and abbreviated revisions. The total savings arising from abbreviated revisions enforceable in 2019 is estimated at 1,738,546,822 CZK and those arising from in-depth revisions at 3,175,635,750 CZK.

Tab. 32 **Overview of final decisions on the revision of reimbursements and the impact on public health insurance funds**

Effective date	Number of SÚKL codes	Number of administrative procedures	Impact on health insurance funds
01/2019	75	3	377 527 068,00 Kč
02/2019	79	10	167 993 400,00 Kč
03/2019	107	18	149 350 659,00 Kč
04/2019	66	4	209 304 064,00 Kč
05/2019	8	1	175 276 088,00 Kč
06/2019	307	7	551 305 581,00 Kč
07/2019	79	11	1 606 873 268,00 Kč
08/2019	70	12	404 338 239,00 Kč
09/2019	83	6	181 524 799,00 Kč
10/2019	117	2	* 0,00 Kč
11/2019	206	11	355 648 982,00 Kč
12/2019	117	11	735 040 424,00 Kč

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

** In-depth revisions of reimbursements of foods for special medical purposes in respect of which availability data are unknown, and hence the amount of public health insurance fund savings cannot be estimated.*

Tab. 33 **Overview of the number of codes of medicinal products/foods for special medical purposes in reimbursement amount zones according to the List of Prices and Reimbursements (SCAU) by month**

Reimbursement zone	01	02	03	04	05	06	07	08	09	10	11	12
Up to 20 CZK incl.	221	220	215	220	202	203	203	208	184	183	185	186
Over 20 CZK to 50 CZK incl.	861	859	847	855	847	844	852	859	870	862	840	848
Over 50 CZK to 100 CZK incl.	1,255	1,261	1,247	1,275	1,275	1,271	1,277	1,287	1,302	1,307	1,324	1,334
Over 100 CZK to 200 CZK incl.	1,564	1,571	1,538	1,575	1,572	1,566	1,561	1,563	1,596	1,608	1,619	1,651
Over 200 CZK to 300 CZK incl.	797	798	794	821	824	822	817	817	827	827	877	878
Over 300 CZK to 500 CZK incl.	872	876	851	862	860	853	850	860	893	890	897	919
Over 500 CZK to 1,000 CZK incl.	1,214	1,210	1,171	1,206	1,208	1,221	1,206	1,209	1,190	1,200	1,222	1,219
Over 1,000 CZK to 2,000 CZK incl.	975	974	975	1,014	1,021	1,036	1,044	1,045	1,041	1,056	1,058	1,063
Over 2,000 CZK to 3,000 CZK incl.	364	366	362	388	395	425	442	442	441	441	442	442
Over 3,000 CZK to 5,000 CZK incl.	397	391	378	395	392	397	389	392	388	388	394	401
Over 5,000 CZK to 10,000 CZK incl.	438	440	432	460	467	472	479	481	480	482	491	501
Over 10,000 CZK to 20,000 CZK incl.	275	271	270	274	274	277	286	299	294	295	297	302
Over 20,000 CZK to 30,000 CZK incl.	129	129	130	133	133	134	120	120	114	114	124	118
Over 30,000 CZK to 50,000 CZK incl.	73	75	76	76	79	82	79	74	71	73	75	73
Over 50,000 CZK to 100,000 CZK incl.	88	97	98	99	101	102	106	111	105	107	108	104
Over 100,000 CZK	93	96	99	103	105	102	99	99	93	94	94	93
Number of codes	**9,616**	**9,634**	**9,483**	**9,756**	**9,755**	**9,807**	**9,810**	**9,866**	**9,889**	**9,927**	**10,047**	**10,132**

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

The overview clearly indicates that in the group of relatively expensive medicinal products with the highest volume of reimbursement from health insurance, there was a significant decrease in the reimbursement for individual packages of medicinal products. The highest reduction was seen in medicinal products included in reference group no. 70/2 HUMIRA and REMICADE (tab. 34).

Tab. 34 **Ten most commonly distributed medicinal products by financial volume in end-user prices reported in compliance with DIS-13, for which reimbursement was changed**

Code	ATC	Name	Name supplement	Financial volume in end-user prices	Original reimbursement (CZK)	New reimbursement (CZK)	Change in reimbursement (CZK)
0210935	L04AB04	HUMIRA	40MG INJ SOL 2X0,4ML I	599 090 725	21 198,78	12 090,84	-43,0
0168904	B01AF01	XARELTO	20MG TBL FLM 98 II	530 223 026	6 167,15	5 788,01	-6,1
0210190	A10AE56	XULTOPHY	100U / ML + 3,6MG / ML INJ SOL 3X3ML	492 646 898	3 244,85	2 724,10	-16,0
0209097	L04AB04	HUMIRA	40MG INJ SOL 2X0,4ML	431 514 900	21 198,78	12 090,84	-43,0
0219085	L02BX03	ZYTIGA	500MG TBL FLM 60 (5X12)	431 316 672	87 170,44	77 328,00	-11,3
0193747	B01AF02	ELIQUIS	5MG TBL FLM 168	363 790 895	5 286,12	4 961,14	-6,1
0168373	B01AE07	PRADAXA	150MG CPS DUR 60X1 I	336 430 108	1 887,90	1 771,84	-6,1
0180087	R03AK07	SYMBICORT TURBUHALER 200 MIKROGRAMŮ / 6 MIKROGRAMŮ / INHALACE	160MCG / 4,5MCG INH PLV 1X120 DÁV	303 142 748	802,48	687,02	-14,4
0194319	L04AA31	AUBAGIO	14MG TBL FLM 28	280 893 651	18 060,85	15 500,76	-14,2
0027283	L04AB02	REMICADE	100MG INF PLV CSL 1	273 042 969	10 278,01	5 862,11	-43,0

The group of medicinal products with the greatest distribution in respect of which reimbursement was changed contains particularly relatively cheap medicinal products. The reimbursements of the aforementioned products were both increased and decreased in 2019. In case of medicinal product NEUROL, the reimbursement was significantly increased, which was also reflected in the increased volume of its supplies (tab. 35).

Tab. 35 **Ten most commonly distributed medicinal products by number of packages reported in compliance with DIS-13 for which reimbursement was changed**

Code	ATC	Name	Name supplement	A (no. of packages)	Original reimbursement (CZK)	New reimbursement (CZK)	B (no. of packages)	Note
0091788	N05BA12	NEUROL	0,25MG TBL NOB 30	176 225	4,70	11,71	194 290	*/
0176954	A03DA02	ALGIFEN NEO	500MG / ML + 5MG / ML POR GTT SOL 1X50ML	363 881	108,44	127,91	349 367	
0140192	A02BC01	OMEPRAZOL STADA	20MG CPS ETD 100		115,18	205,84		x/
0101211	C09AA04	PRESTARIUM NEO	5MG TBL FLM 90 (3X30)		143,09	103,40		x/
0002679	R03AL01	BERODUAL N	21MCG / 50MCG / DÁV INH SOL PSS 200DÁV	255 039	203,90	193,98	254 203	
0206563	J01DD01	TAXIMED	1G INJ / INF PLV SOL 1		65,75	29,47		x/
0056976	C09AA05	TRITACE	2,5MG TBL NOB 20		15,90	11,48		x/
0076064	B03BB01	ACIDUM FOLICUM LÉČIVA	10MG TBL OBD 30	247 662	88,76	73,15	244 786	
0025366	A02BC01	HELICID 20 ZENTIVA	20MG CPS ETD 90 I		103,67	185,26		x/
0002479	R06AX	DITHIADEN	2MG TBL NOB 20		27,28	25,53		x/

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

Validation of Applications

The dropping trend in the number of applications since approx. 2014 was interrupted in 2019, as more than double the number of applications than in 2018 was submitted. The increase in the number of submissions in the last year was caused particularly by the adoption of the Price Regulation and Price Decision effective as of 01 January 2019, stipulating new regulation of medicinal products, whose ATC group was newly not included in the Price Decision, by maximum prices and hence the producers of these products were obliged to submit an application for maximum price determination by 31 January 2019. A significant portion of the total number of applications consisted of applications for determination of the amount and conditions of reimbursement/maximum price and the amount and conditions of reimbursement through the procedure outlined under Section 39g(9) of the Act on Public Health Insurance (so called "similar products"); compared to 2018, the submissions of such applications increased by 65 %.

The most common reason for discontinuing an administrative procedure in the validation stage was withdrawal of the application, followed by an obstacle in procedure (so called litispendence), and obvious legal inadmissibility of the application, the share of those two reasons being the same. The proportion of applications submitted by health insurance companies of the total number of applications remained on the same level as in 2018, amounting to approx. 9 %.

In 2019, 55 medicinal products entered the reimbursement system on the basis of an application for the adoption of producer price and the amount and conditions of reimbursement from an identical reimbursed product.

Tab. 36 **Validation of applications for determination/change/ revocation of maximum prices and/or reimbursement amounts and conditions, for abbreviated revision of maximum price or reimbursement system – 2019**

Period	Submitted applications	Suspended due to defective submission and application shortcomings	Discontinued in the validation phase
January	29	2	0
February	44	0	1
March	45	1	0
April	43	1	0
May	26	0	0
June	36	0	2
July	39	0	2
August	32	1	1
September	27	3	2
October	30	1	0
November	38	2	2
December	48	1	1
Total	**437**	**12**	**11**

Individually Prepared Medicinal Products

Individually prepared medicinal products (hereinafter referred to as IPLP) are subjected to the conditions of material price regulation (hereinafter referred to as "VUC") set forth by the Price Regulation (effective for 2019). This regulation applies to the following groups of medicinal products: individually prepared radiopharmaceuticals (hereinafter referred to as "RF"), individually produced transfusion products and autologous transfusion products (hereinafter referred to as "TP"), parenteral nutrition products for home therapy (hereinafter referred to as "DPV"), individually prepared medicinal products in pharmaceutical care facilities – magistral formulas (hereinafter referred to as "MAG"), and advanced therapy products (hereinafter referred to as "„LPMT").

The conditions for the determination of the amount and conditions of reimbursement by means of general measures (hereinafter referred to as "OOP") are set forth by the Act on Public Health Insurance, specifically its Section 15(5). The drafting of general measures and the method of their publication are governed by Sections 171 to 174 of Act No 500/2004 Coll., the Code of Administrative Procedure.

General Measures (OOPs)

In the course of 2019, six general measure procedures were initiated and properly completed.

As of 01 March 2019, OOP 01-19 for subgroups 12 and 15 TP became effective; in compliance with Decree No 301/2018 Coll., amending Decree No 134/1998 Coll., setting forth the list of healthcare procedures and their point values, as amended, the OOP reflected a change in the minute overhead rate per one minute of time performance from the value of 3.04 points to the new value of 3.12 points. Following Decree No 201/2018 Coll., setting point values, reimbursement amounts for reimbursed services, and regulatory restrictions for 2019, the point value changed from the original amount of 1.03 to the new amount of 1.06 (as per Annex 3 thereto – "Point value, reimbursement amounts, and regulatory restrictions pursuant to Section 7"). Due to these changes, the increase in expenses incurred by the public health insurance was estimated at plus 3.6 mil. CZK.

As of 01 June 2019, OOP 02-19 for subgroup 13 RF took effect; this OOP reflected new price source materials and the effective €/CZK exchange rate as per source documents issued by the Czech National Bank (ČNB). Following Decree No 301/2018 Coll., amending Decree No 134/1998 Coll., setting forth the list of healthcare procedures and their point values, as amended, the point value changed from the original amount of 3.04 points per one minute of time performance to the new value of 3.12 points. Following Decree No 201/2018 Coll., setting point values, reimbursement amounts for reimbursed services, and regulatory restrictions for 2019, the point value changed from the original amount of 1.03 to the new amount of 1.06 (Annex 3 thereto – "Point value, reimbursement amounts, and regulatory restrictions pursuant to Section 7"). Due to revoked marketing authorisation of medicinal product NEUROLITE RAD KIT 1XA + 1XB (SOLV), SÚKL code 0146918, the Institute removed the radiopharmaceutical listed under code 2089 from the list of individually prepared medicinal products, as it was the only product in this group. Upon request, the Institute extended the indicating sites for brain amyloid plaque imaging in patients with Alzheimer's disease by the Department of Neurology of the Central Military Hospital in Prague and by the Neurological Care Centre in Rychnov nad Kněžnou for RF 18F flutemetamol inj. (VIZAMYL). The said OOP also amended the correction factor value for physical breakdown for RF fluoromethylcholine (SÚKL code 2101) from 0.8 to 0.55, which is a value common for all PET radiopharmaceuticals. The list of individually prepared medicinal products was newly extended with TECEOS, a kit for radiopharmaceutical 99mTc butedronate, within the scope of a specific therapeutic programme, intended for non-invasive diagnosis of transthyretin cardiac amyloidosis by nuclear medicine methods. The specific therapeutic programme authorisation is valid until 30 November 2020. All of the aforementioned changes predicted an increased impact upon public health insurance funds, specifically by 0.61 %, which is adequate to the amount of 5.17 mil. CZK.

As of 01 November 2019, OOP 03-19 for the RF subgroup took effect, through which the list of individually prepared medicinal products was newly extended with a product within the scope of a specific therapeutic programme (18F) FMISO 1-8 GBq (18F fluoromisonidazolum). The product is intended for the purposes of positron emission tomography (PET) imaging to establish the degree of solid tumour hypoxia and there is no other available diagnostic alternative thereto. The specific therapeutic programme authorisation is valid until 30 June 2021. Furthermore, in the aforementioned OOP, the Institute amended reimbursement in respect of radiopharmaceutical LEUCO-SCINT (blood elements for 99mTc labelling) in the following manner: only the maximum possible year-to-year price increase cf. to 2018 (i.e. 3 %) was used for the calculation of the price of the radiopharmaceutical, unlike the originally applied 10 % year-to-year price increase. The Institute predicted an increased impact on the public health insurance funds by 1.30 %, which translates to the amount of approx. 11.4 mil. CZK.

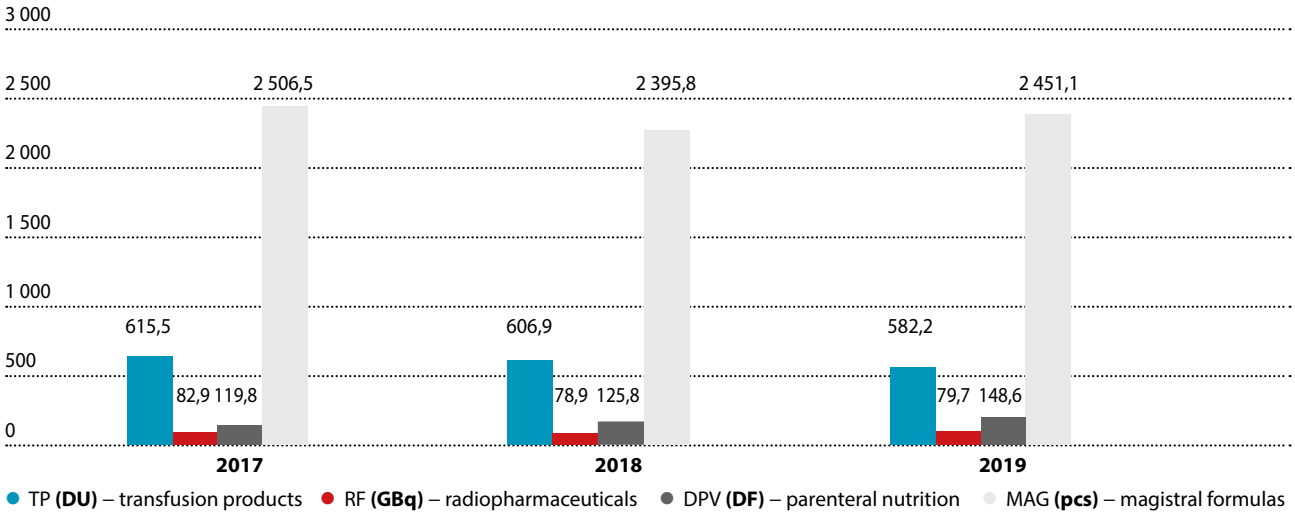
At the end of 2019, OOP 04-19 for radiopharmaceuticals, OOP 05-19 for transfusion products, and OOP 06-19 for parenteral nutrition products for home therapy were adopted with the effective date of 01 January 2020. All of these OOPs were adopted in compliance with Government Regulation No 341/2017 Coll., on the conditions governing salaries of employees working in public services and administration, as amended,

on the basis of which the basic tariff of salaries of healthcare staff was increased by the amount of 1,500 CZK. Furthermore, OOP 04-19 RF and OOP 05-19 TP reflected the change in the minute rate for procedure in accordance with Decree No 269/2019 Coll., amending Decree No 134/1998 Coll., setting forth the list of healthcare procedures and their point values, as amended, with the effective date of 01 January 2020. The minute overhead rate was increased from the original value of 3.12 points per minute of time performance to the new value of 3.19 points. In compliance with Decree No 268/2019 Coll., setting point values, reimbursement amounts for reimbursed services, and regulatory restrictions for 2020, the point value was also increased from the original amount of 1.06 CZK to the new amount of 1.07 CZK per point. In OOP 04-19, the Institute also extended the list of individually prepared medicinal products with radiopharmaceutical 68Ga edotreotide inj. (SomaKit TOC), intended for diagnosis through PET imaging of excessive somatostatin receptor expression in adult patients. Furthermore, in OOP 05-19, the Institute extended the list of individually prepared medicinal products with a new item – deleukotised whole blood for universal administration (blood group 0 with low anti-A and anti-B titres) indicated for and reimbursed in the treatment of acute and massive haemorrhage.

Consumption and Costs of Individually Prepared Medicinal Products Incurred by the Public Health Insurance

The consumption of individually prepared medicinal products is evaluated in defined units (hereinafter referred to as "DU") by individual IPLP subgroups. In case of the TP subgroup, in 2019, consumption decreased, while in respect of the other subgroups, i.e. RF, DPV, and MAG, consumption increased in comparison to the previous period. The values specified for the period of 2018 in the 2018 annual report were updated as of 31 January 2020. Data for the consumption of individually prepared medicinal products in 2019 are available only as at 01 October 2019, due to the delay caused by the hand-over of statistical data by health insurance companies, and hence incomplete data from the Institute of Health Information and Statistics of the Czech Republic (hereinafter referred to as "ÚZIS"). For this reason, the Q4 2019 assumes the form of an estimate of the anticipated expenses using the least squares method. An overview of the consumption of individually prepared medicinal products in DU for the period of 2017-2019 is provided by Fig. 20.

Fig. 20 **Overview of consumption of individually prepared medicinal products for the period from 2017 to 2019 in thous. DU**



In 2019, expenses incurred for individual IPLP subgroups were influenced by the change in the overhead minute rate per minute of time performance from the original value of 3.04 points to the value of 3.12 points in compliance with Decree No 301/2018 Coll., amending Decree No 134/1998 Coll., setting forth the list of healthcare procedures and their point values, as amended. In compliance with Decree No 201/2018 Coll., setting point values, reimbursement amounts for reimbursed services, and regulatory restrictions for 2019, the point value changed from the original amount of 1.03 to the new amount of 1.06. In 2019, two new radiopharmaceuticals were included under the RF subgroup of the IPLP list within the scope of a specific therapeutic programme; these were radiopharmaceutical 99mTc butedronate (TECEOS) and radiopharmaceutical 18F fluoromisonidazolum ([18F] FMISO 1-8 GBq).

The distribution of expenses in the IPLP group for 2019 by individual subgroups is illustrated by Fig. 21.

Fig. 21 **Distribution of total expenses in the IPLP subgroup for 2019**

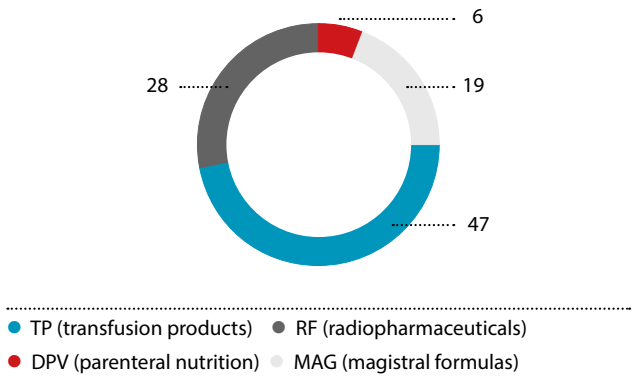


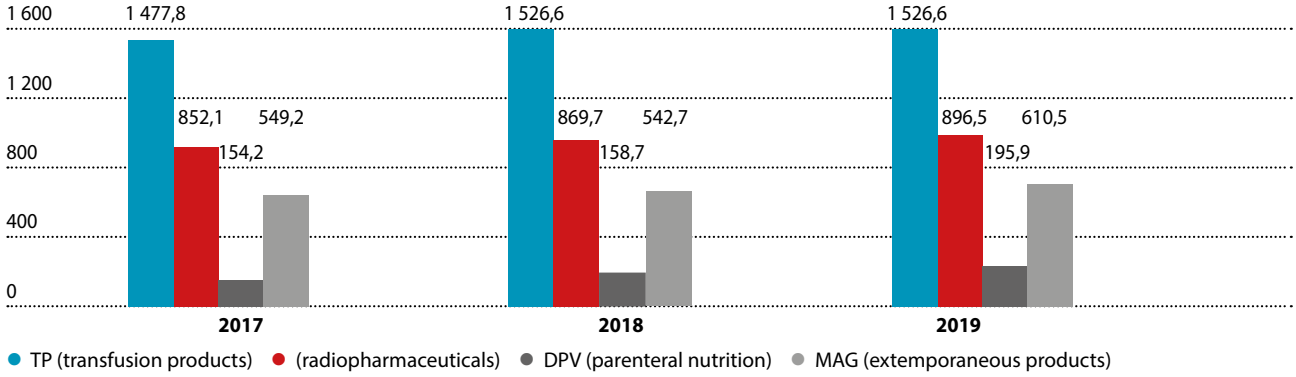
Fig. 22 then illustrates a comparison of expenses in the period of 2017-2019 for individual IPLP subgroups.

In respect of the TP subgroup, expenses incurred by the public health insurance have remained almost constant since 2018.

In respect of the RF subgroup, only a mild increase of expenses was seen, despite the inclusion of two new products within the scope of a specific therapeutic programme.

In respect of the DPV and MAG subgroups, expenses in 2019 increased, particularly due to their increased consumption compared to the previous period.

Fig. 22 **Comparison of expenses by subgroups of individually prepared medicinal products for the period from 2017 to 2019 in mil. CZK**



MEDICAL DEVICES DEPARTMENT

As part of systemisation, in 2019, the Medical Devices Branch was transformed to the Medical Devices Department. With regard to the new Regulations (EU) 2017/745 and 2017/746 of the European Parliament and of the Council, the employees of the Medical Devices Department devoted their effort particularly to the preparation of the new Act on Medical Devices, implementing Regulation No 2017/745, and the preparation of an act amending Act No 268/2014 Coll., on Medical Devices and on Amendment to Act No 634/2004 Coll., on Administrative Fees, on Advertising Regulation, and on Amendment to Act No 468/1991 Coll., on the Operation of Radio and Television Broadcasting. They participated in expert meetings of individual working groups under the European Commission, which focused particularly on the set-up and harmonisation of individual medical device internal market processes and specification of functionalities of the developed European database of medical devices (Eudamed). At the same time, preparation of specifications for the new system for the sphere of medical device regulation and definition of the scope of change requests of the Medical Device Registry were under way, so as to enable the Registry to temporarily replace the unavailable Eudamed database the launch of which was postponed by two years to May 2022.

4.16 Medical Device Clinical Trials and Vigilance Unit

Clinical Trials

Pursuant to the obligation set forth for the sponsors of clinical investigations on medical devices (hereinafter referred to as "CIMD") by Act No 268/2014 Coll., on Medical Devices, 26 applications for authorisation of CIMD conduct and 35 applications for variations to CIMD conditions were submitted to the Institute in 2019 via the Registry of Medical Devices (hereinafter referred to as "RZPRO") Clinical Investigations module. In compliance with Section 9(h) of Act No 268/2014 Coll., on Medical Devices, 24 favourable opinions authorising the conduct of CIMD were issued in administrative procedures, and two procedures were discontinued by resolution.

Furthermore, 35 applications for authorisation of variations to the conditions of CIMD were granted.

Within the scope of inspections of the conduct of clinical investigations on medical devices at providers of healthcare services, seven inspections were carried out, in which seven types of investigational medical devices were inspected. The selection of inspected sites was based upon issued decisions authorising the conduct of CIMD and previously commenced clinical investigations, taking into account the number of included subjects, the duration, and phase of the CIMD. On-site inspections identified 13 shortcomings in total, of which three were critical and 11 major.

In total, 81 serious adverse events (hereinafter referred to as "SAE") were reported from CIMD sites in the Czech Republic.

Within the scope of international cooperation in the sphere of clinical evaluations, in 2019, a representative of the Medical Device Clinical Trials Unit participated in regular meetings of the expert WG on Clinical Investigation and Evaluation of the European Commission. The meetings focused upon the development of implementing regulations and the EUDAMED database in association with Regulation No 2017/745 of the European Parliament and of the Council, and upon exchange of information among the EU Member States.

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

The Institute received reports of 585 adverse events (hereinafter referred to as "AEs") considered to be associated with the use of medical devices in the provision of healthcare services within the territory of the Czech Republic; furthermore, three adverse events arising outside the territory of the Czech Republic associated with medical devices of Czech manufacturers were notified. All of the cases were subjected to investigation. The development of the number of AE reports in 2013-2019 is illustrated by Fig. 23.

The total number of received reports on safety corrective actions regarding medical devices from competent national authorities, manufacturers or their authorised representatives, distributors or importers, as applicable, amounted to 1,160. Of the total number of received reports, 543 concerned medical devices distributed to the Czech market. The development of the number of reports on safety corrective actions in 2013-2019 is illustrated by Fig. 24.

In 2019, the Institute published 466 communications to users – Field Safety Notices (FSN) via the Registry of Medical Devices (RZPRO). FSNs are disseminated by the manufacturer, authorised representative, or distributor in association with an adopted Field Safety Corrective Action (FSCA).

Within the scope of monitoring the implementation of safety corrective actions within the territory of the Czech Republic, three inspections at distributors' and persons servicing medical devices were carried out.

One penalty was imposed for offences in the sphere of adverse events. The offence was sanctioned only by means of an admonition. The Legal Support Unit of the Medical Devices Department (PPZ) was forwarded 185 proposals to impose an administrative penalty for offences committed by manufacturers, persons servicing medical devices or medical device distributors.

As part of monitoring of a safety corrective action set forth by a Czech manufacturer, four reports for competent national authorities (NCAR) were issued and disseminated via the European database of medical devices (EUDAMED).

Within the scope of international cooperation in the field of medical device vigilance, in 2019, the inspectors of the Vigilance Unit participated in 12 teleconferences and two meetings of the Medical Device Expert Group for Vigilance (Post Market Surveillance and Vigilance) focused upon the exchange of information among the EU Member States on current vigilance cases.

In the course of 2019, 20 questions regarding vigilance issues were answered.

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

Fig. 23 **Overview of notified adverse events in 2013–2019**

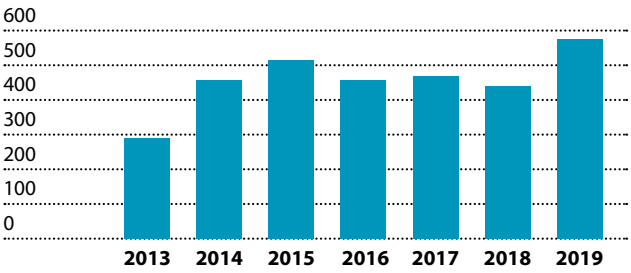
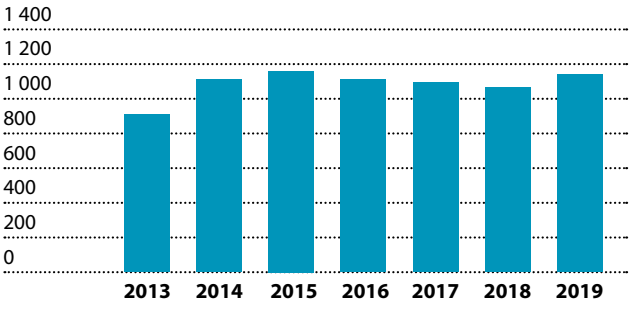


Fig. 24 **Overview of safety corrective actions for medical devices adopted in 2013–2019**



4.17 Registration of Persons and Expert Opinion Unit

In 2019, within the scope of systemisation, the Registration of Persons Unit (ORO) and Expert Opinions and Free Sale Certificates Unit (OPC) were merged into the Registration and Expert Opinion Unit (ROP). ROP is in charge of registration of persons and associated activities pursuant to Act No 268/2014 Coll., on Medical Devices and on Amendment to Act No 634/2004 Coll., on Administrative Fees, as amended, and the drafting of positions and opinions on the basis of external requests and immediate issuance of Free Sale Certificates.

In the last year, specialised ROP staff was involved primarily in the processing of notifications submitted via the RZPRO Registry. In the course of 2019, activities associated with the Free Sale Certificate (FSC) issuance were handed over to the Medical Device Notification Unit (ONZP), as FSC issuance is closely associated with medical device notification.

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

In total, during the past year, the Unit completed 1,124 notifications in the Persons module. In 2019, 1,262 notifications were lodged.

- **Notification of person**

In 2019, the Unit completed 229 submitted notifications of persons.

- **Notification of activity**

In 2019, 69 notifications regarding activities in general were handled – these concerned activities of medical device manufacturers, medical device distributors, medical device importers, persons servicing medical devices, authorised representatives, and clinical investigation sponsors.

- **Notification of changes to data**

In total, 795 notifications of changes to data of a person were processed and completed.

- **Notification of deletion of a person**

In 2019, the Unit processed 30 notifications of deletion of a person.

- **Expert opinion**

Expert opinions are issued on the basis of received requests for the issuance of an expert opinion from external entities as well as on the basis of reports from other units of the Medical Device Department and in response to filed applications for medical device notification in the RZPRO Registry. In 2019, the ROP Unit issued 210 expert opinions concerning nature of a product or medical device classification. The aforementioned activities of the Unit in the processing of opinions regarding product nature are also shared with the Advertising Surveillance Unit in the sphere of pharmaceuticals. Of

the aforementioned number, 35 opinions were issued on the basis of an external request and 175 opinions on the basis of requests from the Legal Support Department of the Medical Devices Department (PPZ).

4.18 Medical Device Notification Unit

The Medical Device Notification Unit (ONZP) is in charge of regulations in the sphere of medical device notification and associated activities as referred to under Act No 268/2014 Coll., on Medical Devices and on Amendment to Act No 634/2004 Coll., on Administrative Fees, as amended.

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

In total, the Unit completed 22,670 applications in the Medical Device module in the last year. In 2019, 14,008 applications were entered in the Medical Device module.

- **Applications for medical device notification**

In 2019, the Unit completed 12,229 administrative procedures regarding applications for medical device notification.

- **Applications for medical device notification renewal**

The Unit completed 59 administrative procedures regarding applications for medical device notification renewal.

- **Applications for change to medical device data**

In total, 9,027 applications for change to medical device data were processed and completed.

- **Applications for medical device deletion**

The Unit completed 1,236 applications for medical device deletion.

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

- **Applications for Free Sale Certificate**

In 2019, 119 applications were submitted, of which 117 were completed .

4.19 Penalties for Breach of the Act on Medical Devices

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

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

In 2019, 62 proposals for the commencement of an administrative procedure on product nature and 23 proposals for the commencement of an administrative procedure on medical device classification were forwarded to the Legal Support Unit.

In 2019, the Institute commenced 62 ex-officio administrative procedures on product nature and 23 ex-officio administrative procedures regarding medical device classification.

In 2019, the Institute received one application for decision regarding product nature and no application for decision on medical device classification.

In 2019, two decisions on medical device classification and 40 decisions on product nature were issued. Furthermore, the Institute issued 54 rulings on administrative procedure termination.

Fig. 25 **Overview of administrative procedures commenced in 2019**

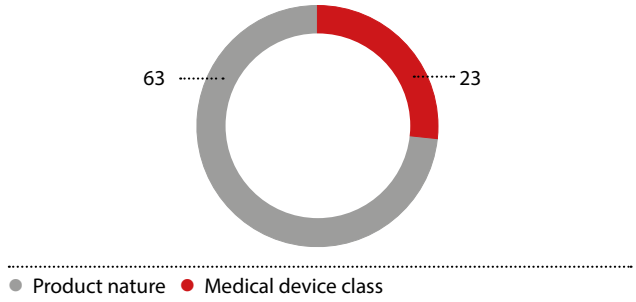


Fig. 26 **Overview of forwarded proposals for the commencement of ex-officio administrative procedures in 2015–2019**

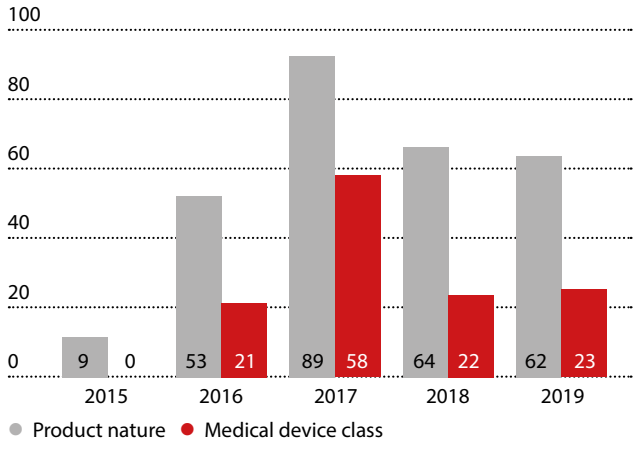
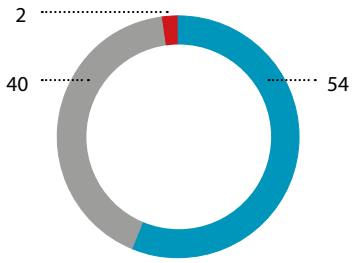


Fig. 27 **Overview of decisions issued in 2019**



Explanatory notes: AP – administrative procedure

Offences

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

In 2019, the Institute imposed fines for breach of the Act on Medical Devices amounting to the total of 4,960,451 CZK. The highest proportion of fines imposed in 2019 for the breach of the Act on Medical Devices were fines imposed upon medical device distributors and healthcare service providers for the breach of their obligations in the provision of healthcare services.

In compliance with the coming into effect of the Act on Medical Devices (on 01 April 2015), the Legal Support Unit has seen an increase in the proposals for commencement of an administrative procedure regarding administrative offences since 2016 within the scope of monitoring of adverse event investigations, particularly breach of the obligation laid down by Section 75 of the Act on Medical Devices, i.e. to inform the Institute of established safety corrective actions and their termination in association with the establishment of a new actus reus in the Act.

Tab. 36 **Overview of forwarded motions for administrative procedure commencement in 2015–2019**

Overview for:	2015	2016	2017	2018	2019
Clinical Trials Unit	-	3	1	-	-
Vigilance Unit	2	47	79	88	185
Control Unit	22	69	64	20	-
Medical Device Notification Unit	-	-	-	-	6
Total	**24**	**119**	**144**	**108**	**191**

Appeals

In 2019, the Legal Support Unit received the total of 54 appeals to be addressed. In compliance with Section 88 of Act No 500/2004 Coll., the Code of Administrative Procedure, as amended, these were forwarded via the Institute to the Ministry of Health of the Czech Republic as the appellate body.

Tab. 37 **Overview of received appeals forwarded to the Ministry of Health of the Czech Republic in 2019**

Unit	No. of appeals	Returned for re-consideration	Granted	Declined	Withdrawn by applicant
Legal Support Unit	35	4	6	1	2
Registration of Persons Unit	2	-	-	-	-
Medical Device Notification Unit	17	1	1	1	1
Total number of appeals for 2019	**54**	***5**	***7**	***2**	**3**

** Number of decisions of the Ministry of Health of the Czech Republic sent back to the Institute.*

4.20. Medical Device Reimbursement Unit

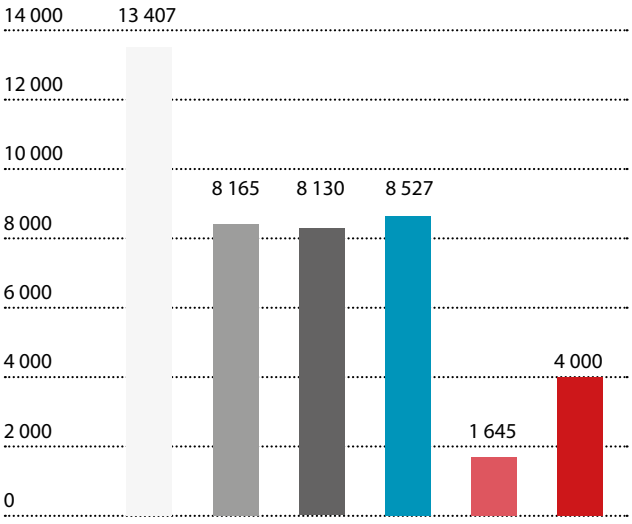
In its finding of 30 May 2017, the Constitutional Court revoked key provisions of the Act on Public Health Insurance (Act No 48/1997 Coll., hereinafter referred to as the "Public Health Insurance Act") that governed the mechanism of determination of reimbursement of medical devices from public health insurance funds in the provision of outpatient healthcare services. The Constitutional Court revoked reimbursement regulation of so called "voucher-based medical devices" (such as incontinence pads, prostheses, wheelchairs, hearing aids, or glucometers and other devices for diabetic patients). Specifically, those provisions that stipulated that the insured person's entitlement to medical device reimbursement applied to the economically least demanding alternative established by health insurance companies via market research were revoked.

On 01 January 2019, the amended Public Health Insurance Act came into effect and brought new rules for the reimbursement regulation of medical devices prescribed on vouchers and reimbursed from the public health insurance funds, and the medical device reimbursement agenda was assigned to the State Institute for Drug Control.

The new reimbursement regulation has been based on a notification principle. Decisions on the classification of a specific medical device under a particular reimbursement group are primarily not taken via administrative procedures. Manufacturers themselves notify the Institute of the classification of their medical device in a reimbursement group. Prior to the notification proper, the notifying person registers and obtains login details. The system for the obtaining of login details for the agenda information system was launched on 15 April 2019. It is possible to notify a new classification, change or removal of a medical device from the reimbursement group, which influences its reimbursement from the public health insurance funds. In case a medical device is assigned to an improper reimbursement group, the Institute initiates an administrative procedure regarding non-inclusion in the reimbursement group or removal from a reimbursement group. In respect of those medical devices whose reimbursement had been determined prior to the effect of the amended Public Health Insurance Act, so called re-notification was conducted in the course of June. Where the manufacturer failed to submit this re-notification, the respective medical device stopped to be reimbursed from the public health insurance funds as of 01 August 2019. Re-notified medical devices began to be reimbursed pursuant to the new legislation as of 01 December 2019.

Notifications of medical devices newly entering the reimbursement system may be lodged at any time. The validity of the reimbursement is set forth by law. Prior to the start of the new reimbursements, the Institute was issuing so called Consolidated List, on the basis of which medical devices were reimbursed.

Fig. 28 **Medical device reimbursement notifications in June 2019**



Tab. 38 **Reimbursement notifications in 2019**

Reimbursement notifications	Number of SÚKL codes
Total submissions	11,603
Re-notifications	9,387
New notifications	2,216
Included in the list of medical devices	10,759
Suspended	844

Tab. 39 **Overview of administrative procedures commenced in 2019**

Administrative procedures regarding non-inclusion of a medical device to a reimbursement group	Number of SÚKL codes
Commenced	30
Decided	0
Pending appeals procedure	0
Concluded	4
Administrative procedures regarding removal from a reimbursement group	**Number of SÚKL codes**
Commenced	9
Decided	0
Pending appeals procedure	0
Concluded	5

STATE AGENCY FOR MEDICAL CANNABIS

In compliance with Act No. 167/1998 Coll., on Dependency-Producing Substances, as amended, the Institute fulfils the tasks of the State Agency for Medical Cannabis. The Unit of the State Agency for Medical Cannabis was established for these purposes on 01 January 2013. Its activities are associated with the granting of licences for growers of cannabis for medical use (hereinafter referred to as "medical cannabis"), controlling compliance of the cultivation, processing, and storage with legislative requirements, ensuring purchases of grown and harvested cannabis and its safe storage, transport, and distribution, and ensuring its export outside the territory of the Czech Republic, where applicable. Furthermore, the Unit fulfils all obligations in terms of providing information to the Ministry of Health of the Czech Republic and the Czech Police.

4.21 Unit of State Agency for Medical Cannabis

In 2019, the Unit of the State Agency for Medical Cannabis (hereinafter referred to as "OSALK") safeguarded the processes and activities to ensure the availability of the medical cannabis active substance for Czech patients from a domestic grower. In 2019, the Institute took over and placed in distribution 24.7 kg of medical cannabis from the winner of the public contract for the supply of medical cannabis, Elkoplast Slušovice s.r.o. By means of third and fourth medical cannabis order, the Institute ordered the total of 16 kg of medical cannabis from the successful supplier, which ensured continuity of medical cannabis supplies onto the Czech market. The unit supervised the organisation of safe storage, transportation, and distribution of medical cannabis to pharmacies via the Institute's contract distributor, Alliance Healthcare s.r.o. It also mediated the process of concluding framework contracts on the transfer of medical cannabis between pharmacy operators and the Institute. OSALK was preparing expert source materials for issues regarding medical cannabis for the Press and Information Department, other expert units, and the management of the Institute. It also ensured the determination of the price of medical cannabis for operators of pharmaceutical care facilities and the administration of the published pricelist of medical cannabis. The Unit also safeguarded compliance with the Institute's information and notification obligation to the Czech Police and to the Ministry of Health of the Czech Republic as referred to under Act No 167/1998 Coll., on Dependency-Producing Substances. As in the previous year, OSALK cooperated with the Inspectorate for Narcotic and Psychotropic Substances of the Czech Ministry of Health. As part of its operation, OSALK communicated and cooperated with top Czech and foreign experts in the field of medical cannabis, patient organisations, professional societies, chambers, and doctors. The employees of the Unit also gave lectures intended for professionals. In 2019, 138 doctors complying with the requirements set forth by all applicable legal regulations and authorised to prescribe medical cannabis for patients in indications defined by law, and 82 pharmacies meeting the statutory requirements for the ordering, preparation, and dispensing of magistral formulas containing medical cannabis grown in the Czech Republic were registered. This, as well as other updated information relevant to issues pertaining to medical cannabis, incl. up-to-date statistics, are published by OSALK on a regular basis on its website at www.sakl.cz and on SÚKL's website at www.sukl.cz (Cannabis for medical use).

Tab. 40 **Cannabis dispensing in 2019 by months**

Month	1	2	3	4	5	6	7	8	9	10	11	12
No. of issued e-prescriptions	159	189	237	287	311	239	279	318	354	440	477	434
No. of patients for whom medical cannabis was prescribed (unique)	159	189	237	287	311	239	279	318	354	440	477	434
Dispensed amount of medical cannabis (g)	699,66	1 048,08	1 073,73	1 133,78	1 338,21	1 064,1	1 273,51	1 552,01	1 717,45	2 089,43	2 112,89	1 896,88

COORDINATION OF EXPERT ACTIVITIES

4.22 Expert Activity Coordination Unit

As part of systemisation, the Expert Activity Coordination Unit (hereinafter referred to as "KOČ") was established in 2019. KOČ is a unit reporting directly to SÚKL's Director. KOČ represents the Institute in activities stipulated by Act No 378/2007 Coll., on Pharmaceuticals and on Amendments to Some Related Acts (Act on Pharmaceuticals), in areas securing availability of medicinal products for patients in the Czech Republic.

As stipulated by the provisions of Section 11 of the Act on Pharmaceuticals, the primary role of creating conditions allowing to secure availability of medicinal products important for the provision of healthcare services lies with the Ministry of Health and the Institute is obliged by the Act to provide maximum cooperation in the analysis and implementation of individual procedures. For this reason, in the beginning of 2019, the Expert Activity Coordination Unit, together with the Pharmaceuticals and Medical Devices Unit of the Ministry of Health of the Czech Republic prepared a methodological guideline on approaching the availability of pharmaceuticals in document "ENSURING THE AVAILABILITY OF MEDICINAL PRODUCTS – COMMON MoH AND SÚKL METHODOLOGY".

Activities of the Expert Activity Coordination Unit in Respect of Securing the Availability of Medicinal Products

1. Administration of Market Report – report from marketing authorisation holders (hereinafter referred to as "MAH") referred to under Section 33(2) of the Act on Pharmaceuticals

- Marketing authorisation holders are obliged to report to the Institute the placement of a medicinal product onto the market in the Czech Republic, and its suspended, restored, or terminated supplies onto the market in the Czech Republic, within timelines stipulated by the Act and Decree. Reporting is done via electronic form available from the Institute's website. Data from these reports are copied to the database of medicinal products and presented on the Institute's website in the "Medicinal Product Supply Disruptions".
- The task of KOČ assessors is to evaluate the reported suspensions or terminations of supplies in view of ensuring the availability of medicinal products important for the provision of healthcare services. The Institute always assesses the replaceability of each medicinal product individually (with regard to the characteristic properties of the medicinal product, its current consumption and duration of supply disruption). The KOČ employee always allocates the replacement medicinal product or evaluation of replaceability with another therapy to the individual reports. Information on irreplaceable or difficult-to-replace medicinal products are entered in a table shared by the Institute and the Ministry of Health of the Czech Republic. The table also specifies individual steps addressing the disrupted supply of the respective medicinal product. Information on unavailability of critical medicinal products is sent to the Czech Medical Association of J. E. Purkyně and to concerned professional societies. The method of addressing the disrupted supply of an irreplaceable medicinal product is chosen with a view to the duration of the supply disruption, levels of stock, importance of the medicinal product in the provision of healthcare, and reason for the disrupted supply of the medicinal product.
- KOČ employees also make entries into the database of medicinal products in case the electronic report functionality fails, when changes to the reports are notified, or in case the MAH report is submitted through a channel different than the electronic report form, and they answer questions on the availability and check for availability with the MAHs in case reporting discrepancies arise.

1.1. Reporting statistics of the Market Report in 2019:

- Suspended supplies: 2,260 reports (in 2/3 of these, supplies have already been restored);
- Terminated supplies: 802 reports;
- Restored supplies: 1,733 reports;
- Initiated supplies: 1,326 reports;
- Irreplaceable medicinal products: 148.

2. Addressing medicinal product unavailability

2.1. Addressing disrupted supplies of medicinal products within the Institute

- Check/solution of the current situation with medicinal products the disrupted supply of which has been caused by reasons constituting procedural or marketing authorisation causes or quality defects.

2.2. Allowing for placement of a foreign-language batch of a medicinal product into circulation

- Pursuant to Section 38 of the Act on Pharmaceuticals, having regard to public health protection, the Institute may allow for the omission of certain data in the labelling and package leaflet of the concerned medicinal product; the Institute may also allow for the labelling and package leaflet to be partially or fully in a language other than the Czech.
- When assessing applications for the placement of individual batches of a medicinal product into circulation where the labelling is in a language other than the Czech, the KOČ employee abides by the particulars stipulated by Section 3(6)(b) of Decree No 228/2008 Coll.
- In 2019, the Institute issued the total of 93 decisions allowing for the placement of a foreign-language batch into circulation.

2.3. Identification of possible individual import of non-authorised medicinal products

- Pursuant to the provision of Section 8(3) of the Act on Pharmaceuticals, it is possible to prescribe or use a non-authorised medicinal product in cases when the authorised medicinal product is not available.
- KOČ employees check the database in compliance with Art. 57 (EMA database, Regulation [EC] No 726/2004 of the European Parliament and of the Council) to see whether in the EU, medicinal products which could be used as a replacement for the unavailable medicinal products have been authorised. Furthermore, KOČ employees check guideline DIS-13 to see whether such medicinal products are imported to the Czech Republic, or, if applicable, they contact medicinal product distributors about possible import of unauthorised medicinal products.
- In the application of Section 77(1)(i) of Act No 378/2007 Coll., on Pharmaceuticals, and Section 46 of Decree No 229/2008 Coll., on Manufacture and Distribution, the KOČ unit assesses and issues approvals of submitted applications for import of non-authorised medicinal products from third countries. In 2019, 21 approvals of import of non-authorised medicinal products from third countries were issued in total.

2.4.Drafting of opinions on specific therapeutic programmes (hereinafter referred to as "SpTP")

- Where the supply of a foreign-language presentation of a medicinal product cannot be organised and the Institute considers the product irreplaceable, the Ministry of Health of the Czech Republic, having regard to the anticipated duration of supply disruption, authorises

the Institute within the meaning of the provision of Section 2a(b) of Minister's Order No 20/2011, "Coordination of the activities of the Ministry of Health of the Czech Republic and SÚKL in addressing certain specific processes to safeguard the availability of medicinal products important for the provision of health care", to publish a communication about the emergency need and call for proposals of specific therapeutic programmes using non-authorised medicinal products for human use.

- In 2019, 14 calls in total were published.
- In compliance with Section 49 of Act No 378/2007 Coll., on Pharmaceuticals, and Section 2 of Decree No 228/2008 Coll., on marketing authorisation of medicinal products, the Unit also safeguards the preparation of opinions on the submitted applications for specific therapeutic programmes using non-authorised medicinal products for human use (guideline UST-20), the purpose of which is the treatment, prophylaxis, or diagnosis of life-threatening conditions for a defined patient group.
- In 2019, there were 152 ongoing programmes and the Institute drafted opinions on 66 new applications.

2.5. Ensuring possible extemporaneous preparation of medicinal products (hereinafter referred to as "extemporaneous products") in pharmacies

- Extemporaneous products offer a way how to resolve a medicinal product availability problem on a temporary basis. Nevertheless, medicinal products prepared in this manner are not identical with authorised proprietary medicinal products. KOČ employees consult this possibility with pharmaceutical specialists.

3. Communication with the Public

- As part of their activities, KOČ employees also address questions from doctors, pharmacists, and patients regarding unavailability and replaceability of medicinal products.

4. Medicinal Product Replaceability Assessment in Relation to the Activities of Other Units

- KOČ employees also assess medicinal product replaceability for the Quality Defects Unit and the Marketing Authorisation Section. In total, this concerned 48 replaceability assessments for the Quality Defects Unit and 16 assessments of exemptions from the sunset clause for the Marketing Authorisation Section.

5. Preventive Measures Related to Restricted Re-export of Medicinal Products

5.1. In compliance with Section 77c of Act No 378/2007 Coll., on Pharmaceuticals, the Institute collects information on the volume of medicinal products on the market in the Czech Republic and on the volume of medicinal products dispensed and used in the provision of healthcare services from marketing authorisation holders, distributors, and pharmacies. The Institute processes this information and assesses whether the quantities of a medicinal product irreplaceable with another medicinal product of adequate therapeutic properties or of medicinal products mutually replaceable in terms of their therapeutic properties sufficiently covers the current needs of patients in the Czech Republic. If, on the basis of evaluation of the stated facts, the Institute arrives at a conclusion that the current stock of the concerned medicinal product or medicinal products no longer adequately covers the current needs of patients in the Czech Republic and the lack of this medicinal product would jeopardise the availability and efficacy of treatment of patients in the Czech Republic with a direct impact upon the protection of the people's health and upon the provision of healthcare services, it notifies the Ministry of Health to this effect and provides source materials and information on the basis of which the Institute drew this conclusion. In 2019, KOČ sent the total of 20 reports on jeopardised availability for 52 codes of medicinal products in total.

5.2. In case the Institute receives a report from a distributor as referred to under Section 77(1)(q) of Act No 378/2007 Coll., on Pharmaceuticals, concerning an intention to export a medicinal product placed on the list of medicinal products whose distribution abroad has to be reported by distributors to the Institute, KOČ employees assess whether such distribution abroad would, in the coming period, cause a shortage of the medicinal product that is not replaceable with another medicinal product of adequate therapeutic properties or of medicinal products that are mutually replaceable in terms of their therapeutic properties, for the current needs of patients in the Czech Republic. In case the availability of treatment for patients in the Czech Republic is jeopardised, with a direct impact upon the protection of the people's health and the provision of healthcare services, the Institute submits a motion to the Ministry of Health for the issuance of a general measure as per Section 77d of Act No 378/2007 Coll., on Pharmaceuticals, through which the Ministry of Health would prohibit the distribution of the concerned medicinal product(s) abroad. In 2019, KOČ submitted four reports suggesting prohibition of distribution abroad.

6. Preparation, Sharing, Communication, and Addressing of Availability on the European Level within the Scope of the HMA/EMA Task Force on Availability of Medicinal Products

6.1. In 2019, the Czech Republic was represented in the Supply Chain Disruptions Working Group via the Expert Activity Coordination Unit; the group prepared a specimen uniform format for the sharing of information about cases of unavailability affecting several EU countries, and was involved in the SPOC (Single Point of Contact) pilot project, where the representatives of national agencies share information on the availability of critical medicinal products with each other.

5 PROCESSING AND PROVISION OF INFORMATION

5.1 Information Technologies

In 2019, the implementation of the security perimeter hardware modernisation whose first stage had begun in 2018, was completed. The purpose of this modernisation was to ensure a higher level of protection of the systems operated in the Institute against the increasing activity of cyberattacks aimed at systems operated across state administration. As part of internal system modernisation, in 2019, the back-up system was completely replaced with a more advanced and effective one. This replacement included not only the replacement of hardware and software, but also a change in the set-up and complete re-working of the back-up system to a more efficient and robust one. In this year, the mailroom's scanning line software was upgraded to reflect the needs for scanning hard-copy documents to the required new versions of the PDF format.

A third data centre was built; this data centre serves primarily as another back-up centre for the ePrescription system.

In 2019, works on the end-user computer technology replacement continued – new notebooks and PCs were procured. In association with PC replacement, all-in-one computers were procured for the first time. These computers were allocated to a selected group of users for pilot operation. After approx. one year of the testing operation, this type of computers proved useful and it will continue to be used in the future. The particular benefit of all-in-one computers is the easier handling during replacement and allocation of the computer to new users. The replacement of computers was also associated with the approaching expiry of the Microsoft Windows 7 operating system support by the manufacturer and transition to the new Microsoft Windows 10 operating system version.

It may be stated that in 2019, the Information Technology Department continued to implement numerous measures to further increase the security level of operated systems and the availability of the Institute's information systems in line with the global trends in this area.

ePrescription

Electronic prescriptions and the establishment of the ePrescription information system are legislatively stipulated by Act No 378/2007 Coll., on Pharmaceuticals, as amended. By means of the ePrescription system, the doctor issues an electronic prescription (ePrescription) to the patient; on the basis of this prescription the pharmacy dispenses the medicinal product. The Central Repository of Electronic Prescriptions (hereinafter referred to as "CÚER") collects and stores all ePrescriptions under conditions set forth by effective legislation. The established ePrescription system is one of the eHealth services and since 01 January 2018, its operation in the Czech Republic has been mandatory. Pursuant to Section 81f of Act No 378/2007 Coll., on Pharmaceuticals, exceptional situations when it is possible to continue to issue prescriptions in hard copies are permissible.

In relation to the requirement for mandatory electronic prescription, the process of modernisation of the entire system, also with a view to its inclusion in eHealth National Strategy of Electronic Healthcare and Strategic eGovernment Development Framework 2014+, commenced as early as in 2015. The implementation of the ePrescription project was carried out according to the effective schedule and the project was completed in December 2017. The ePrescription system has been included under the critical infrastructure of the state, and hence has been subjected to the tightest security measures as referred to under the Act on Cyber-Safety and related legal regulations. An ongoing system support has been established and on the basis of initiatives raised by professionals as well as the general public, the system is being continuously improved, which is consistent with the performance of the service agreement on the provision of service support for this system (with regard to Section 81 of the Act on Pharmaceuticals, the ePrescription system includes the CÚER repository, a Registry of Restricted Medicinal Products [hereinafter referred to as "RLPO"] and other components).

Since 01 January 2018, the system has been operated in the mode of mandatory electronic prescription. Throughout 2019, its operation did not exhibit any major problems. Health insurance companies routinely download batches of ePrescriptions for their insureds, which provides the former with a complete overview of dispensing. Since the launch of mandatory electronic prescription, applications for doctors, patients, and pharmacists have been also made available. In their application, doctors have the possibility to prescribe an ePrescription outside their offices. The patient application allows patients to view a list of those ePrescriptions prescribed for them, in which the individual patient was clearly identified in the registry of inhabitants (hereinafter referred to as "ROB"). The pharmacist's application allows the pharmacist to find out information about the ePrescription in case standard communication with the ePrescription system is not available.

To date, the ePrescription system has been providing a wealth of benefits particularly for the patient. Although there is still the possibility of handing the identifier to the patient in the form of a hard-copy sheet, and this option is still the most commonly used one, **electronic delivery of the ePrescription identifier – via SMS or e-mail messages has been gaining an ever growing popularity. The final volume for 2018 amounted to 3 million of SMS messages and 492 thousand e-mail messages; in 2019 these figures increased to more than 10.5 million and 702.5 thousand messages, respectively.**

Since the launch of the electronic prescription, the www.epreskripce.cz website is being continuously updated. In autumn 2019, a section for the sharing of the patient's medication record and all related information was added.

Within the scope of operation of the electronic prescription system, the Institute provides also support for the users of the given system. A free

hotline has been available to professional as well as lay users during working days from 7:00 a.m. to 5:00 p.m.

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

In 2018, 58.5 million ePrescriptions in total were issued; 56 million were dispensed; the total value of reimbursements of the dispensed reimbursed medicinal products prescribed via the ePrescription system exceeded 26,118,000 thous. CZK.

In 2019, more than 73.5 million ePrescriptions in total were issued; 71.5 million were dispensed; the total value of reimbursements of the dispensed reimbursed medicinal products prescribed via the ePrescription system exceeded 33,154,301 thous. CZK, which represents a more than 25 % increase. **The record of the year was achieved on Monday 16 December 2019, when more than 445.5 thous. ePrescriptions were prescribed.**

Almost 50 thousand doctors and dentists, i.e. their vast majority, had SÚKL generate access data for them. In 2019, application verifications with all professional chambers was carried out on a continuous basis. Dispensing of the prescribed medicinal products may be executed practically in all pharmacies in the Czech Republic. As of 31 December 2019, 45,230 doctors, 18,251 healthcare facilities, and 2,873 pharmacies were actively involved.

In the course of 2019, an ongoing system support was provided and on the basis of initiatives raised by both professionals and the general public, the system was being improved on a continuous basis. A rather significant change in this period was the change of the primary carrier of the identifier from a one-dimensional code to a QR code. This change was planned in the long term in order to improve the quality of identifier scanning in pharmacies (QR code is less prone to damage).
Furthermore, in mid-2019, the Institute launched its back-up system (the third data centre). The purpose of the backup system is to support the flawless operation of electronic prescription dispensing within the territory of the Czech Republic in case of a sudden failure of the primary ePrescription system that provides for this service. The back-up part of the ePrescription information system is completely independent of the primary ePrescription system and is located completely separately.

On 01 January 2020, the Ministry of Labour and Social Affairs and the Czech Social Security Administration (ČSSZ) launched an electronic sick note system. Authentication to the B2B channel uses the same SSL communication certificate as that used by the healthcare service provider (healthcare facility) for communication with the ePrescription system. In October 2019, the testing of electronic sick notes commenced and SÚKL provided ČSSZ with maximum cooperation during the implementation of the project. This project is an important positive step taken in favour of professionals as healthcare staff may avail of the current authentication means for another system implemented nationally by the state administration.

The adoption of amendment to Act No 378/2007 Coll., on Pharmaceuticals that came into effect on 01 December 2019 and subsequent publication of the new Decree No 329/2019 Coll., on the prescribing of medicinal products, effective as of 01 January 2020 brought many changes relevant for the area of electronic prescription. The most awaited change was the sharing of the patient's medication record, which is, in principle, a register of all issued and, where applicable, dispensed ePrescriptions for a particular patient with an established identity. The medication record may be viewed only by the patient who was unequivocally identified against the ROB registry at the time the medicinal product was prescribed. Following a careful consideration of the situation in the Czech Republic and having regard to the actual benefit and practicality of the patient medication record, an opt-out system was selected, so that the patient's medication record may be viewed by the doctor, pharmacist or clinical pharmacist unless the patient expresses his/her disagreement with such access. The list of all granted or revoked consents is managed through the consent administration of the ePrescription system that was launched on 01 December 2019. The patient has a right to express his/her global disagreement with doctors or pharmacists viewing his/her medication record. Equally, he/she may grant an explicit consent exclusively for a selected specific doctor or pharmacist. Parents also have the right to express their disagreement with a doctor or pharmacist viewing the shared medication records of their children.

The patient's consents or disagreements may be entered via the patient web application; other channels that may be used are the patient's data mailbox or a letter signed with an officially authenticated signature.

Viewing the patient's medication record proper will be made possible from 01 June 2020. Along with the launch of the shared medication record, it will be possible to avail also of the medicinal product prescription duplicity check.

Another change to the ePrescription system was implemented with regard to the established reimbursement of medical cannabis from health insurance. Since 01 January 2020, the ePrescription system has been providing support in the registration of the dispensed quantity of 30 g of cannabis with a 90 % price reimbursement from public health insurance. This change was associated with a complete change to the

prescription codes for cannabis, the registration of both maximum dispensing limits (the existing maximum total dispensing of 180 g per month and the new maximum amount of cannabis with the 90 % price reimbursement from the public health insurance) as well as amendment of services for pharmacists who, during dispensing, need to distinguish whether they dispense reimbursed cannabis or cannabis that is not subject of reimbursement.

A major change implied by effective legislation is the obligation to digitise hard-copy prescriptions in the pharmacy. This is a completely new functionality and for the purposes of registration of the digitised prescriptions (electronic dispensing records), it was necessary to prepare new services for pharmacists and health insurance companies who obtain the information about digitised prescriptions for the purposes of establishment of reimbursement for pharmacies for these activities.

The legislation, moreover, implied other minor changes that had to be reflected in the ePrescription system as of 01 January 2020. These concern the cancellation of two-item prescriptions, as starting from 01 January 2020, electronic prescriptions may bear the maximum of one item per ePrescription, and starting from 01 June 2020, this rule will apply also to hard-copy prescriptions; consolidation of the prescription validity to 14 days; and the addition of patient contact data (telephone or address of residence) at the time of illness on the ePrescription. Furthermore, the web and mobile applications were amended to be consistent with the current legislative requirements.

In addition to the legislative changes, a new functionality of the provision of important information on medicinal products was deployed on 01 January 2020. This will result in better availability of information for doctors and pharmacists as well as for patients. Via the ePrescription system, it is possible to display product related information about the prescribed or dispensed medicinal product. This concerns primarily educational materials, Direct Healthcare Professional Communications (DHPC) or other important information.

In July 2018, SÚKL and its partner, the Region of Vysočina, became involved in the Deployment of Cross Border Services in the Czech Republic (NIX-ZD.CZ II) project. The objective of the project is to create, test, and deploy the cross-border ePrescription service, i.e. the provision of access to ePrescriptions issued in one EU Member State for pharmacists in another participating EU Member State. The project implementation is scheduled from 01 July 2018 to 30 June 2022. Seventy-five per cent of the project costs are covered by the CEF TELECOM European subsidy.

In the course of 2019, the technical solution for the process of dispensing products on the Czech ePrescription abroad was being prepared. In November 2019, the team of authors successfully completed testing on the European level. Furthermore, preparations for the implementation of another scenario, i.e. dispensing of products on foreign electronic prescriptions in Czech pharmacies, commenced. The objective for 2020 is to successfully complete multi-round testing of both scenarios.

5.2 Database of Medicinal Products and Monitoring of Supplies to Pharmacies

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

Registry of Active Substances

At present, the DLP Component Library contains 18,619 components (incl. combined components). In 2019, 370 new components were entered.

- In 2019, an update of flagging of doping components and of products containing such substances in the DLP was carried out pursuant to The 2018 Prohibited List – The World Anti-Doping Code effective as of 01 January 2019. Thereafter, flagging was performed on a quarterly basis.
- Furthermore, a revision of substances labelled as doping by the CD-Info database took place. According to this database, 105 components were newly labelled or their labelling was changed.
- New and renamed components were entered and more than one half of components from revised and corrected monographs of the Czech Pharmacopoeia 2019 Supplement amended, together with corresponding data from the European Pharmacopoeia, 9th edition.
- Components from lists proposed by INN WHO issued in 2019 were entered and an adjustment of components from the Recommended INN WHO Lists was performed.
- Data about psychotropic substances were updated and new components entered in compliance with Government Regulation on the lists of dependency-producing substances – Annex 4.
- The revision of the entire DLP Component Library has been underway and is still ongoing; on the basis of this revision, 5,855 components were deleted and new information on revised components was added.
- Some groups of more complex substances were revised so that their names and records thereof were consistent with new approaches and consolidated (e.g. macrogols, polymers, copolymers, and silicones).

Registry of Medicinal Products

In 2019, the Institute granted 484 marketing authorisations (3,037 SÚKL codes). Authorisation was revoked for 484 marketing authorisation numbers, which corresponds to 4,234 codes. The authorisation was revoked either upon request of the marketing authorisation holder (339 marketing authorisation numbers), or due to the sunset clause (101 marketing authorisation numbers), or due to the fact that the

holder did not apply for marketing authorisation renewal (44 marketing authorisation numbers). The validity of 5,403 codes in total expired (the period of the code final sale expired or marketing authorisation was revoked).

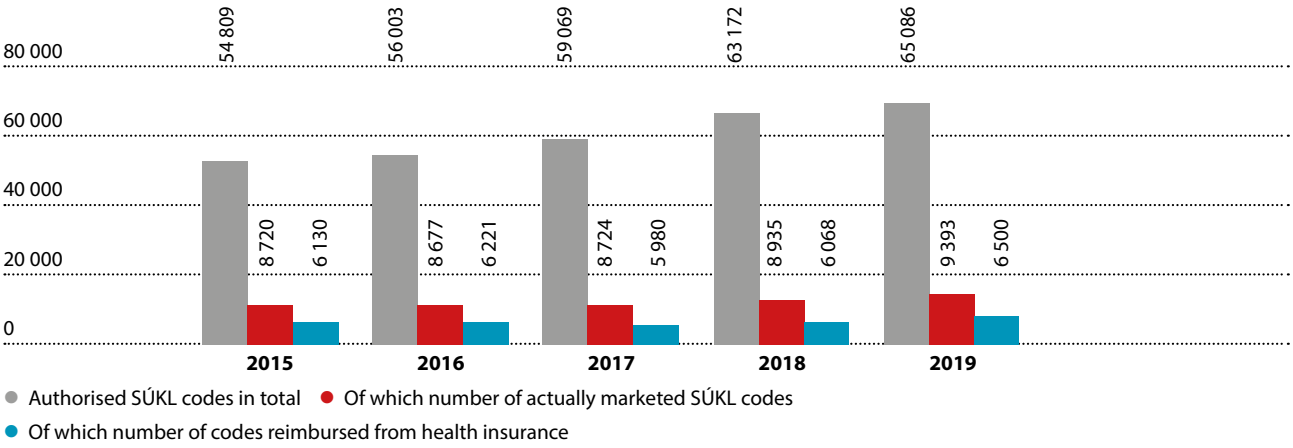
In the course of 2019, no distribution was reported for 55,693 codes (86 %) of medicinal products, excluding homeopathic preparations. Hence despite having a valid marketing authorisation, these products were not placed on the market.

Authorised medicinal products contained 2,707 various active substances in total.

Tab. 41 **Selected subgroups of authorised medicinal products recorded in the Institute's database as of 31 December 2019**

	Total no. of authorisation numbers / marketed authorisation numbers	Total no. of SÚKL codes / marketed SÚKL codes
Medicinal products in total (excl. homeopathic preparations)	**17,887/6,202**	**65,086/9,393**
Of which by MA numbers:		
MA numbers granted by the Institute	6,448/4,876	53,622/8,061
MA numbers of products authorised via Community Centralised Procedure	11,439/1,325	11,464/1,331
Of which by content:		
Single-component	14,377	51,722
Multi-component	3,516	13,350
Of which by type of dispensing:		
Prescription-only medicinal products	17,037/5,492	60,621/8,148
OTC medicinal products	891/717	4,346/1,225
Restricted OTC medicinal products	8/5	49/7
Restricted prescription-only medicinal products	7/6	70/8
Homeopathic preparations	274/270	865/350

Fig. 29 **Authorised medicinal products in the period of 2015–2019**



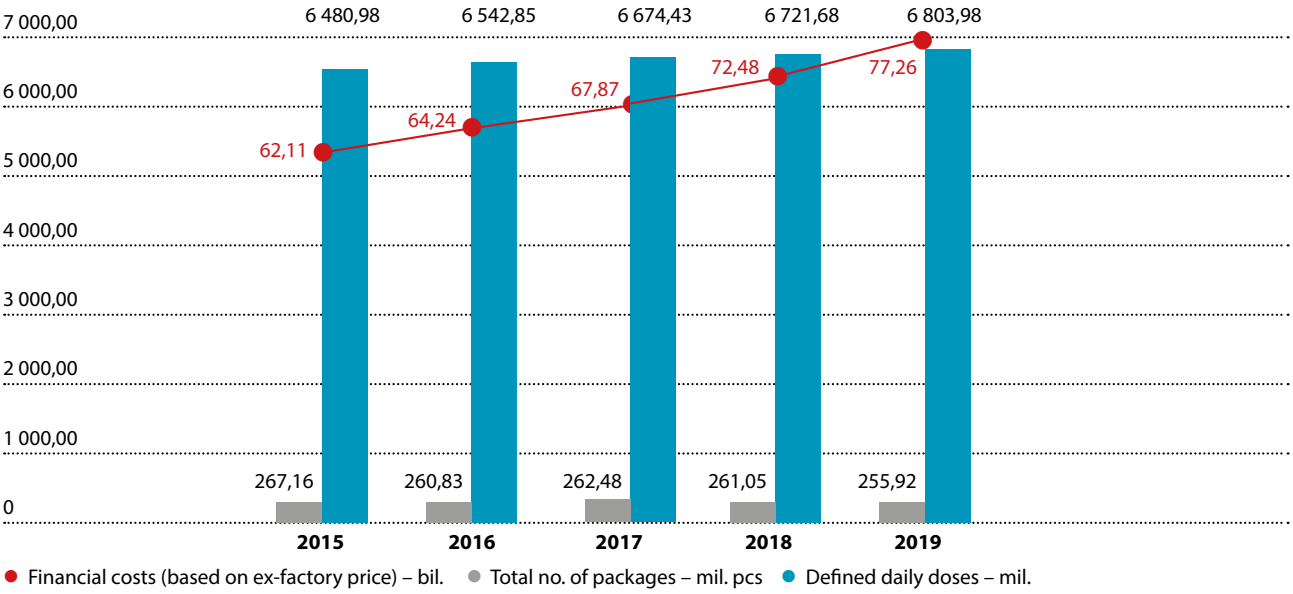
Regular Outputs from the Database of Medicinal Products

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

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

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

Fig. 30 **Deliveries of medicinal products in 2015–2019**



Tab. 42 **Deliveries of distributed medicinal products in 2019**

Medicinal products in total	**Number**
Deliveries to pharmacies and healthcare facilities (mil. packages)	255.923
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	77,257.910
Deliveries to pharmacies and healthcare facilities (mil. DDD)	6,803.975
DDD/1,000 inhabitants/day	1,752.340
Prescription-only medicinal products	**Number**
Deliveries to pharmacies and healthcare facilities (mil. packages)	177.640
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	69,900.209
Deliveries to pharmacies and healthcare facilities (mil. DDD)	6,205.745
DDD/1,000 inhabitants/day	1,598.268
OTC and selected pharmaceuticals	**Number**
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. packages)	78.019
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. CZK based on ex-factory price)	7,321.076
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. DDD)	598.132
DDD/1,000 inhabitants/day	154.047
Restricted OTCs	**Number**
Deliveries to pharmacies and healthcare facilities (mil. packages)	0.264
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	36.625
Deliveries to pharmacies and healthcare facilities (mil. DDD)	0.098
DDD/1,000 inhabitants/day	0.025
Homeopathic preparations	**Number**
Deliveries to pharmacies (mil. packages)	1.885
Deliveries to pharmacies (mil. CZK based on ex-factory price)	192.888

Evaluation of Deliveries of Distributed Medicinal Products

In 2019, evaluation of deliveries of distributed medicinal products based upon the mandatory reporting from entities authorised to distribute medicinal products in the Czech Republic was performed on a monthly basis. The subject-matter of the reports concerned deliveries of medicinal products to pharmacies and other healthcare facilities in the Czech Republic and abroad. In addition to authorised medicinal products, also products included in specific therapeutic programmes and non-authorised products supplied on medical prescription for a specific patient were included in the evaluation.

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

In 2019, 255.92 million packages of medicinal products were distributed, which corresponds to approx. 6,803.98 mil. DDD. The value of these deliveries amounted to 77.26 billion CZK (based on ex-factory price).

In 2019, the Data Analysis Unit processed the total of 5,200 data outputs pertaining to data from the database of medicinal products (DLP), reports on deliveries of medicinal products to medicinal product distribution authorisation holders, reports on medicinal products dispensed by operators authorised to dispense medicinal products, reports on medicinal product deliveries to the Czech Republic conducted by medicinal product marketing authorisation holders, and other data sources.

5.3 Information Activities

The primary task of the Press and Information Department (TIO) is to provide information on SÚKL's activities to the general and professional public. The most important sources of information about the Institute are the website www.sukl.cz, information portal for the public www.olecich.cz, and the website of the campaign Nebezpečné léky (Dangerous Drugs) located at www. nebezpecneleky.cz, which are administered by TIO and which serve both of the aforementioned groups. TIO is also in charge of social networks (Facebook, Twitter) through which it answers questions mostly from the general public as part of user interactivity. The information portal www.olecich.cz provides patients with information from the sphere of pharmaceuticals, such as a database of medicines, database of pharmacies, and database of clinical studies. Available is also a vaccination schedule with essential information regarding both mandatory and optional vaccination, incl. relevant vaccines. For several years now, the general public may avail of the "Ask Us" service, within the scope of which doctors and pharmacists answer the questions of the public. Via the "Ask Us" service, the following specialists answered questions raised by the public: a general practitioner, a paediatrician, and two pharmacists. Thanks to that, it was possible to answer 132 patient questions. In 2019, the largest proportion of the questions concerned drug interactions. TIO also administers a specialised library and is responsible for publication activities, represented by the preparation and publication of SÚKL's Bulletin, the drug bulletin Farmakoterapeutické informace (Pharmacotherapeutic Information, a member of the International Society of Drug Bulletins – ISDB), and the Adverse Drug Reactions Bulletin. All of the above-mentioned publications are available from www.sukl.cz. In 2019, TIO addressed 48 requests for information pursuant to Act No 106/1999 Coll., on Free Access to Information, as amended. Furthermore, it answered another 3,277 inquiries from the general public and from professionals which were sent via e-mail or post. Approximately 2,054 more inquiries were handled through the infoline.

The Department drafted responses to 242 inquiries from journalists and provided regular statements for radio or TV broadcasting. Fourteen press releases and two reactions were published on the Institute's website.

6 FINANCIAL AND MATERIAL RESOURCES OF THE INSTITUTE

6.1 The 2019 Income and Expenditure Account

Income

In 2019, extra-budgetary income in the total amount of 550,017 thous. CZK was achieved. The major part of this income was generated by the reimbursement of costs of expert activities that were conducted by the Institute upon request from manufacturers, distributors, vendors, and other legal entities as well as natural persons. The major part of the overall volume was represented by income from applications in the sphere of marketing authorisations of medicinal products. The income from completed expert activities was used piecemeal by the Institute in compliance with Act No 378/2007 Coll., on Pharmaceuticals, as amended, Act No 296/2008 Coll., on Human Tissues and Cells, as amended, and Act No 268/2014 Coll., on Medical Devices and Amendment to the Act on Administrative Fees, as amended, for the funding of payroll, operating and investment expenditures not covered by allocated financial resources from the state budget. In 2019, the total amount of 467,610 thous. CZK was used in this manner through permissible excess expenditure. Of this amount, 429,714 thous. CZK were used for non-investment expenditure and 37,896 thous. CZK for the financing of investment needs.

In addition to income from the reimbursement of costs of expert activities, another portion of income came from the revenues of the state budget, e.g. collected administrative fees for submitted applications amounting to 28,800 thous. CZK, income from imposed fines amounting to 8,261 thous. CZK, income from lease in the amount of 289 thous. CZK, income from the sale of goods amounting to 2,169 thous. CZK (medical cannabis), refunds of excess advance payments made, related fully to the previous budgetary years, and other compensations amounting to 432 thous. CZK, etc. An overview of the reported budget income as of 31 December 2019 is provided in Tab. 43.

Tab. 43 **Tab. 43 State budget funds (thous. CZK)**

Item	Approved budget	Actual
Administrative fees	19,800	28,800
Received penalty payments	1,000	8,261
Income from lease	0	289
Income from the sale of goods	0	2,169
Income from the provision of services	0	20
Received non-capital contributions and compensation	0	432
Transfers from the reserve fund	0	467,610
Transfers from other own funds	0	270
TOTAL	**20,800**	**507,851**

Expenditure

Data concerning expenditures incurred in 2019 broken down by individual categories are provided in Table 44.

Total investment expenditure amounted to 37,882 thous. CZK from extra-budgetary resources. Investment resources were used to finance the replacement security technologies as part of data centre development (3,720 thous. CZK), the provision of the back-up system (1,573 thous. CZK), and the development of the third data centre for ePrescription back-ups (1,287 thous. CZK). Furthermore, 923 thous. CZK were used for the purchase of licences; 4,013 thous. CZK for the technical upgrade of applications and software (ePrescription, eSSL Athena, and others), 4,296 thous. CZK for the purchase and replacement of hardware; and 469 thous. CZK for websites (portal). HSM modules were procured (1,628 thous. CZK), as well as a PROXY SMS gateway (212 thous. CZK), and electronic notice board (317 thous. CZK). A general reconstruction of the substation in Building No 24 was carried out (2 184 thous. CZK), and in the Brno building, a lift was built and underground premises reconstructed (5,514 thous. CZK). For laboratories, apparatuses in the total value of 10,972 thous. CZK were purchased (polarimeter, biological incubator, multifunctional microplate reader, water treatment apparatus, and liquid chromatography device with a mass spectrometer). Furthermore, the CCTV system was upgraded (50 thous. CZK) and so was the attendance system (178 thous. CZK) and air-conditioning in Building No 24 (53 thous. CZK). In total, 122 thous. CZK were incurred for the extension of the data distribution system and the optical network, and 371 thous. CZK for project studies for construction projects under preparation (data centre reconstruction project and Building 23 A reconstruction project – demolition and design works).

Non-investment expenditures, including mandatory expenditures, were utilised in the total amount of 590,046 thous. CZK, of which 159,913 thous. CZK came from the state budget and claimed unused expenditures amounted to 797 thous. CZK; 429,336 thous. CZK were taken from extra-budgetary resources. Extra-budgetary resources included resources from abroad provided for the EURIPID project (utilised amount: 18 thous. CZK), the STARS project (utilised amount: 13 thous. CZK), and the NIX-ZD.CZ project (utilised amount: 2,373 thous. CZK).

Tab. 44 **Expenditures (thous. CZK)**

Indicator	Approved budget	Final budget	Actual
Employee salaries	23,537	42,943	42,943
Civil servant salaries	89,706	275,971	275,942
Other payments for completed work, severance pay, surrenders	3,603	15,120	15,118
Mandatory insurance premium	39,728	111,596	111,579
Contribution to the Fund of Social and Cultural Needs	2,265	6,403	6,402
Operating acquisitions and related expenditure	1,074	138,391	138,062
Acquisition of long-term tangible and intangible fixed assets	0	37,896	37,882
TOTAL	**159,913**	**628,320**	**627,928**
Of which: operating expenditure	1,074	590,424	590,046
capital expenditure	0	37,896	37,882

Expenditures for International Projects within the EU

The EURIPID project has been under way since 2008. It concerns a voluntary association of competent authorities in charge of the pricing and reimbursements of medicinal products. The association was established for the purposes of setting up a joint database of reimbursed medicinal product prices. At present, more than 24 European countries are involved. In 2015, the project obtained European support for the extension of the database and for the processing of technical and expert recommendations for the conduct of so-called external price references. An important output from the grant will be an open publication of a set of recommendations that will help to prevent or minimise the potential negative impact on the availability of medicinal products resulting from incompetent utilisation of foreign price references. In 2019, 17,522.50 CZK from foreign funds were utilised for the purposes of the project (travel allowances).

The Institute has been also involved in a joint action on health technology assessment on the European Union level within the EUnetHTA project, Joint Action 3 (JA3 2016-2020). The objective of JA3 is to define and implement a sustainable model for multinational cooperation in the area of health technology assessment (HTA) in Europe. In the EUnetHTA project, the Institute, in cooperation with the Ministry of Health, is so called associated partner. In total, more than 78 organisations from 29 countries are involved in the project. This joint action is co-funded by the European Commission and the Member States, with the EC covering 60 % of the project costs. In 2019, no funds were incurred for the project.

Since 2019, the Institute, along with 17 other EU Member States, has been acting as a partner in the three-year Strengthening Training of Academia in Regulatory Science (STARS) project. This is a European project receiving the Horizon 2020 grant support. The objective of the project is to analyse and improve the education of academic staff in the area of "regulatory science" both on the national and European level, and thus further improve regulatory scientific advice. Another object of the project is also support for academic research in the form of consultation provision. In 2019, a survey in selected sites involved in academic research took place as well as a survey among regulatory agencies regarding the provision of consultations. In the next two years, a complex list of existing support activities for regulatory scientific advice in Europe will be created; and analysis of the aforementioned surveys will be performed; and, as part of a pilot project, specific training in support of academic staff will be conducted and experience shared among the participating countries. In 2019, 13,466 CZK from foreign funds were utilised for the project (travel allowances – business trip abroad in association with the annual meeting of project representatives in Bonn, Germany).

As early as in 2018, SÚKL, together with the main partner – the Vysočina Region – became involved in the Deployment of Cross Border Services in the Czech Republic (NIX-ZD.CZ II) project. The objective of this project is to create, test, and deploy a cross-border ePrescription service. The total duration of project implementation has been scheduled from 01 July 2018 until 30 June 2022. Of the total project costs, 75 % will be covered by the CEF TELECOM European subsidy. In the course of 2019, a major progress in project implementation was achieved, starting with the necessary national legislation amendment in relation to cross-border exchange, and ending with the primary testing of data exchange between the Czech Republic and other Member States that may be rated as highly successful. The project team is going to work intensively and develop technical solutions proper also in the next year, so that the patient in particular may draw a maximum benefit from the output of this project. In 2019, project expenditures amounted to 2,611,400.93 CZK, of which 2,373,000 CZK were utilised foreign funds.

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Other

A total of 3,423 thous. CZK was used for foreign business trips. In 2019, 380 foreign business trips took place, of which 170 were fully covered by SÚKL and 210 trips were fully or partially refunded by the organising institutions (EC, EU Council, EMA, etc.); 33 foreign trips were educational and nine foreign trips were covered by funds allocated to EU projects (EURIPID, STARS, NIX- ZD.CZ II.). The purpose of most business trips was participation in regular meetings of various committees and

working groups resulting from membership in relevant bodies. SÚKL has its members or alternates in more than 70 groups across the EU institutions and international organisations. The employees of the Institute actively cooperate with the European Medicines Agency (EMA), the European Directorate for the Quality of Medicines (EDQM), the European Commission, Council of Europe, etc., and are involved in the activities of the aforementioned bodies. Cooperation in the bodies of the European Commission, EU projects, and other similar programmes is also of importance and much benefit. Other business trips were approved with regard to SÚKL's priorities, the relevance and benefits of the discussed topics for SÚKL.

Assets

The total assets as of 31 December 2019 amounted to 1,244,051 thous. CZK, of which fixed assets represented 413,782 thous. CZK and current assets 830,269 thous. CZK. Of the total liabilities of 1,244,051 thous. CZK, equity amounted to 1,196,685 thous. CZK and borrowed capital to 47,366 thous. CZK. Selected types of assets and liabilities are listed in Tab. 45.

Tab. 45 **Overview of selected types of assets and liabilities of the organisation (thous. CZK)**

Item	Past period 2018	Current period 2019
ASSETS	**1,163,656**	**1,244,051**
A. Total fixed assets	**428,201**	**413,782**
of which:		
I. Long-term intangible fixed assets – total	115,833	95,350
II. Long-term tangible fixed assets – total	312,368	318,432
of which:		
Lots	4,619	4,530
Buildings	241,954	243,363
Separate tangible movables and sets of tangible movables	41,584	70,022
Unfinished tangible fixed assets	24,211	517
B. Total current assets	**735,455**	**830,269**
of which:		
I. Inventory - total	384	1,951
II. Short-term receivables - total	4,781	12,317
III. Short-term financial assets - total	730,290	816,001
LIABILITIES	**1,163,656**	**1,244,051**
C. Equity	**1,126,964**	**1,196,685**
of which:		
I Assets of the accounting entity and adjustments	228,869	227,425
II. Funds of the accounting entity	698,839	781,888
Fund for Cultural and Social Needs	2,080	2,224
Reserve Fund	696,759	779,664
III. Economic result	–597,682	–729,643
Economic result for the current accounting period	–107,543	–131,961
Economic result for the previous accounting periods	–490,139	–597,682
IV. Income and expenditure account of the budget management	796,938	917,015
D. Total borrowed capital	**36,692**	**47,366**
of which:		
I. Total long-term liabilities	0	0
II. Total short-term liabilities	36,692	47,366

Auditing

In the period from 05 June 2019 to 31 July 2019 (following expiry of the timeline for submission of objections) the Revenue Authority for the Capital City of Prague, Territorial Office for Prague 1, Asset Tax Unit, conducted an audit in SÚKL, focusing upon administrative fee management in the period of 2017–2018. The audit did not identify any shortcomings.

On 21 May 2019, the Revenue Authority for the Capital City of Prague commenced a tax audit to identify facts decisive for the proper identification and possible imposition of a tax liability arising from a breach of budgetary discipline as referred to under the provision of Section 44 and Section 44a of Act No 218/2000 Coll., on Budgetary Rules and on Amendment to Some Related Acts (Budgetary Rules), as amended, in the utilisation of state budget funds within the scope of a contract on the provision of legal aid concluded with Advokátní kancelář Němec, Bláha & Navrátilová, s.r.o., of 08 February 2011 and its Amendment No 1 dated 20 December 2013, on the basis and within the scope of report no. 16/18-NKU140/213/17 sent by the Supreme Audit Office. The audit identified breach of the provision of Section 45(2) of the Act on Budgetary Rules. For the breach, a fine in the amount of 31,460 CZK and a penalty in the amount of 31,460 CZK were imposed. On the basis of an application for waiver of the tax liability for breach of budgetary discipline, on 12 December 2019, the General Financial Directorate issued a decision waiving the full amount of the fine and penalty in the amount of 27,804 CZK. The difference in the amount of 59,264 CZK resulting from the decision of the General Financial Directorate was refunded to the Institute's account in January 2020.

No other audits performed by public administration authorities pursuant to the Act on Financial Audit or by the Supreme Audit Office took place.

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7 FOCUS UPON EMPLOYEES

7.1 Personnel Issues

Organisational Structure

In compliance with the Institute's systemisation approved for 2019 pursuant to Act No 234/2014 Coll., on Civil Service, organisational changes have been implemented since 01 January 2019 in order to optimise the number of systemised positions and to increase the effectiveness of work, in the total number of 560 positions, of which 463 are civil service positions and 97 employment positions.

As part of the organisational changes associated with the Institute's systemisation effective as of 01 January 2019, in addition to the increased number of civil service and employment positions compared to 2018 (required by new activities implied by the legislation, such as the Institute's duty to take over activities associated with Brexit), several substantial changes were implemented, particularly within the organisational structure of selected regulatory sections and departments.

In the course of 2019, several other modifications of the organisational structure were implemented with effect as at 01 March 2019, 01 May 2019, and 01 July 2019; these modifications concerned primarily the hierarchy of units of selected regulatory sections (e.g. the establishment of a new Health Technology Assessment Department in the Pricing and Reimbursement Section in order to increase the effectiveness of the organisation of expert assessment of the submitted documentation in parallelly running administrative procedures of various types, to increase the effectiveness of human resource planning, and safeguard the mandatory timelines in individual administrative procedures and in-depth revisions).

The number of physical employees on the Institute's payroll as of 31 December 2019 was 511 persons, of which 398 were women (i.e. 77.9 %) and 113 were men (i.e. 22.1 %).

Within the scope of the Personal and Working Life Harmonisation Policy, as of 31 December 2019, the total of 72 employees of the Institute (of which 70 were women), i.e. 14.1 % of the total number of employees, worked part-time.

Converted to full-time equivalents (FTEs) worked under non-employment agreements (work agreement and agreement to perform work), a total of 33.5 employees were employed as of 31 December 2019. Compared to 2018, this was an 11.3 % increase.

Age Structure of Employees

The average age of all employees compared to 2018 increased by 0.9 %, i.e. to 42.88 years.

Tab. 46 **Age structure of employees as of 31 December 2019**

Year	% of employees do 35 let	% of employees aged 36 to 55 years	% employees older than 55 years
2018	32.6	49.7	17.7
2019	31.5	50.7	17.8

Qualification Structure of Employees

Tab. 47 **Qualification structure of employees by achieved level of education as of 31 December 2019 (number / % of the total number of employees)**

Highest achieved education	Primary	Secondary technical	Secondary general	Secondary with GCE	Technical colleges	University bachelor's degree	University – master's degree	Postgraduate
Number of employees	1	5	13	76	6	12	385	12
% of the total number of employees	0.2	0.98	2.55	14.9	1.18	2.35	75.49	2.35

Staff Turnover

The overall staff turnover taking into account all start-ups and departures, amounted to 10 % (compared to 2018, this was a 16.6 % decrease).

In total, 275 tenders were completed on the basis of which the total of 101 employees were admitted.

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

	Civil service		Employment	
	No. of positions to be staffed through tenders	Staffed	No. of positions to be staffed through tenders	Staffed
Total	**1173**	**57**	**102**	**44**

Tab. 49 **Overview of employment and civil service terminations in 2019 by reason of employment/civil service termination**

	Employment	Civil service
Cancellation of employment/civil service in probationary period	9	6
Agreed time expiry	4	2
Termination by agreement (Section 49 of the Labour Code)	3	-
Notices given by employees/termination of civil service upon request of the civil servant	5	13
Notices given due to organisational reasons/by decision of the civil service authority	3	-
Termination of civil service performance with the Institute due to transfer of the civil servant to another civil service authority	-	2
Retirement	2	1
Total	**26**	**24**

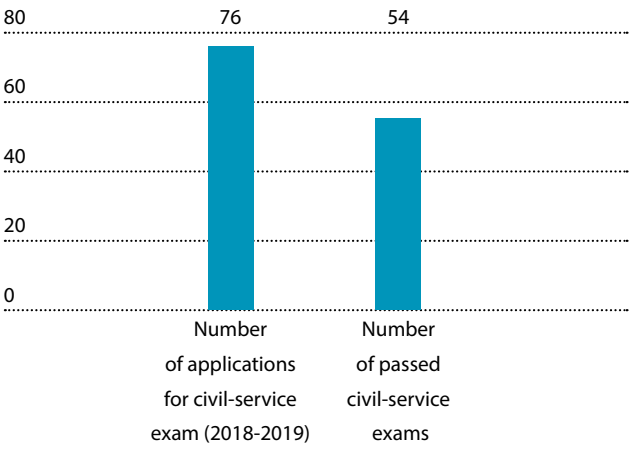
Civil-service exam

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

Forty applications were brought forward from 2018 to the next calendar year and in the course of 2019, 36 applications lodged by the employees of the Institute were newly registered, which amounts to 76 applications in total. In 2019, 54 employees successfully passed both parts of the civil-service exam. The remaining 22 employees will take the exam in 2020 (within 12 months of their recruitment as civil servants, as stipulated by the Act on Civil Service).

Of the total number of civil-service exams taken, only one employee was unsuccessful on the first attempt (in the specialised part of the civil-service exam); this employee successfully passed the exam on a second attempt.

Fig. 31 **Civil-service exams in 2019**



7.2 Employee Education

In 2019, the area of employee education focused upon the development of expert, soft, and language skills. Within the scope of initial education, all new members of the staff were trained in all topics set forth by effective legislation: employee evaluation, basic information about the Institute and its internal regulations, information security incl. personal data protection, quality management, the Code of Ethics, internal regulation of conflict of interest, human rights protection, equality, prohibited discrimination, and environmental responsibility.

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

Concurrently, in 2019, the Institute implemented management courses intended for the education of senior and managerial staff, which were organised in the form of individual and group couching focused upon the development of personal qualities and management skills, making use of model situations, case studies, and results of research in the area of neuroscience and occupational psychology.

Furthermore, in 2019, language education for the employees also took place; it was based upon the current needs, strategy, and objectives of the Institute. Language courses were organised particularly for employees of regulatory units who use English for necessary purposes, and for employees representing the Institute in international and multinational institutions, audits, and inspections.

In 2019, the Information Security (Cybersecurity) Manager and the Data Protection Officer organised a mandatory training for all employees in the area of information security and personal data protection. The training focused upon compliance with the basic requirements implied by the new Decree No 82/2018 Coll., on Cybersecurity, and by the General Data Protection Regulation (EU) 2016/679 (GDPR).

The total volume of funds incurred for all types of educational activities amounted to **2,811,000 CZK.**

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

Type of event	Number of events	Number of hours	Number of attendees
Specialised courses & training; language courses	1,503	5,830	1,071
Mandatory training	116	230	745
Foreign specialised training	27	728	35

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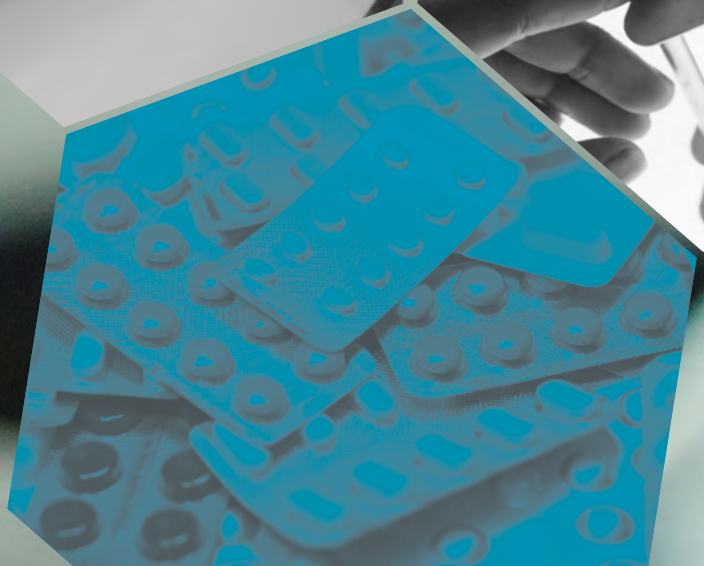

8 FOCUS UPON QUALITY

The continuous intention of the Institute in the area of quality is to execute its activities at a high standard, in a predictable manner, with transparent documentation, in shortest practicable timelines and required quality, with openness to reports and initiatives, while observing ethical rules, environmental conduct, and occupational safety. All of the aforementioned is aimed at increasing stakeholder satisfaction, developing a positive image of the Institute, and winning international acknowledgement.

In 2019, the quality management system was being maintained and developed in compliance with the requirements of the ČSN EN ISO 9001:2016 standard. In December 2019, the LL-C (Certification) Czech Republic s.r.o. certification body conducted a review of some of the Institute's certified processes and noted that the Institute's quality management system continued to meet the requirements of this standard.

The functionality of the quality management system was verified on an ongoing basis also within the scope of internal audits; in compliance with the annual plan, 20 such internal audits took place in 2019.

In June 2019, the Institute hosted a meeting of the Working Group of Quality Managers (WGQM) of European medicines agencies, under the HMA. The long-term objective of this Working Group is to share experience and best practice examples in the sphere of quality management systems. Among other topics, the new training system for quality auditors or the BEMA medicines agencies benchmarking (peer review) were debated at the meeting.

9 INFORMATION SECURITY MANAGEMENT POLICY

Also in 2019, the Institute continued to pay much attention to the security of information – not only in light of the fact that the agendas administered by the Institute include one of the most extensive databases of sensitive personal data in the Czech Republic – the ePrescription, but also with regard to the seriousness of extended information security of all systems that facilitate computerisation of agendas and supporting legal activities imposed upon the Institute as a state administration and surveillance authority.

For this reason, in 2019, recommendations from the security testing completed in 2018 in cooperation with the National Cyber and Information Security Agency were integrated and further evaluated; also, a management communication table-top exercise was conducted with the employees of the National Cyber and Information Security Agency, within the scope of which SÚKL's preparedness for and reactions to various types of attacks, including the provision of information on their impacts to professionals, were tested.

Furthermore, in 2019, an audit (to be continued in 2020) was performed in the Institute by the Office for Personal Data Protection, in compliance with Regulation (EU) 2016/679 of the European Parliament and of the Council (GDPR); the subject-matter of the audit was observation of the obligations stipulated by the GDPR in the area of personal data processing in the Central Repository of Electronic Prescriptions (ePrescription).

In 2019, the Institute successfully passed the second surveillance audit of the information security management system as per the ČSN ISO/IEC 27001:2014 standard, and so has been the holder of the relevant certificate for 12 years now.

Even in the coming period, SÚKL shall strive to develop and deploy new technical and organisational measures aimed at effective reactions to the situation when the number of cyber-attacks keeps growing, so as to be prepared to face new cybernetic threats.

10 OUTLOOK FOR 2020

In 2020, the Institute shall focus upon other new functionalities and development of the ePrescription system. A new key functionality of the ePrescription system is so-called shared medication record that has been introduced by the amended Act on Pharmaceuticals. As of 01 June 2020, it will hence be possible for doctors, pharmacists, and clinical pharmacists providing healthcare services to the patient to view the patient's shared medication record. Although it is in the interest of each patient that his/her treating doctors and pharmacists contribute to safe and successful treatment, each citizen has the right to freely express disagreement with the viewing of his/her record. Patients may express their disagreement with the viewing of their medication records from 01 December 2019. Prior to the launch of the shared medication record, the Institute together with the Ministry of Health of the Czech Republic shall inform patients as well as healthcare professionals about the new functionality.

In the course of 2020, the Institute shall also focus upon the education of the general public in the area of storage and disposal of pharmaceuticals. Within the scope of the "Don´t Throw Medicines in the Bin" campaign, the STEM/MARK agency organised a survey called "Actual Utilisation of Pharmaceuticals and Its Financial Impact upon the Healthcare System in the Czech Republic", whose research finding will be presented to the public as part of the campaign. Furthermore, in 2020, a sociological survey focused upon the use of antibiotics and the public awareness of antimicrobial resistance shall be conducted under the auspices of the Institute.

11 LIST OF ABBREVIATIONS

AMR	Antimicrobial resistance
ARTHIQS	Assisted Reproductive Technologies and Haematopoietic stem cells Improvements for Quality and Safety throughout Europe
ASRW	Assessment Report Worksharing
ATC	Anatomical Therapeutic Chemical group
BEMA	Benchmarking of European Medicines Agencies
BI	Business intelligence
BPM	Business process management
CAP	Centrally Authorised Product
CDFA	China Food and Drug Administration
CDNÚ	Central Database of Adverse Drug Reactions
CD-P-PH	The European Committee on Pharmaceuticals and Pharmaceutical Care
CKS	End-user price
CKS NAP	Central Coordination Group of the National Antibiotic Programme
CMS	Concerned Member State
CRS	Chemical reference substance
CTFG	Clinical Trials Facilitation Group
CÚER	Central Repository of Electronic prescriptions
ČAV	Czech Academy of Sciences
CP	Czech Pharmacopoeia
DCP	Decentralised Procedure for marketing authorisations
DU	Defined unit
DL	Diagnostic laboratory
DLL	Active substance importers
DMS	Data management software
DPV	Parenteral nutrition products for home therapy
DSUR	Development Safety Update Report
ECDC	European Centre for Disease Prevention and Control
eCDT	Format for the submission of marketing authorisation applications
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EFPIA	European Federation of Pharmaceutical Industries and Associations
EPC	European Pharmacopoeia Commission
EMA	European Medicines Agency
EUDAMED	European Database of Medical Devices
EudraGMP	European Community of Manufacturing Authorisations and of Certificates of Good Manufacturing Practice
EUnetHTA	European Commission and Council of Ministers targeted Health Technology Assessment
EU-NTC	EU Network Training Centre
EURIPID	European Integrated Price Information Database
EV EWG	EudraVigilance Expert Working Group
FAQ	Frequently Asked Questions
FIH	First-in-human
FSC	Free Sale Certificate
FSCA	Field Safety Corrective Action
FSN	Field Safety Notice
FV	Pharmacovigilance
GDPR	General Data Protection Regulation
GMP	Good Manufacturing Practice
HAV	Human autogenous vaccines
HLP	Medicinal Products for Human Use
HMA	Heads of Medicines Agencies

HR	In-depth revision
HTA	Health Technology Assessment
CHMP	Committee for Medicinal Products for Human Use
IMPD	Investigational Medicinal Product Dossier
INN WHO	International Non-proprietary Name
IPLP	Individually prepared medicinal product
JVP	Joint Visit Programme
CT	Clinical trial
KHZP	Clinical evaluation of medical devices
CIMD	Clinical investigation of medical devices
LP	Medicinal product
LTB	Human tissues and cells
MAG	Magistral formulas
MC	Maximum price
MDEG	Medical Devices Expert Group
MHRA	Medicines & Healthcare Products Regulatory Agency (United Kingdom)
MMR	Measles, Mumps, Rubella
MOFCOM	Ministry of Commerce of the People's Republic of China
MRA	Medicine Regulatory Authority
MRP	Mutual Recognition Procedure
MoH	Ministry of Health of the Czech Republic
NCAR	National Competent Authority Report (medical devices)
NOOL	National Medicines Verification Organisation (Národní organizace pro ověřování pravosti léčiv)
OCABR	Official Control Authority Batch Release
OECD	Organisation for Economic Co-operation and Development
OMCL	Official Medicines Control Laboratories
ONM	Nuclear Medicine Department
OOP	General Measure
OOVL	Detached pharmaceuticals dispensing unit
OP	Profit margin
OPC	Expert Opinions and Free Sale Certificates Unit
ORN	Registration and Notification Department
OSALK	Unit of State Agency for Medical Cannabis
OZ	Donation Centre
PČR	Czech Police
Ph.Eu	European Pharmacopoeia
PhV	Pharmacovigilance
PhV BT	Pharmacovigilance Business Team
PhV IWG	Pharmacovigilance Inspectors Working Group
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PPZ	Legal Support Unit (medical devices)
PRAC	Pharmacovigilance Risk Assessment Committee
PSUR	Periodic Safety Update Report
PSUSA	Periodic Safety Update Single Assessment
RA	Rapid Alert
RAB	Rapid Alert System for Blood and Blood Components
RAN	Rapid Alert Network
RATC	Rapid Alert System for Human Tissues and Cells
RF	Radiopharmaceuticals
RLPO	Registry of Restricted Active Substances

RMS	Reference Member State
RSI	Reference Safety Information
RA	Rapid alert
RZPRO	Registry of Medical Devices
SAE	Serious Adverse Event
SAKL	State Agency for Medical Cannabis
SCOPE	Strengthening Collaboration for Operating Pharmacovigilance in Europe
GDP	Good Distribution Practice
SEAI	List of essential anti-infectives
SKAP	Subcommission for Antibiotic Policy
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
AP	Administrative Procedure
SÚKL	State Institute for Drug Control
SUSAR	Suspected Unexpected Serious Adverse Reaction
SVP	Good Manufacturing Practice
SWP	Safety Working Party
SZPI	Czech Agriculture and Food Inspection Authority (CAFIA)
ŠÚKL	Slovak State Institute for Drug Control
TIO	Press and Information Unit
TNK	Technical standardisation Committee
TP	Transfusion products
TZ	Tissue centres
UHR	Reimbursement
ÚJČ AV	Czech Language Institute, Czech Academy of Sciences
ÚNMZ	Czech Office for Technical Standardisation, Metrology, and State Testing (Úřad pro technickou normalizaci, metrologii a státní zkušebnictví)
VaPú	Amount and conditions of reimbursement
VHP	Voluntary Harmonisation Procedure
VILP	Highly innovative medicinal products
VUC	Materially regulated price
WHO	World Health Organisation
ZNR	Serious adverse reaction
ZNU	Serious adverse event
ZoL	Act on Pharmaceuticals
ZoRR	Acton Advertising Regulation
ZP	Health insurance
ZP	Medical device
ZTS	Blood centre
ROP	Registration and Expert Opinion Unit
ONZP	Medical Device Notification Unit
MAH	Marketing authorisation holder
ČSSZ	Czech Social Security Administration
DHPC	Direct Healthcare Professional Communications
DDD	Daily Defined Doses
FTE	Full-Time Equivalent
KOČ	Expert Activity Coordination Unit
ADR	Adverse Drug Reaction

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