SÚKL

ANNUAL REPORT **2020**
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, EUROPEAN, AND OTHER INTERNATIONAL INSTITUTIONS

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

In 2020, the Institute very 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 2020, cooperation within the scope of the legislative process of the proposed amendment to Act No 378/2007 Coll., on Pharmaceuticals, as amended (hereinafter referred to as the "Act on Pharmaceuticals") was carried out. This concerned implementation of Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC (hereinafter referred to as "Regulation 2019/6"). In this respect, Regulation (EU) 2019/4 of the European Parliament and of the Council of 11 December 2018 on the manufacture, placing on the market and use of medicated feed, amending Regulation (EC) No 183/2005 of the European Parliament and of the Council and repealing Council Directive 90/167/EEC was also implemented into the national legal order (hereinafter referred to as "Regulation 2019/4"). Regulation 2019/6 stipulates the legal framework for the regulation of veterinary medicinal products reflecting the scientific progress, current market conditions, and economic reality. The regulatory framework for veterinary medicinal products should take into account the needs of veterinary pharmaceutical enterprises and trade with veterinary medicinal products within the EU. Regulation 2019/4 then lays down the rules governing medicated feed that have a significant impact upon the breeding of animals, including non-food-producing animals, and upon the production of products of animal origin. Maintaining a high standard of human health protection is one of the major objectives of the EU food law.

Although the aforementioned Regulations fall within the substantive scope of the Ministry of Agriculture, they essentially influence also the powers of the Institute with regard to the necessity of extensive Amendment to the Act on Pharmaceuticals that substantively governs veterinary medicinal products. The importance of distinguishing between the method of handling human and veterinary medicinal products therefore required the Institute's involvement in the drafting of the veterinary amendment to the Act on Pharmaceuticals. In the course of the legislative work, the Institute also extensively cooperated with the Institute for State Control of Veterinary Biologicals and Medicines.

Furthermore, in cooperation with the Ministry of Health of the Czech Republic and the Institute of Health Information and Statistics of the Czech Republic, the Institute was involved in the adjustments of the proposed draft act on electronization in healthcare. Electronization in healthcare represents electronization of processes and digitalisation of agendas aimed at achieving a greater effectivity in the provision of healthcare services, their reimbursement, and control. Electronization in healthcare forms an integral part of the healthcare system, although it does not replace it or create parallel management and administration structures. The current legal base covers only some elements introducing electronization in healthcare. The current fragmented form of partial legal bases does not allow for effective management of electronic healthcare systems. A systemic, complex legal base for the introduction of new technologies in the sphere of electronization in healthcare is clearly missing and so is the basic infrastructure for healthcare electronization, legally defined roles and responsibilities of entities within the electronic healthcare system, and definitions of associated terms, standards of communication, and rules of sharing or provision of medical documentation. With a view to the aforementioned, works on the drafting of a new act on electronization in healthcare have been commenced; the said draft will be relevant for the Institute particularly in relation to the ePrescription system administered by the Institute. This was one of the reasons why the Institute was substantially involved in the commenting on the draft act so as to ensure that the potential changes affect the ePrescription system users as little as possible and that further smooth operation of the system be safeguarded.

Legislative changes influenced also the area of marketing authorisation of medicinal products. The Institute, in cooperation with the Ministry of Health of the Czech Republic, prepared a proposed amendment to Decree No 228/2008 Coll., on marketing authorisation of medicinal products, that was forwarded for the purposes of complete adaptation of the national part of the legal order of the Czech Republic to 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. The provision of Article 117 of the Regulation amends Directive 2001/83/EC, on the Community code relating to medicinal products for human use, by amending the text of Annex I(3.2)(12) to this Directive. Furthermore, the draft Decree harmonised the text of the Decree with the current wording of the Act on Pharmaceuticals after the implemented amendments, particularly adaption of Regulation 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, and with the guidance of the European Medicines Agency, responding thus to real-world findings in terms of leaving out some requirements that were obsolete in the current context.

This was not, however, the only change in the area of medicinal products; legislative amendments were introduced also to Decree No 226/2008 Coll., on Good Clinical Practice and Detailed Conditions Governing Clinical Trials on Medicinal Products. The proposed amendment to the Clinical Decree was presented with regard to the adaptation of Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, implemented through amendment to the Act on Pharmaceuticals. Also in this case the Institute approached the legislative amendments to the implementing legal regulations in a manner reflecting the amendments to the European legislation.

In the sphere of medical devices, the Institute and the Ministry of Health continued their previous cooperation in the preparation 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, (hereinafter referred to as the "MDR"), 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 (hereinafter referred to as the "IVDR"). In the course of 2019, a draft of a new Act on Medical Devices was prepared as a complement to the aforementioned Medical Device 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 Device 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. In 2019, this suite of bills was forwarded to the Legislative Council of the Government for assessment and subsequently was approved by the Government. In the course of 2020, both bills were discussed by the Chamber of Deputies of the Parliament of the Czech Republic as Chamber Documents nos. 696 and 697, approved by the MPs, and forwarded to the Senate of the Parliament of the Czech Republic for discussion as Senate Documents nos. 32 and 33.

In association with the aforementioned Chamber document no. 696, the Institute drafted also its amendment introducing a brand new legal base for so called eOrders, i.e. electronic orders on which the holder is to be dispensed a medical device prescribed thereon. The said amendment was approved by the MPs and currently has been included under Senate Document no. 32; eOrder thus represents another step towards healthcare modernisation.

In 2020, the Institute, in cooperation with the Ministry of Health of the Czech Republic, was significantly involved in the drafting of a new joint act on medical devices and in vitro diagnostic medical devices. The joint act is the implementation of MDR and IVDR into the national legal order and aims to simplify the legal base to make it friendlier for application in practice. The anticipated date of coming into effect of the MDR is 26 May 2021; this means that the coming into force of the MDR has been postponed by one year from the original schedule. The IVDR will hence come into force on 26 May 2022. In order to meet the liabilities of the Czech Republic implied by its membership in the EU, it is hence necessary to implement the aforementioned Regulations in an appropriate and timely manner into the national legal order. The draft joint act covers the adaptation provisions of both Regulations as well as areas not explicitly covered by the Regulations, such as medical device servicing. In association with the legal order adaptation to the Regulations, amendments to other legal regulations were also drafted, specifically those to Act No 40/1995 Coll., on Advertising Regulation, and Act No 634/2004 Coll., on Administrative Fees. The purpose of the aforementioned Regulations is to ensure a smooth working of the internal market in terms of medical devices and in vitro diagnostic medical devices, based on a high standard of patient and user health protection, and taking into account small and medium enterprises operating in this industry. At the same time, these Regulations lay down a high standard for the quality and safety of medical devices and in vitro diagnostic medical devices in order to address general safety issues associated with these products. At present, the bill is at the start of ordinary legislative process and legislative works are anticipated to continue also in 2021.

In addition to direct legislative activities, the Institute also participated in the assessment of individual amendments pertaining to Chamber Documents of interest currently discussed by the Chamber of Deputies of the Parliament of the Czech Republic. Specifically, these concerned Government amendment to Act No 48/1997 Coll., on Public Health Insurance, that, with regard to the discussed matter in question, involved particularly the Pricing and Reimbursement Section; and the Government amendment to Act No 167/1998 Coll., on Dependency-Producing Substances, that aims, inter alia, to set a new legal basis in the area of medical cannabis and so called blue-stripe prescriptions. Upon the Ministry's request, the Institute provides its opinions on the individual amendments, through which it specifies its expert position on the issues in question, which allows it to actively participate in the discussion on such amendments.

In addition to activities associated with these major legislative tasks, the Institute also paid due attention to cooperation in the sphere of providing comments to other legislative proposals governing other areas of relevance for its operation, including also the sphere of consumer protection.

In cooperation with the Ministry of Industry and Trade and relevant units of the Institute, the Institute was also involved in fulfilling the obligations stipulated by Regulation (EU) 2018/1724, establishing a single digital gateway. Within the scope of this cooperation, information regarding requirements for products, for declaration of conformity or mutual recognition in a user-friendly form was provided.

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 of opinions of the Czech Republic on preliminary questions raised before the European Court of Justice regarding the sphere of powers of the Institute continued also during the last year.

The Institute was also actively involved in the fulfilment of the Public Administration Service Catalogue as per the Act on the Right for Digital Services.

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, in particular, 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 total, this involved 160 queries, of which 138 were raised by the Czech Police, six by courts of justice, two by a public prosecution office, six by the Customs Administration, one by a tax authority, two by the Industrial Property Office, one by the General Police Inspectorate (GIBS), one by the Municipality of the Capital City of Prague, one by a municipal authority, and two by the Prison Service.

3.2 Cooperation with EU Institutions and Other Foreign Partners

The Institute has been actively involved in international cooperation in more than 80 working groups and committees. These represent, in particular, bodies of the EU Council, the European Commission, and the European Medicines Agency (EMA), 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. In 2020, the role of this executive support was much enhanced due to the COVID-19 pandemics, the meetings were transferred into the virtual sphere and new groups necessary for crisis management were formed.

The Institute is a member of HMA working groups and management structures and it is involved in the implementation of the joint HMA/EMA strategy. 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. In 2020, the Institute was actively involved in the preparation of a new joint HMA/EMA strategy for 2020–2025 and together with Germany was responsible for the drafting of the strategy, coordination of comments, and the processing of the final version of one of its six defined areas of priority.

Relevant strategic information from international meetings is forwarded via membership in sectoral and cross-sectoral bodies also down to the national level. One of the key problems addressed on the global international level is e.g. the area of antimicrobial resistance (AMR) or availability of medicinal products.

The issue of AMR was successfully included among six new strategic priorities of the European network of medicines agencies and the Institute undertook co-management of the development of this part of the new strategy. Even during the COVID-19 pandemics, and with emphasis upon extension to other public health threats, the perception of AMR as a threat of a slowly progressing, extremely serious pandemics, essentially jeopardizing the entire concept of advanced medicine, was successfully included as a threat the awareness of which has to be raised. It is necessary to consider the special role of anti-infectives among other pharmaceuticals as well as the necessity to approach the solution of this problems in the context of the One Health principle. The Institute will continue this activity by means of its membership in the working group for the implementation of the joint strategy and any knowledge gained therefrom will be transferred to the national level. Preparations for implementation should commence in mid-2021 and should reflect also the lessons learned during the control of the current pandemics.

The Institute's international activities on the EU level include also involvement in the process of adoption of new European legislation and discussions on non-legislative proposals in the EU Council falling under the Institute's responsibility. In 2020, the Institute, as the managing authority, continued to represent the Czech Republic in a 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 the educational strategy for the entire medicines regulatory network of the European Union and of the EEA and in the development of cooperation with other stakeholders in this area, particularly with the academia. In 2020, the Institute was also involved in the launch of a project for a new EU NTC model, initiated by EMA, to ensure appropriate adaptation to current as well as future challenges for the European regulatory network of pharmaceuticals.

In early 2020, the International Conference on Harmonisation (ICH) accepted the Institute's offer to organise an international meeting of the Quality Drafting Group (ICH QDG), which was to be held in Prague in April 2020 and attended by experts from all over the world. Due to the restrictions adopted because of the COVID-19 pandemics, the event was rescheduled for autumn and later on cancelled. With regard to the global situation, the Institute did not organise any other international events in 2020.

In the second half of 2022, the Czech Republic will hold the Presidency the EU Council for the second time and preparatory works aimed at ensuring a successful fulfilment of this demanding task have been under way since 2019. The Institute has been participating in these activities as well, particularly through activities focused upon the planning of international meetings to be organised by the Institute within the scope of the Presidency. The Institute has been also involved in updating sectoral agendas that represent a more detailed plan of the priorities of the Czech Republic as the country presiding the EU Council in the aforementioned period.

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4 REGULATORY ACTIVITIES OF SÚKL

4.1 Record System

In 2020, the electronic record system of the Institute, incl. its regional workplaces, registered 97,748 delivered documents and 65,101 dispatched documents (Tab. 1, 2). The decrease in the number of received documents was associated with the termination of the agenda of so called medical device reimbursement re-notifications, carried out in June 2019, reflecting the transitory provisions of the Act on Public Health Insurance. The priority channel for official document delivery are data mailboxes.

Tab. 1 **Registration of documents in 2018–2020**

	2018	2019	2020
Received documents	103 833	112 034	97 748
Dispatched documents	101 229	78 902	65 101

Tab. 2 **Overview of communication channels in 2020**

	Mailroom	E-mail messages	Data messages	Medical device reimbursement notifications	Total
Received documents	34 954	49 647	10 658	2 489	97 748

	Dispatch room	E-maily messages	Data messages	Electronic notice board	Total
Dispatched documents	5 108	1 050	50 666	8 277	65 101

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 intended for patients 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 intended for patients, 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. The Marketing Authorisation Section also assesses submitted applications for variations to marketing authorisation, marketing authorisation renewals, transfers and revocations of marketing authorisation as well as applications for the authorisation of parallel import and variations to, renewals of or revocations of parallel import authorisations. At the same time, 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 subset clause application.

The Clinical Trials of Medicinal Products Department assesses applications for authorisation/notification of clinical trials, supervision over the conduct of clinical trials, and assessment of applications for hospital exemptions; it also 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 in charge of safeguarding the safety of medicinal products and conducting 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 2020, 546 applications in total were forwarded for expert assessment following successful validation. Most of them were applications for MRP/DCP marketing authorisations. The total number of applications for marketing authorisation increased from 539 applications in 2019 to 573 applications in 2020. 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 2020, the number of received applications for DCP marketing authorisation with the Czech Republic as the Reference Member State increased – from 69 applications in 2019 to 85 applications in 2020.

Marketing Authorisation Renewals

In 2020, 360 applications in total were forwarded for expert assessment following successful validation. Most of them were applications for MRP/DCP marketing authorisation renewals; in 2020, the total number of received applications for marketing authorisation renewal was similar to that in 2019.

Variations to Marketing Authorisation

In 2020, the number of received applications for variations to MRP/DCP marketing authorisations slightly decreased, but, at the same time, the number of received applications for variations to national marketing authorisations slightly increased. The total number of received applications remained similar. At the same time, the number of submitted applications for transfers of MRP/DCP marketing authorisations as swell as national marketing authorisations decreased from the total number of 432 applications in 2019 to 221 applications in 2020.

Parallel Import

In 2020, the number of submitted applications for parallel import authorisation decreased, specifically from 58 applications in 2019 to 30 applications in 2020. At the same time, the number of submitted applications for variations to parallel import authorisations decreased from 121 applications in 2019 to 43 applications in 2020. On the contrary, the number of decided applications for variations to parallel import grew from 77 applications in 2019 to 124 decided applications in 2020.

Marketing Authorisation Revocations

In 2020, 320 applications for revocation of marketing authorisation were decided.

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

Process of marketing authorisation of medicinal products	Submitted in 2020	Decided in total in 2020	Pending as of 31 December 2020
New marketing authorisations	**573**	**491**	**771**
- of which national	19	31	77
- of which MRP-RMS	17	21	51
- of which DCP-RMS	85	93	112
- of which CMS (MRP and DCP)	452	346	531
MA renewals	**340**	**366**	**373**
- of which national	14	31	82
- of which RMS	39	44	37
- of which CMS	287	291	254
National variations to MAs	**2,512**	**2,487**	**502**
- of which MA transfers	68	57	11
- of which PIL and labelling	93	78	20
- of which bulk NAT variations	2,351	2,352	471
MRP-RMS variations	**774**	**779**	**155**
- of which MA transfers	31	33	1
- of which PIL and labelling	45	43	4
- of which bulk MRP-RMS variations	698	703	150
MRP-CMS variations	**4,296**	**4,081**	**1,360**
- of which MA transfers	122	135	3
- of which PIL and labelling	176	169	27
- of which bulk MRP-CMS variations	3,998	3,777	1,330
MA revocations	**318**	**320**	**0**
Parallel import	**30**	**40**	**28**
Parallel import variations	**43**	**124**	**6**
Parallel import renewals	**29**	**20**	**15**
Parallel import revocations	**11**	**11**	**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 Procedur

Expiry/Non-expiry of Marketing Authorisations

In 2020, the Institute conducted 97 administrative procedures concerning the granting of an exemption from the sunset clause.

In the course of 2020 the sunset clause as referred to under Section 34a of the Act on Pharmaceuticals applied to 118 MA numbers and the marketing authorisation of these medicinal products was terminated.

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

	Conducted in 2020
Administrative procedures for exemption from the sunset clause	**97**
- of which: submitted applications	**97**
- of which: ex officio initiated administrative procedures	**0**
- granted	72
- declined	10
- suspended as undue	14
- suspended as unjustified	0
- suspended for failure to provide amendment	0
- withdrawal of application	1

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 2020, the Institute gave twelve oral consultations (including consultations in the form of teleconferences) and issued 23 written opinions on process-regulation and expert requests for consultations.

In 2020, the Institute issued 13 written opinions on requests for consultations about medicinal product names.

In 2020, the annual seminar for companies regarding news in the area of marketing authorisation of medicinal products was not held due to the adverse epidemiological situation.

4.3 Cooperation with the European Medicines Agency and CHMP

In 2020, 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:

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

Along with the aforementioned, the Institute provided comments on other centralised procedures. It regularly and actively participated in discussions held during meetings of the CHMP and other committees (COMP, PDCO, CAT, PRAC) and workgroups.

4.4 Clinical Trials

The 2020 COVID-19 pandemics affected also the area of clinical trials, with a pronounced increase in the agenda associated with the implementation of emergency measures governing new or ongoing clinical trials and the assessment of clinical trials on COVID-19 therapies or prevention was given priority; such studies were assessed by means of an abbreviated, expedite procedure. On 13 March 2021, SÚKL issued its first opinion on the use of special procedures in clinical trials which are not permissible under normal situation, such as conducting remote study visits, delivery of investigational medicinal products to trial subjects by a courier service, videoconference monitoring, etc. In the course of the year, the opinion was updated eleven times in total, in order to reflect the epidemic situation and the development of the pandemics.

Tab. 5 **Clinical trials in 2020**

	Pending from the previous period	**Applications received in 2020**	**Number of decisions issued in 2020**	**Of which declined**	**Of which withdrawn**
Applications for CT authorisation	26	360	136	0	13
CT notifications	61		222	0	10
Notifications of amendments to CTs	---	4 401	3 688	---	---

In 2020, the total of 360 applications for clinical trial authorisation/notification were submitted, which was nine applications less than in the previous year. In total, 358 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 358 decided applications for clinical trial authorisation/notification, 19 were for clinical trials submitted by non-commercial entities (academic research), 38 applications concerned orphan drugs, (medicinal products for rare diseases), 42 were applications for clinical trials enrolling also children or intended directly for the paediatric population (paediatric clinical trials), six concerned clinical trials on advanced therapy products (four somatic cell therapies; one gene therapy; and one tissue engineering therapy), five applications were for first-in-human (FIH) trials. In the course of the assessment process, 23 applications in total were withdrawn (13 applications for clinical trial authorisation and 10 applications concerning clinical trial notifications); no application was declined.

Tab. 6 **Numbers of applications in 2020 by clinical trial phase**

	Applications received in 2020	Applications assessed in 2020
Phase I	22	21
Phase II	108	106
Phase III	191	195
Phase IV	18	14
Bioequivalence studies	21	22

Tab. 7 **Indication groups of clinical trials assessed in 2020**

Indication group	Number
Oncology	99
Metabolic disorders + endocrinology	0
Healthy volunteers	26
Neurology	39
Cardiovascular system	23
Respiratory + allergology	19
Infectious	11
Dermatology	18
Rheumatology	22
Haematology	10
Psychiatry	8
GIT	15
Urogenital diseases	8
ENT	0
Gynaecology	5
Ophthalmology	12
Paediatrics	3
Internal medicine	4
Transplantations	1
Anaesthesiology and resuscitation	1
Investigations	1
Diabetology	16
Other	2
Pain	0
Vaccination	8
Pharmacokinetics	7

Since the start of the year, Development Safety Update Report (DSUR) assessment and control of SUSAR reports continued to be carried out. During the year, 610 DSURs were submitted. In 2020, 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 2020, 11 Member States were involved and 67 assessment reports were drafted, which is the same number as in 2019 and 83 reports less than in 2018. The reason for the decrease is a pronounced drop in the number of assessors seen in the EU in 2019, the largest of which occurred in Ireland. Unfortunately, it was not possible to increase the number of assessors in 2020, either. The Czech Republic drafted three ARs, of which one DSUR was newly assessed and two DSURs were updated. In association with the prioritisation of activities with regard to the COVID-19 pandemics, DSUR assessment and assessment report drafting had to be reduced. Within the scope of the ASR-WS project, our assessors took part in six teleconferences of the CTFG (Clinical Trials Facilitation Group) – Safety Group.

Also in 2020, we continued our 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). In the second half of the year, the Institute significantly reduced the acceptance of studies as the RMS due to the workload of all assessors and their reduced numbers. Within the scope of the VHP, 196 applications for clinical trial authorisation/notification were submitted in the EU, of which the Czech Republic was asked to participate in 65 assessments and it accepted participation in 62 VHP procedures – three studies were declined at the time of the first wave of the pandemics in March. In respect of 22 VHPs, the Czech Republic asked to act as the RMS; in 20 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 2020, the total of 655 substantial amendments were submitted within the scope of VHPs, of which 310 were in the Czech Republic, and in 79 cases, the Czech Republic conducted the assessment procedure as the RMS. In 2020, 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 19 VHP-plus procedures and in four cases, it was appointed as the RMS.

Also in this year, the preparatory activities regarding the implementation of Regulation No 536/2014, on clinical trials, represented a large proportion of work and so did involvement in the CTIS (Clinical Trials Information System) activities. 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 and the CTFG.

Due to the pandemics, the meetings of the Ethics Committee Forum were cancelled. One offline working meeting with the representatives of multicentric ethics committees was organised.

Planned seminars were also cancelled as a result of the pandemic situation. In 2020, the Institute gave 24 consultations for 15 pharmaceutical companies and nine non-commercial entities (academicians, researchers, and representatives of healthcare service providers).

4.5 Pharmacovigilance

In compliance with the Act on Pharmaceuticals (Act No 378/2007 Coll.), SÚKL's Pharmacovigilance Department operates a system of spontaneous reports of suspected adverse drug reactions from the Czech Republic. In 2020, SÚKL received 2,904 suspected adverse drug reaction (ADR) reports from the territory of the Czech Republic, of which 1,526 were reports filed by medicinal product marketing authorisation holders (pharmaceutical companies), and 1,378 were reports sent to SÚKL directly by healthcare professionals and patients (of which, 815 were reports from healthcare professionals and 597 were reports from 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 2020, the Pharmacovigilance Assessment Unit assessed 924 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 13 PSUSA procedures (i.e. PSUR single assessment for a particular substance) from the position of so called PSUSA - Lead Member State (LMS) in the course of 2020. The Institute acts as the PSUSA LMS for 52 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, SÚKL performed the assessment of 18 procedures in total in the course of 2020. In total, we have been appointed the PRAC rapporteur for 17 centrally authorised medicinal products. In 2020, we became EU PRAC rapporteur for medicinal product Veklury (remdesivir), indicated for the treatment of COVID -19. With regard to a more thorough monitoring of the safety of treatment of the COVID-19 infection, we evaluated monthly safety reports for medicinal product Veklury, in total seven of them during 2020; in late 2020, we initiated a detailed evaluation of acute kidney damage signal. This signal will be concluded in early 2021.

We actively participated in eleven meetings of the PRAC pharmacovigilance committee 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), and the EMA PhV Business Team. During the training of pharmacovigilance assessors organised by EMA we had a presentation on conditional marketing authorisation based on our experience with medicinal product Veklury (conditional marketing authorisation was granted also to Veklury). We have been actively involved in the creation of several EMA documents – revision of document "EU Individual Case Safety Report Implementation Guide, GVP Module XVI Risk minimisation measures: selection of tools and effectiveness indicators (Rev 3)" and "Module XVI Addendum II – Methods for effectiveness evaluation", whose first revision was successfully completed and approved by PRAC. In February 2021, a public consultation will commence.

In cooperation with other units of the Marketing Authorisation Section, conclusions adopted by CHMP and the PRAC pharmacovigilance committee were being transferred to Czech clinical practice on an ongoing basis. On its website, the Institute published ten communications intended for healthcare professionals or for the general public on medicinal product safety. In cooperation with marketing authorisation holders, the Institute published educational materials on 79 medicinal products and 28 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 looked at the pharmacovigilance section; in 2020, they prepared 971 reports on pharmacovigilance documentation in total.

The Pharmacovigilance Department continues to issue the Adverse Drug Reactions Bulletin (Nežádoucí účinky léčiv). In 2020, we published three issues (of which one was a double issue). 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.

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

In 2020, the Pharmacovigilance Inspection and Data Support Unit carried out the total of twelve inspections of the pharmacovigilance system of marketing authorisation holders. Of the completed inspections, four were conducted as part of EMA CAP programme, where the Institute acts as the supervising authority for the concerned centrally authorised medicinal products. One inspection was carried out upon CHMP's request and one ad hoc, in response to a report from a whistleblower. Due to the anti-epidemic measures, it was necessary to conduct five inspections in a remote manner, via a videoconference; in this respect, SÚKL was one of the pioneering national authorities in the EU who started to conduct distant pharmacovigilance inspections. The Pharmacovigilance Department communicates with the public, it answers questions from healthcare professionals, the general public as well as pharmaceutical companies. In 2020, 515 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 five presentations within the scope of professional congresses or seminars for doctors and pharmacists or courses of the Institute for Postgraduate Medical Education (IPVZ). Compared to previous years, the number of presentations was significantly reduced due to the ongoing pandemics. The Institute also focuses upon the education of pharmaceutical companies in the proper conduct of pharmacovigilance. In 2020, we continued the tradition of organising two one-day seminars for companies on news in pharmacovigilance from the previous year. Due to the anti-epidemic measures, these seminars were organised as remote.

In spring 2020, we completed the demanding implementation of a new project – inclusion of important information on the safety of pharmaceuticals in the electronic prescription system. The approved educational materials (EM), Direct Healthcare Professional Communications (DHPC), and other important information are currently not only published in full on SÚKL's website, but also in the electronic prescription. During the prescribing or dispensing of the concerned proprietary medicinal product, an alert is displayed informing that EM/DHPC are available for this code and that they may be displayed by the doctor or pharmacist if he/she ticks them. The doctor as well as the pharmacist can see information intended for the patient so that the former can provide it to the latter. Information for patients is displayed also in the patient web or mobile ePrescription application. All of the educational materials approved to date (280) were checked in terms of professional accuracy or holders were asked to update them and to create joint EMs; these are piecemeal manually uploaded to the ePrescription system. At present, all of the newly approved EMs/DHPCs as well as 62 % of all EMs approved prior to the rollout of this functionality have been uploaded to the system, and the objective is to complete the implementation in the course of 2021
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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. Inspection of medicinal product handling are carried out also in 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 and safeguards activities to eliminate potential jeopardy caused by a pharmaceutical or an excipient of inadequate quality, including assessments of measures proposed/adopted by regulated entities. It is also in charge of issues of counterfeit or stolen medicinal products in the legal distribution network, and addresses also cases of unsuccessful verification of safety features on medicinal products in compliance with effective legislation in order to protect the public from counterfeit medicinal products. This activity also includes assessment of requests filed in compliance with Section 11(r) of the Act on Pharmaceuticals.

The exercise of surveillance over compliance with the Act on the Regulation of Advertising in the sphere of advertising for medicinal products for human use (HMPs) and sponsorship in this area (with the exception of radio and television broadcasting) is performed by the Department of Advertising Regulation Unit. It conducts investigations into complaints pertaining to inappropriate advertising for HMPs, gives expert opinions on advertising materials and on advertising regulation issues. The Unit is also involved in enforcement in those cases where illegal situation has been identified – i.e. illegal handling of pharmaceuticals, and in decision making on whether a product is a medicinal product or not.

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 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 of the Department 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 2020, verification of the established quality system by a group of EDQM auditors took place, due to the pandemic situation, it was conducted as a remote audit and the attest is currently valid until December 2021. International recognition of the quality management system is a precondition for participation in international studies of control of centrally authorised medicinal products organised by EMA/EDQM, recognition of the results of MRP/DCP product analyses, and international recognition of batch release certificates for selected medicinal products (OCABR) within the EU.

The results of sample analyses conducted in 2020 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 2020***

Project name	Number of analysed products	Number of analysed samples	Number of compliant samples	Number of non-compliant samples	Number of comments on MA dossier
3/2019 – Pharmacy samples	102	232	226	6	1
5/2018 – Enalapril maleinate	23	12	23	0	2
1/2019 – Control of Braille on medicinal product labelling	80	94	90	6	0
1/2018 – Medicinal products containing omeprazole	8	16	16	0	0
6/2018 – Medicinal products containing ibuprofen	13	26	26	0	0
7/2018 – Syrups for children with dispenser	16	28	28	0	1
Individually Prepared Medicinal Products project	6	12	11	1	0
BIO/1/2019 – Control of nasal product quality compliance with pharmacopoeial requirements in the area of sterility and microbiological quality	27	55	55	0	0
BIO/3/2018 – Microbiological monitoring of aqua purificata	2 (bulk AP and finished AP)	143	134	9	1
Total	**277**	**618**	**596**	**22**	**5**

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 SÚKL's Quality Team. In 2021, works on the following projects have been under way: control of medicinal products containing pregabalin, desloratadin and losartan and control of selected cardiac and diuretic products, verification of microbiological quality of oromusocal products, verification of packagerd aqua puritificata microbiological quality. Pharmaceutical samples and Braille on the labelling of medicinal products continue to be controlled and analyses of identified counterfeit and illegal samples continue to be carried out, particularly upon request of the Czech Police. A project controlling influenza vaccines for the 2020/2021 season is approaching its completion.

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

Product type	No. of medicinal products	No. of reported batches	Released on the basis of certificate	Released after lab. control	Total number of released batches*	Not released	Completed within timeline
Blood derivatives	71	799	779	20	799	0	799
Vaccines	27	257	257	0	257	0	257
Others	1	1	0	1	1	0	1

** 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	31	30	1
Suspected counterfeit, illegal samples*	50	-	-
International OMCL studies *	11	-	-
Internal quality control of purified water	122	117	5
Verification of quality of a reference substance for Ph. Eur.	1	1	0
Verification of draft pharmacopoeia monographs	2	2	0
Other analyses **	12	12	0
Total	**229**	**162**	**6**

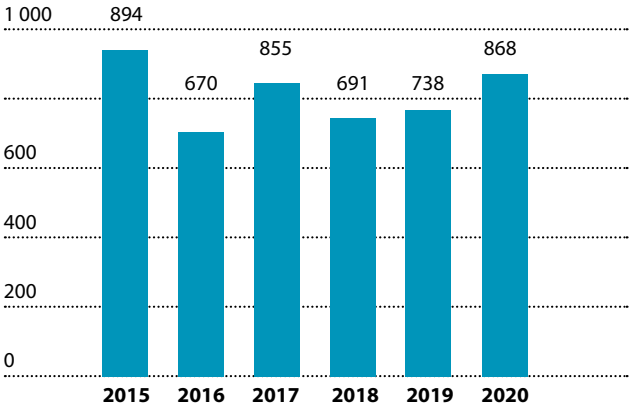
** Sample compliance cannot be evaluated.*

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

The tables above indicate that in the Laboratory Control Department, 868 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) decreased to 3.2 % (vs. 4.2 % in 2019; 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) and also within the scope of the Braille on Medicinal Product Labelling project. Otherwise, the quality of proprietary medicinal products available on the Czech market has been very good. This defect was confirmed only for one sample evaluated as part of suspected quality defect.

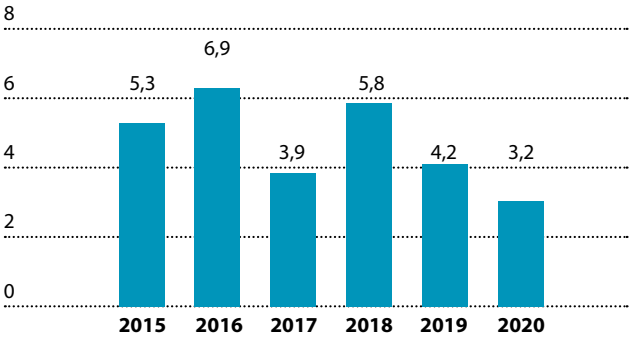
Within the scope of the statutory task of batch release, all of the reported batches were released onto the market in time, i.e. within timelines stipulated by the law. Fig. 1 illustrates the number of released batches of blood derivatives and vaccines; for some blood derivatives, an internationally recognised certificate (OCABR – Official Control Authority Batch Release) was issued after laboratory testing. Although the number of released vaccine batches has been slightly dropping, the batch volumes are larger, and hence the number of released vaccine doses has been greater than in the past few years (2018 – 3,389,764 doses; 2019 – 4,012,430 doses; 2020 – 4,054,936 doses).

Fig. 1 **Number of sample analyses in 2015–2020**



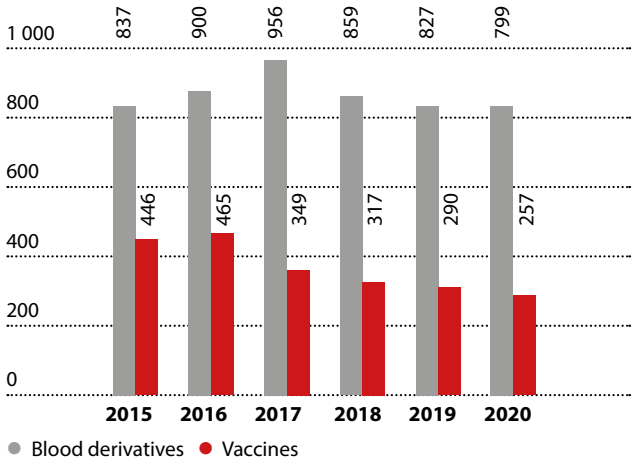
Legend: Number of analysed samples

Fig. 2 **Development in the number of non-compliant samples in 2015–2020 (%)**



Legend: Non-compliant samples (%)

Fig. 3 **Number of released batches in 2015–2020**



International Cooperation in the Sphere of Laboratory Control

The Department has been 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 2020, the Laboratory Control Department participated in collaborative international studies listed in Table 11.

Tab. 11 **Participation in international studies**

Study	Study name	Rating
PTS 202	Immunoglobulin molecular-size distribution	good
PTS 203	Bacterial endotoxins (vaccines samples)	good
PTS 204	Potentiometric determination of pH	good
PTS 206	Loss on Drying	good
CRS	Gammacyclodextrin	good
SUP 009	Suspected unknown product	good
CAP 2020/46	Xagrid	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.

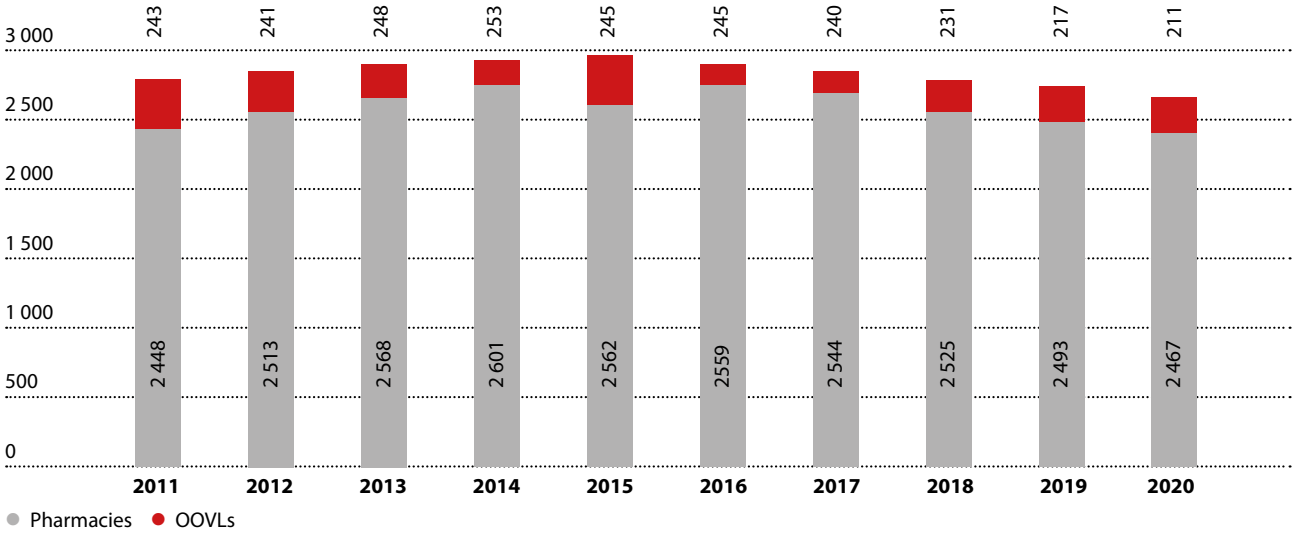
SUP – A comparative study to verify the laboratory's ability to analyse Suspected Unknown Products.

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 2020, the Institute kept a record on 2,467 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 211 detached pharmaceuticals and medical device dispensing units (hereinafter referred to as "OOVL"), 3,124 vendors of selected medicinal products for human use, 42 nuclear medicine departments of healthcare facilities, and 401 wholesale distributors of medicinal products. Compared to 2019, the total number of pharmacies decreased by 26 entities and the number of OOVLs by six units (Fig. 4).

Fig. 4 **Number of pharmacies and OOVLs in the last 10 years (as of 31 December 2020)**



In 2020, the inspectors of the Pharmacy and Distribution Department conducted the total of 570 inspections in pharmaceutical care facilities – pharmacies, of which 22 were hospital pharmacies of inpatient care providers. Of the total number of completed inspections, 19 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 344 pharmacies.

Price control focusing upon compliance with the Act on Prices and rules of price regulation was conducted in 98 pharmacies and ten wholesale distributors.

On the basis of facts identified during the conducted inspections, the total of eight admonitions and 110 final decisions on imposition of a fine for breach of obligations stipulated by the Act on Pharmaceuticals in the total amount of 18,125,000 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. One fine in the total amount of 150,000 CZK was imposed for failure to cooperate during the inspection. In eight cases, the preparation of medicinal products was suspended for a pharmacy due to unverified or non-validated equipment (weights, laminar boxes).

The main reasons for the issuance of a decision imposing an administrative penalty included serious shortcomings in the record-keeping of the number of pieces received, stocked and dispensed; dispensing of medicinal products without medical prescription or on invalid prescriptions, dispensing by unauthorised staff; dispensing of products with a quality defect for which they should have been withdrawn from the market; illegal distribution and export of medicinal products from the pharmacies 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 or active substances and excipients without quality documentation for preparation.

Within the scope of inspections of the handling of dependency-producing substances in pharmacies, in 2020, identification of major breaches of the Act on Dependency-Producing Substances resulted in the total of one admonition and 22 final decisions on fine imposition upon pharmacy operators, of which the fines for offences referred to under this Act amounted to the total of 250,000 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 control of handling precursors, no final decision on fine imposition pursuant to the Act on Precursors was issued in 2020, only one aggregate fine.

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.

Inspections focusing on compliance with price regulation rules in pharmacies identified a breach of price regulations in 52 cases. In 2020, 17 decisions on administrative penalty imposition became final, of which two cases involved financial sanctions amounting to 54,000 CZK and the other cases were imposed admonitions for price offences concerning 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.

Within the scope of regular inspection activities of the Institute, no breach of the ban on the offering and provision of advantageous sale in the dispensing of prescription-only medicinal products reimbursed from the public health insurance was identified.

In 2020, the total of five decisions on fine imposition for the breach of the Act on Public Health Insurance identified in the previous period became final; the fines amounted to 611,000 CZK in total; in one case an admonition was issued instead of a financial sanction.

In 2020, moreover, 178 inspections of the handling of medicinal products in healthcare facilities were carried out. The inspections took place in 11 inpatient departments of healthcare service providers and in 167 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 six targeted inspections were performed. In total, four admonitions and ten final decisions on fine imposition in the total amount of 1,370,000 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 administrative penalty imposition included, in particular, procedures contrary to the summary of the product characteristics; evidenced storage of medicinal products outside the scope of the authorisation for healthcare service provision; shortcomings associated with recalls of medicinal products due to their quality defects; serious or multiple breaches of the obligations governing the handling of medicinal products set forth by implementing legal regulations; or illegal activities associated with the electronic prescription system.

In 2020, inspections of vendors of selected medicinal products involved 107 outlets in total, of which two were targeted inspections. In total, two admonitions and 28 final decisions on fine imposition in the total amount of 270,000 CZK for breach of the obligations implied by the Act on Pharmaceuticals were issued. One fine for failure to cooperate during the inspection in the amount of 10,000 CZK was finally imposed. 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 15 inspections were carried out; the findings from the inspections did not result in the need for the imposition of any administrative penalty.

Summary results from inspections completed in 2020 are provided in Table 12.

Tab. 12 **Inspection surveillance over pharmacies, nuclear medicine departments, healthcare facilities, and vendors of selected medicinal products in 2020**

			Classification of defects						Penalties		
Inspected entity	**Inspection type**	**Number**	**1**	**%**	**2**	**%**	**3**	**%**	**A**	**B**	**C**
Pharmacies	Regular inspections	*570	364	64,0	144	25,3	61	10,7	8	-	119
	Price controls	98	-	Not rated by classification of defects					-	-	17
	Inspections of dependency -producing substances and precursors	344	289	84,0	45	13,1	10	2,9	-	-	23
ONMs		12	11	91,7	-	-	1	8,3	-	-	-
HAVs		3	1	33,3	2	66,7	-	-	-	-	-
Healthcare facilities		178	131	73,6	38	21,3	9	5,1	-	-	14
Vendors of selected medicinal products		107	69	64,5	21	19,6	17	15,9	-	-	31

** One pharmacy inspection not rated.*

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 – Administrative penalty imposed (final decision)

In 2020, inspectors from the Pharmacy and Distribution Department took a total of 213 samples of medicinal products during inspections in pharmacies, of which 84 were samples of pharmaceutical products intended for the preparation of magistral formulas in the pharmacy. Out of 129 pharmacy samples (medicinal products prepared in pharmacies), seven were out-of-specification, the defect being out-of-specification content of active substances in four cases, and out-of-specification pH in the remaining three cases. In five samples intended for dispensing, defects in their labelling were identified.

Other activities of the Pharmacy and Distribution Department include issuance of binding opinions on the technical and material equipment of pharmacies for the purposes of gaining authorisation for the provision of healthcare services. In 2020, the total of 230 applications for issuance of an opinion were received from pharmacy operators and 229 favourable binding opinions were issued.

In 119 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 five cases, with an inspection of the OOVL (Table 13 refers). Furthermore, in this context, 129 consultations on the technical equipment of existing pharmacies or the construction of new pharmacies, and 418 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. 13 **Other activities of the Pharmacy and Distribution Department**

Other activities of the Pharmacy Distribution Department	Other activities of the Pharmacy and Distribution Department	Other activities of the Pharmacy Distribution Department
119	46/7	72/13
Initial OOVL inspection	**Consultations on material and technical equipment**	**Other consultations**
5	129	418

Distribution of Medicinal Products

In 2020, the number of distributors exhibited a year-to-year decrease by nine entities to the total of 401 medicinal products distribution authorisation holders. Of the total number of authorised distributors, 111 entities were both a distribution authorisation holder and a pharmacy operator.

In 2020, 34 new distribution authorisations and 128 decisions on variations to distribution authorisations were issued, and 34 authorisations were revoked upon request of their holders. In four cases, the distribution authorisation expired in compliance with Section 76(4) of the Act on Pharmaceuticals and in respect of five entities, the authorisation was revoked by the decision of the Institute pursuant to Section 76(3) of the Act on Pharmaceuticals.

The total of ten entities applied for entry into, variation to entry in, or deletion from the Registry of Brokers of Human Medicinal Products in 2020; as of 31 December 2020, the Registry included 49 entities in total. Table 14 provides an overview of received applications and issued decisions in respect of distribution authorisation, variations thereto or revocation thereof, and the registration of brokers of medicinal products.

Tab. 14 **Distribution and brokerage of pharmaceuticals in 2020**

	Received applications	Decisions issued/Registry entries made
Application for distribution authorisation	32	34
Application for variation to distribution authorisation	114	128
Application for revocation of distribution authorisation	30	34
Application for entry in the Registry /variation to entry in the Registry/deletion from the Registry	10	9

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

In 2020, the total of 259 inspections of distributors and seven inspections of brokers were conducted, of which eleven were targeted inspections carried out on the basis of internal and external reports. In total, 12 reports on the operation of distributors were received; in five cases, a declaration of non-compliance with the rules of Good Distribution Practice (GDP) was 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, control of compliance with the distributor's obligation to notify in advance of their intention to export a medicinal product placed on the list of the Ministry of Health of the Czech Republic abroad and observation of the ban on export, 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 187 rated inspections of distributors (follow-up and targeted inspections), 76 % were rated with grade 1 (good), 15.5 % with grade 2 (satisfactory), and 8.5 % with grade 3 (not satisfactory). On the basis of identified facts, in 24 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 16 post-inspection good distribution practice certificates were issued, of which six certificates were of limited validity (for one year in two cases; for two years in two cases; and in respect of two 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, with the authorisation of the Strasbourg EDQM inspectorate and the Institute's Laboratory Control Department, 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 43 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, HPRA or EMA).

The Good Distribution Practice Unit organised a good distribution practice seminar for distributors; due to a high number of those wishing to participate, the seminar was held on two different days. The content of the seminar focused particularly upon the issue of information system validations; other presentations concentrated on the control of safety features and ensuring the availability of medicinal products.
In 2020, ten 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 six 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.

On the basis of facts identified during the completed inspections, distributors were imposed three admonitions and the total of 17 final decisions on fine for breach of obligations set forth by the Act on Pharmaceuticals and its implementing regulations amounting to 2,415,000 CZK in total (incl. also finalised administrative procedures based on inspections conducted in the previous period).

The main reasons for the proposed fine imposition included failure to comply with GDP rules; failure to file an application for variation to the distribution authorisation in case of changes concerning the distributor; distribution of medicinal products to unauthorised clients; distribution outside the territory of the Czech Republic contrary to the issued measure of the Ministry of Health of the Czech Republic; failure to notify of the intention to distribute a medicinal product placed on the list of the Ministry of Health of the Czech Republic abroad; and serious shortcomings in the keeping of regulatory and record documentation of the distributor.

In five cases, the distribution authorisation was suspended and declarations of non-compliance with GDP rules were issued due to serious breaches of the obligations laid 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 2020 are shown in Table 15.

Tab. 15 **Inspection surveillance over distributors**

	Number of inspections				Inspection rating			Measures	
Total	Initial	Follow-up	Targeted	Variation	1	2	3	NCR	Proposed fine
259	36	176	11	36	142	29	16	5	24

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 com¬pliance with the principles of good distribution practice is expressed by the following rating:

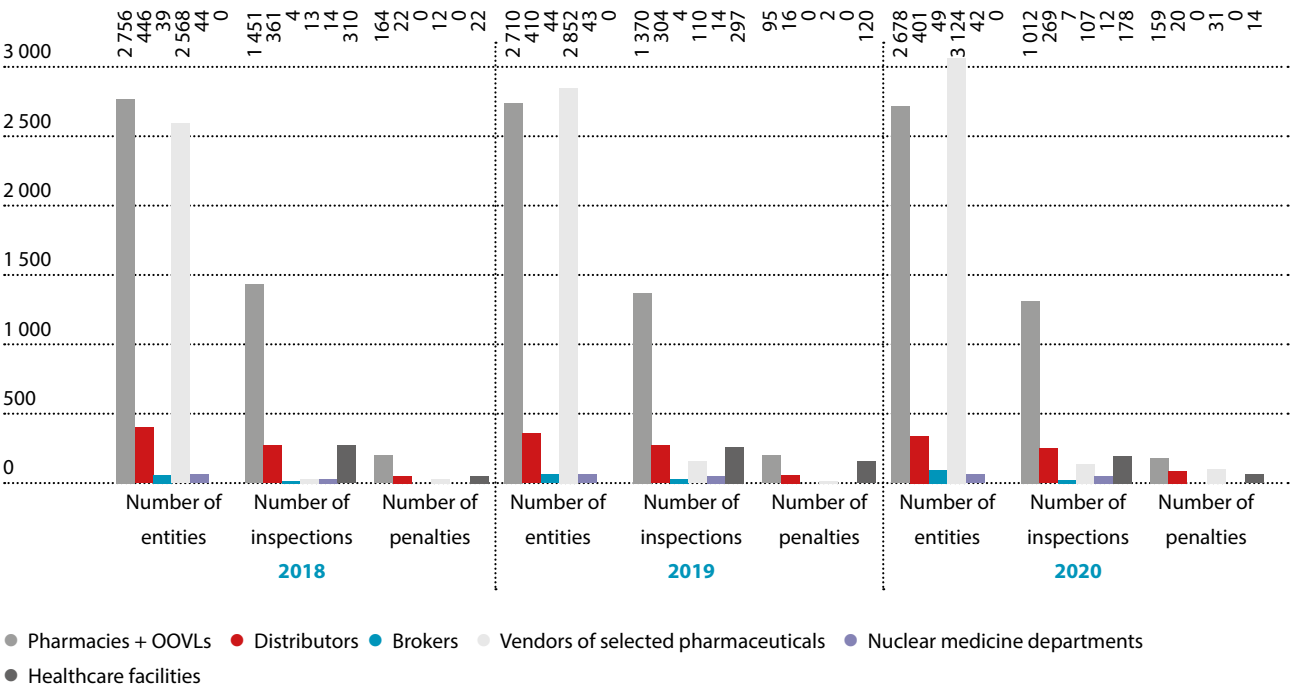
1 – Good;

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. 5.

Fig. 5 **Information on surveillance activities in 2017–2020**



4.8 Surveillance in the Area of Manufacture of Pharmaceuticals, Human Tissues and Cells, Good Laboratory Practice and Good 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 of active substances, 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 provides for 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 118 applications for manufacturing authorisation or variations thereto were received (Tab. 16). The number of cases brought forward from one year to another corresponds to the intervals for application processing.

Human Tissues and Cells

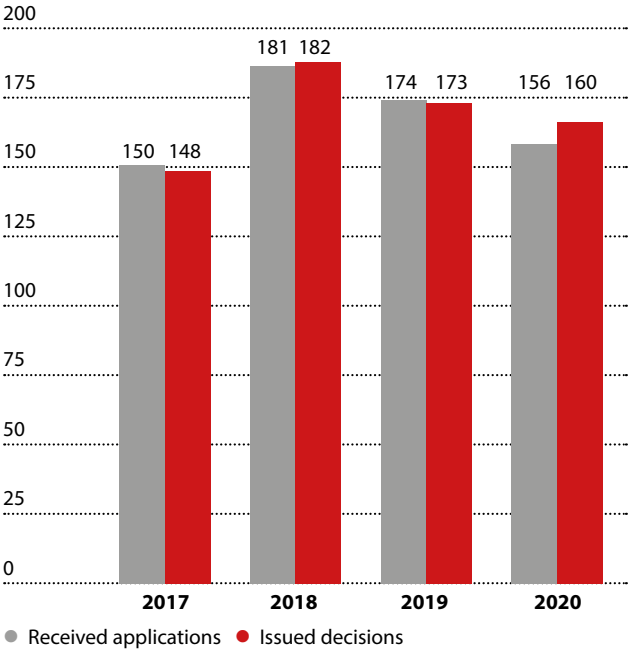
This is an area regulated by the Institute pursuant to Act No 296/2008 Coll., on Human Tissues and Cells.

In 2020, 38 applications for authorisation to engage in an activity and applications for variations thereto were received.

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

Typ žádosti		2017		2018		2019		2020	
		Received applications	Issued decisions	Received applications	Issued decisions	Received applications	Issued decisions	Received applications	Issued decisions
Application for manufacturing authorisation	Manufacturers of medicinal products	4	4	2	1	2	2	4	4
	Control laboratories	1	1	2	0	1	3	0	0
	Blood centres	2	3	1	1	3	3	1	1
Application for variation to manufacturing authorisation	Manufacturers of medicinal products	56	53	58	57	59	60	53	52
	Control laboratories	2	3	3	3	1	1	5	5
	Blood centres	27	26	39	40	45	44	49	47
Application for manufacturing authorisation revocation	Manufacturers of medicinal products	0	1	5	5	4	5	6	6
	Control laboratories	2	2	3	3	1	1	0	0
	Blood centres	1	1	1	1	0	0	0	0
Application for operating authorisation for:	Tissue centre	3	2	4	5	1	1	1	3
	Distribution of tissues and cells	1	0	3	4	1	1	1	1
	Donation centre	0	0	0	0	0	0	0	0
	Diagnostic laboratory	3	2	1	1	1	0	0	1
Application for variation to operation of:	Tissue centre	40	39	44	48	43	38	27	32
	Distribution of tissues and cells	-	-	1	0	0	1	0	0
	Donation centre	1	1	0	0	0	0	0	0
	Diagnostic laboratory	4	6	4	4	9	9	7	7
Application for revocation of operation of:	Tissue centre	1	1	7	6	0	1	1	1
	Distribution of tissues and cells	-	-	-	-	0	0	0	0
	Donation centre	0	0	0	0	2	2	1	1
	Diagnostic laboratory	2	2	3	3	1	1	0	0
Total		**150**	**148**	**181**	**182**	**174**	**173**	**156**	**160**

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



In 2020, 230 inspections in total were completed, of which 53 inspections were associated with the regulated area of tissues and cells. Their character and resulting ratings are provided in Table 17. A comparison of the number of inspections and breaches of the Act on Pharmaceuticals, or of the Act on Human Tissues and Cells, where applicable, in the period of 2017–2020 is provided in Table 17 and in Fig. 7 and 8.

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 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 rating of other criteria. 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 92 inspections at manufacturers' of medicinal products and active substances or in control laboratories, no breach of the Act on Pharmaceuticals was identified. 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. 17 **Inspections conducted in 2020 and their outcomes**

	Number of inspections						Inspection rating		
	Total	Initial	Follow-up	Targeted	Variation	Complian[1)]	Non -compliant	Breach of law	Fine/ Order
Manufacturers of medicinal products	56	5	39	2	10	44	0	1	0
Manufacturers of active substances	22	1	14	4	3	15	0	0	0
Control laboratories	10	0	8	0	2	8	0	0	0
Active substance importers	4	4	0	0	0	4	0	0	0
Blood centres	62	1	47	6	8	48	0	0	0
Blood banks	2	0	2	0	0	2	0	0	0
GCP inspections – Ethics Committees	2	0	0	2	0	0	0	0	0
GCP inspections – others	19	0	0	18	1	0	0	0	0
TC, DC, DL, DIS inspections	53	5	36	3	9	41	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. 18 **Inspections conducted in 2017–2020**

	2017		2018		2019		2020	
	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	57	8	58	9	59	2	56	1
Manufacturers of active substances	20	1	14	0	23	3	22	0
Control laboratories	22	0	8	0	17	0	10	0
Active substance importers	5	0	2	0	4	0	4	0
Blood centres	57	0	51	0	64	0	62	
Blood banks	22	0	19	0	11	0	2	0
GCP inspections + ethics committees	25	0	34	1	33	1	21	0
Tissue centres, donation centres, diagnostic laboratories	84	0	101	0	59	0	53	0
Total	**292**	**9**	**286**	**10**	**270**	**6**	**230**	**0**

Fig. 7 **Number of manufacturers of medicinal products and of active substances and control laboratories and an overview of completed inspections**

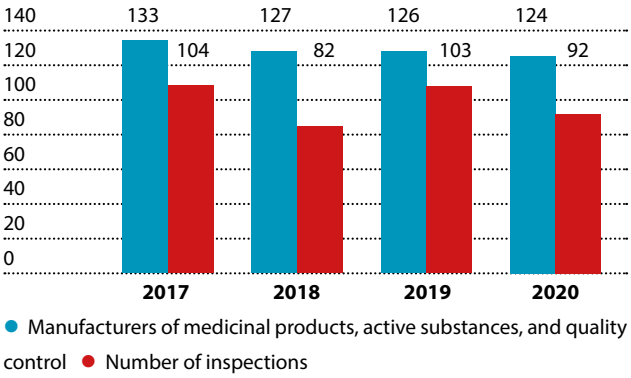
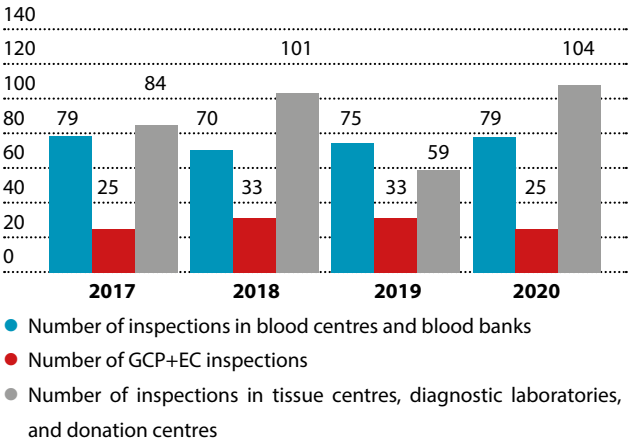


Fig. 8 **Overview of completed inspections in the area of blood centres + blood banks, GCP + EC, and HTC (tissue centres, diagnostic laboratories, donation centres) in the period of 2017–2020**



Haemovigilance

In 2020, 36 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, twelve SARs involved blood or blood component donors and 14 SARs concerned post-transfusion reactions in transfusion product recipients (eight cases of anaphylaxis; three haemolytic reactions arising from AB0 system incompatibility; and three cases of a transfusion-related acute lung injury (TRALI)). In twelve 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 one patient, the reaction resulted in mild consequences; and in another patient in severe consequences. In eight cases, the donors of blood or blood components fully recovered from the SAR; one donor suffers mild consequences; in three cases it was not possible to find out the result.

Furthermore, 15 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. Five cases did not constitute a SAE; one suspected SAE is still pending. Two cases constituted product confusion; two cases involved dispensing of inappropriate transfusion product; two cases donor's retrospective report about an illness; two cases a sample NAT positivity of an already dispensed transfusion product; one case concerned quarantine at transfusion department. 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), in 2020, the Institute received ten new reports and twelve complementary reports from six countries. All of the cases involved an epidemiological situation (in six cases associated with the occurrence of the West Nile virus; in three cases with COVID-19, and in one case with the occurrence of the dengue fever).

Good Laboratory Practice (GLP)

In 2020, 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, four follow-up inspections were completed.

Good Clinical Practice (GCP)

Due to the emergency measures associated with the COVID-19 pandemics, in 2020, the number of good clinical practice inspection dropped compared to previous periods.

In the course of 2020, the total of 21 inspections of good clinical practice were conducted. Of the said number, 18 concerned a targeted inspection of a trial site (a GCP inspection at the investigator's), one was a follow-up inspection of a contract research organisation on the basis of an application for the issue of a Good Clinical Practice Certificate, and two were targeted ethics committee inspections.

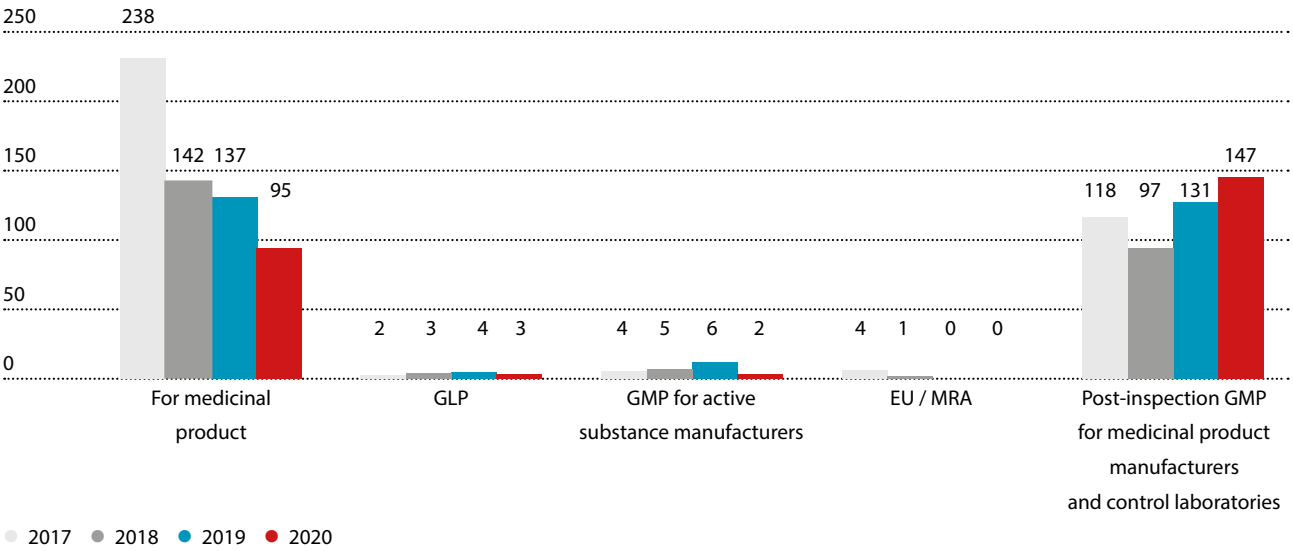
Actions and Penalties

In 2020, one breach of the Act on Pharmaceuticals was identified.

Certification

In total, 247 various certificates were issued. Post-inspection good manufacturing practice certificates are 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. 9 **Issued certificates**



Assessment of GMP Compliance within the Scope of Marketing Authorisation Activities

A total of 1,017 cases were received (a 24% decrease compared to 2019); all of them were processed within predefined timelines.

Foreign Inspections

In 2020, two good manufacturing practice inspections at foreign entities were conducted.

Tab. 19 **Foreign inspections**

	2017	2018	2019	2020
Number of inspections	8	4	7	2
Certificate issuance	3	1	4	1
Issued non-compliance	0	0	1	0

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 (Table 20 refers).

Tab. 20 **Number of reports received in 2020**

Quality defects	2014	2015	2016	2017	2018	2019	2020
Reports received in total	345	333	420	443	496	497	496
Reports from the Czech Republic	181	181	243	277	286	284	304
Reports from abroad	164	152	177	166	210	213	192
Resulted in recall (in SÚKL codes)	60	79	72	79	89	59	47
Administrative procedure (since 04/2017)	-	-	-	20	33	81	55
Rapid Alert	6	11	17	22	6	15	1

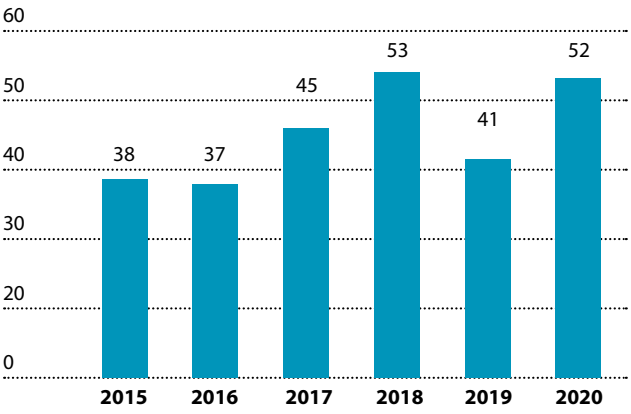
Explanatory notes: Rapid alert = a rapid alert notification sent by the Institute within the scope of the international Rapid Alert system

Within the scope of addressing quality defects, effective actions have been taken to reduce the impact of quality defects of pharmaceuticals upon patient health. In 2020, 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 192 reports on quality defects of pharmaceuticals.

The Quality Defects Unit addresses also motions to initiate an administrative procedure regarding the possibility to distribute, dispense, place on the market, or use 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 2020, 55 administrative procedures were commenced and 55 final decisions were issued; these concerned 99 medicinal products (in SÚKL codes) and 165 batches of medicinal products.

The Quality Defects Unit addresses also reports concerning the occurrence of counterfeit medicinal products in the legal distribution chain or their theft. In 2020, the Quality Defects Unit addressed 52, such cases in total, of which four cases concerned theft of medicinal products from the legal distribution chain.

Obr. 10 **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 2020, the Quality Defects Unit received and evaluated 23 such reports in total. Furthermore, the Quality Defects Unit monitored the recall of five medicinal products (in SÚKL codes) for marketing authorisation reasons (changed method of dispensing and ongoing European review).

An overview of measures taken in this year for individual medicinal products (in SÚKL codes) is provided in Table 21. All of these cases concerned actions taken and implemented by the marketing authorisation holders or operators themselves; the Institute was only monitoring or adjusting their actions.

Tab. 21 **Actions taken in 2020, (related to SÚKL codes)**

Actions taken	Number
Recall from distributor level	0
Recall from healthcare facility level	46
Recall from patient level	1
Suspended distribution, dispensing and/or use	4
Released distribution, dispensing, and use	4
Permitted distribution, dispensing, marketing, and use in the provision of healthcare services through an administrative procedure	99 (number of batches: 165)

Mutual exchange of information and cooperation with the Slovak authority, ŠÚKL in Bratislava, continued and in 2020, the Quality Defects Unit cooperated with ŠÚKL in several cases.

The Quality Defects Unit was involved in the preparation of adaptation of Regulation 161/2016, 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 2020, working meetings

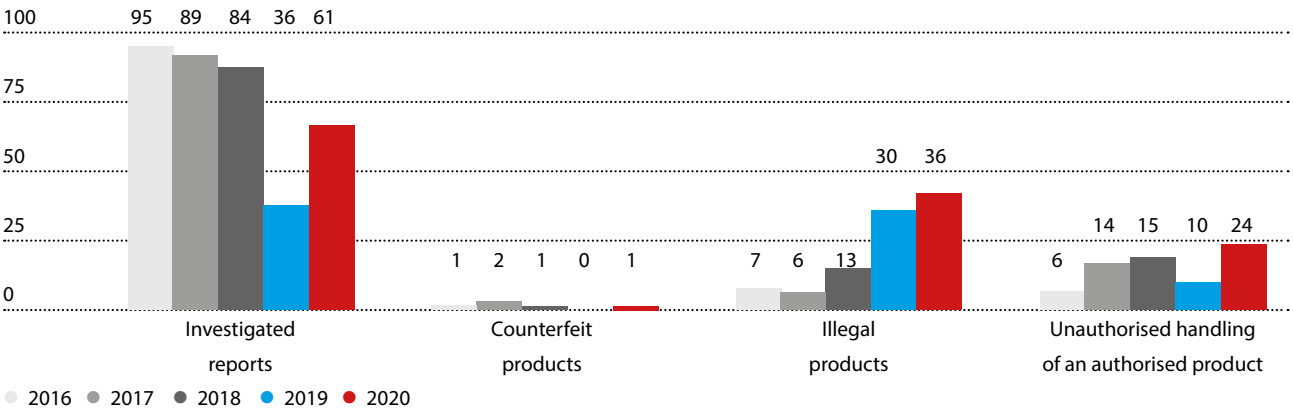
aimed at enhancements to the web interface and electronic form for the reporting of unsuccessful verification of safety features by the concerned entities were held. The representatives of the Institute regularly participated in the meetings of the expert group for safety features and in international teleconferences.

For 2020, the Institute recorded the total of 216,880 reports on unsuccessful safety feature verification (for the entire period from 9 February 2019 to 31 December 2020, this number amounted to 1,140,270 reports in total). In the course of this year, the Quality Defects Unit communicated with 20 marketing authorisation holders in respect of whose products a high number of such reports was identified. In the course of 2020, the Unit issued favourable recommendations for the total of eight medicinal products and 16 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 38 reports concerning suspected broken anti-tamper devices (ATDs).

4.10 Enforcement

In 2020, 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.

Fig. 11 **Control activities in the period of 2016–2020**



In 2020, a total of 61 reports (either the Institute's own or received reports) were investigated. In 2020, the Institute was monitoring and detecting illegal offers of medicinal products in the internet environment and executed 24 control purchases. Thirty-six cases of handling of unauthorised medicinal products and 24 cases of unauthorised handling of authorised medicinal products were identified.

In 2020, the Institute prepared a total of 150 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 2020, the Institute investigated a total of 134 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 2020, the Institute received five new reports less than in 2019 (139 newly received reports in 2019). In 2020, seven administrative procedures were completed which resulted in the imposition of eight fines in the aggregate amount of 1,090,000 CZK.

The subject of investigation into advertising was printed advertising matter (72 %) and websites (28 %).

Advertising for prescription-only medicines accounted for 51 % of the investigated cases, advertising for over-the-counter medicines represented 49 % of cases.

Pharmaceutical companies or their legal representatives filed 4 % of reports on suspected breaches of law, 2 % of reports were filed anonymously, 6 % were lodged by private individuals, 4 % by state administration bodies, and 84 % by SÚKL employees.

Tab. 22 **Overview of investigated reports of suspected breaches of the Act on Advertising Regulation in 2020**

	Reports brought forward from 2019	Newly received reports in 2020	Total
Number of reports	3	131	134
Investigation completed	3	117	120
Forwarded for commencement of administrative procedure	0	11	11
Completed administrative procedures	0	4	4
Number of finally imposed fines	0	4	4

Fig. 12 **Overview of investigated reports of suspected breaches of the Act on Advertising Regulation (2016–2020)**

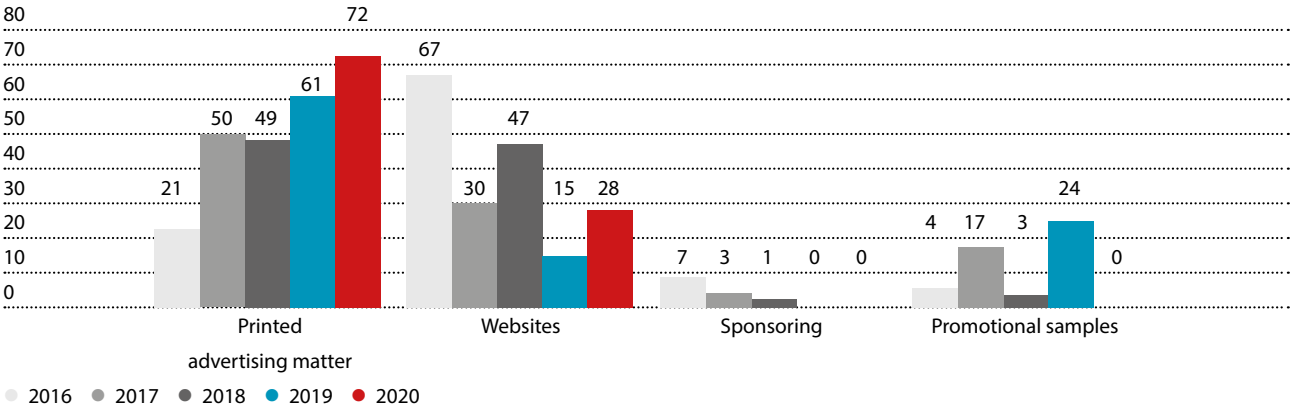
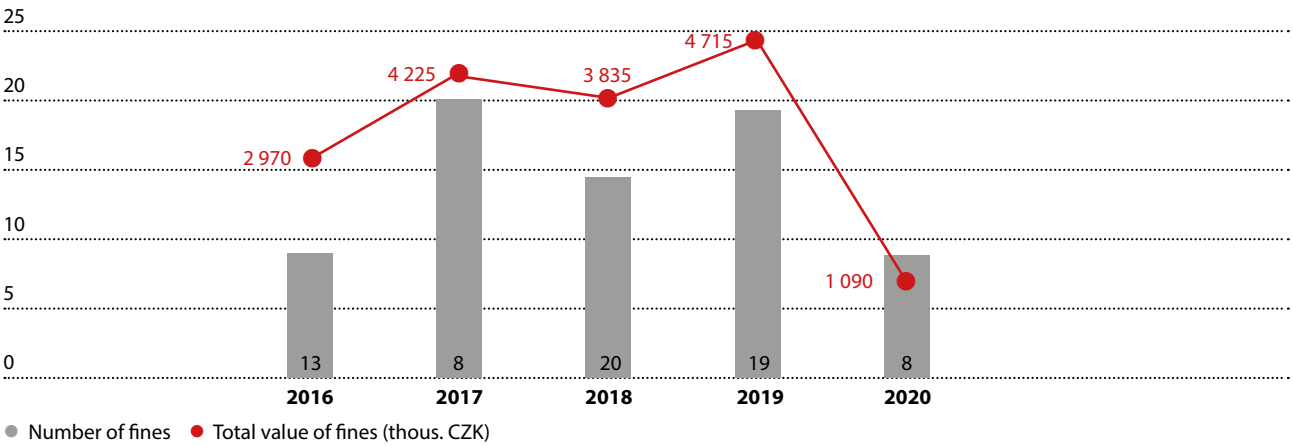


Fig. 13 **Overview of fines imposed for breaches of the Act on Advertising Regulation (2016–2020)**



Upon request, the Institute issued/provided 60 expert opinions/consultations on the issue of proposed advertising for medicinal products for human use.

The inspectors of the Advertising Regulation Unit completed 20 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 2020, the Institute commenced investigation into 96 cases of various products, most often dietary supplements and cosmetic products, for suspected classification as a medicinal product. In 37 cases, an administrative procedure regarding the nature of the product was initiated ex officio or upon request. In 2020, the Institute reclassified the total of 17 products to the group of medicinal products. Upon request, it provided four 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 2020, the Pharmacopoeia employees prepared for print third supplement to the Czech Pharmacopoeia 2020 (hereinafter referred to as "Suppl. 2020"). In its European part, it contains the translations of the body of the tenth edition of the European Pharmacopoeia Ph. Eur. 10.0 and its two supplements (Suppl. 10.1 and 10.2). Nevertheless, as the amount of texts is rather extensive (including not only the 10th edition, but also two subsequent supplements), it was necessary to split the publication into two sections and apply a different order of chapters than the one used in the previous years. The first section contains the National Part, the General Part of the European Part, and beginning of the Special Part (vaccines for human and veterinary use, herbal drugs, radiopharmaceuticals, homeopathic products, and sutures). In the second section, the Special Part of the European Part continues with new and revised chemical and biological monographs for active substances, excipients, and medicinal products.

The European part contains the total of 766 texts, of which the General Part includes 70 general texts (of which five are new ones), six general articles, and ten revised general articles concerning pharmaceutical forms. The Special Part contains texts for 33 vaccines for human use (of which one is new) and 40 monographs on veterinary vaccines (of which one is new), two revised monographs on immunosera for human use, four revised monographs on radiopharmaceuticals, 47 herbal drug monographs (of which four are new), twelve monographs on homeopathic products (of which one is new), and two revised monographs of surgical sutures for use in man. The number of chemical and biological monographs on active substances, excipients, and medicinal products amounted to 540 (of which 15 were new).

The National Part of Suppl. 2020 contains 22 texts in total. Its General Part includes the full version of Tables I, II, III, IV, V, X, and XII, which contain active substances included in Czech Pharmacopoeia 2017, in Suppl. 2018, in Suppl. 2019 as well as in Suppl. 2020. 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 and reference substances used in national monographs.

The Special Part of the National Part contains a new monograph *Adeps suillus stabilisatus* and redrafted and revisited monograph *Butamirati citras*. Furthermore, due to minor corrections, the following monographs were revised: *Acaciae mucilago, Aqua carminativa rubra, Aqua conservans, Mannitoli infusio, Propranololi hydrochloridi solutio cum acido citrico, Propranololi hydrochloridi solutio cum natrii hydrogenophosphate, Ethanolum benzino denaturatum, Ibuprofeni suppositorium, Paracetamoli suppositorium, Paracetamoli suppositorium pro infantibus,* and *Sulfathiazoli globulus.*

For monograph *Butamirati citras,* new national reference substances were prepared (CRLN; five in total).

Monograph Deferasiroxum was deleted from the National Part (due to replacement with the European monograph *Deferasiroxum* (2933), published in Ph. Eur. – Suppl. 10.3, binding as of 1 January 2021).

Monographs *Adeps suillus stabilisatus* and **Butamirati citras** were presented for public inquiry and notified under no. 2020/348/CZ as per Directive (EU) 2015/1535 of the European Parliament and of the Council of 9 September 2015 laying down a procedure for the provision of information in the field of technical regulations and of rules on Information Society services.

Czech Pharmacopoeia 2017 – Suppl. 2020 was published in cooperation with the Grada Publishing house in two volumes as binding from 1 December 2020 and it is available also in electronic format (on a USB). The electronic version is complete and it contains all unrevised texts of Czech Pharmacopoeia 2017 along with new and revised texts of Suppl. 2018, Suppl. 2019, and Suppl. 2020.

Tab. 23 **Number of texts in the European Part of Czech Pharmacopoeia 2017 – Suppl. 2020**

European Part	General Part	Special Part	Total
New	5	22	27
Revised	81	658	739
Total	**86**	**680**	**766**

Concurrently with the proof-reading and print preparation of Suppl. 2020, translations and revisions of three other European Pharmacopoeia supplements were under way (Suppl. 10.3, 10.4, and 10.5). The three European editions will form part of Czech Pharmacopoeia 2017 – Supplement 2021 (hereinafter referred to as "Suppl. 2021"). In the European Part, this concerns approximately 380 texts.

In the second half of 2020, works on the National Part of Suppl. 2020 began; also in this case, updated tables will be included.

In September 2020, in cooperation with the laboratories and the Pharmacy Section of the Pharmacopoeia Commission, the "Shelf-Life of Magistral Formulas" project was completed; 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%. The results are contained in revised Table XVI: Storage and shelf-life of products prepared in pharmacies (revision in Suppl. 2021).

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 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 2020, these meetings were only virtual).

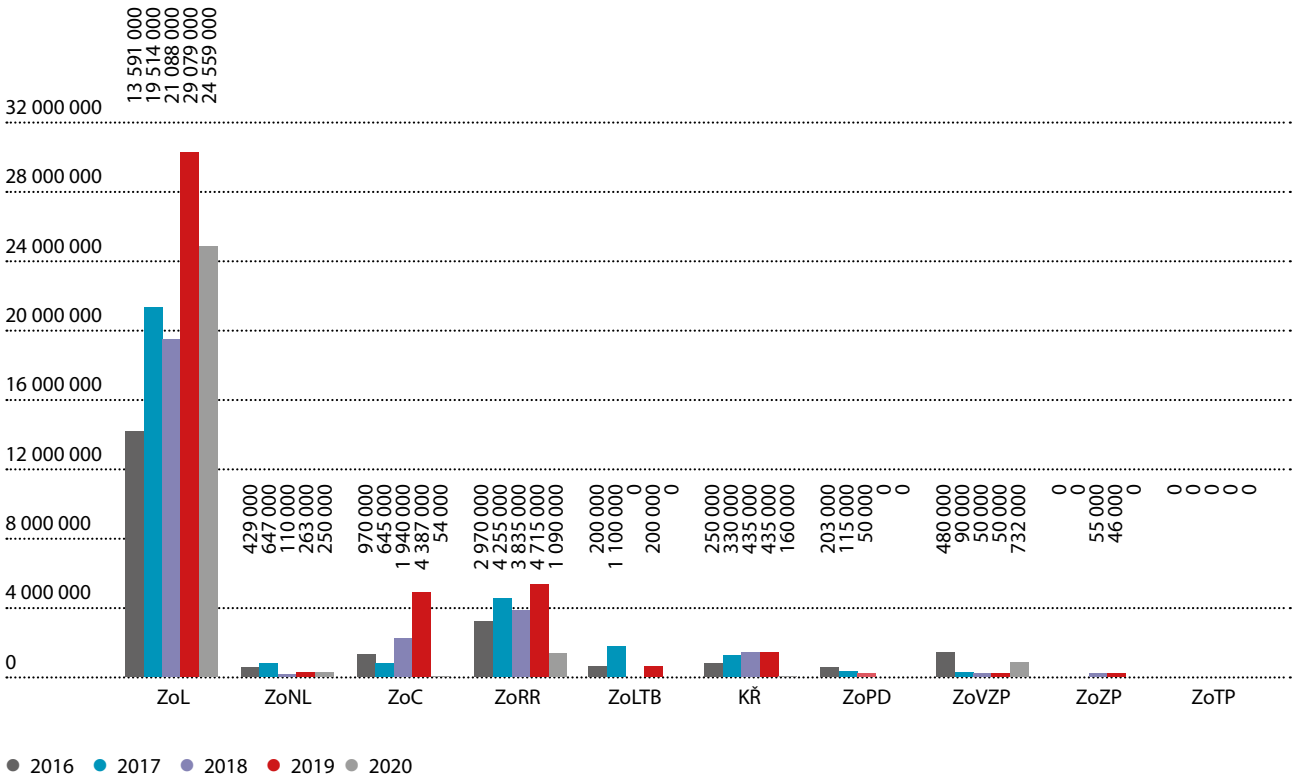
State Institute for Drug Control

Annual Report **2020**

4.13 Imposed Penalties

Based on its *ex-officio* findings or findings from reports received from the Czech Police and other administrative bodies of the Czech Republic as well as on the basis of 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 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 2020. 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 2020, in the area of penalties, the Institute continued also the imposition of penalties in the form of so-called aggregate fines for committed 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, as amended, in its practice of administrative penalisation. Pursuant to this Act, the Institute has also the option to impose an admonition as an administrative penalty instead of a financial sanction where less serious offences are concerned. Compared to 2019, the Institute availed of this option more often in 2020.

Fig. 14 **Imposed penalties which became final in 2015–2020 (in mil. CZK)**



- *ZoL* *Act on Pharmaceuticals*
- *ZoNL* *Act on Dependency-Producing Substances*
- *ZoC* *Act on Prices*
- *ZoRR* *Act on Advertising Regulation*
- *ZoLTB* *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 on Products*

■ 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..

4.14 Pricing and Reimbursements

In the course of 2020, the Section continued in the initiation of in-depth reimbursement revisions in accordance with the schedule. For 2020, the initiation of 17 in-depth revisions was scheduled, of which 15 in-depth revisions (254 SÚKL codes) were actually commenced. The difference in the number of scheduled and initiated in-depth revisions reflects the 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 practice in the Czech Republic.

For 2020, in-depth revisions of maximum prices of medicinal products subjected to price regulation through the determination of maximum price for which the maximum price had been determined were planned and also completed during the year. In compliance with the Act on Public Health Insurance, maximum price revisions were conducted for each reference group or group of principally therapeutically replaceable products separately.

Maximum Ex-factory Prices

Tab. 24 **Overview of administrative procedures in 2020**

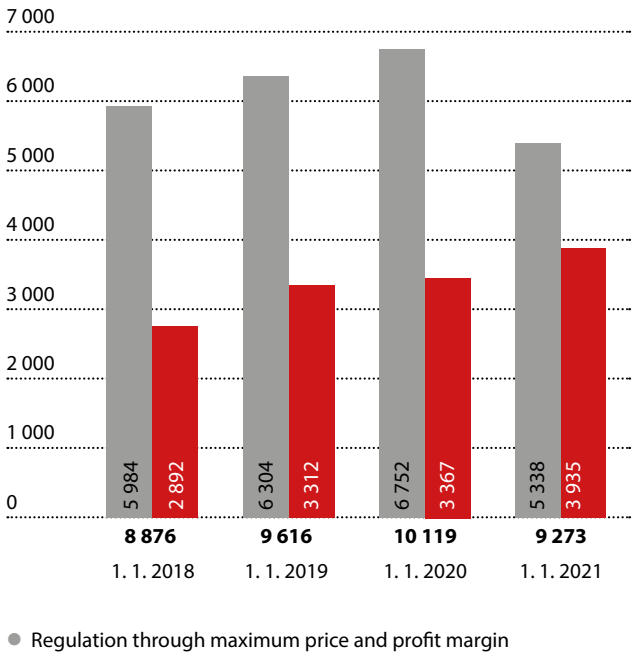
Applications for maximum ex-factory price determination	Number of SÚKL codes
Initiated	254
Decided	252
Appeal procedure pending	0
Became final	252
Applications for maximum ex-factory price change	
Initiated	221
Decided	140
Appeal procedure pending	2
Became final	134
Applications for maximum ex-factory price reduction – abbreviated procedure	
Initiated	2
Decided	2
Appeal procedure pending	0
Became final	2
Applications for maximum ex-factory price revocation	
Initiated	1
Decided	0
Appeal procedure pending	0
Became final	0
Maximum price in-depth revisions	
Initiated	3 327
Decided	1 866
Appeal procedure pending	0
Became final	1 866

The principal legislation governing the area of price regulation for 2020 was the Price Regulation of the Ministry of Health of the Czech Republic 1/2020/CAU, 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 5/2020/CAU, 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 – the Price Regulation with effect as of 1 January 2020 and the Price Decision with effect as of 1 March 2020; and due to the change in the Price Decision, the number of applications for maximum price determination increased in 2020.

In 2020, 134 administrative procedures regarding the maximum ex-factory price change were commenced (compared to 47 administrative procedures in 2019); applications filed by marketing authorisation holders prevailed (17 applications were filed by health insurance companies and 117 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. Compared to 2019, however, the share of products regulated by profit margin only apparently increased in 2020 (Fig. 15)

Fig. 15 **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. 25), it may be stated that in the individual months of 2020, the numbers of medicinal products in all of the maximum price zones were decreasing continuously throughout the year. The most significant decrease occurred in the zone of More than 1,000 CZK up to 2,000 CZK incl. and More than 500 CZK up to 1,000 CZK incl.

Development of Average End-User Prices

In 2020, there was no change to the profit margins or to the VAT, the rate of which for medicinal products remained 10 % also in 2020. In respect of medicinal products regulated by the maximum price (maximum price determined by an administrative procedure and profit margin as per the Price Regulation), the average end-user price increased by 9.9 %. The highest increase of average prices occurred in the highest price zone. 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 26.6 %, with the highest increase in the seventh price zone. The situation in ex-factory price levels (ex. profit margin and VAT) focusing upon a more detailed comparison of the latest quarters of 2019 and 2020 is illustrated by Fig. 16 and 17.

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

Price regulation zone	01	02	03	04	05	06	07	08	09	10	11	12
Up to 20 CZK incl.	21	21	20	19	19	19	18	18	18	20	20	21
More than 20 CZK up to 50 CZK incl.	410	403	312	291	289	293	275	269	273	279	279	282
More than 50 CZK up to 100 CZK incl.	886	881	786	704	705	701	687	689	708	726	730	733
More than 100 CZK up to 200 CZK incl.	1,096	1,088	1,010	947	961	960	948	917	929	923	927	923
More than 200 CZK up to 300 CZK incl.	558	563	527	490	494	490	479	481	492	494	482	491
More than 300 CZK up to 500 CZK incl.	645	637	573	523	525	524	518	523	539	537	537	526
More than 500 CZK up to 1,000 CZK incl.	804	805	696	616	629	641	650	647	640	636	639	632
More than 1,000 CZK up to 2,000 CZK incl.	718	722	572	532	534	536	520	520	519	519	521	526
More than 2,000 CZK up to 3,000 CZK incl.	292	293	230	203	202	203	203	199	213	216	215	204
More than 3,000 CZK up to 5,000 CZK incl.	367	367	319	289	287	278	272	274	273	273	272	272
More than 5,000 CZK up to 10,000 CZK incl.	342	342	278	261	260	258	255	259	257	264	266	265
More than 10,000 CZK up to 20,000 CZK incl.	247	248	181	167	165	170	169	172	179	181	180	172
More than 20,000 CZK up to 30,000 CZK incl.	98	95	80	72	72	74	76	78	78	79	81	81
More than 30,000 CZK up to 50,000 CZK incl.	80	80	70	69	71	70	70	69	66	65	65	63
More than 50,000 CZK up to 100,000 CZK incl.	108	108	86	82	82	84	84	85	84	87	87	87
More than 100,000 CZK	80	80	75	74	75	76	76	76	75	75	75	75
Number of codes	**6,752**	**6,733**	**5,815**	**5,339**	**5,370**	**5,377**	**5,300**	**5,276**	**5,343**	**5,374**	**5,376**	**5,353**

Fig. 16 **Prices of pharmaceuticals regulated by maximum price – comparison of average prices in Q4 2019 and Q4 2020 by price zones**

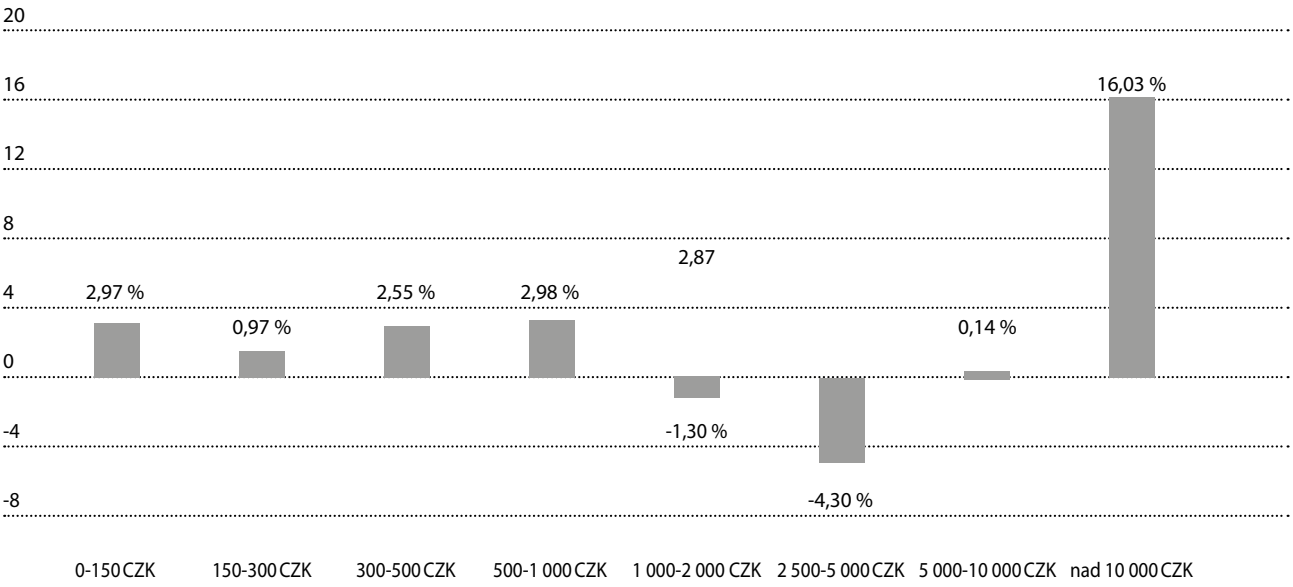
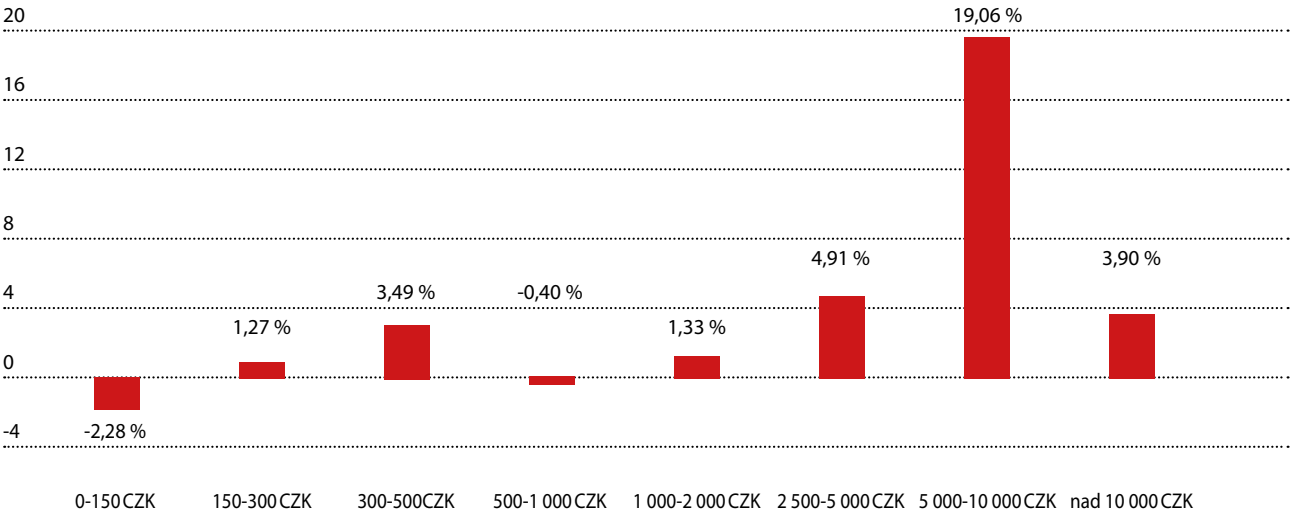


Fig. 17 **Prices of pharmaceuticals regulated by profit margin – comparison of average prices in Q4 2019 and Q4 2020 by price zones**



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

On the basis of 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 changed.

In 2020, 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. The biggest change in terms of maximum price increase occurred for medicinal product PROSTAPHLIN, where the original price increased due to an increased maximum price with regard to public interest in compliance with the provision of Section 9 of Decree No 376/2011 Coll. (Tab. 26).

Tab. 26 **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 (%)
0233016	J01CF04	PROSTAPHLIN	1000MG INJ PLV SOL 1	617,700	38.94	94.83	+ 143.5
0206563	J01DD01	TAXIMED	1G INJ/INF PLV SOL 1	604,390	59.66	47.46	– 20.4
0140192	A02BC01	OMEPRAZOL STADA	20MG CPS ETD 100	536,758	131.18	76.43	– 41.7
0030434	C03DA01	VEROSPIRON	25MG TBL NOB 100	504,428	139.60	191.22	+ 37.0
0216572	H02AB09	HYDROCORTISON VUAB	100MG INJ PLV SOL 1 II	401,709	32.34	39.10	+ 20.9
0166423	C02AC06	RILMENIDIN TEVA	1MG TBL NOB 90	384,412	327.99	302.92	– 7.6
0100339	J01FF01	DALACIN C	300MG CPS DUR 16	330,526	87.00	84.22	– 3.2
0000168	C03AA03	HYDROCHLOROTHIAZID LÉČIVA	25MG TBL NOB 20	328,366	38.45	28.24	– 26.6
0046444	N06AX05	TRITTICO AC	150MG TBL RET 60	322,843	311.85	266.26	– 14.6
0093109	N01BB58	SUPRACAIN	40MG/ML+5MCG/ML INJ SOL 10X2ML	293,491	180.71	173.78	– 3.8

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. 27).

Tab. 27 **Ten 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 MC v % price (%)
0210190	A10AE56	XULTOPHY	100U/ML+3,6MG/ML INJ SOL 3X3ML	500 181 577	3 199,53	2 823,30	– 11,8
0193826	A10AE06	TRESIBA	200U/ML INJ SOL 3X3ML	355 164 663	1 416,73	1 314,90	– 7,2
0210402	A10AE04	TOUJEO	300U/ML INJ SOL 3X1,5ML	350 539 308	914,57	815,49	– 10,8
0027953	A10AE04	LANTUS SOLOSTAR	100U/ML INJ SOL 5X3ML	342 066 407	1 154,97	981,46	– 15,0
0029740	A10BD08	EUCREAS	50MG/1000MG TBL FLM 60 I	206 694 189	652,70	606,87	– 7,0
0210026	A10BK03	JARDIANCE	10MG TBL FLM 90X1	173 286 589	2 813,41	2 780,68	– 1,2
0026096	A16AB07	MYOZYME	50MG INF PLV CSL 1	170 895 536	11 794,52	10 899,49	– 7,6
0209033	J05AR18	GENVOYA	150MG/150MG/200MG/ 10MG TBL FLM 30	151 646 018	30 315,00	17 783,72	– 41,3
0194361	R03AL04	ULTIBRO BREEZHALER	85MCG/43MCG INH PLV CPS DUR 30X1+INH	147 236 503	1 229,22	901,70	– 26,6
0166423	C02AC06	RILMENIDIN TEVA	1MG TBL NOB 90	143 882 423	327,99	302,92	– 7,6

Amounts and Conditions of Reimbursements from Health Insurance

Tab. 28 **Overview of administrative procedures in 2020**

Applications for determination or change of the amount and conditions of reimbursement	Number of SÚKL codes
Initiated	490
Decided	252
Appeal procedure pending	53
Became final	192
Applications for determination or change of maximum price and the amount and conditions of reimbursement	
Initiated	178
Decided	85
Appeal procedure pending	26
Became final	62
Applications for reimbursement revocation	
Initiated	198
Decided	70
Appeal procedure pending	0
Became final	59
Applications for maximum price and reimbursement revocation	
Initiated	188
Decided	179
Appeal procedure pending	0
Became final	177
Ex officio initiated procedures	
Initiated	426
Decided	337
Appeal procedure pending	197
Became final	134
Procedures concerning similar products	
Initiated	613
Decided	582
Appeal procedure pending	41
Became final	523

In 2020, 24 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 2020, savings of public health insurance funds were generated both by in-depth and abbreviated revisions. The total savings arising from abbreviated revisions enforceable in 2020 is estimated at 1,486,137,348 CZK, and those arising from in-depth revisions at 2,038,474,824 CZK.

Tab. 29 **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
01/2020	*98*	*9*	*450 369 636 Kč*
02/2020	*53*	*13*	*40 060 867 Kč*
03/2020	*60*	*12*	*108 305 629 Kč*
04/2020	*16*	*4*	*2 508 266 Kč*
05/2020	*233*	*10*	*930 873 513 Kč*
06/2020	*513*	*11*	*899 553 639 Kč*
07/2020	*47*	*4*	*90 315 393 Kč*
08/2020	*216*	*9*	*355 303 640 Kč*
09/2020	*171*	*10*	*269 405 510 Kč*
10/2020	*117*	*9*	*101 532 932 Kč*
11/2020	*102*	*8*	*228 756 527 Kč*
12/2020	*24*	*4*	*47 626 620 Kč*

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

Tab. 30 **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
Do 20 CZK, incl.	178	175	174	154	167	167	166	165	163	163	162	161
More than 20 CZK up to 50 CZK, incl.	837	835	832	745	766	782	776	775	761	764	769	759
More than 50 CZK up to 100 CZK, incl.	1,334	1,325	1,339	1,222	1,275	1,302	1,290	1,273	1,316	1,316	1,301	1,291
More than 100 CZK up to 200 CZK, incl.	1,673	1,677	1,685	1,517	1,541	1,611	1,573	1,583	1,612	1,606	1,601	1,594
More than 200 CZK up to 300 CZK, incl.	870	853	857	748	752	718	708	722	749	769	799	794
More than 300 CZK up to 500 CZK, incl.	950	954	959	851	817	903	902	879	884	862	881	885
More than 500 CZK up to 1 000 CZK, incl.	1,199	1,204	1,202	1,064	1,087	1,054	1,049	1,057	1,050	1,069	1,057	1,067
More than 1 000 CZK up to 2 000 CZK, incl.	1,079	1,073	1,075	984	990	898	895	902	898	918	910	910
More than 2 000 CZK up to 3 000 CZK, incl.	397	408	408	366	371	369	367	382	393	396	393	386
More than 3 000 CZK up to 5 000 CZK, incl.	388	392	394	363	362	353	351	351	348	343	337	347
More than 5 000 CZK up to 10 000 CZK, incl.	516	519	520	466	468	447	440	434	434	436	439	436
More than 10 000 CZK up to 20 000 CZK, incl.	302	303	303	276	284	297	301	307	313	314	318	305
More than 20 000 CZK up to 30 000 CZK, incl.	121	120	120	104	107	113	116	119	115	113	114	110
More than 30 000 CZK up to 50 000 CZK, incl.	72	71	70	69	76	78	78	77	76	78	78	79
More than 50 000 CZK up to 100 000 CZK, incl.	107	106	108	96	100	102	103	103	102	99	100	99
More than 100 000 CZK	96	97	96	88	90	89	88	88	87	87	87	87
Number of codes	**10,119**	**10,112**	**10,142**	**9,113**	**9,253**	**9,283**	**9,203**	**9,217**	**9,301**	**9,333**	**9,346**	**9,310**

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 LUCENTIS and EYLEA (Tab. 31).

Tab. 31 **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)	Změna reimbursement (%)
0223046	L01XC17	OPDIVO	10MG/ML INF CNC SOL 1X24ML	804 926 010	77 934,68	70 829,68	–9,1
0210773	L01XC17	OPDIVO	10MG/ML INF CNC SOL 1X10ML	639 159 310	32 472,79	29 454,43	–9,3
0168904	B01AF01	XARELTO	20MG TBL FLM 98 II	579 195 191	5 788,01	4 472,93	–22,7
0193696	S01LA05	EYLEA	40MG/ML INJ SOL 1X0, 1ML	577 068 733	22 283,04	16 258,18	–27,0
0210187	L01EL01	IMBRUVICA	140MG CPS DUR 90	545 705 324	139 866,69	137 507,53	–1,7
0194569	S01LA04	LUCENTIS	10MG/ML INJ SOL 1X0, 165ML	509 272 642	22 560,31	16 258,24	–27,9
0193747	B01AF02	ELIQUIS	5MG TBL FLM 168	429 223 520	4 961,14	5 339,52	7,6
0168373	B01AE07	PRADAXA	150MG CPS DUR 60X1 I	362 457 226	1 771,84	1 891,17	6,7
0194319	L04AA31	AUBAGIO	14MG TBL FLM 28	346 577 793	15 500,76	18 060,85	16,5
0210317	L04AC10	COSENTYX	150MG INJ SOL PEP 2X1ML	313 046 058	26 160,75	26 228,05	0,3

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 2020. In case of medicinal product KALIUM CHLORATUM, the reimbursement was significantly increased, which was also reflected in a slightly increased volume of its supplies (Tab. 32).

Tab. 32 **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
0243240	*A11CC05*	*VIGANTOL*	*0,5MG/ML POR GTT SOL 1X10ML*	*527 513*	*94,70*	*49,04*	*731 462*	
0234736	*A12CC30*	*MAGNOSOLV*	*365MG POR GRA SOL SCC 30*	*484 945*	*107,27*	*121,92*	*513 906*	
0200935	*A12BA01*	*KALNORMIN*	*1G TBL PRO 30*	*216 532*	*45,03*	*59,33*	*213 501*	*/
0140192	*A02BC01*	*OMEPRAZOL STADA*	*20MG CPS ETD 100*	*284 659*	*205,84*	*97,76*	*260 288*	
0025366	*A02BC01*	*HELICID*	*20MG CPS ETD 90 I*	*255 290*	*185,26*	*87,98*	*266 637*	
0030434	*C03DA01*	*VEROSPIRON*	*25MG TBL NOB 100*		*210,38*	*130,57*		*x/*
0017189	*A12BA01*	*KALIUM CHLORATUM BIOMEDICA*	*500MG TBL ENT 100*	*92 409*	*75,05*	*98,89*	*96 088*	*/
0045010	*J01FA10*	*AZITROMYCIN SANDOZ*	*500MG TBL FLM 3*	*216 278*	*119,70*	*56,06*	*150 551*	
0109415	*A02BC02*	*NOLPAZA*	*40MG TBL ENT 84*	*146 546*	*172,91*	*82,12*	*190 267*	
0164979	*A02BC01*	*OMEPRAZOL TEVA PHARMA*	*20MG CPS ETD 100*	*167 197*	*205,84*	*97,76*	*174 482*	

** – 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*

Table 33 presents a list of essential changes to the reimbursement system in 2020, with impact upon clinical practice. The table provides a summary overview of new innovative pharmaceuticals that entered the reimbursement system for the first time, as well as previously reimbursed pharmaceuticals in respect of which reimbursement was newly extended to a new diagnosis or a broader patient population.

Tab. 33 **Overview of newly reimbursed original pharmaceuticals and significant extensions of reimbursement in 2020**

Name of the medicinal product and active substance	Indication (clinical use)	Reimbursement effective from
OPDIVO (nivolumab)	First-line treatment of moderate/poor prognosis renal carcinoma (combination with ipilimumab); Treatment of advanced head and neck carcinoma	March 2020
OPDIVO + YERVOY (nivolumab + ipilimumab)	First-line treatment of locally advanced or metastatic melanoma	March 2020
OPDIVO (nivolumab) TECENTRIQ (atezolizumab)	Second-line treatment of locally advanced or metastatic non-small cell lung carcinoma	August 2020 (OPDIVO), March 2020 (TECENTRIQ)
OPDIVO (nivolumab)	Second-line treatment of locally advanced or metastatic melanoma	May 2020
KEYTRUDA (pembrolizumab)	First-line treatment of locally advanced or metastatic non-small cell lung carcinoma	August 2020
OPDIVO (nivolumab)	Adjuvant treatment of malignant melanoma	October 2020
AVASTIN (bevacizumab)	Metastatic, recurrent or persisting cervical carcinoma not indicated for surgical management and/or radiotherapy	October 2020

ADCETRIS (brentuximab vedotin)	CD30+ refractory or relapsing Hodgkin's lymphoma After at least two prior therapies	January 2020
ADCETRIS (brentuximab vedotin)	CD30-positive peripheral T-lymphoma in first-line treatment	August 2020
ADCETRIS (brentuximab vedotin)	CD30+ Hodgkin's lymphoma (HL) with increased risk of relapse or progression following autologous stem cell transplantation (ASCT)	July 2020
MYLOTARG (gemtuzumab ozogamicin)	Previously untreated de novo CD33-positive primary acute myeloid leukaemia	June 2020
BESPONSA (inotuzmab ozogamicin)		
BLINCYTO (blinatumomab)	Relapsing or refractory acute lymphoblastic leukaemia	February 2020
VENCLYXTO (venetoclax)	Chronic lymphatic leukaemia (in combination with rituximab) after failure of treatment with ibrutinib or idelalisib	April 2020
KYPROLIS (carfilzomib)	Multiple myeloma in patients who completed previous 1–3 treatment lines	November 2020
HEMLIBRA (emicizumab)	Routine prophylaxis of haemorrhagic episodes in patients with severe haemophilia A (HA) without factor VIII inhibitors	December 2020
XARELTO (rivaroxaban)	First-line prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation	November 2020
AIMOVIG (erenumab) AJOVY (fremanezumab) EMGALITY (galcanezumab)	Prevention of migraine in patients with at least 4 days with migraine per month after previous treatment failure	February 2020 (AIMOVIG), May 2020 (AJOVY), October 2020 (EMGALITY)
SKYRIZI (risankizumab)	Moderate to severer psoriasis	June 2020
ENBREL, ERELZI (etanercept) HUMIRA, HYRIMOZ, AMGEVITA, IDACIO (adalimumab) CIMZIA (certolizumab) SIMPONI (golimumab)	Rheumatoid arthritis with moderate disease activity in patients previously treated with conventional therapy	February 2019 (ENBREL, first medicinal product with extended reimbursement in this indication), other products gradually in the course of the year
PRALUENT (alirocumab)	Lipid metabolism disorders in which target LDL-C values are not achieved through maximally intensive hypolipidemic treatment (at least 3.1 mmol/l in case of heterozygous familial hypercholesterolemia or at least 2.5 mmol in nonfamilial hypercholesterolemia or mixed dyslipidaemia)	October 2020

For these ongoing administrative procedures, the outcome of which may be important both for the general public and for professionals in terms of the addressed expert issue (application for the determination of reimbursement for a new active substance, application for determination of reimbursement for a new indication, application for substantial variation to the conditions of reimbursement), the Institute has been newly publishing a so-called Assessment Report Summary at its website on an ongoing basis since 2020. The Institute has been publishing such Summaries for individual pharmaceuticals/procedures at its website in order to facilitate access of the general public to basic data and information about the assessed pharmaceuticals.

Validation of Applications

Compared to 2019, a mild increase in the number of submitted applications, specifically by 5 %, was seen in 2020. The highest proportion of the total number of submissions was observed in the first quarter (approx. 32 %). In this period, a Price Regulation became effective that newly regulated, through the producer price and maximum profit margin, orphan medicinal products used in outpatient and inpatient care without determined reimbursement for outpatient care; producers of such medicinal products hence became obliged to apply for maximum price determination. As of 1 March 2020, a Price Decision became effective, which, in accordance with the Price Regulation, newly regulated, through maximum price, medicinal products whose ATC group with the respective route of

administration was newly not included in the Price Decision, and all producers therefore had the obligation to apply for maximum price determination. In the third quarter, and even more profoundly in the fourth quarter, the number of applications for change of maximum price grew in association with the issued decisions from in-depth maximum price revisions.

Compared to 2019, the proportion of applications submitted by health insurance companies increased from 9 to 15 %. Administrative procedures initiated on the basis of an application for the determination of the amount and conditions of reimbursement/maximum price by ways stipulated under the provision of Section 39g(9) of the Act on Public Health Insurance (so called "similar products") accounted for 32 % of the total number of procedures on request.

In 2020, 34 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 code.

Tab. 34 **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 – 2020**

Period	Submitted applications	Suspended due to defective submission and application shortcomings	Discontinued in the validation phase
January	58	3	2
February	114	0	6
March	131	3	7
April	65	1	1
May	42	0	1
June	52	0	0
July	97	0	9
August	53	2	1
September	65	2	1
October	54	0	0
November	124	0	5
December	80	1	1
Total	**935**	**12**	**34**

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 2020). 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 the provisions of Sections 171 to 174 of Act No 500/2004 Coll., the Code of Administrative Procedure, as amended.

General Measures (OOPs)

In the course of 2020, six general measure procedures were initiated and properly completed.

As of 1 April 2020, OOP 01-20 for a group of radiopharmaceuticals became effective. By means of this OOP, a new radiopharmaceutical, 177Lu oxodotreotide inj. (medicinal product LUTATHERA), was included in the IPLP List. The Institute estimated an increase in public health insurance funds by 11.63 %, i.e. the amount of 104 mil. CZK, as a consequence of including the new radiopharmaceutical.

As of 1 May 2020, OOP 02-20 for the group of otherwise unclassified magistral formulas became effective; the general measure revoked the amount and conditions of reimbursement for individually prepared medicinal products containing cannabinoids. From 1 January 2020, the price and reimbursement regulation of individual prepared medicinal products containing medical cannabis has been governed by the effective Price Regulation.

As of 1 May 2020, OOP 05-20 for transfusion products became effective through an abbreviated procedure; the general measure placed new items on the IPLP List – Convalescent plasma and Pathogen-inactivated

convalescent plasma, which has been reimbursed for patients with moderate or severe course of COVID-19 infection. After the inclusion of the two new items, the Institute estimated the increase of costs from public health insurance funds to amount to approx. 2.9 mil CZK per year providing the consumption is 500 units.

As of 1 June 2020, three general measures became effective – OOP 03-20 and OOP 04-20 for advanced therapy medicinal products and OOP 06-20 for radiopharmaceuticals.

OOP 03-20 included advanced therapy medicinal product ALOFISEL in the IPLP List; this product has been reimbursed for the treatment of complex perianal fistulas in adult patients with inactive or mildly active luminal Crohn's disease who did not respond to at least one conventional and biological treatment and at least one surgical treatment. The Institute assumed that in the first five years, 10 to 82 patients would be treated with this product which would represent an impact onto the budget in the amount of 17.2 to 138.2 mil. CZK. Nevertheless, due to a cost limitation agreement, the actual impact may be expected to be lower.

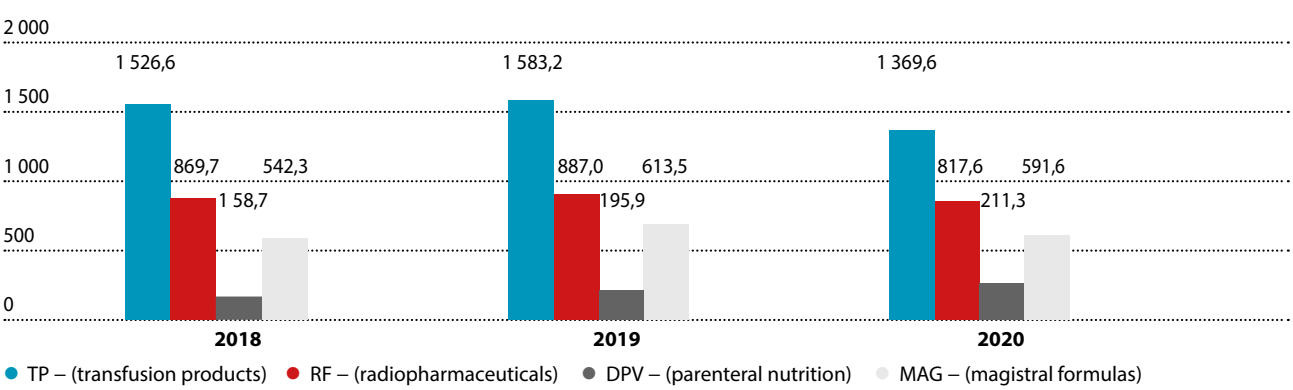
OOP 04-20 included advanced therapy medicinal product HOLOCLAR in the IPLP List; this product has been reimbursed for adult patients with moderate to severe limbal stem cell deficit caused by physical or chemical eye burns. The Institute assumed that in the next five years, ten to twelve patients would be treated with this product, which would represent an impact onto the budget in the amount of 20 to 24 mil. CZK. In case of repeated administration in 25 % of the patients, it would increase to 25-30 mil. CZK.

OOP 06-20 for radiopharmaceuticals reflected new pricing source materials and the effective €/CZK exchange rate according to materials published by the Czech National Bank. The said OOP included non-authorised medicinal product 68Ga-PSMA-11 into the IPLP List within the scope of a specific therapeutic programme. A non-authorised radionuclide generator Galli Ad, 0.74–1.85 GBq is used for the preparation of this product. Furthermore, upon request and following approval by the Czech Nuclear Medicine Society, the Institute extended the indications for radiopharmaceutical 18F fluoromethylcholine with the localisation of adenoma or parathyroid gland hyperplasia with suspected primary hyperparathyroidism. In this OOP, the Institute also newly reflected the costs of environmental sterility monitoring as per guideline LEK-17 in the final reimbursement as referred to under Art. IV(6)(d) of the Price Regulation, specifically in the amount of 0.05 CZK/MBq for radiopharmaceuticals intended for diagnosis, and in the amount of 0.01 CZK/MBq for radiopharmaceuticals intended for therapy. The total estimated impact of all of the aforementioned changes hence amounts to approx. 23 mil. CZK.

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 DPV subgroup, in 2020, the consumption increased, while in respect of the other subgroups, i.e. RF, TP, and MAG, consumption decreased in comparison to the previous period. The values specified for the period of 2019 in the 2019 annual report were updated as of 28 January 2021. Data for the consumption of individually prepared medicinal products in 2020 are available only as at 01 October 2020, 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 and future cost prediction using the least squares method. An overview of the consumption of individually prepared medicinal products in DU for the period of 2018-2020 is shown on Fig. 18.

Fig. 18 **Overview of consumption of individually prepared medicinal products for the period of 2018-2020 in thous. DU**



In 2020, 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 3.12 points to the value of 3.19 points in compliance 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 effect from 1 January 2020. In compliance with Decree No 268/2019 Coll., setting point values, reimbursement amounts for reimbursed services, and regulatory restrictions for 2020, the point value also changed from the original amount of 1.06 CZK to the new amount of 1.07 CZK per point. In compliance with Government Regulation No 341/2017 Coll., on civil servant salaries, as amended, the salaries of healthcare professionals in the basic tariff were raised by the amount of 1,500 CZK.

In 2020, three new radiopharmaceuticals were included in the RF group of the IPLP List. With effect as of 1 January 2020, radiopharmaceutical 68Ga edotreotide inj. (medicinal product SomaKit TOC) was included, as of 1 April 2020 it was radiopharmaceutical 177Lu oxodotreotide inj. (medicinal product LUTATHERA), and as of 1 June 2020 it was radiopharmaceutical 68Ga-PSMA-11 within the scope of a specific therapeutic programme. In 2020, three new items from the transfusion product group were included in the IPLP List. With effect from 1 January, Whole blood, deleukotised, for universal administration (blood group 0 with low anti-A and anti-B titres) was included and with effect from 1 May 2020, Convalescent plasma and Pathogen-inactivated convalescent plasma were included.

Celkové výdaje na skupinu IPLP uhrazené z prostředků veřejného zdravotního pojištění za rok 2019 představovaly 3 279,6 mil. Kč. V roce 2020 dosáhly hodnoty 2 990,1 mil. Kč, což představuje snížení výdajů oproti roku 2019 o 289,5 mil. Kč, v procentuálním vyjádření o 8,83 %.

Fig. 19 **Distribution of total expenses in the IPLP group for 2020**

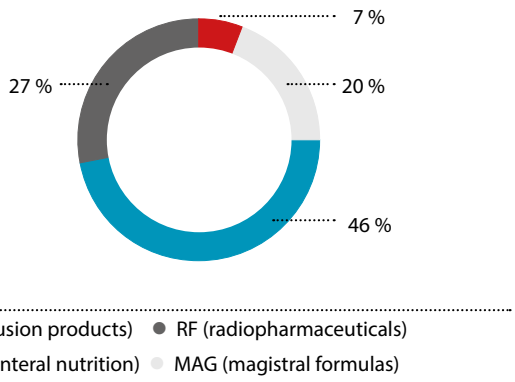
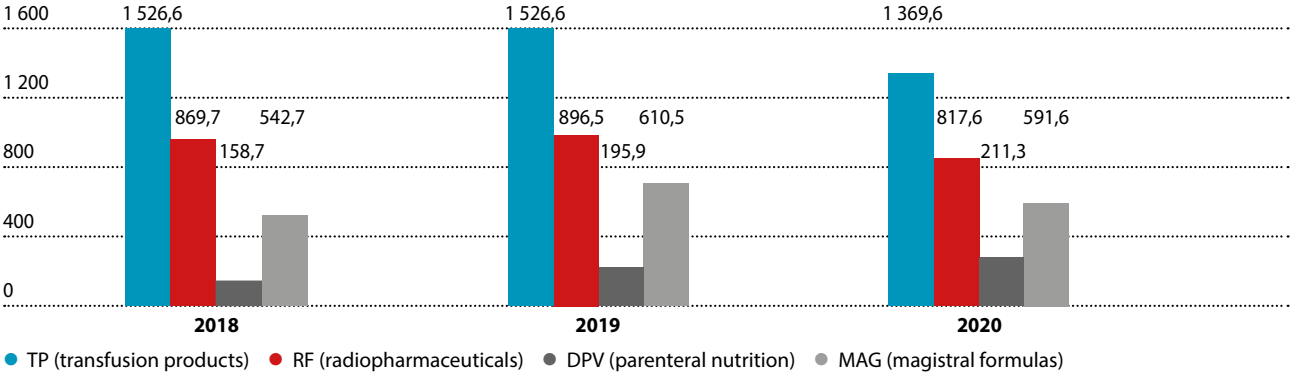


Fig. 20 illustrates a comparison of expenses in the period of 2018-2020 for individual IPLP groups.

Compared to 2019, an increase in costs reimbursed from the public health insurance funds occurred only in the DPV subgroup; other subgroups, i.e. TP, RF, and MAG, exhibited a decrease, which corresponds also to their lower consumption compared to 2019.

Fig. 20 **Comparison of expenses by subgroups of individually prepared medicinal products for the period of 2018-2020 in mil. CZK**



The total expenses for the IPLP group reimbursed from public health insurance funds amounted to 3,279.6 mil. CZK in 2019. In 2020, this amount was 2,990.1 mil. CZK, which is a decrease in expenses by 289.5 mil. CZK, i.e. by 8.83 %, compared to 2019.

MEDICAL DEVICES DEPARTMENT

Practically throughout 2020, the Medical Devices Department (OZP) had to handle measures aimed against the spread of the COVID-19 infection both in terms of staffing and in terms of the provision of information and answers to frequent questions asked both by professionals and the general public. With regard to the coming effect of Regulation (EU) 2017/745 of the European Parliament and of the Council on medical devices (hereinafter referred to as "MDR") and

Regulation 2017/746 (hereinafter referred to as the "IVD Regulation"), the staff of the Department were busy preparing new processes and defining the scope of change requirements in the Registry of Medical Devices (hereinafter referred to as the "RZPRO") in a situation, when the roll-out of the main tool for the implementation of both Regulations, the European Database of Medical Devices (hereinafter referred to as the "EUDAMED"), has been delayed by approximately two years, with the anticipated roll-out date in May 2022. In the second half of 2020, the employees of the Department, in cooperation with the Ministry of Health, were significantly involved in the drafting of a new act on medical devices and on in vitro diagnostic medical devices that adapt both of the aforementioned Regulations in parallel, with expected effective date consistent with the IVD Regulation effective date, which is 26 May 2022. They also participated in the meetings of various expert working groups of the European Commission focusing, in particular, on the set-up and harmonisation of individual processes in the medical device internal market and the specification of functionalities in the EUDAMED database. Furthermore, the preparation of specifications of a new system for the medical devices agenda was also completed.

4.15 Medical Device Control and Expert Opinion Unit (KOP)

Controls

The Institute's surveillance activities over persons handling medical devices are stipulated by Act No 268/2014 Coll., on Medical Devices and on Amendment to Act No 634/2004 Coll., on Administrative Fees, as amended (hereinafter referred to as the "Act on Medical Devices") that sets forth competencies within the sphere of control activities pursuant to this Act and Act No 22/1997 Coll., on Technical Requirements for Products and on Amendments to Some Acts, as amended. Such persons are healthcare service providers in the sphere of medical devices use as well as medical devices manufacturers, distributors, importers, persons servicing medical devices, and persons selling and dispensing medical devices. This surveillance activity includes also the agenda of assessments of proper placement of medical devices onto the market.
The objective of both scheduled and ad hoc controls conducted by the Institute is to ensure that medical devices supplied onto the market in the Czech Republic were safe and functional and that health care were provided using appropriate, safe, and effective medical devices in a manner preventing any damage to the health of users or patients in the proper use of the devices for their intended purposes.
In 2020, the inspectors of the Control Unit conducted the total of 123 inspections, of which 43 were inspections at providers of healthcare services (both state and non-state healthcare facilities) and 80 were inspections at medical devices manufacturers, importers, distributors, and persons selling, dispensing or servicing medical devices. During these inspections, 250 medical devices were inspected. The tables below provide a more detailed statistics regarding the total number of inspected medical devices and persons.

Forty-three inspections were carried out at providers of healthcare services, within the scope of which documents certifying compliance with the conditions for the medical device use in the provision of health care were checked. Furthermore, 80 inspections were conducted as part of market surveillance, in which compliance with the requirements of medical devices placement onto the market was checked. The number of shortcomings identified in respect of persons subjected to market surveillance was 126.

The Medical Devices Inspection and Expert Opinion Unit forwarded the total of 116 motions to the Legal Support Department of the Medical Devices Department.

Tab. 35 **Overview of KOP inspections**

Number of inspections	123
Number of inspections instigated by a motion (of the total number of inspections)	25
Number of inspected medical devices	*250
Number of inspected Legally Controlled Measuring Instruments (of the total number of inspected medical devices)	0
Number of shortcomings identified in inspected medical devices	*126
Number of motions forwarded to the Legal Support Department (proposals for administrative procedure initiation)	*116

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

Tab. 36 **KOP inspection rating**

Entity	Number of inspections	1*	2*	3*
POS – providers	43	27	16	0
CEN – price control	1	0	0	0
DIS – distributors	33	12	7	12
DOV – importers	23	10	6	8
PRO – persons selling medical devices	12	11	1	0
SER – persons servicing medical devices	14	8	4	0
VYD – persons dispensing medical devices	6	6	0	0
VYR – manufacturers	26	1	18	7
Miscellaneous	4	2	0	0

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

Inspection rating is performed using the internal classification of shortcomings; the inspector evaluates and rates the shortcoming (DN – minor or no shortcoming – 1, VN – significant shortcoming – 2, KN – critical shortcoming – 3). The inspection is rated as follows: the rating of the most serious shortcoming determines the numerical classification of the inspection.

Expert Opinions

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 Devices Department and in response to filed applications for medical devices notification in the RZPRO Registry. In 2020, the KOP Unit issued 168 expert opinions concerning the nature of a product or medical devices 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, 43 opinions were issued on the basis of an external request and 125 opinions on the basis of requests from the Legal Support Department of the Medical Devices Department (PPZ).

4.16 Medical Devices Clinical Trials and Vigilance Unit (KHV)

Clinical Trials

Pursuant to the obligation set forth for the sponsors of clinical investigations on medical devices (hereinafter referred to as "CIMD") by the Act on Medical Devices, 35 applications for authorisation of CIMD conduct and 41 applications for variations to CIMD conditions were submitted to the Institute in 2020 via the Registry of Medical Devices (hereinafter referred to as "RZPRO") Clinical Investigations module.

In compliance with Section 9(h) of the Act on Medical Devices, 25 favourable opinions authorising the conduct of CIMD were issued in administrative proceedings. Furthermore, 33 applications for authorisation of variations to CIMD were granted.

With regard to the COVID-19 pandemics, three inspections of the conduct of clinical investigations on medical devices at providers of healthcare services were carried out, in which three 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 one case of non-compliance with the plan and, subsequently, it was proposed to initiate administrative proceedings with the sponsor.

In total, 89 serious adverse events (hereinafter referred to as "SAE") were reported from ongoing CIMDs in the Czech Republic.

Within the scope of international cooperation in the sphere of clinical evaluations, in 2020, a representative of the Medical Device Clinical Trials Unit participated in regular web 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 the Medical Devices Regulation and its postponed effect by one year, and upon exchange of information among the EU Member States.

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

The Institute received reports of 753 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, eight 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 2013-2020 is illustrated by Fig. 21.

The total number of received reports on safety corrective actions regarding medical devices from competent national authorities, manufacturers or their authorised representatives, distributors or importers, as applicable, amounted to 934. Of the total number of received reports, 473 concerned medical devices distributed on the Czech market. The development of the number of reports on safety corrective actions in 2013-2020 is illustrated by Fig. 22.

In 2020, the Institute published 408 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).

The inspections at distributors' and persons servicing medical devices scheduled as part of monitoring the implementation of safety corrective actions within the territory of the Czech Republic were not carried out due to the adverse epidemiological situation.

Sixty-six penalties were imposed for offences in the sphere of adverse events. The Legal Support Unit of the Medical Devices Department (PPZ) was forwarded 65 proposals to impose an administrative penalty for offences committed by healthcare service providers, manufacturers, persons servicing medical devices or medical device distributors.

As part of monitoring of a safety corrective action set forth by a Czech manufacturer, six reports for competent national authorities (NCAR), the European Commission and the competent bodies of EU Member States were issued and disseminated via the EUDAMED database.

In 2020, the inspectors of the Vigilance Unit participated in regular meetings of the PMSV (Post Market Surveillance and Vigilance) Working Group and the Medical Devices Coordination Group (MDCG) of the European Commission; they participated in two meetings and twelve teleconferences focused upon the exchange of information among the EU Member States regarding current vigilance cases and the course to

be taken in their solution. They took active part in consultations and repeated commenting on documents distributed by the European Commission, specifically consultations concerning implementation of Art. 83(4) of MDR 2017/745 and provision of comments on the sections regarding vigilance of draft document Guidance on Eudamed alternative pathway before Eudamed becomes available.

SÚKL updated the vigilance sections of its website – specifically the "Medical devices (suspected) adverse event report", a section concerning the new version of the MIR (Manufacturer Incident Report) form, including questions and answers on the implementation of this form, and IMDRF (International Medical Devices Regulators Forum) documents – the terminology for AE report classification, including annexes A–G.

In the course of 2020, 33 questions regarding vigilance issues were answered in total.

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

Fig. 21 **Overview of notified adverse events in 2013–2020**

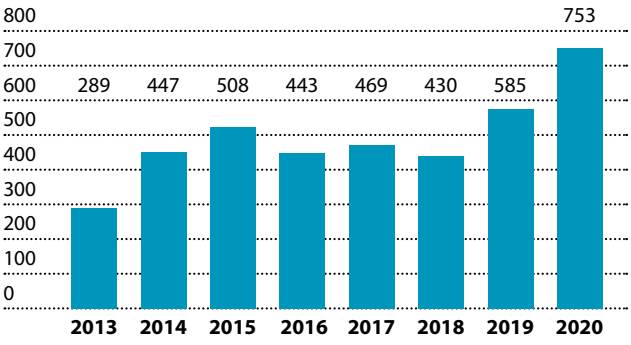
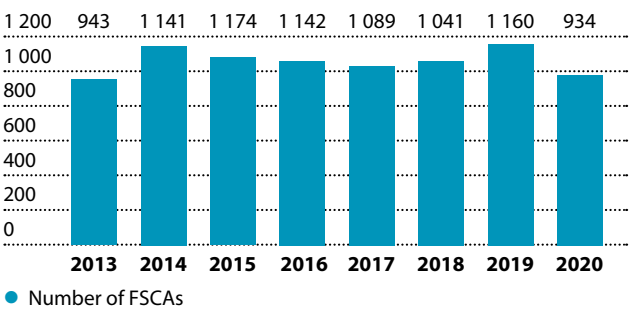


Fig. 22. **Overview of safety corrective actions for medical devices adopted in 2013–2020**



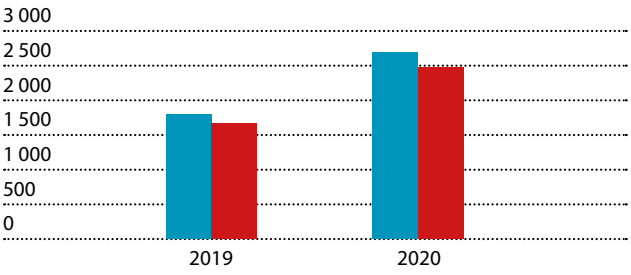
4.17 Registration and Notification Unit (RAN)

On the basis of systemisation, effective as of 1 January 2020, the name of the organisational centre of Medical Devices Notification Unit (ONZP) was change to Registration and Notification Unit (RAN) and its agenda was extended with registration of persons. RAN is in charge of registration of persons and associated activities, regulation in the area of medical devices notifications and associated activities, and the issuance of certificates of free sale in compliance with the Act on Medical Devices.

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 2,521 notifications in the Persons module. In 2020, 2,674 notifications were lodged. A comparison of submitted and concluded notifications (completed procedures governed by the Code of Administrative Procedure – Act No 500/2004 Coll.) is illustrated by Fig. 23.

Fig. 23 **Proportion of submitted and concluded notifications**



- **Notification of Person**

  In 2020, RAN concluded 406 submitted notifications of persons.

- **Notification of Activity**

  In 2020, 115 notifications regarding activities in general were handled – these concerned activities of manufacturers, distributors, importers, persons servicing medical devices, authorised representatives, and clinical investigation sponsors.

- Notifications of changes to data

  In total, 1,133 notifications of changes to data of a person were processed and completed.

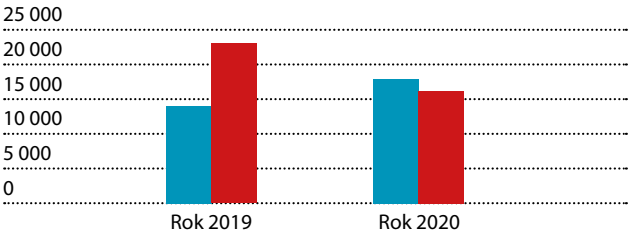
- Notification of deletion of a person

  In 2019, the RAN Unit processed 33 notifications of deletion of a person.

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

In total, the Unit completed 15,946 applications in the Medical Devices module in the last year. In 2020, 18,269 applications were entered in the Medical Devices module. A comparison of submitted and concluded applications (completed procedures governed by the Code of Administrative Procedure – Act No 500/2004 Coll.) is illustrated by Fig. 24.

Fig. 24 **Proportion of submitted and concluded applications**



- Number of applications lodged in the Medical Devices module
- Number of applications concluded in the Medical Devices

Note: The chart does not reflect data on certificates of free sale.

- Applications for medical device notification
  In 2020, the Unit completed 5,528 administrative procedures regarding applications for medical devices notification.

- Applications for medical devices notification renewal
  In total, 900 administrative proceedings regarding applications for medical device notification renewal.

- Applications for change to medical device data
  In total, 8,530 applications for change to medical device data were processed and completed.

- Applications for medical device deletion
  The Unit completed 988 applications for medical device deletion.

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

- Applications for Certificates of Free Sale
  In 2020, 198 applications were submitted, of which 185 were completed.

4.18 Legal Support Unit of the Medical Devices Department (PPZ)

Penalties for Breach of the Act on Medical Devices

In compliance with the Act on Medical Devices, 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 determination and proper classification of medical devices.

Where the Institute identifies any justified 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 devices notification, it commences an administrative proceedings with the party in question.

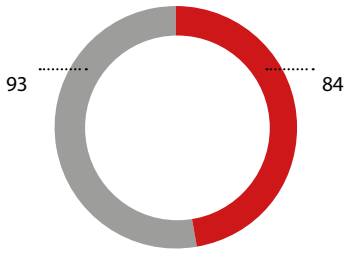
In 2020, 93 proposals for the commencement of an administrative proceedings on product nature and 85 proposals for the commencement of an administrative proceedings on medical devices classification were forwarded to the Legal Support Unit.

In 2020, the Institute commenced 93 ex-officio administrative proceedings on product nature and 84 ex-officio administrative proceedings regarding medical devices classification.

In 2020, the Institute received no application for decision regarding product nature and two applications for decision on medical devices classification.

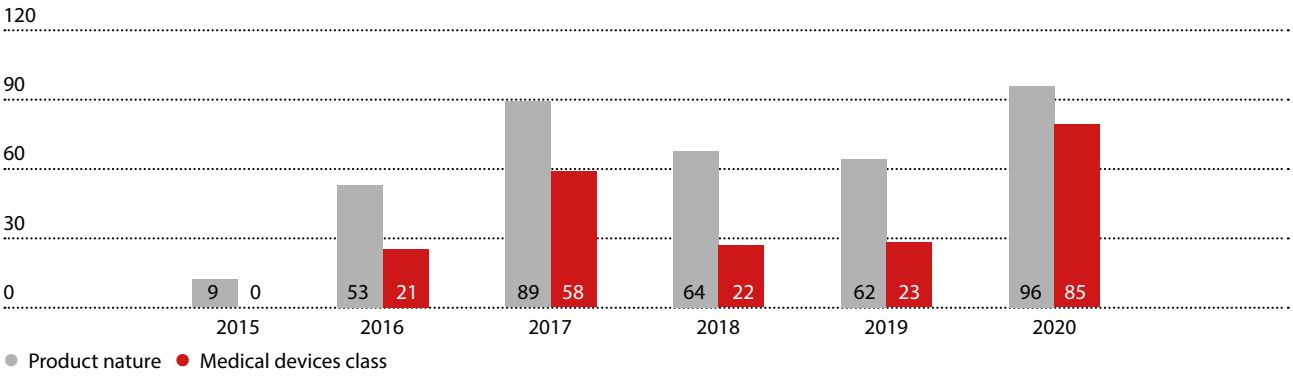
In 2020, 19 decisions on medical devices classification and 23 decisions on product nature were issued. Furthermore, the Institute issued 81 rulings on administrative proceedings termination.

Fig. 25 **Overview of administrative proceedings commenced in 2020**



Product nature Medical device class

Fig. 26 **Overview of forwarded proposals for the commencement of ex-officio administrative proceedings in 2015–2020**



Offences

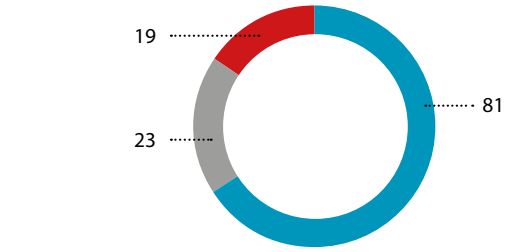
The Institute, as a first-instance administrative authority, commences administrative proceedings regarding offences in case a breach of obligations imposed by the Act on Medical Devices is identified, particularly with reference to the inspection activity conducted at providers of healthcare services,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

In 2020, the Institute imposed fines for breach of the Act on Medical Devices amounting to the total of 4,917,478 CZK. The highest proportion of fines imposed in 2020 for the breach of the Act on Medical Devices were fines imposed upon medical devices distributors and healthcare service providers.

In 2020, 156 orders and 23 decisions were issued. Furthermore, the Institute issued six rulings regarding administrative proceedings termination.

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 administrative proceedings 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.

Fig. 27 **Overview of decisions issued in 2020**



Explanatory notes: AP – administrative proceedings

Tab. 37 **Overview of forwarded motions for administrative proceedings commencement in 2015–2020**

Overview for:	2015	2016	2017	2018	2019	2020
Clinical Trials Unit	-	3	1	-	-	-
Vigilance Unit	2	47	79	88	185	65
Control Unit	22	69	64	20*	-*	116
Medical Device Notification Unit	-	-	-	-	6	-
Total	**24**	**119**	**144**	**108**	**191**	**181**

** In the period from 1 August 2018 to 31 December 2019, surveillance over the medical device market was the responsibility of SÚKL's Surveillance Section.*

Recalls and Withdrawals

In 2020, the Institute issued one decision on medical device recall and one decision on medical device withdrawal from circulation and recall pursuant to Section 39 of the Act on Medical Devices.

Appeals

In 2020, the Legal Support Unit received the total of 77 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. 38 **Overview of received appeals forwarded to the Ministry of Health of the Czech Republic in 2020**

Unit	No. of appeals	Returned for re-consideration	Granted	Declined	Withdrawn by applicant
Legal Support Unit	67	1	1	4	4
Medical Devices Reimbursement Unit	2	2	-	-	-
Registration and medical device Notification Unit	8	-	5	-	-
Total number of appeals for 2020	**77**	***3**	***6**	***4**	***4**

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

4.19 Medical Devices Reimbursement Unit (UZP)

The 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 proceedings. 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.

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 proceeding regarding non-inclusion in the reimbursement group or removal from a reimbursement group.

Notifications of medical devices reimbursements may be lodged at any time. The maximum amount of reimbursement is stipulated by law.

A major part of the Unit's operation represents a year-to-year producer price increase, which is implemented in compliance with Price Regulation 1/2019/CAU, regulating medical devices prices.

The major output from the Unit's operation is, in particular, the process of issuing the Medical Devices Reimbursement and Price List for medical devices reimbursed on order, which is the main index for reporting care associated with reimbursements for medical devices reimbursed on order. It is updated in compliance with effective legislation always as of the 20th day of the month. On 31 December 2020, the Medical Devices Reimbursement and Price List contained 11,542 items in total.

Tab. 39 **Medical devices reimbursement notifications in 2020**

Reimbursement notifications	Number of SÚKL codes
Total submissions	**3,944**
New notifications	1,608
Change notifications	1,213
Year-to-year producer price increase	789
Included in the list of medical devices	1,331
Removed from the list of medical devices	91
Suspended	243

Tab. 40 **Overview of administrative proceedings**

Administrative proceedings	Number of SÚKL codes
Commenced	9
Decided	31
Concluded	10

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 its 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

4.20 Unit of State Agency for Medical Cannabis

In 2020, 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 2020, the Institute took over and placed in distribution 11,610 grams of medical cannabis (as per the licence of 2017) and 6,510 grams (as per the current, 2020 licence) from the winner of the public contract for the supply of medical cannabis, Elkoplast Slušovice s.r.o. By means of the fifth to seventh medical cannabis order (as per the 2017 licence), the Institute ordered the total of 11,410 grams medical cannabis from the successful supplier, and 19,000 grams of medical cannabis by means of the first order as per the 2020 licence, 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 Unit, 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, i.e. in 2019, 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 2020, 263 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 93 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. 41 **Cannabis dispensing in 2020 by months**

Month	1	2	3	4	5	6	7	8	9	10	11	12
No. of issued e-prescriptions	920	1 007	1 045	855	1 053	1 324	1 389	1 165	1 408	1 363	1 331	1 307
No. of patients for whom medical cannabis was prescribed (unique)	733	790	796	735	920	1103	1087	998	1199	1197	1127	1103
Dispensed amount of medical cannabis (g)	3 398,79	3 820,45	4 527,53	4 001,53	5 078,38	6 050,09	6 409,41	5 607,99	6 857,49	7 160,22	7 064,54	6 789,16

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■ COORDINATION OF EXPERT ACTIVITIES

4.21 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 and it 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 – reports 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 as well as its suspended, restored, or terminated supplies onto the market in the Czech Republic, within timelines stipulated by the Act and Decree. The reporting is done via an 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" section.
- 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 other than 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 2020:

- Suspended supplies: 1 898 reports (in 80 % of which supplies have already been restored);
- Terminated supplies: 628 reports;
- Restored supplies: 1 756 reports;
- Initiated supplies: 982 reports;
- Irreplaceable medicinal products: 124.

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 on the labelling and in the 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 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 Czech, the KOČ employee abides by the particulars stipulated by Section 3(6)(b) of Decree No 228/2008 Coll.
- In 2020, the Institute issued the total of 131 decisions allowing for the placement of a foreign-language batch into circulation, which is a 40% increase compared to the previous year.

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 an 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 products 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 2020, 41 approvals of import of non-authorised medicinal products from third countries were issued in total, which is 95 % more than in the previous year.

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 2020, 4 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 group of patients.
- In 2020, the Institute drafted opinions on 79 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 to authorised proprietary medicinal products. KOČ employees consult such alternative options with pharmaceutical specialists.

2.6 In 2020, the KOČ unit drafted three opinions on submitted applications for the implementation of a specific therapeutic programme as referred to under Section 49(6-9) of Act No 378/2007 Coll., on Pharmaceuticals.

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 products replaceability for the Quality Defects Unit and the Marketing Authorisation Section. In total, this concerned 21 replaceability assessments for the Quality Defects Unit and 18 assessments of exemptions from the sunset clause for the Marketing Authorisation Section in 2020.

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. A major increase in the number of procedures has been observed also in respect of this activity. In 2020, KOČ sent the total of 37 reports on jeopardised availability for 209 codes of medicinal products in total and six proposals for exclusion from the list for 33 codes 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 2020, the Institute validated 831 applications for distribution of listed products abroad submitted by distributors, which represented a year-to-year growth of 1,350 %. 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 a significant impact on 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 2020, KOČ submitted 13 motions 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 2020, the Czech Republic was represented in the Supply Chain Disruptions Working Group by the KOČ Unit; the group prepared a template 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.

7. Activities associated with the COVID-19 pandemics

7.1 Throughout the pandemics, the KOČ Unit carried out monitoring of availability of medicinal products necessary for the treatment of hospitalised patients. This concerned, in particular, pharmaceuticals intended for intensive care units. The scope of monitored medicinal products was derived from the lists of essential medicinal products of EMA and EC working groups.

7.2. For the Ministry of Health, the KOČ Unit drafted six expert opinions on non-authorised medicinal products as referred to under Section 8(6) of Act No 378/2007 Coll., on Pharmaceuticals, and compiled lists of medicinal products whose re-export is to be restricted during emergency situations.

7.3 The KOČ Unit was assessing the impact of restricted API manufacture in China, restricted export from India, and Brexit on the availability of medicinal products.

7.4 The KOČ Unit was involved in the provision of comments on the COVID-19 vaccination strategy.

5 PROCESSING AND PROVISION OF INFORMATION

5.1 Information Technologies

In the area of information technologies, 2020 was affected by the outbreak of COVID-19 pandemics. As a priority, employees were provided with technical means allowing them to work in the home office mode, which was the major method of work of internal staff due to the pandemics. It concerned, in particular, the procurement of new notebooks, headphones sets, and web cameras. Furthermore, during 2020, IT technology was being replaced according to a predefined schedule. This mostly concerned the provision of mobile technology (especially notebooks) to end users.

With regard to the aforementioned reasons, last year, the performance of infrastructure components was enhanced, in particular that of the electronic prescription system, on the database and application server level. Furthermore, the performance of the terminal environment was enhanced with a view to the abnormal number of employees working in the home office mode in association with the aforementioned COVID-19 pandemics. The terminal environment was extended with new virtual servers so as to be able to provide the needed capacity for the work of large number of users working from home. In association with this, also end-user support provided by the IT staff in the implementation of home office work was enhanced.

In terms of internal system operation, in 2020, new tenders were opened for some areas of servicing, reflecting the new requirements for cybersecurity and the situation associated with a higher degree of risk of cyber-attacks. In late 2020, preparatory works concerning the reconstruction of the second data centre in Prague to be implemented in 2021 took place.

It may be stated that in 2020, the Information Technology Department continued to implement numerous measures to further increase the security level of operated systems as well as the availability of the Institute's information systems in line with the global trends in this area and the growing risk of potential cyber-attacks aimed at the Institute's systems.

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"), as one of the components of the ePrescription system, 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 paper-based prescriptions 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. In an open tender in 2020, a new service agreement was awarded that ensures support and development of all of the ePrescription system components that, pursuant to Section 81 of the Act on Pharmaceuticals, includes the CÚER repository, a Registry of Restricted Medicinal Products ("RLPO"), the medication record, consent administration, and other components listed therein.

Since 01 January 2018, the system has been operated in the mode of mandatory electronic prescription. Throughout 2020, as well as in the previous years, its operation did not exhibit any major problems. Health insurance companies routinely download batches of ePrescriptions for their clients, 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"). Furthermore, parents have the option to view ePrescriptions issued for their underage children. 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.

The ePrescription system provides numerous 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 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, and, in 2020, as many as the record 28.5 million SMS messages and 840 thousand e-mail messages.**

Since the launch of the electronic prescription, the www.epreskripce.cz website is being continuously updated. This website is the publication

point for any information concerning the ePrescription or medication record and other news from the sphere of eHealth.

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 and operator 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.

In 2020, more than 79 million ePrescriptions were issued; almost 77 million were dispensed; the total value of reimbursements of the dispensed reimbursed medicinal products prescribed via the ePrescription system exceeded 32,981,849 thous. CZK, which only confirms the routine operation and usage of the system. Another piece of evidence, moreover, may be also the fact that on 2 November 2020, the number of ePrescriptions issued since January 2018 reached 200 million.

Almost 50 thousand doctors and dentists, i.e. their vast majority, had SÚKL generate access data for them. In 2020, 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 2020, 45,763 doctors, 18,247 healthcare facilities, and 2,875 pharmacies were actively involved.

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 nationwide 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 numerous changes relevant for the area of electronic prescription.

The most eagerly awaited change is the sharing of the patient's Medication List, which is, in principle, a register of all issued and, where applicable, dispensed ePrescriptions for a particular patient with an established identity. The Medication List may be viewed only for a 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 List, an opt-out system was selected, so that the patient's Medication List 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. At any time, the patient has a right to express his/her global disagreement with doctors or pharmacists viewing his/her Medication List. Equally, the patient 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 List of their children.

The patient's consents or disagreements may be set up as the patient desires via the patient web application, the patient's data mailbox or a letter signed with an officially authenticated signature.

Viewing the patient's Medication List proper has been possible since 01 June 2020. Along with the launch of the shared Medication List, it is possible to avail also of the medicinal product prescription duplicity check. In case the healthcare professional wishes to view the patient's shared Medication List, the process is exactly defined by legislation. Pursuant to the effective legislative provision, the initial viewing of the patient's shared Medication List by the doctor who, to date, has not prescribed any ePrescription for the patient, is possible only upon the presentation of the patient's identification document. Nevertheless, where an established link between the doctor and patient is evidenced by the fact that this doctor prescribed an ePrescription for the patient in the past, which was then dispensed in the pharmacy, the presentation of the identification document is not required. The pharmacist may view the list only if the

patient presents his/her identification document or when the pharmacist dispenses an ePrescription which is valid (i.e. may be dispensed).

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 paper-based 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. These concern the cancellation of two-item prescriptions as of 01 June 2020; 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 into the system, 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.

As of 1 April 2020, the citizens of the Czech Republic may apply for an excerpt of ePrescriptions issued and dispensed for them in a selected period of time from the ePrescription system at a public administration contact point (Czech POINT). Thanks to this functionality, the patient may have his/her electronic prescriptions printed out at a Czech POINT site. The scope of the data to be provided is defined by the relevant legislation.

As of 1 June 2020, the patient has a new option to provide a list of all of the identifiers of his/her ePrescriptions for dispensing in a pharmacy by presenting his/her machine-readable identification document – primarily the ID card. On the basis of the patient's presented document, the pharmacist can retrieve a list of all ePrescriptions issued for the patient. The medicinal product dispensing proper is then carried out as usual on the basis of the obtained ePrescription identifiers.

The ePrescription system has proven to be much valuable particularly at the time of the COVID-19 pandemics in the Czech Republic. During this difficult period, the electronic prescription rather effectively supported the desirable social distancing, significantly reducing the need for patients to come to doctors' offices, which much contributed to safeguarding the protection of health for all citizens of the Czech Republic.

Fig. 28 **Number of prescribed and dispensed ePrescriptions in individual months of 2020 (mil.)**

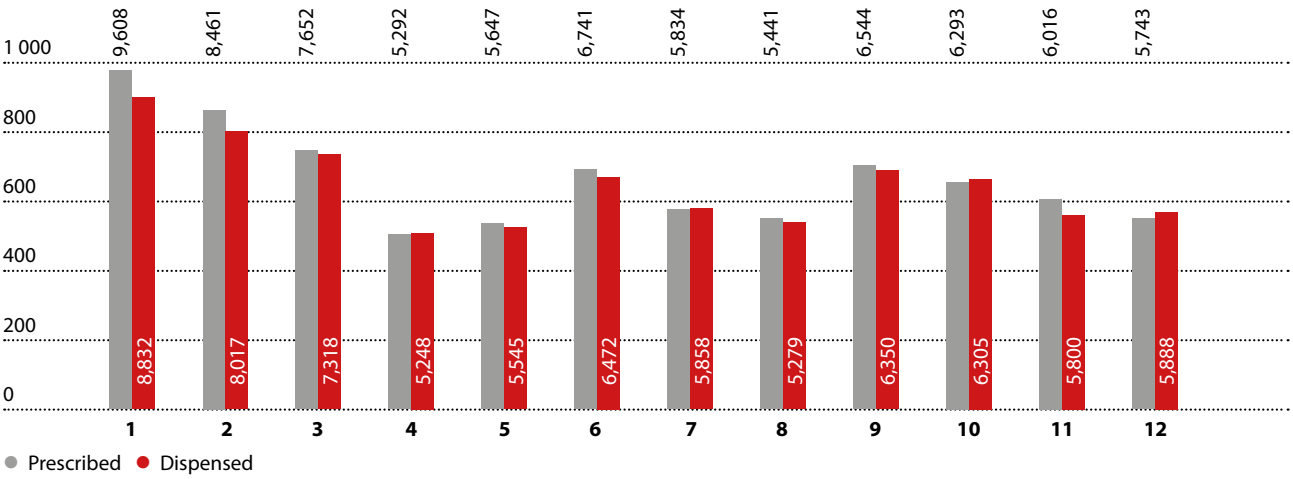
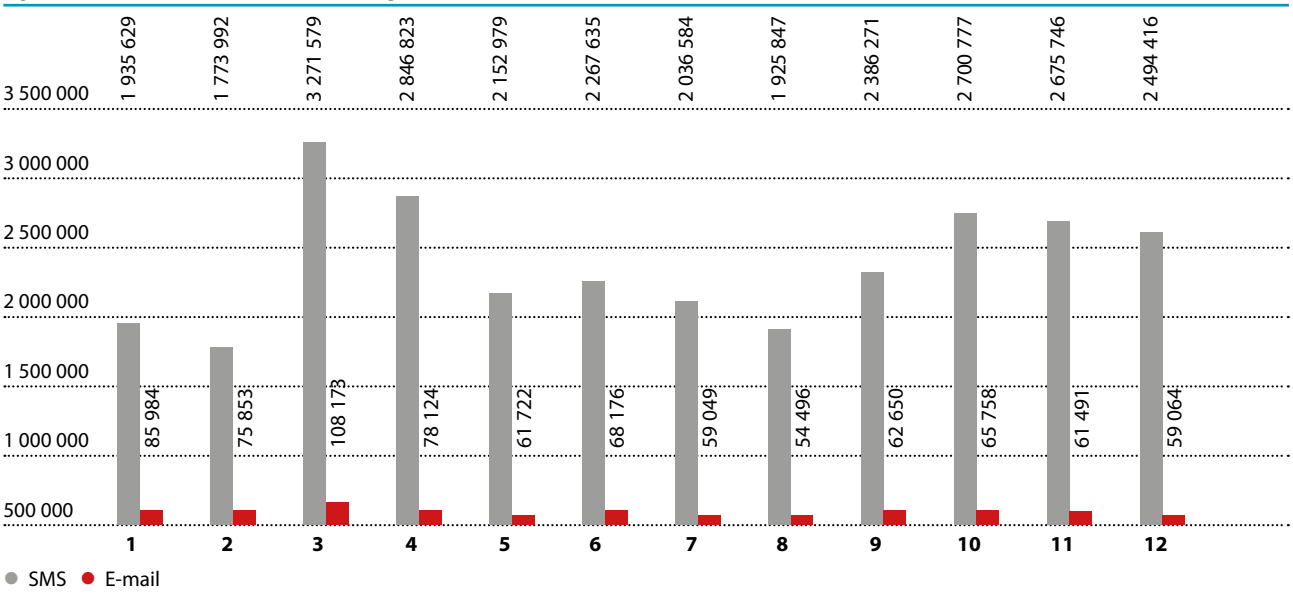


Fig. 29 **Number of e-mail and SMS messages sent in 2020 (thous.)**



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 ("DLP") is used, which is updated on an ongoing basis.

Registry of Active Substances

At present, the DLP Component Library contains 18,983 components (incl. combined components). In 2020, 405 new components were entered.

- In 2020, an update of flagging of doping components and of products containing such substances in the DLP was carried out pursuant to The 2020 Prohibited List – The World Anti-Doping Code effective as of 01 January 2020. 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, 93 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 2020 Supplement amended, together with corresponding data from the European Pharmacopoeia, 10th edition.
- During revisions of pharmacopoeias, synonyms were amended to be consistent with the new concept of the DLP Component Library (dedicated lines for certain literature sources).
- 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 dependency-producing and psychotropic substances were updated in compliance with Government Regulation on the lists of dependency-producing substances.
- The revision of the entire DLP Component Library has continued.

Registry of Medicinal Products

In 2020, the Institute granted 401 marketing authorisations (2,221 SÚKL codes). Authorisation was revoked for 485 marketing authorisation numbers, which corresponds to 4,727 codes. The authorisation was revoked either upon request of the marketing authorisation holder (340 marketing authorisation numbers), or due to the sunset clause (118 marketing authorisation numbers), or due to the fact that the holder did not apply for marketing authorisation renewal (27 marketing authorisation numbers). The validity of 5,598 codes in total expired (the period of the code final sale expired or marketing authorisation was revoked).

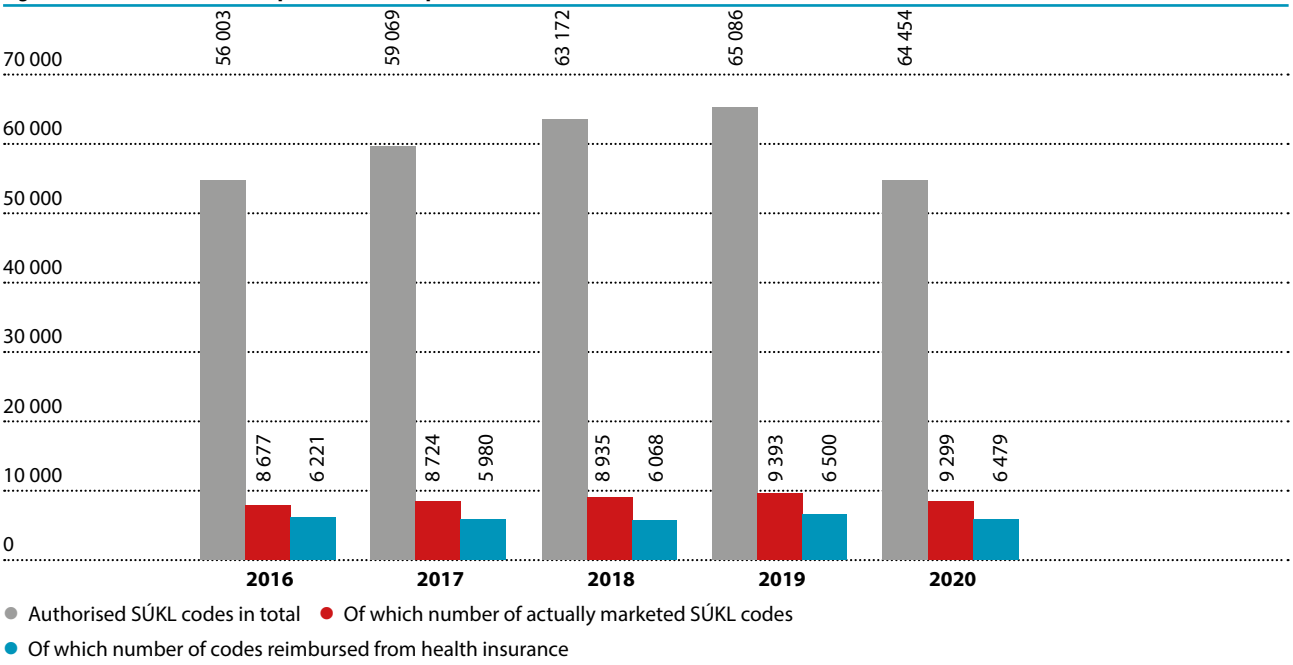
In the course of 2020, no distribution was reported for 55,155 codes (86 %) of medicinal products, excluding homeopathic preparations. Hence, despite having a valid marketing authorisation, these products were not placed on the market.

Authorised medicinal products contained 2,767 various active substances in total.

Tab. 42 **Selected subgroups of authorised medicinal products recorded in the Institute's database as of 31 December 2020**

	Total no. of marketing authorisation (MA) numbers / marketed MA numbers	Total no. of MA numbers / marketed MA numbers
Medicinal products in total (excl. homeopathic preparations)	**18,385/6,308**	**64,454/9,299**
Of which by MA numbers:		
MA numbers granted by the Institute	6,416/4,875	52,456/7,859
MA numbers of products authorised via Community Centralised Procedure	11,969/1,432	11,998/1,440
Of which by content:		
Single-component	14,790	51,767
Multi-component	3,600	12,672
Of which by type of dispensing:		
Prescription-only medicinal products	17,535/5,618	60,162/8,114
OTC medicinal products	893/698	4,172/1,168
Restricted OTC medicinal products	6/5	38/6
Restricted prescription-only medicinal products	7/6	82/8
Homeopathic preparations	274/274	865/409

Fig. 30 **Authorised medicinal products in the period of 2016–2020**



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 publication 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.

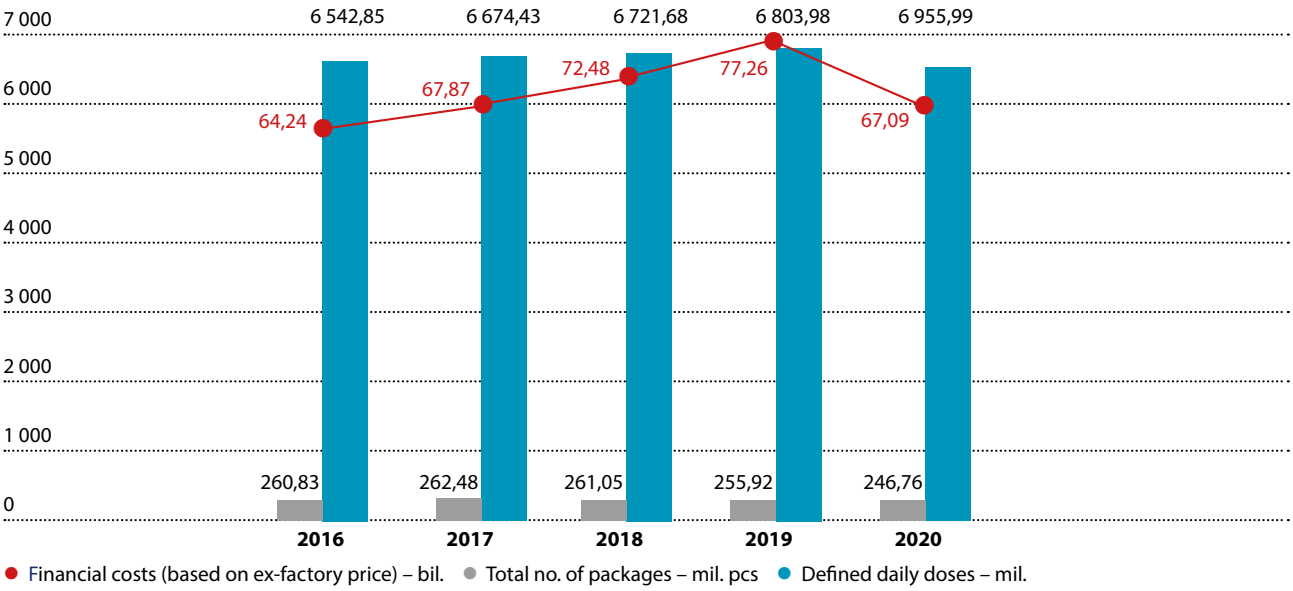
Evaluation of Deliveries of Distributed Medicinal Products

In 2020, 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 2020, the Institute has been receiving data about the price of a medicinal product only for medicinal products in respect of which reimbursement from the public health insurance funds has been established. Since 2008, the Institute's website provides 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 2020, 246.76 million packages of medicinal products were distributed, which corresponds to approx. 6,955.99 mil. DDD. The value of these deliveries amounted to 67.09 billion CZK (based on ex-factory price).

Fig. 31 **Deliveries of medicinal products in 2016–2020**



In 2020, the Data Analysis Unit processed the total of 5,320 data outputs pertaining to data from the database of medicinal products (DLP), reports on deliveries of medicinal products made by 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.

Tab. 43 **Deliveries of distributed medicinal products in 2020**

Medicinal products in total	**Number**
Deliveries to pharmacies and healthcare facilities (mil. packages)	246.757
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	67,086.737
Deliveries to pharmacies and healthcare facilities (mil. DDD)	6,955.987
DDD/1,000 inhabitants/day	1,784.216
Prescription-only medicinal products	**Number**
Deliveries to pharmacies and healthcare facilities (mil. packages)	171.479
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	66,811.104
Deliveries to pharmacies and healthcare facilities (mil. DDD)	6,323.345
DDD/1,000 inhabitants/day	1,621.943
OTC and selected pharmaceuticals	**Number**
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. packages)	75.077
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. CZK based on ex-factory price)	275.633
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. DDD)	632.556
DDD/1,000 inhabitants/day	162.251
Restricted OTCs	**Number**
Deliveries to pharmacies and healthcare facilities (mil. packages)	0.201
Deliveries to pharmacies and healthcare facilities (mil. DDD)	0.086
DDD/1,000 inhabitants/day	0.022
Homeopathic preparations	**Number**
Deliveries to pharmacies (mil. packages)	1.646

5.3 Information Activities

The primary task of the Press and Information Unit (TIO) is to provide information on SÚKL's activities to the general public and to professionals. The most important sources of information about the Institute are the websites 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 were answering questions raised by the public: a general practitioner, a paediatrician, and two pharmacists. Thanks to that, it was possible to answer 131 patient questions. In 2020, 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.

The transfer of the issue of anti-microbial resistance (AMR) onto the national level meant also continued information campaign concerning AMR and the prudent use of antibiotics and the impact of their consumption on the development of resistance of infectious disease agents; a series of articles published in the Farmakoterapeutické informace bulletin; and the preparation of an awareness-raising campaign concerning proper use of antibiotics and antimicrobial resistance. The Institute strives to become a respected partner in this area both on the national and international level, in order to safeguard public health protection also in the coming period.

In 2020, TIO answered 3,738 inquiries from the general public and from professionals which were sent via e-mail or post. Approximately 2,431 more inquiries were handled through the infoline.

The Department drafted responses to 230 inquiries from journalists and provided regular statements for radio or TV broadcasting. Forty-two press releases and two reactions were published on the Institute's website.

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6 FINANCIAL AND MATERIAL RESOURCES OF THE INSTITUTE

6.1 The 2019 Income and Expenditure Account

Income

In 2020, extra-budgetary income in the total amount of 581,662 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 costs and investment expenditures not covered by allocated financial resources from the state budget. In 2020, the total amount of 504,584 thous. CZK was used in this manner through permissible excess expenditure. Of this amount, 483,451 thous. CZK were used for non-investment expenditure and 21,133 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 29,660 thous. CZK, income from imposed fines amounting to 7,739 thous. CZK, income from lease in the amount of 282 thous. CZK, income from the sale of goods amounting to 4,434 thous. CZK (medical cannabis), refunds of excess advance payments made, related fully to the previous budgetary years, and other compensations amounting to 849 thous. CZK, etc. Transfers from the reserve fund line shows the volume of extra-budgetary income used for the funding of expenditures in 2020. An overview of the reported state budget income as of 31 December 2020 is provided in **Tab. 44.**

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Tab. 44 **State budget funds (thous. CZK)**

Item	Approved budget	Item
Administrative fees	19,800	29,660
Received penalty payments	1,000	7,739
Income from lease	0	282
Income from the sale of goods	0	4,434
Income from the provision of services	0	5
Received non-capital contributions and compensation	0	849
Transfers from the reserve fund	0	504,584
CELKEM	**20 800**	**547 553**

Expenditure

Data concerning expenditures incurred in 2020 broken down by individual categories are provided in Table 45.

The total investment expenditure from extra-budgetary resources amounted to 21,128 thous. CZK. Investment resources were used to finance demolition of administrative building 23 A (4,101 thous. CZK), for the purchase of videoconference equipment (383 thous. CZK) and for the purchase of air-conditioning (86 thous. CZK). The costs of procured licences amounted to 1,855 thous. CZK, the costs of technical upgrades of applications and SW to 8,667 thous. CZK (ERP, eSSL Athena, etc.), the purchase and replacement of HW cost 2,453 thous. CZK and the infrared spectrometer upgrade 168 thous. CZK. For laboratories, apparatuses in the total value of 1,431 thous. CZK were purchased (a UHQ water treatment apparatus, refractometer, melting point apparatus, and automatic temperature monitoring system). On the security features of interactive parts of the web (form), 1,984 thous. CZK were spent.

Non-investment expenditures were utilised in the total amount of 646,546 thous. CZK, of which 163,032 thous. CZK came from the state budget and claimed unused expenditures amounted to 391 thous. CZK; 483,123 thous. CZK were taken from extra-budgetary resources. Extra-budgetary resources included resources from abroad provided for the EURIPID project (utilised amount: 25 thous. CZK), the STARS project (utilised amount: 16 thous. CZK), and the EUnetHTA project (utilised amount: 10 thous. CZK).

Tab. 45 **Expenditures (thous. CZK)**

Indicator	Approved budget	Final budget	Actual
Employee salaries	24,155	50,202	50,201
Civil servant salaries	91,783	287,323	287,304
Other payments for completed work, severance pay, surrenders	3,603	13,111	13,109
Mandatory insurance premium	40,405	117,384	117,371
Contribution to the Fund of Social and Cultural Needs	2,319	6,786	6,785
Operating acquisitions and related expenditure	967	172,268	171,776
Acquisition of long-term tangible and intangible fixed assets	0	21,133	21,128
TOTAL	**163,232**	**668,207**	**667,674**
Of which: operating expenditure	163,232	647,074	646,546
capital expenditure	0	21,133	21,128

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 products prices. At present, more than 26 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. The output from the grant was an open publication of a set of recommendations helping to minimise the potential negative impact on the availability of medicinal products resulting from incompetent utilisation of foreign price references. In 2018, the project received European support to enhance cooperation among Member States in the sphere of medicinal product pricing. At present, discussions on possible extension of the EURIPID database to include medicinal products not subjected to reimbursement and, in the future, also medical devices, are under way. In 2020, 32,889 CZK were utilised for payroll and statutory deductions in the project (of which 23,847 CZK were covered from foreign funds in 2020).

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 a 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 2020, 7,713 CZK were utilised for the project from foreign funds (payroll, incl. statutory deductions and travel allowances).

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 objective of the project is the provision of support for academic research in the form of consultation provision. In 2020, on the basis of a survey carried out in 2019 in selected sites involved in academic research, and on the basis of experience shared among the Member States, an educational event pilot project for three selected Member States – Hungary, Austria, and Italy – was prepared; the project is to be implemented in 2021. The Institute, along with The Netherlands, was chosen as the educational institution in this pilot project. In the next two years, a complex list of existing support activities for regulatory scientific advice in Europe will be created; an analysis of the aforementioned educational pilot project will be performed; and a specific plan of training in support of academic staff will be prepared. In 2020, 15,447.32 CZK from foreign funds were utilised for the project (travel allowances).

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 1 July 2018 until 30 June 2022. Of the total project costs, 75 % will be covered by the CEF TELECOM European subsidy. During 2020, attention was principally focused on testing the data exchange between the Czech Republic and other Member States. On the basis of these tests of interaction with other Member States, the Czech cross-border exchange interface was continuously improved and modified. In the second half of the year, the interface proper was upgraded to Wave 4 involvement specifics, which required numerous adjustments in the solution proper. In the course of the year, also communication with pharmacy SW vendors was intensified, as it may be assumed that the major output from this project will be utilised particularly in Czech pharmacies. In the next year, the project team will focus primarily upon successful completion of audit tests, so as to pass the scheduled audit process with the European Commission in the autumn months and to be able to roll-out the production version of the system. In 2020, project expenditures amounted to 2,611,315 CZK (extra-budgetary funds of the Institute).

Other

A total of 428,237.96 CZK were used for foreign activities (such as expert assistance, participation in international institutional programmes, education). The conduct of foreign business trips was strongly limited due to the COVID-19 pandemics. In 2020, 44 foreign business trips took place, of which 14 were covered by SÚKL and 30 trips were fully or partially refunded by the organising institutions (EC, EU Council, EMA, etc.); 32 foreign trips were cancelled due to the COVID-19 pandemics and 264 were conducted online, i.e. mostly without any other costs incurred by the Institute; five attendances at foreign educational events took place.

The purpose of most business trips was participation in regular meetings of various committees and working groups resulting from membership in the relevant bodies. SÚKL has its members or alternates in more than 80 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 beneficial. Other business trips were approved in compliance with the principles, such as association with SÚKL's priorities, the relevance and benefits of the discussed topics for SÚKL.

Assets

The total assets as of 31 December 2020 amounted to 1,298,284 thous. CZK, of which fixed assets represented 388,522 thous. CZK and current assets 909,762 thous. CZK. Of the total liabilities of 1,298,284 thous. CZK, equity amounted to 1,255,740 thous. CZK and borrowed capital to 42,544 thous. CZK. Selected types of assets and liabilities are listed in Tab. 46.

Tab. 46 **Overview of selected types of assets and liabilities of the organisation (thous. CZK)**

Item	Past period	Current period
	2019	2020
ASSETS	**1,244,051**	**1,298,284**
A. Total fixed assets	**413,782**	**388,522**
of which:		
I. Long-term intangible fixed assets – total	95,350	93,085
II. Long-term tangible fixed assets – total	318,432	295,437
of which:		
Lots	4,530	4,530
Buildings	243,363	231,920
Separate tangible movables and sets of tangible movables	70,022	54,416
Unfinished tangible fixed assets	517	4,571
B. Total current assets	**830,269**	**909,762**
of which:		
I. Inventory - total	1,951	905
II. Short-term receivables - total	12,317	14,193
III. Short-term financial assets - total	816,001	894,664
LIABILITIES	**1,244,051**	**1,298,284**
C. Equity	**1,196,685**	**1,255,740**
of which:		
I Assets of the accounting entity and adjustments	227,425	226,626
II. Funds of the accounting entity	781,888	858,661
Fund for Cultural and Social Needs	2,224	1,873
Reserve Fund	779,664	856,788
III. Economic result	–729,643	–866,683
Economic result for the current accounting period	–131,961	–137,040
Economic result for the previous accounting periods	–597,682	–729,643
IV. Income and expenditure account of the budget management	917,015	1,037,136
D. Total borrowed capital	**47,366**	**42,544**
of which:		
I. Total long-term liabilities	0	0
II. Total short-term liabilities	47,366	42,544

Auditing

In 2020, no audits conducted by public administration bodies pursuant to the Act on Financial Audits 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 2020 pursuant to Act No 234/2014 Coll., on Civil Service, as of 01 January 2020, the number of systemised positions was 571 positions, of which 460 were civil service positions and 111 employment positions.

As part of the organisational changes associated with the Institute's systemisation effective as of 1 January 2020, in addition to the increased number of civil service and employment positions compared to 2019 (required by new activities implied by the legislation), several substantial changes were implemented, particularly within the organisational structure of selected regulatory sections and departments.

In the course of 2020, several other systemisation modifications were implemented with effect as at 15 March 2020, 1 May 2020, 1 August 2020, and 1 October 2020; these modifications concerned primarily the workplace changes in order to safeguard consistency in the decision-making practice, methodological cooperation among individual units of the Section of Pricing and Reimbursement Regulation, continuous expert education, and, last but not least, better communication and cooperation both within the horizontal job structure (within a single unit and among various positions) and the vertical structure (between the management and the units), and increased effectiveness in fulfilling the activities prescribed by law; other partial changes pertained to the subordination in respect of some specific service positions.

The number of physical employees on the Institute's payroll as of 31 December 2020 was 530 persons, of which 423 were women (i.e. 79.8 %) and 107 were men (i.e. 20.2 %).

Within the scope of the Personal and Working Life Harmonisation Policy, as of 31 December 2020, the total of 72 employees of the Institute (of which 70 were women), i.e. 13.6 % of the total number of employees, worked part-time.

Tab. 47 **Numbers of employees at local workplaces**

Brno	38
České Budějovice	5
Hradec Králové	7
Olomouc	5
Ostrava	4
Plzeň	2
Praha	469

Age Structure of Employees

Average age: females 43.3 years; males 42.3 years. The overall average age of all employees is 43 years.

Tab. 48 **Age structure of employees as of 31 December 2020**

Year	% of employees under 35 years	% 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
2020	28,9	53	18,1

Qualification Structure of Employees

Tab. 49 **Qualification structure of employees by achieved level of education as of 31 December 2020**

Highest achieved education	Primary	Secondary	Technical colleges	University – bachelor's degree	University – master's degree	Postgraduate Postgraduální
Number of employees	2	98	5	26	357	42
% of the total number of employees	0.4	18.5	0.9	4.9	67.4	7.9

Staff Turnover

The overall staff turnover taking into account all start-ups and departures, amounted to 10.13 %, which was comparable to 2019.

In total, 218 tenders were completed on the basis of which the total of 98 employees were admitted.

In 2020, 53 employees terminated their employment or civil service.

Tab. 50 **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	**128**	**55**	**90**	**43**

Tab. 51 **Overview of employment and civil service terminations in 2020 by reason of employment/civil service termination**

	Pracovní poměr	Služební poměr
Cancellation of employment/civil service in probationary period	8	4
Agreed time expiry	4	0
Termination by agreement (Section 49 of the Labour Code)	7	0
Notices given by employees/termination of civil service upon request of the civil servant	4	17
Notices given due to organisational reasons/by decision of the civil service authority	2	1
Termination of civil service performance with the Institute due to transfer of the civil servant to another civil service authority	0	1
Retirement	1	4
Celkem	26	27

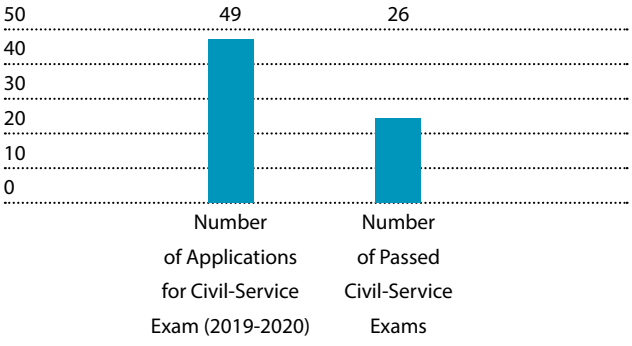
Civil-service Exam

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).

Fifteen applications were brought forward from 2019 to the next calendar year and in the course of 2020, 34 applications lodged by the employees of the Institute were newly registered, which amounts to 49 applications in total. Of the total number in 2020, 26 employees successfully passed both parts of the civil-service exam. The remaining 23 employees will take the exam in 2021 (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 two employees did not succeed on the first attempt (in the specialised part of the civil-service exam). The first employee successfully passed the exam on a second attempt; the other one will repeat the exam in 2021, before the definite period of time expires for him.

Fig. 32 **Civil-service exams in 2020**



7.2 Employee Education

In 2020, employee educations was profoundly affected by the epidemiological situation caused by the COVID-19 disease. The dates of many specialised trainings or conferences were postponed (or cancelled), depending on the currently effective government regulations and measures associated therewith (such as limited number of attendees, cancelled events). For this reason, employees took part mostly in seminars or conferences organised online.

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 education, 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. There were practically no foreign educations events, as the global epidemiological situation did not allow for their organisation.

Due to the COVID-19 disease, management training of managerial staff was organised within the necessary scope in the form of online education in 2020. When the measures were lifted, education took place in the necessary scope and it focused upon the development of personal talents and management skills.

The epidemiological situation hindered also language education, which was suspended for a substantial period of time. Individual language courses were resumed as the measures were lifted (group classes did not take place). The new term was started fully in online format. Language education was organised primarily for the employees of regulatory units who use the English language for necessary work purposes, and for employees representing the Institute in international and multinational institutions, audits, and inspections.

In 2020, the Information Security (Cybersecurity) Manager and the Data Protection Officer organised a mandatory training via an external entity in the form of e-learning for all employees of the Institute (a cybersecurity basics course and a course for cybersecurity managers).

The total volume of funds incurred for all types of educational activities amounted to **1 376 000 Kč**.

Tab. 52 **Overview of educational activities in 2020 – follow-up education**

Type of event	Number of events	Number of hours	Number of attendees
Specialised courses & training; language courses	865	2 525	465
Mandatory training	89	188	677
Foreign specialised training	4	112	5

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8 FOCUS UPON QUALITY

The continuous intention of the Institute in the area of quality management 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 2020, the quality management system was being maintained and further developed in compliance with the requirements of the ČSN EN ISO 9001:2016 standard. In November 2020, the LL-C (Certification) Czech Republic s.r.o. certification body conducted a re-certification audit of some of the Institute's processes and noted that the Institute's quality management system continued to meet the requirements of this standard, granting the Institute an ISO 9001 certificate for the next three years.

The Laboratory Control Department, which is part of the Surveillance Section, has developed a quality system compliant with the ČSN EN ISO/IEC 17025:2018 standard. In October 2020, a successful compliance check of the established quality system with the standard was carried out in the form of an international audit (MJA – Mutual Join Audit).

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, 23 such internal audits took place in 2020.

9 INFORMATION SECURITY MANAGEMENT POLICY

2020 brought new risks as well as challenges for the Institute in terms of security of information systems and information processed therein. With regard to the government and internal measures aimed at preventing the spread of the COVID-19 infection, a huge volume of communication with the Institute moved to the electronic format, as information was provided/shared via e-mail, data and documents were collected by means of electronic forms, and teleconferences and meetings replaced personal meetings. A global shift towards this form of communication encouraged an extraordinary spread of hacker activities and cyber-attack attempts. The prevailing type of attacks were phishing or spearphishing attempts, but a significant increase was also seen in so called outer perimeter scanning and attempts to break into systems in this manner.

To date, the implementation of ad hoc measures and recommendations from relevant national security authorities as well as of own measures based upon the analyses of attempted attacks has successfully warded off such attacks.

In May 2020, the Institute successfully passed a recertification audit of the information security management system (ISMS) as per the ČSN ISO/IEC 27001:2014 standard, which means that it has been the holder of the relevant certificate for as long as 13 years.

The high standard of information security system implemented in the Institute has been repeatedly noted also by international audits conducted by concerned European quality authorities.

The achieved level of information security in the Institute, however, does not mean that it is possible to relax and ease off the measures established through constant development of security actions, both on the technical and operational level. The activities and methods of potential attackers should be expected to grow quantitatively as well as qualitatively. For this reason, the development of the information security system remains a high priority of the Institute also in the coming years.

10 OUTLOOK FOR 2021

In 2021, the State Institute for Drug Control shall focus much of its attention upon activities associated with the COVID-19 disease. Through its representatives in the committees of the European Medicines Agency, it has been actively involved in the authorisation of vaccines against this disease, the recording, processing, and evaluation of reported suspected adverse reactions to these vaccines, and also in the activities of administrative batch release for the Czech Republic.

In the area of marketing authorisation of medicinal products, it is possible to anticipate an increase in the number of requests for abbreviated procedures and regulatory flexibility for medicinal products needed for supportive treatment of COVID-19 (such as medicinal oxygen) as well as a greater involvement in centralised marketing authorisations of pharmaceuticals intended directly for the treatment or prevention of the COVID-19 infection (monoclonal antibodies, vaccines). In the area of pharmacovigilance, an increased interest in suspected adverse reaction reporting for COVID-19 vaccines is anticipated, with enhanced demands for the monitoring of their safety. The requirements for abbreviated timelines will influence also the Clinical Trials Department, where clinical trials on pharmaceuticals for the treatment or prevention of the COVID-19 infection are assessed in abbreviated procedures. The interest in consultations regarding new COVID-19 medicines is also expected to increase.

In terms of medicinal products availability, the current priority is to safeguard medicinal products for intensive care, which is being constantly monitored by the Institute due to the ongoing pandemics; to safeguard sufficient manufacturing and distribution capacities for medicinal oxygen; and to draft expert opinions on new treatment options for COVID-19.

In 2021, the Medical Devices Department will continue to intensively cooperate with the Customs Administration, so as to ensure that medical devices non-compliant with the legislative requirements be held prior to their entry into the Czech Republic and prevented from being placed on to the market. Furthermore, inspections of face mask manufacturers will be completed to see whether the manufacturers and the devices manufactured thereby meet the requirements stipulated by legislation. Furthermore, an intensive control of antigen test and face mask vendors has been under way, during which labelling and storage of these devices are primarily checked.

In 2021, Regulation (EU) 745/2017 on medical devices (MDR) and, in 2022, Regulation (EU) 746/2017 on in vitro diagnostic medical devices (IVDR) are to become effective, bringing major changes to the method of inspecting and enhanced demands for the sharing of information about the surveillance activities conducted by the competent authorities on the EU level; all this will require organisational, staffing, and process changes in this area. Last but not least, a new Act on Medical Devices will become effective, the draft of which newly incorporates surveillance over advertising under the surveillance activity powers.

The new system for the management and keeping of administrative procedures of the Pricing and Reimbursement Section will comply with the requirements for advanced agenda systems. The new system should support administrative activities that may be automated, and hence facilitate the management of the Section.

The Surveillance Section, inter alia, completed a Good Manufacturing Practice (GMP) certification of COVID-19 vaccine manufacturers, specifically Novavax CZ, a.s., Czech Republic, and SK Bioscience Co. Ltd., South Korea. Further inspections aimed at verification of compliance with the GMP requirements or extended validity of the issued certificates will be carried out in both entities also in 2021.

In 2021, new legislation introducing a new eHealth instrument, an electronic order for medical devices, is to become effective. It is expected that this new module will be developed and implemented in the ePrescription system, safeguarding electronic communication among the prescriber, patient, dispensary, and health insurance company.

Furthermore, the ePrescription system is planned to be extended with a cross-border prescribing and dispensing option within EU Member States. In 2020, the system was created and tested. In 2021, it is expected to be attested and rolled out into routine operation. This system will allow for dispensing of medicinal products also outside the home country.

In 2021, the Institute will also focus upon the planning and implementation of the project of its new websites that are to become a modern platform presenting information in a standard corresponding to the current trends and demands for availability of information, straightforward navigation, visual layout, and search options.

In the course of 2021, the Institute will also focus upon the education of the general public in the area of storage and disposal of pharmaceuticals. STEM/MARK implements a research project called "Practical Use of Medicines and Its Financial Impact upon the Healthcare System in the Czech Republic", the results of which are being presented to the public.

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
DJ	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
PV	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 (zdravotnické prostředky)
NOOL	National Organisation for the Verification of Medicines (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 of Medical Device Department
PRAC	Pharmacovigilance Risk Assessment Committee
PSUR	Periodic Safety Update Report
PSUSA	Periodic Safety Update Single Assessment
RA	Rapid Alert
RAB	Rapid Alert System for Blood and Blood Components
RAN	Rapid Alert Network
RATC	Rapid Alert System for Human Tissues and Cells
RF	Radiopharmaceuticals
RLPO	Registry of Restricted Active Substances

RMS	Reference Member State
RSI	Reference Safety Information
RV	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
MAH	Marketing authorisation holder
ČSSZ	Czech Social Security Administration
DHPC	Direct Healthcare Professional Communications
DDD	Daily Defined Doses
KOČ	Expert Activity Coordination Unit
ADR	Adverse Drug Reaction
OZP	Medical Device Department
IVD	in vitro diagnostic medical devices
KOP	Medical Device Control and Expert Opinion Unit
KHV	Medical Device Clinical Trials and Vigilance Unit
RAN	Registration and Notification Unit
ONZP	Medical Device Notification Unit
UZP	Medical Device Reimbursement Unit

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