SÚKL

ANNUAL REPORT **2021**
STATE INSTITUTE FOR DRUG CONTROL

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CONTENT

1 INTRODUCTION

In 2021, the State Institute for Drug Control (hereinafter referred to as the "Institute" or "SÚKL") continued its highly intensive cooperation with the Ministry of Health of the Czech Republic (hereinafter referred to as the "Ministry"), particularly in the implementation of tasks within the scope of EU cooperation in the area of pharmaceuticals and medical devices as well as in the preparation and subsequent legislative process of the adoption of new legal regulations with relevance for the scope of the Institute's operation.

In cooperation with the Ministry of Health, the Institute commenced preparatory works on the new Act on Pharmaceuticals, specifically its splitting into the human and veterinary parts. Discussions are to continue in 2022. Furthermore, in 2021, the Institute continued its cooperation with the Ministry and with the Institute of Health Information and Statistics of the Czech Republic in the sphere of amendments to the approach to the draft act on healthcare electronisation. As further detailed herein, legislative amendments that the Institute was involved in, concerned also marketing authorisations of medicinal products, clinical trials on medicinal products, the area of medical devices, medical cannabis, and other topics. In cooperation with the Ministry of Health of the Czech Republic and with the Institute of Health Information and Statistics of the Czech Republic, the Institute was also involved in the modifications to the conception of the draft act on electronisation in healthcare.

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

The Institute has been actively involved in international cooperation in more than 100 working groups, subgroups, and committees. These are, in particular, the bodies of the EU Council, European Commission, and the European Medicines Agency (EMA), the World Health Organisation (WHO), the Council of Europe and its European Directorate for the Quality of Medicines and Health Care (EDQM) or the Organisation for Economic Cooperation and Development (OECD). Constant priorities of the Institute include primarily representation in EMA scientific committees which address the issues associated e.g., with the safety of medicinal products on the EU market or the approval of new pharmaceuticals. Last but not least, the Institute has been actively involved in informal groups of experts from various countries in the field of regulation of pharmaceuticals and medical devices, pricing, health technology assessment (HTA) or regulation of human tissues and cells. The main one of these informal groups is the Heads of Medicines Agencies (HMA) network that, along with EMA, form the European medicines regulatory network. The Institute has been involved in this network not only via the Institute's Director's membership, but also through direct involvement in the team for the executive support of the steering group of the entire network.

Following successful validation, the total of 616 applications were submitted for expert assessment to the Marketing Authorisation Section. In 2021, a growth in the number of received applications for DCP marketing authorisations with the Czech Republic as the Reference Member State was seen; the number of these applications increased from 85 in 2020 to 107 in 2021. Furthermore, 293 applications for the revocation of marketing authorisation were processed.

The lasting COVID-19 pandemics again affected also the area of clinical trials, with an increase in the agenda associated with the implementation of emergency measures applicable to new or ongoing clinical trials and the assessment of clinical trials on COVID-19 treatment or prevention was given priority and such studies were assessed via an abbreviated, rapid procedure. The number of consultations and queries associated with the preparation of clinical trial dossiers by academic sponsors increased. In 2021, the total of 409 applications for clinical trial authorisation/notification were submitted, which is 49 more than in the previous year. In total, 408 decisions were issued. Most applications concerned phase III studies, international, multicentric, randomized, blinded, placebo- or active-controlled clinical trials conducted by foreign sponsors.

In 2021, 13,759 suspected adverse drug reaction (ADR) reports were received from the territory of the Czech Republic. Of the total number of the received reports, 10,631 concerned COVID-19 vaccines. The remaining 3,153 reports concerned all other medicinal products. Each individual spontaneous report delivered to the Institute is processed, individually assessed, entered to the database of ADRs from the Czech Republic (CDNÚ) and, at the same time, sent to the pan-European EudraVigilance database as well as to the global WHO database.

The Laboratory Control Department completed 674 sample analyses. The number of samples rated as non-compliant slightly decreased (to 3.0 %). Defects were confirmed primarily in pharmacy samples. Otherwise the quality of proprietary medicinal products available on the Czech market is very good.

As of the end of 2021, the Institute registered the total of 2,476 pharmacies and 3,454 vendors of selected human medicinal products, 42 nuclear medicine departments of healthcare facilities, 385 medicinal product distributors, and 53 brokers of medicinal products for human use. In 2021, the inspectors of the Pharmacy and Distribution Department completed the total of 668 inspections of pharmacy care facilities – pharmacies, of which 39 concerned hospital pharmacies of inpatient care providers. In 2021, the inspections of vendors of selected medicinal products involved 130 shops in total; distributors were subjected to 242 inspections and brokers to three inspections.

In 2021, the Inspection Department conducted the total of 262 inspections as part of its surveillance activities in the area of manufacture of pharmaceuticals (incl. the manufacture of transfusion products and raw materials for further manufacture of pharmaceuticals), of which 59 inspections focused upon the regulated area of tissues and cells.

In 2021, the Quality Defects Unit that deals with cases concerning the occurrence of counterfeit medicinal products in the legal distribution chain addressed the total of 33 such cases, of which two were cases of theft of medicinal products from the legal distribution chain.

In 2021, the Institute addressed the total of 135 instigations concerning a breach of Act No 40/1995 Coll., on Advertising Regulation, as amended. In 2021, the number of addressed instigations was the same as in 2020. In 2021, twelve administrative procedures were completed and as a result thereof, 13 penalties amounting to the total of 1,330,000 CZK to for the breach of the Act on Advertising Regulation were imposed.

The Institute, as the supervisory authority, also conducts inspections of manufacturers, importers, distributors, persons servicing, selling, and dispensing medical devices, as well as activities in the field of assessments of proper placement of medical devices onto the market. The objective of both scheduled and ad hoc inspections conducted by the Institute is to ensure that medical devices supplied onto the market in the Czech Republic are safe and functional and that health care is 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 2021, the inspectors of the Control Unit conducted the total of 109 inspections, of which 47 were inspections at providers of healthcare services (both state and non-state healthcare facilities) and 62 were inspections at medical devices manufacturers, importers, distributors, and persons selling, dispensing or servicing medical devices.

In the course of 2021, the Section of Pricing and Reimbursement Regulation continued to commence in-depth reimbursement revisions as planned. The plan for 2021 included the commencement of 16 in-depth revisions; actually, 19 were commenced (233 SÚKL codes). In 2021, 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 2021 are estimated at 1,356,373,520 CZK and at 1,771,167,648 CZK, respectively.

In 2021, 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 2021, the Institute took over and placed into distribution 42,570 grams of medical cannabis from the winner of the public tender for medical cannabis supply, Elkoplast Slušovice s.r.o.

The ePrescription system keeps bringing a wealth of benefits to the patients as well as healthcare professionals and proved particularly valuable at the time of the COVID-19 pandemic 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 substantially contributed to safeguarding the protection of health for all citizens of the Czech Republic.

Electronic delivery of the ePrescription identifier – via SMS or e-mail messages – has been gaining an ever-growing popularity. The final total volume for 2021 grew to the record amount of almost 34 million SMS messages and 688 thousand e-mail messages. In 2021, more than 76 million ePrescriptions were issued and almost 75 million were dispensed, which only confirms the routine operation and usage of the system.

The Institute has been continuously extending the system. One of the changes is e.g., the electronisation of so-called blue-stripe prescriptions, i.e., prescriptions for medicinal products containing highly addictive substances listed under Annex 1 or 5 to Government Regulation on the List of Dependency-Producing Substances. Another new functionality is the electronic registry of vaccination records. Doctors have been obliged to make a record of applied vaccination since 01 January 2022 and this obligation is applicable to all vaccinations, regular, special, extraordinary as well as voluntary ones, reimbursed or non-reimbursed, with the temporary exception of COVID-19 vaccination. Furthermore, works on the amendment to external identities should be mentioned, which will cater for the authentication of other categories of healthcare professionals, incl. the use of the National Identity Authority, in association with the planned launch of electronic order (eOrder).

As part of its obligation to inform both the professionals and the general public, the Institute administers the following websites: www.sukl.cz, www.olecich.cz, www.epreskripce.cz and the OSALK website at www.sakl.cz. The Press and Information Unit also provides for publication activities, specifically the preparation and publication of the Newsletter, the Farmakoterapeutické informace (Pharmacotherapeutic Information) drug bulletin, and the Zpravodaj nežádoucích účinků léčiv (Adverse Drug Reaction Newsletter).

2 SÚKL'S ORGANISATIONAL STRUCTURE

Organisational structure from 1. 1. 2021

DIRECTOR

- UnitInternal Audit and Control

- OfficePress and Information Unit
- UnitHuman Resources and Education Unit
- UnitExpert Activity Coordination Unit

Marketing Authorisation Section

- Assistant
- Lawyer

Pharmaceutical Documentation Assessment Department

- Assistant
- Chemical and Herbal Products Assessment Unit
- Unit of Biological Product Assessment, Incl. Clinical Trials
- Variation Assessment and Parallel Import Unit
- Chemical Products in Clinical Trials Assessment Unit

Clinical Trials of Medicinal Products Department

- Assistant
- Clinical Trials of Pharmaceuticals Unit
- Coordination and Administrative Unit

Administrative and Procedural Support Department

- Assistant
- European Assessment Implementation Unit
- MA Section Validation Unit
- National Applications Unit
- MRP Applications Unit
- MA Data Support Unit

Coordination and Regulation Department

- Assistant
- MA Procedures Coordination Unit
- National Regulation Unit

Pharmacovigilance Department

- Pharmacovigilance Assessment Unit
- Pharmacovigilance Inspection and Data Support Unit

Non-Clinical and Clinical Assessment Department

- Regulatory Manager
- Centralised procedures coordinator
- Clinical Assessment Unit
- Non-clinical and Bioanalysis Assessment Unit

Surveillance Section

- Assistant
- Lawyer
- Advertising Surveillance Unit
- Quality Defects Unit
- Data Analysis Unit

Inspection Department

- Assistant
- Clinical Practices Unit
- Good Manufacturing Practice Unit
- Surveillance over Biological Materials Unit

Pharmacy and Distribution Department

- Regional Pharmaceutical Control Units 31210-31280
- Good Distribution Practice Unit

Laboratory Control Department

- Analytical Chemistry Unit
- Biological Methods Unit

Department of Director's Office

- Quality Manager
- Unit of International Relations
- Unit of State Agency for Medical Cannabis
- Director's Support Unit
- Legal and Legislative Unit

Section of Pricing and Reimbursement Regulation

- Assistant
- Validation and Administrative Support Unit

Pricing and Legal Support Department

- Data and Analytics UnitUnit
- Unit of Administrative Procedure Coordination
- Unit of Selected Types of Administrative Proceedings

Health Technology Assessment Department

- Medicines Evaluation Unit
- Health Economics Unit

Service Activities Section

- Assistant
- Information Security Manager
- Documentary Service and Mailroom Unit
- Public Contracts, Project Management and Investment Unit

Information Technology Departmente

- Assistant
- Security Manager IT
- Lawyer
- Operations Unit
- Management Support Unit
- Prescription Unit
- Business Analysis and Development Unit

Operations and Economics Department

- Accounting Unit
- Budget and Financing Unit
- Operations and Transport Unit

Medical Devices Department

- Assistant
- Registration and Notification Unit
- Medical Devices Clinical Trials and Vigilance Unit
- Legal Support Unit
- Medical Devices Reimbursement Unit
- Medical Devices Market Surveillance and Expert Opinions Unit

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

3.1 Cooperation with the Ministry of Health in the Area of Legislation

In 2021, 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 the scope of the Institute's operation.

Primarily, it should be mentioned that the Institute, in cooperation with the Ministry of Health, commenced preparatory works on the Act on Pharmaceuticals, specifically the splitting of the existing Act No 378/2007 Coll., on Pharmaceuticals, to a human and veterinary part. It was decided to prepare a new act due to the need of the actual division of regulation in the human and veterinary sectors, and also with a view to the excessive number of amendments made to the Act that significantly hindered the clarity of the Act which, in itself, is rather extensive.

Therefore, the Institute, as an authority in charge of, inter alia, drug policy, has been significantly involved in the drafting of the new wording of the Act. In 2021, in this respect, discussions were held with the Ministry of Agriculture and with the Institute for State Control of Veterinary Biologicals and Medicines. In the course of 2021, joint meetings with the Ministry of Health, the purpose of which was the preparation of the new legal regulation as such, took place. These meetings are to continue also in 2022. All concerned SÚKL's units have been actively involved in this process.

In 2021, the Institute continued its cooperation with the Ministry of Health of the Czech Republic and with the Institute of Health Information and Statistics of the Czech Republic in the sphere of amendments to the approach to the draft act on healthcare electronisation. Healthcare electronisation comprises of electronisation of processes and digitalisation of agendas aimed at increasing the effectiveness in the provision of healthcare services, their reimbursement and control. Healthcare electronisation forms an integral part of the healthcare system, nevertheless, it does not replace it or create parallel management and administration structures. The current legislation covers only some elements introducing healthcare electronisation. The existing fragmentary form of partial legislative regulation does not allow for effective management of healthcare electronisation systems. Quite clearly, a systemic and comprehensive legal basis for the introduction of new technologies in the sphere of healthcare electronisation, basic healthcare electronisation infrastructure, legally defined roles and responsibilities of entities in the healthcare electronisation system, and definitions of terms associated therewith, as well as communication standards and rules of sharing or transferring of medical documentation are missing. With a view to the aforementioned, it was decided to commence works on the preparation of a new act on healthcare electronisation, the draft of which will concern the Institute particularly in relation to the ePrescription system administered by SÚKL. This was one of the reasons why the Institute was so much involved in the provision of comments on the draft act to ensure that the proposed changes affected the ePrescription system users as little as possible and that the system was able to work as smoothly as to date. The Act on Healthcare Electronisation was published in the Collection of Laws as Act No 325/2021 Coll.; an accompanying Act that concerns, inter alia, also the amendments to the Act on Pharmaceuticals, was published in the Collection of Laws as Act No 326/2021 Coll.

The legislative amendments concerned also the marketing authorisation of medicinal products. In cooperation with the Ministry of Health of the Czech Republic, the Institute drafted an amendment to Decree No 228/2008 Coll., on marketing authorisation of medicinal products, which was presented with the aim to complete the adaptation of the national part of the legislative order of the Czech Republic in relation to Regulation (EU) 2017/745 of the European Parliament and of the Council 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 changing the text of section 3.2(12) of Annex 1 thereto. Furthermore, the draft Decree harmonised the text of the Decree with the current wording of the Act on Pharmaceuticals following the adopted amendments (in particular, adapting Regulation No 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 EMA guidelines, responding to real-world evidence by deleting some requirements which have currently proven to be obsolete. In 2021, the legislative process progressed through comment procedures up to the level of working commissions of the Legislative Council of the Government.

In the area of marketing authorisation of medicinal products, however, this was not the only change; the legislative amendments touched also upon the sphere of clinical trials on medicinal products. For this reason, the Institute prepared a brand new decree taking account of the adaptation of Regulation (EU) 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, completed via the amendment to the Act on Pharmaceuticals. The legislative process of drafting the new decree was successfully completed by publication in the Collection of Laws as Decree No 463/2021 Coll., on detailed conditions governing the conduct of clinical trials on human medicinal products, with effect as of 31 January 2022. At the same time, as at 31 January 2025, this implementing regulation revokes the original Decree No 226/2008 Coll., on good clinical practice and detailed conditions of clinical trials on medicinal products.

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 05 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 05 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 suitable complement to the 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 legal order 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. Following discussion on both bills by the Chamber of Deputies and Senate of the Parliament of the Czech Republic, the new Act on Medical Devices was published in the Collection of Laws as Act No 89/2021 Coll. The accompanying amending act was published as Act No 90/2021 Coll. In respect of the aforementioned accompanying act, the name and the subject-matter of the original Act No 268/2014 Coll. was also changed and the Act is newly referred to as the Act on in Vitro Diagnostic Medical Devices. The new legislation came in to effect on 26 May 2021, in line with the effective date of the MDR.

With regard to the aforementioned legal basis, the Institute, in cooperation with the Ministry of Health, drafted also the implementing decrees. For Act No 89/2021 Coll., new decrees were prepared and published in the Collection of Laws as Decree No 186/2021 Coll., implementing certain provisions of the Act on Medical Devices, and Decree No 170/2021 Coll., on the determination of reimbursement of costs of expert activities performed by the State Institute for Drug Control on request pursuant to the Act on Medical Devices.

In the area of in vitro diagnostic medical devices, the original Decree No 62/2015 Coll. was amended and, moreover, a new Decree No 171/2021 Coll., on the determination of reimbursement of costs of expert activities performed by the State Institute for Drug Control on request pursuant to the Act on in Vitro Diagnostic Medical Devices was drafted. The effective date of the Decrees was defined to be identical to that of the acts, i.e., 26 May 2022.

With reference to the powers defined by the provision of Section 29(6) of Act No 89/2021 Coll., the Institute also drafted a new decree governing the area of eOrder. In future, the eOrder will allow for electronic prescription also on the medical device level and in principle, it is an analogy to the well-established electronic prescription of medicinal products via the ePrescription system. This legislative process for this Decree is expected to be completed in early 2022.

In 2021, 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. In order to meet the obligations of the Czech Republic implied by its membership in the EU, it was 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 devices 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. In 2021, the draft of the joint act, incl. the accompanying amending act, passed the comments procedure and discussions in the working commissions of the Legislative Council of the Government. With regard to the effective date of the IVDR, which has been established at 26 May 2022, the proper completion of the legislative process is expected by early 2022 so that the Czech Republic properly fulfilled the obligations implied by its EU membership. The effective date of the proposed legislation has been established to be identical to that of the IVDR.

Furthermore, the preparation of legal regulations implementing the aforementioned joint Act started as early as in 2021. The structure of these legal regulations, however, reflects the previously adopted decrees. Also in this case, the legislative process is expected to be completed by the effective date of the IVDR.

The Institute also contributed to the finalisation of the legislative process concerning major legislative standards governing the field of pharmaceuticals, specifically the amended Act on Dependency-Producing Substances, which was published in the Collection of Laws as Act No 366/2021 Coll., and amended Act on Public Health Insurance, which was published as Act No 371/2021 Coll. Both regulations take effect on 01 January 2022. With a view to the adoption of the aforementioned, rather extensive amendments, it was necessary to amend the implementing legal regulations. For this reason, the Institute, in cooperation with the Ministry of Health, drafted an amendment to so called mega-decree implementing some provisions of the Act on Public Health Insurance. This amended decree passed the ordinary legislative process and was published in the Collection of Laws as Decree No 525/2021 Coll. In association therewith, moreover, a brand new decree was drafted, i.e., the decree on the determination of reimbursement of costs of expert activities conducted on request

and the method of determination of reimbursement of costs of expert consultations given by the State Institute for Drug Control pursuant to the Act on Public Health Insurance. This amended decree also passed the ordinary legislative process and eventually was published as Regulation No 527/2021 Coll. The latter brings a new approach in terms of the reimbursement of costs of expert activities and consultations that the Institute may claim on the basis of this decree. The effective dates of both aforementioned decrees are then identical to that of the Act, i.e., 01 January 2022.

In association with the amended Act on Dependency-Producing Substances, it was also necessary to amend a large amount of implementing legal regulations and the Institute was substantially involved in the drafting of these amendments. Due to this, amendments to the following regulations were adopted: Decree No 84/2008 Coll., on good pharmaceutical practice, detailed conditions of handling pharmaceuticals in pharmacies, healthcare facilities and at other operators and facilities dispensing medicinal products; Decree No 85/2008 Coll., on the list of active substances and excipients that may be used for the preparation of medicinal products; furthermore, Decree No 236/2015 Coll., on the conditions governing the prescribing, preparation, distribution, dispensing, and use of individually prepared medicinal products containing medical cannabis; and Decree No 123/2006 Coll., on the record-keeping and documentation of dependency-producing substances and products. Furthermore, the Institute was involved in the preparation of amendment to Decree No 329/2019 Coll., on the prescribing of medicinal products in the provision of healthcare services.

The preparation of drafts of completely new decrees also commenced, specifically of a decree on the determination of the amount of reimbursement of costs of expert activities performed by the State Institute for Drug Control on request pursuant to the Act on Dependency-Producing Substances, and a decree on good growing practice. Analogously to the reimbursement decree pertaining to the Act on Public Health Insurance, the Institute will be able to collect the reimbursement of costs for expert activities performed thereby on request of entities pursuant to the Act on Dependency-Producing Substances. This legislative process is expected to be completed in early 2022.

In addition to other direct legislative works, the Institute was also involved in the assessment of individual proposed amendments to the Chamber documents of interest that were discussed by the Chamber of Deputies of the Parliament of the Czech Republic.

In addition to activities associated with these major legislative tasks, the Institute was also involved in providing comments to other legislative proposals governing areas of relevance for its operation, including also the sphere of consumer protection. In this respect, the Institute held discussions with the Ministry of Industry and Trade as the gestor of amended Act No 634/1992 Coll., on Consumer Protection, as the prepared amendment introduces new powers entrusted to the Institute.

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

As in the previous years, cooperation with the Ministry of Health of the Czech Republic in drafting opinions of the Czech Republic on preliminary questions raised before the European Court of Justice and falling within powers of the Institute continued also during the last year.

3.2 Cooperation with Other State Institutions in the Czech Republic

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.

As in the previous years, in 2021, the Institute continued its intensive cooperation with other public authorities through providing answers to their queries in the area of the Institute's powers. The majority of requests came from law enforcement authorities and a growing trend in the transfer of information and data from information systems administered by the Institute, particularly the ePrescription system, was apparent.

In total, this involved 210 queries, of which 182 were raised by the Czech Police, four by courts of justice, one by a public prosecution office, four by the Customs Administration of the Czech Republic, seven by tax authorities, one by the Industrial Property Office, five by the General Police Inspectorate (GIBS), two by the Prison Service, one by an insolvency administrator, two by the appellate financial directorate, one by the Ministry of Defence.

The Institute, in cooperation with the Ministry of Health and the Ministry of Interior, continued its involvement in the filling of the public administration service catalogue pursuant to the Act on the Right for Digital Services.

3.3 Cooperation with EU Institutions and Other Foreign Partners

The Institute has been actively involved in international cooperation in more than 100 working groups, subgroups, 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. Since 2020, the role of this executive support has been much enhanced as 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 their 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 2021, the Institute was actively involved in the implementation of a new joint HMA/EMA strategy for 2020-2025 and together with Germany was responsible for 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 medicinal product availability or antimicrobial resistance (AMR).

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 problem in the context of the "One Health" principle (i.e., a principle that recognises that the wellbeing of people and of animals is mutually interconnected and that diseases are transferred from people to animals and vice versa, and for this reason, they have to be to be addressed in both at the same time. The "One Health" approach includes also the environment which is another connecting line between people and animals and also a potential source of new resistant microorganisms, as mentioned in the Communication from the Commission to the European Parliament and the Council on the "One Health" European action plan against antimicrobial resistance (AMR), 2017).

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.

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 2021, 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 is to be carried out in four areas, specifically: a) joint clinical assessments; b) joint scientific consultations; c) identification of emerging health technologies suitable for joint assessment; and d) voluntary cooperation among Member States. The Council debate was successfully concluded during the Portuguese presidency and in December 2021, the European Parliament adopted the final text of the Regulation with applicability as of January 2025.

The Institute was also involved in the discussion on the proposal for a Regulation of the European Parliament and of the Council on a reinforced role for the European Medicines Agency in crisis preparedness and management for medicinal products and medical devices and proposal for a Council Regulation on a framework of measures for ensuring the supply of crisis-relevant medical countermeasures in the event of a public health emergency at Union level.

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.

Due to the COVID-19 pandemics, in 2021, the absolute majority of international meetings were organised in the on-line mode. In 2021, the Institute completed only six foreign business trips (of which four were foreign inspections, one was an expert meeting, and one trip was educational).

In the second half of 2022, the Czech Republic will hold the Presidency of the EU Council for the second time and preparatory works aimed at ensuring a successful fulfilment of this 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.

4 REGULATORY ACTIVITIES OF SÚKL

4.1 Record System

In 2021, the electronic record system of the Institute, incl. its regional workplaces, registered 102,484 delivered documents and 77,488 dispatched documents (Tab. 1, 2). The increase in the number of received documents was associated with the growing agenda of the Registration and Notification Unit in the Registry of Persons and Medical Devices system. The priority channel for official document delivery are data mailboxes (Tab. 2).

Tab. 1 **Registration of documents in 2019–2021**

	2019	2020	2021
Received documents	112,034	97,748	102,484
Dispatched documents	78,902	65,101	77,488

Tab. 2 **Overview of communication channels in 2021**

	Mailroom	E-mail messages	Data messages	Medical device reimbursement notifications	Total
Received documents	35,658	54,090	11,071	1,665	102,484

	Dispatch room	E-mail messages	Data messages	Electronic notice board	Total
Dispatched documents	5,290	1,655	63,092	7,451	77,488

■ 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 as well as applications for the authorisation of parallel import and variations to, renewals 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 medicinal products (e.g., referrals, uniform PSUR assessments, PRAC recommendations on pharmacovigilance signals or paediatric work-sharing), for the development of lists of medicinal products jeopardized or extinct due to the sunset clause application, and for the conduct of administrative procedures regarding exceptions from the sunset clause application.

The Clinical Trials on 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 intended for risk minimisation; and the provision of new safety information both to professionals and to the general public.

4.2 Marketing Authorisation of Medicinal Products

Applications for New Marketing Authorisation

In 2021, 616 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 573 applications in 2020 to 642 applications in 2021. 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 2021, the number of received applications for DCP marketing authorisation with the

Czech Republic as the Reference Member State increased – from 85 applications in 2020 to 107 applications in 2021.

Marketing Authorisation Renewals

In 2021, 301 applications in total were forwarded for expert assessment following successful validation. Most of them were applications for MRP/DCP marketing authorisation renewals; in 2021, the total number of received applications for marketing authorisation renewal was slightly lower than in 2020.

Variations to Marketing Authorisation

In 2021, the number of received applications for variations to MRP/DCP marketing authorisations slightly increased, but, at the same time, the number of received applications for variations to national marketing authorisations slightly decreased. The total number of received applications remained similar. At the same time, the number of submitted applications for transfers of national marketing authorisations significantly increased from the total of 68 applications in 2020 to 146 applications in 2021. In respect of MRP/DCP marketing authorisation transfers, the number of submitted applications remained similar.

Parallel Import

In 2021, the number of submitted applications for parallel import authorisation significantly increased, specifically from 30 applications in 2020 to 57 applications in 2021. At the same time, the number of submitted applications for variations to parallel import authorisations increased from 43 applications in 2020 to 77 applications in 2021.

Marketing Authorisation Revocations

In 2021, 293 applications for revocation of marketing authorisation were decided.

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

Process of marketing authorisation of medicinal products	Submitted in 2021	Decided in total in 2021	Pending as of 31 December 2021
New marketing authorisations	**642**	**500**	**917**
- of which national	45	36	72
- of which MRP-RMS	20	21	50
- of which DCP-RMS	107	55	167
- of which CMS (MRP and DCP)	470	388	628
MA renewals	**321**	**335**	**340**
- of which national	14	25	73
- of which RMS	87	58	46
- of which CMS	220	252	221
National variations to MAs	**2,236**	**2,278**	**467**
- of which MA transfers	146	148	9
- of which PIL and labelling	79	94	8
- of which bulk NAT variations	2,011	2,033	450
- of which MA transfers	857	749	206
- of which PIL and labelling	37	38	0
- of which bulk MRP-RMS variations	38	32	8
- of which MA transfers	782	679	198
MRP-CMS variations	**4,301**	**4,245**	**1,319**
- of which MA transfers	111	109	1
- of which PIL and labelling	179	177	11
- of which bulk MRP-CMS variations	4,011	3,959	1,307
MA revocations	**308**	**293**	**0**
Parallel import	**57**	**45**	**41**
Parallel import variations	**77**	**76**	**7**
Parallel import renewals	**24**	**32**	**9**
Parallel import revocations	**3**	**3**	**0**

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

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

Expiry/Non-expiry of Marketing Authorisations

In 2021, the Institute conducted 110 administrative procedures concerning the granting of an exemption from the sunset clause.

In the course of 2021, the sunset clause as referred to under Section 34a of the Act on Pharmaceuticals applied to 81 MA numbers and the marketing authorisation of these medicinal products was terminated.

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

	Conducted in 2021
Administrative procedures for exemption from the sunset clause	**110**
- of which: submitted applications	**110**
- of which: ex officio initiated administrative procedures	**0**
- granted	90
- declined	0
- suspended as undue	20
- suspended as unjustified	0
- suspended for failure to provide amendment	0
- withdrawal of application	0

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

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

In 2021, we gave seven oral consultations (including consultations held in the form of teleconferences) and issued 18 written opinions on regulatory and expert issues.

In 2021, we issued 19 written opinions on requests for consultations concerning medicinal product names.

In 2021, 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 2021, 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;
- 18 times it assessed type I and II variations to centralised marketing authorisations;
- once it assessed a referral;
- four times it assessed documentation for MA renewal;
- once it assessed rolling review documentation.

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 working groups.

4.4 Clinical Trials

In 2021, the persisting COVID-19 pandemics again affected also the area of clinical trials, with a continuous increase in the agenda associated with the implementation of emergency measures governing new or ongoing clinical trials; the assessment of clinical trials on COVID-19 therapies or prevention was given priority and such studies were assessed by means of an abbreviated, rapid procedure; the number of consultations and questions related to the preparation of the clinical trial dossier by academic sponsors increased. SÚKL´s 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., was updated with regard to the epidemiological situation and development of the pandemics and its expiry was set at 30 June 2021. In association with the new wave of the COVID-19 disease, on 22 November 2021, a new SÚKL´s opinion on the possibility to use special procedures in clinical trials was issued.

In spring 2021, an independent audit of the EU portal (CTIS – Clinical Trial Information System) was completed, on the basis of which the launch of the EU portal for clinical trials was approved. The audit outcome report was published in the Bulletin of the European Commission with the established effective date of Regulation 536/2014 and the launch of the EU portal as at 31 January 2022. In association therewith, activities to establish a new ethics committee of the Institute were initiated; legislation associated with the regulation was completed by the issuance of Decree No 463/2021 on the conduct of clinical trials on pharmaceuticals and attendance at EMA´s training in the EU portal operation was organised. For internal employees and regulated entities, SÚKL prepared training on Regulation 536/2014, amended Act No 378/2007 as amended with regard to the Regulation, the new decree, and the use of the EU portal. These activities are to continue also in 2022.

Tab. 5 **Clinical trials in 2021**

	Pending from the previous period	Applications received in 2021	Number of decisions issued in 2021	Of which declined	Of which withdrawn
Applications for CT authorisation	37	409	152	0	19
CT notifications	53		256	0	29
Notifications of amendments to CTs	---	4,864	3,951	---	---

In 2021, the total of 409 applications for clinical trial authorisation/notification were submitted, which was 49 applications more than in the previous year. In total, 408 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 408 decided applications for clinical trial authorisation/notification, 26 were for clinical trials submitted by non-commercial entities (academic research), 38 applications concerned orphan drugs, (medicinal products for rare diseases), 39 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 (three somatic cell therapies; three gene therapies; and no tissue engineering therapy), and eleven applications were for first-in-human (FIH) trials. In the course of the assessment process, 48 applications in total were withdrawn (19 applications for clinical trial authorisation and 29 applications concerning clinical trial notifications); no application was declined.

Tab. 6 **Numbers of applications in 2021 by clinical trial phase**

	Applications received in 2021	Applications assessed in 2021
Phase I	30	30
Phase II	114	117
Phase III	218	214
Phase IV	23	23
Bioequivalence studies	24	24

Tab. 7 **Indication groups of clinical trials assessed in 2021**

Indication group	Number
Oncology	99
Metabolic disorders + endocrinology	6
Healthy volunteers	31
Neurology	44
Cardiovascular system	23
Respiratory + allergology	25
Infectious	27
Dermatology	17
Rheumatology	24
Haematology	11
Psychiatry	4
GIT	20
Urogenital diseases	16
ENT	0
Gynaecology	13
Ophthalmology	21
Paediatrics	1
Internal medicine	11
Transplantations	0
Anaesthesiology and resuscitation	0
Investigations	0
Diabetology	7
Other	4
Pain	1
Vaccination	1
Pharmacokinetics	2

Despite the complicated conditions caused by the COVID-19 pandemics and, in particular, by the intensive preparations for the coming into force of Regulation 536/2017, Development Safety Update Report (DSUR) assessment and control of Suspected Unexpected Serious Adverse Reaction (SUSAR) reports continued to be carried out. In 2021, 91 DSURs were submitted. For the above-mentioned reasons, the activity of the Assessment Safety Report Worksharing (ASR-WS) project (i.e., joint assessment and creation of assessment reports on DSURs) was significantly subdued in 2021. In this year, ten Member States were involved and 51 assessment reports were drafted, which is 16 reports less than in 2020. The reason for the decrease was the determination of the effective date of Regulation 536/2014, when all Member States focused particularly upon the preparation for the launch of the EU portal and the involvement of their agencies. Within the scope of the ASR-WS project, our assessors took part in four teleconferences of the CTFG (Clinical Trials Facilitation Group) – Safety Group.

Also in 2021, 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). With regard to the publication of the effective date of Regulation 536/2014, the end date for the receipt of applications and their assessment via the VHP was set at 15 October 2021. Within the scope of the VHP, 119 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 46 VHPs. In respect of five VHPs, the Czech Republic asked to act as the RMS; in eight VHPs, the Czech Republic conducted the assessment process as the RMS; in three cases, it acted as the RMS for newly accessing countries in previously approved procedures. In 2021, the total of 522 substantial amendments were submitted within the scope of VHPs, of which 227 were in the Czech Republic, and in 74 cases, the Czech Republic conducted the assessment procedure as the RMS. In 2021, the Czech Republic continued to participate in the VHP-plus project (involvement of multicentric ethics committees in the joint assessment within the scope of VHPs). The Czech Republic accepted involvement in seven VHP-plus procedures and in two cases, it was appointed as the RMS.

Also in this year, we were actively involved in the activities of the EMA working group for the creation of the EU portal and the new European database of clinical trials as well as those of other international groups – CTFG (Clinical Trials Facilitation Group), CTEG (Clinical Trial Expert Group), CTIS (Clinical Trial Information System-Working Group), CAT (Committee for Advanced Therapies). Two coordinators were involved as Master Trainers and they participated in EMA training and the testing of the EU portal. At the end of the year, they were testing the functionality of the EU portal upon request also with some sponsors.

Due to the pandemics, only one meeting of the Ethics Committee Forum took place, which we attended with presentations on the current situation in the sphere of clinical trials, the Regulation and national legislation, and with a presentation on clinical trials in the diabetes mellitus indication. In 2021, we did not organise any working meeting with the representatives of ethics committees for multicentric clinical trials; the members had the chance to attend our seminars.

In 2021, we organised seven seminars, all of them in the on-line form due to the pandemics. In the autumn, we were involved in the "Call for the 21st Century", an expert discussion forum organised by the Association of Pharmaceutical Medicine together with SÚKL, which was attended by the representatives of sponsors, CROs, healthcare service providers as well as investigators.

In 2021, we gave 24 consultations for 14 pharmaceutical companies and ten 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 (OFV) operates a system of spontaneous reports of suspected adverse drug reactions (ADR) from the Czech Republic. In 2021, the reports of suspected ADRs were mostly those associated with COVID-19 vaccination – the number of reports concerning these particular vaccines increased. While in the previous years, the average number of reports per year ranged around 3,000, in 2021, SÚKL received the total of 13,759 reports (the figure may slightly vary as the report duplicity and validity checks continue to be performed on an ongoing basis). Of the total number of reports, 1,844 were reports filed by medicinal product marketing authorisation holders (pharmaceutical companies) and 11,915 were reports sent to SÚKL directly by healthcare professionals and patients (of which, 4,939 were reports from patients – some reports were filed both by the healthcare professional and the patient).

Of the total number of 13,759 received reports, 10,631 concerned COVID-19 vaccines. In respect of all other medicinal products, 3,153 reports were received (25 reports were for COVID-19 vaccines and another medicinal product at the same time), which is consistent with the approximate number of reports from previous years and slightly higher than in 2020. To date, no other medicinal product has been administered in such large quantities over a relatively short period of time as COVID-19 vaccines during 2021. This fact, along with the pronounced interest of the public in the safety of these vaccines, resulted in the unprecedented number of reports. Nevertheless, all of the reports concerned merely suspected ADRs, which should serve for the identification of possible new ADRs on the basis of large amount of collected similar reports. In order to safeguard transparency, SÚKL regularly publishes an overview or all reported suspected ADRs to COVID-19 vaccines. To be able to carry out a detailed evaluation, adequate report quality is necessary – i.e., important information about the patient´s history, concomitant medication, a good clinical

description of the reaction, its detailed progress, etc. When the report is received, it is often necessary to contact the reporter to ask for additional missing important data, in particular where a very serious or unexpected ADR is suspected. While in 2020, we contacted the reporter in 121 cases to ask for additional important information on the report (so called follow-up), in 2021, 1,100 follow-up requests were raised. This is also associated with the increased interest in the safety of COVID-19 vaccines and the need to obtain complete important data for a more precise characterisation of the report.

Due to the COVID-19 vaccination, 2021 became a completely unique year in terms of pharmacovigilance – never before had we worked with such an immense volume of data at such a great speed, as actual new ADRs to COVID-19 vaccines need to be identified from the reports and recommendations on these ADRs issued so as to safeguard the maximum safety of further vaccination.

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 78 active substances on the pan-European level. In 2021, the Pharmacovigilance Assessment Unit assessed 923 monthly ADR reports from the EudraVigilance database regarding substances for which the Czech Republic acts as the 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 20 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 2021. The Institute acts as the PSUSA LMS for 54 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 2021. In total, we have been appointed the PRAC rapporteur for 22 centrally authorised medicinal products.

Due to the aforementioned unprecedented necessity to carry out pharmacovigilance activities associated with the monitoring and evaluation of safety, particularly that of COVID-19 vaccines, but also of medicinal products for the treatment of this infection, the pharmacovigilance activities that SÚKL has been involved in significantly increased also on the pan-European level. We actively participated in eleven regular meetings of the PRAC pharmacovigilance committee in the European Medicines Agency (EMA); due to the pandemics, most of these meetings took place online. Furthermore, ten one-day teleconference meetings of the PRAC committee took place as well as six extraordinary meetings summoned for the purposes of urgent assessment of COVID-19 vaccine safety. In the course of 2021, we acted as PRAC co-rapporteur for amfepramone referral, the evaluation of which was presented by the Institute at PRAC meetings in two rounds. We also submitted 150 written comments on procedures conducted by other countries.

Furthermore, we are 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. We are an active member of the group for harmonisation of risk management plans (HARP), for which we prepare our own assessments and provide comments on assessments drafted by other members.

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 nine communications intended for healthcare professionals or for the general public on medicinal products safety. In cooperation with marketing authorisation holders, the Institute published 146 educational materials on the safer use of medicinal products and 28 letters to healthcare professionals focused upon increased safety of medicinal product use, of which nine brought important safety information regarding COVID-19 vaccines.

Assessors from the Pharmacovigilance Assessment Unit were involved in the assessment of marketing authorisation dossiers where they looked at the pharmacovigilance section; in 2021, they prepared 1,992 reports on pharmacovigilance documentation in total.

The Pharmacovigilance Department continues to issue the Adverse Drug Reactions Bulletin (Nežádoucí účinky léčiv). In 2021, we published four issues. 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 important pharmacovigilance outputs. Furthermore, articles on important safety information concerning COVID-19 vaccines were published in the Bulletin.

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

In 2021, the Pharmacovigilance Inspection and Data Support Unit carried out the total of eleven inspections of pharmacovigilance systems of marketing authorisation holders. Of the completed inspections, three were inspections of the complete pharmacovigilance system, where the marketing authorisation holder´s PSMF is stored in the Czech Republic. Eight inspections focused upon the pharmacovigilance activities of MA holder local representation in the Czech Republic.

One inspection to be carried out within the scope of EMA´s CAP programme, where the Institute acts as the supervising authority for the concerned centrally authorised medicinal products, was postponed following consultation with EMA due to an initiated referral.

Due to the anti-epidemic measures, it was necessary to conduct four inspections in a remote mode, via a videoconference. In the course of the inspections, critical shortcomings were identified only with one marketing authorisation holder.

The Pharmacovigilance Department communicates with the public, it answers questions from healthcare professionals, the general public as well as pharmaceutical companies. In 2021, the number of questions increased profoundly due to the interest in the COVID-19 vaccine safety and 1,049 questions were answered in writing or by phone, which was more than double the number from 2020.

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 eight presentations within the scope of professional congresses or seminars for doctors and pharmacists or courses of the Institute for Postgraduate Medical Education (IPVZ) or as part of student education. Compared to previous years, the number of presentations was reduced due to the ongoing pandemics. The Institute also focuses upon the education of pharmaceutical companies in the proper conduct of pharmacovigilance. In 2021, 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 also organised online.

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. Inspections 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 is in charge of addressing quality defects of pharmaceuticals and excipients available on the market in the Czech Republic and it 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 it 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 Advertising Regulation 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 Advertising Regulation Unit. It conducts investigations into complaints pertaining to inappropriate advertising for HMPs and provides 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 2021, another verification of the established quality system by a group of EDQM auditors took place; due to the pandemic situation, it was conducted as remote audit. 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 2021 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 2021***

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
3/2020 – Pharmacy samples	98	213	200	13	0
2/2019 – Medicinal products containing pregabalin	13	23	23	0	0
5/2019 – Medicinal products containing ivabradine and trimetazidine	11	20	20	0	0
4/2019 – Medicinal products containing desloratadine	9	21	21	0	0
7/2019 – Medicinal products containing losartan	8	15	15	0	0
BIO/3/2020 – Microbiological quality monitoring of packed aqua purificata	-	55	55	0	3
BIO/2/2020 – Microbiological quality monitoring of oromucosal products	17	31	31	0	0
Total	**156**	**378**	**365**	**13**	**3**

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 2022, works on the following projects have been under way: control of medicinal products containing quetiapine fumarate, atomoxetine, lisinopril and captopril, metamizole, levetiracetam, allopurinol, and verification of the microbiological quality of oromucosal products and preparations for the project of herbal tea microbioplogical quality are under way. 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..

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	49	728	715	13	728	0	728
Vaccines	29	429	429	0	429	0	429

** 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	38	35	3
Suspected counterfeit, illegal samples*	101	-	-
International OMCL studies *	5	-	-
Internal quality control of purified water	131	127	4
Verification of quality of a reference substance for Ph. Eur.	2	2	0
Other analyses **	6	6	0
Total	**283**	**170**	**7**

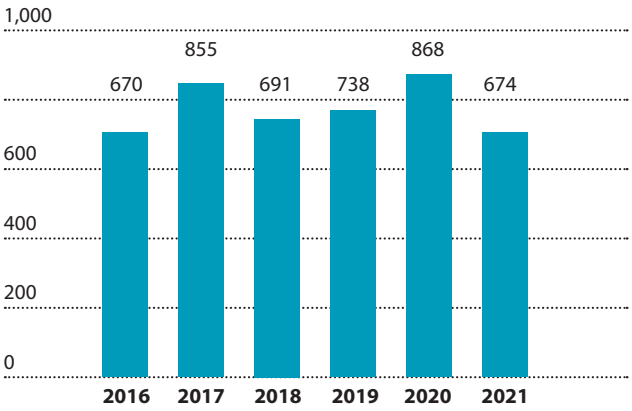
* *Sample compliance cannot be evaluated.*

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

The tables above indicate that in the Laboratory Control Department, 674 sample analyses were completed. Compared to the last year, the number of samples rated as non-compliant (ex. counterfeit and illegal products and samples from international studies) slightly decreased to 3.0 % (vs. 3.2 % in 2020; 4.2 % in 2019; 5.8 % in 2018; 3.9 % in 2017; 6.3 % in 2016). Quality defects were confirmed particularly for pharmacy samples (incl. adjusting defects). Otherwise, the quality of proprietary medicinal products available on the Czech market has been very good.

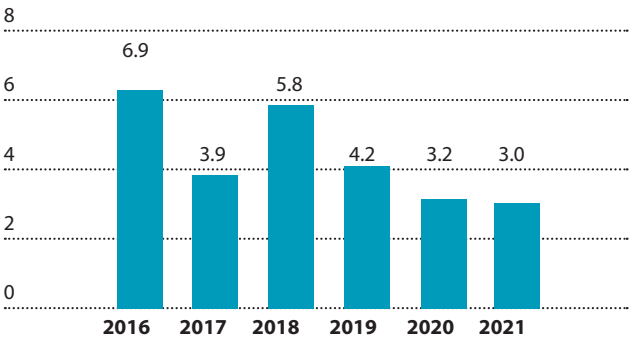
Within the scope of the statutory task of batch release, all of the reported batches were released onto the market in time, i.e., within timelines stipulated by the law, which, in the last year, concerned also COVID-19 vaccines – for this reason, the number of released batches of vaccines increased compared to the previous years. Fig. 3 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.

Fig. 1 **Number of sample analyses in 2016–2021**



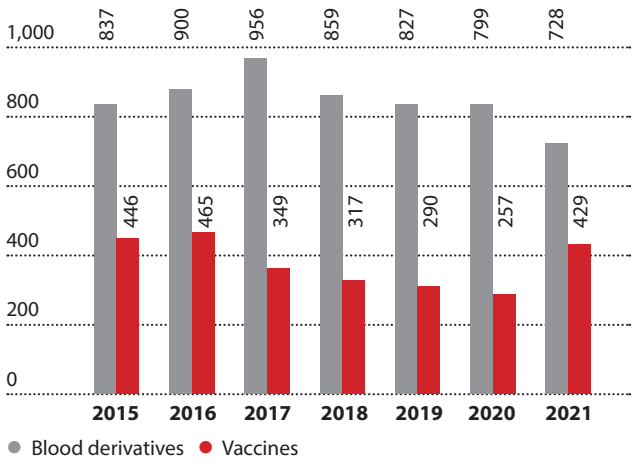
Number of analysed samples

Fig. 2 **Development in the number of non-compliant samples in 2016–2021 (v %)**



Non-compliant samples (%)

Fig. 3 **Number of released batches in 2016–2021**



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 medicinal products authorised via MRP or DCP), laboratory proficiency testing for the conduct of various analytical methods, and verification of the quality of reference substances for the European Pharmacopoeia.

In 2021, the Laboratory Control Department participated in collaborative international studies listed in Table 11.

Tab. 11 **Participation in international studies**

Study	Study name	Rating
PTS 207	UV-VIS Spectrophotometry	good
PTS 208	Liquid Chromatography	good
PTS 215	Volumetric Titration	good
PTS 217	Relative density	good
CRS	Clobetasol propionate	good
CRS	Isomalt	good
SUP 010	Suspected unknown product	good

Legend to abbreviations:

PTS – 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.

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

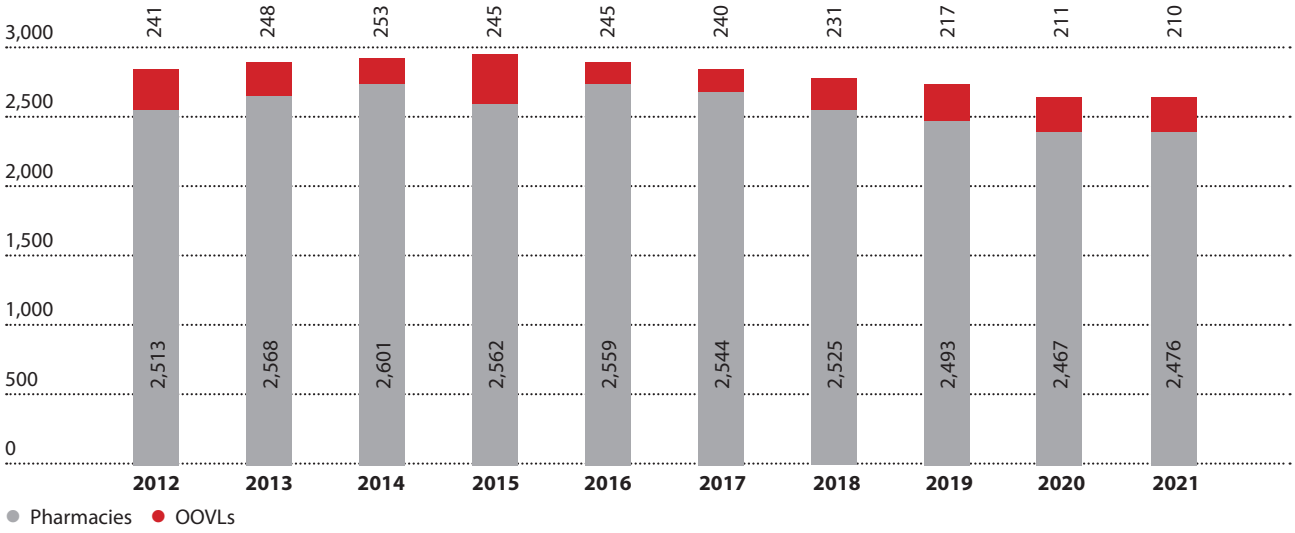
SUP – A comparative study to verify the laboratory's ability to analyse Suspected Unknown Products.

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. The control activities are 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 and brokers of medicinal products. 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 lists of the aforementioned regulated entities with the exception of healthcare facilities.

By the end of 2021, the Institute kept a record on 2,476 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 210 detached pharmaceuticals and medical devices dispensing units (hereinafter referred to as "OOVL"), 3,454 vendors of selected medicinal products for human use, 42 nuclear medicine departments of healthcare facilities, 385 wholesale distributors and 53 brokers of medicinal products for human use. Compared to 2020, the total number of pharmacies increased by nine entities and the number of OOVLs decreased by one unit (Fig. 4).

Fig. 4 **Number of pharmacies and OOVLs in the last 10 years (as of 31 December 2021)**



In 2021, the inspectors of the Pharmacy and Distribution Department conducted the total of 668 inspections in pharmaceutical care facilities – pharmacies, of which 39 were hospital pharmacies of inpatient care providers. Of the total number of completed inspections, 20 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 423 pharmacies.

Price control focusing upon compliance with the Act on Prices and rules of price regulation was conducted in 100 pharmacies and ten wholesale distributors.

On the basis of facts identified during the conducted inspections, the total of 87 final decisions on imposition of a fine for breach of obligations stipulated by the Act on Pharmaceuticals in the total amount of 54,900,000 CZK, incl. aggregate fines (see below), and on finalised administrative procedures based on inspections carried out in the previous period, and one admonition were adopted in respect of pharmacy operators. Three fines in the total amount of 350,000 CZK were imposed for failure to cooperate during the inspection. In five cases, the preparation of medicinal products was suspended for a pharmacy due to unverified or non-validated equipment (weights used during preparation).

The main reasons for the issuance of a decision imposing an administrative penalty included very serious shortcomings in the proper record-keeping of the medicinal products received, stocked, and dispensed; illegal distribution and export of medicinal products from pharmacies abroad; 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; 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 or preparation using non-verified weights.

Within the scope of inspections of the handling of dependency-producing substances in pharmacies, in 2021, identification of major breaches of the Act on Dependency-Producing Substances resulted in the total of 18 final decisions on fine imposition upon pharmacy operators, of which the fines for offences referred to under this Act amounted to the total of 160,000 CZK. In other cases, pharmacy operators committed offences referred to also by the Act on Pharmaceuticals, 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 2021.

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 45 cases. In 2021, 26 decisions on administrative penalty imposition in total became final, of which 21 cases involved financial sanctions amounting to 332,000 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 sale; 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 2021; 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 67,000 CZK in total.

In 2021, moreover, 235 inspections of the handling of medicinal products in healthcare facilities were carried out. The inspections took place in two inpatient departments of healthcare service providers and in 233 separate outpatient offices of general practitioners and medical specialists and in other healthcare facilities. On the basis of reports received by the Institute in respect of the operation of healthcare facilities where health care is provided, a total of 19 targeted inspections were performed. In total, twelve final decisions on fine imposition in the total amount of 630,000 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). One final fine in the amount of 100,000 CZK was imposed for failure to cooperate during the inspection.

The major reasons for the issuance of the decision on administrative penalty imposition included, in particular, storage of medicinal products above the scope of the authorisation for healthcare service provision; shortcomings associated with recalls of medicinal products due to their quality defects; procedures contrary to the summary of the product characteristics; serious or multiple breaches of obligations governing the handling of medicinal products set forth by implementing legal regulations, primarily incorrect storage of medicinal products or failure to keep the required documentary records.

In 2021, inspections of vendors of selected medicinal products involved 130 outlets in total. Twenty-two final decisions on fine imposition in the total amount of 300,000 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]), 18 inspections in total were carried out; the findings from the inspections did not result in the need for the imposition of any administrative penalty. In 2021, one decision on imposition of a fine in the amount of 15,000 CZK for shortcomings identified during the preparation of radiopharmaceuticals in the previous period became final.

Summary results from inspections completed in 2021 are provided in Table 12.

Tab. 12 **Inspection surveillance over pharmacies, nuclear medicine departments, healthcare facilities, and vendors of selected medicinal products in 2021**

			Classification of defects						Penalties		
Inspected entity	**Inspection type**	**Number**	**1**	**%**	**2**	**%**	**3**	**%**	**A**	**B**	**C**
Pharmacies	Regular inspections	*668	449	67.3	127	19	91	13.7	5	-	91
	Price controls	100	Not rated by classification of defects						-	-	26
	Inspections of dependency-producing substances and precursors	423	330	78.0	71	16.8	22	5.2	-	-	18
ONMs		17	16	94.1	1	5.9	-	-	-	-	1
HAVs		1	-	-	1	100	-	-	-	-	-
Healthcare facilities		*235	163	69.7	59	25.2	12	5.1	-	-	13
Vendors of selected medicinal products		130	84	64.6	17	13.1	29	22.3	-	-	23

** One pharmacy inspection and one healthcare facility inspection were 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 2021, inspectors from the Pharmacy and Distribution Department took a total of 220 samples of medicinal products during inspections in pharmacies, of which 77 were samples of pharmaceutical products intended for the preparation of magistral formulas in the pharmacy. Out of 143 pharmacy samples (medicinal products prepared in pharmacies), five were out-of-specification, the defect being out-of-specification content of active substances in two cases, an out-of-specification content and pH in one case, an out-of-specification weight in one case, and one tested sample did not pass the mass uniformity test. In three 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 2021, the total of 222 applications for issuance of an opinion were received from pharmacy operators and 212 favourable binding opinions were issued.

In 109 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 four cases, with an inspection of the OOVL (Table 13 refers). Furthermore, in this context, 111 consultations on the technical equipment of existing pharmacies or the construction of new pharmacies, and 420 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 13 also provides data on newly established and defunct pharmacies/OOVLs.

Tab. 13 **Other activities of the Pharmacy and Distribution Department**

Initial pharmacy inspection	Establishment of a new pharmacy/OOVL	Defunct pharmacies/OOVLs
109	70/6	61/7
Initial OOVL inspection	**Consultations on material and technical equipment**	**Other consultations**
4	111	420

Distribution of Medicinal Products

In 2021, the number of distributors exhibited a year-to-year decrease by 16 entities to the total of 385 medicinal products distribution authorisation holders. Of the total number of authorised distributors, 96 entities were both a distribution authorisation holder and a pharmacy operator.

In 2021, 20 new distribution authorisations and 111 decisions on variations to distribution authorisations were issued, and 33 authorisations were revoked upon request of their holders. In three cases, the distribution authorisation expired in compliance with Section 76(4) of the Act on Pharmaceuticals and in respect of two entities, the authorisation was revoked by the decision of the Institute pursuant to Section 76(3) of the Act on Pharmaceuticals.

The total of six entities applied for entry into, variation to entry in, or deletion from the Registry of Brokers of Human Medicinal Products in 2021; as of 31 December 2021, the Registry included 53 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 2021**

	Received applications	Decisions issued/Registry entries made
Application for distribution authorisation	22	20
Application for variation to distribution authorisation	119	111
Application for revocation of distribution authorisation	36	33
Application for entry in the Registry /variation to entry in the Registry/deletion from the Registry	6	6

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

In 2021, the total of 242 inspections of distributors and three inspections of brokers were conducted, of which nine were targeted inspections carried out on the basis of internal and external reports. In total, 25 reports on the operation of distributors were received; in one case, a declaration of non-conformity with the rules of Good Distribution Practice (GDP) was issued and in five cases, an administrative procedure regarding fine imposition was initiated 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 185 rated inspections of distributors (follow-up and targeted inspections), 75 % were rated with grade 1 (good), 19 % with grade 2 (satisfactory), and 6 % with grade 3 (not satisfactory). On the basis of identified facts, in 20 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 142 post-inspection Good Distribution Practice Certificates were issued, of which seven Certificates were of limited validity (for one year in five cases; for two years in two cases). 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 50 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, EMA).

In 2021, ten price controls of distributors focusing upon control of compliance with the Act on Prices and with effective Pricing Regulations issued by the Ministry of Health for the regulation of prices of medicinal products and foods for special medical purposes were conducted. A breach of pricing regulations was identified in two cases and they consisted of inadequate price record-keeping and failure to comply with the procedure set forth by material conditions, rules or procedures governing the establishment of official prices, changes thereto, and the method of their negotiation, application, and accounting as required by the pricing authority pursuant to Section 5(5) of the Act on Prices. In 2021, six fines in the total amount of 540,000 CZK were finally imposed for committed pricing offences.

In 2021, on the basis of facts identified during the completed inspections, distributors were imposed the total of 19 final decisions on fine for breach of obligations set forth by the Act on Pharmaceuticals and its implementing regulations amounting to 3,219,000 CZK in total (incl. also finalised administrative procedures based on inspections conducted in the previous period). Three final decisions on imposition of a fine in the amount of 300,000 CZK were imposed for failure to cooperate during the inspection.

In addition to failure to comply with GDP rules, the main reasons for the proposed fine imposition included 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 two cases, the distribution authorisation was suspended and declarations of non-conformity with GDP rules were issued due to serious breaches of the obligations implied by the Act on Pharmaceuticals and conditions of Good Distribution Practice; these were entered in the EudraGMDP database.

The results of inspections at distributors´ in 2021 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
242	22	176	9	35	139	35	11	1	20

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:

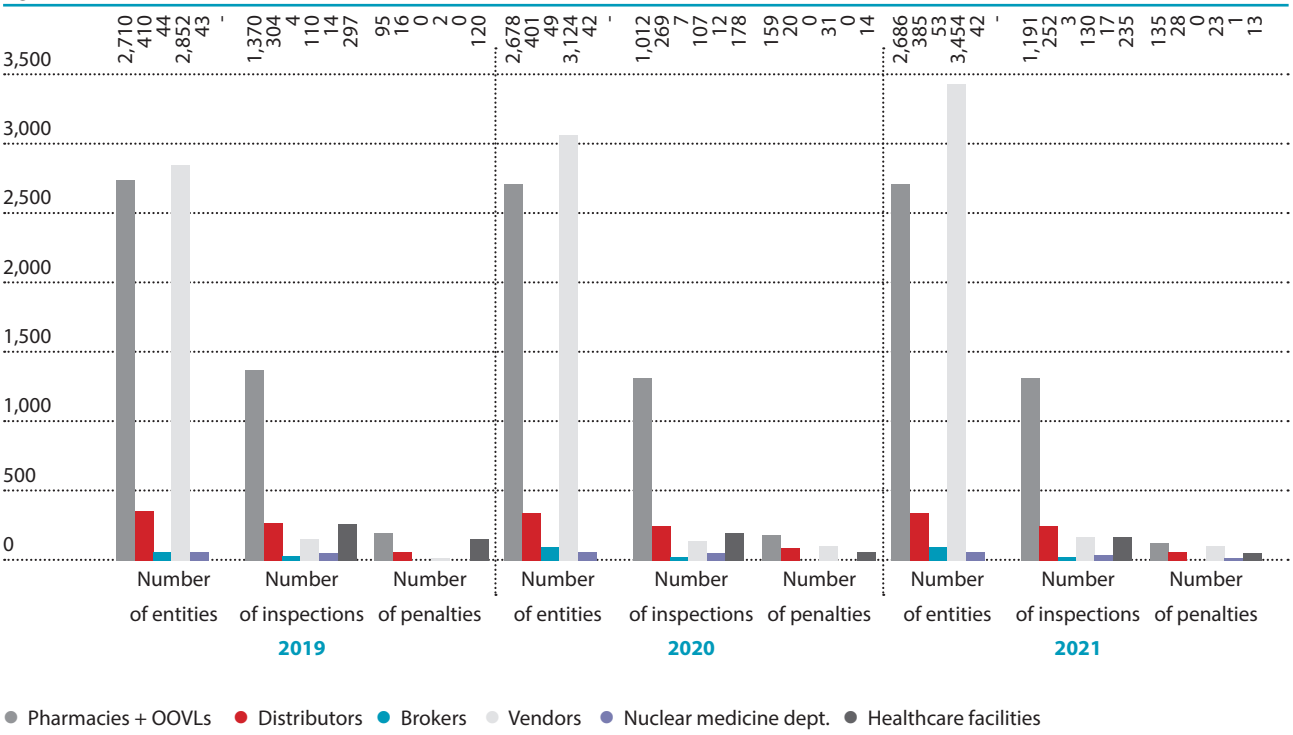
1 – Good;

2 – Satisfactory;

3 – Not satisfactory

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

Fig. 5 **Information on surveillance activities in 2018–2021**



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

The Inspection Department carries out surveillance activities in the sphere of manufacture of pharmaceuticals (including the manufacture of transfusion products and starting materials for further manufacture of pharmaceuticals – hereinafter referred to as "TP"), Good Clinical Practice and Good Laboratory Practice, issuance of binding opinions on the import 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 also 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 of pharmaceuticals are available from the Institute's website.

In the area of manufacturers (incl. blood centres), the total of 99 applications for manufacturing authorisation or variations thereto were received (Tab. 16 refers). The number of cases brought forward from one year to another corresponds to the timelines governing application processing.

Human Tissues and Cells

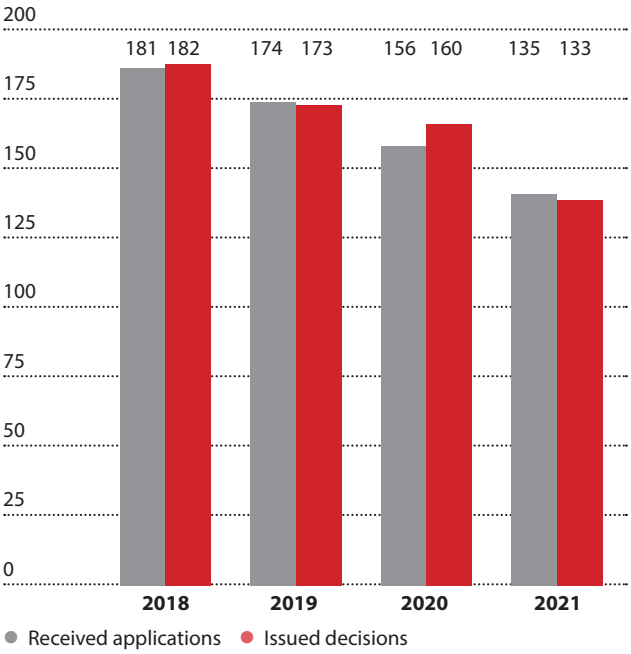
This is an area regulated by the Institute pursuant to Act No 296/2008 Coll., on Human Tissues and Cells.

In 2021, 33 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**

Application type		2018		2019		2020		2021	
		Received applications	Issued decisions	Received applications	Issued decisions	Received applications	Issued decisions	Received applications	Issued decisions
Application for manufacturing authorisation	Manufacturers of medicinal products	2	1	2	2	4	4	1	0
	Control laboratories	2	0	1	3	0	0	1	1
	Blood centres	1	1	3	3	1	1	3	3
Application for variation to manufacturing	Manufacturers of medicinal products	58	57	59	60	53	52	53	53
	Control laboratories	3	3	1	1	5	5	2	2
	Blood centres	39	40	45	44	49	47	39	43
Application for manufacturing authorisation revocation	Manufacturers of medicinal products	5	5	4	5	6	6	2	2
	Control laboratories	3	3	1	1	0	0	1	1
	Blood centres	1	1	0	0	0	0	0	0
Application for operating authorisation for:	Tissue centre	4	5	1	1	1	3	0	1
	Distribution of tissues and cells	3	4	1	1	1	1	0	0
	Donation centre	0	0	0	0	0	0	0	0
	Diagnostic laboratory	1	1	1	0	0	1	1	1
Application for variation to operation of:	Tissue centre	44	48	43	38	27	32	29	24
	Distribution of tissues and cells	1	0	0	1	0	0	0	0
	Donation centre	0	0	0	0	0	0	0	0
	Diagnostic laboratory	4	4	9	9	7	7	2	2
Application for revocation of operation of:	Tissue centre	7	6	0	1	1	1	0	0
	Distribution of tissues and cells	-	-	0	0	0	0	0	0
	Donation centre	0	0	2	2	1	1	0	0
	Diagnostic laboratory	3	3	1	1	0	0	0	0
Total		**181**	**182**	**174**	**173**	**156**	**160**	**135**	**133**

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



In 2021, 262 inspections in total were completed, of which 59 inspections were associated with the regulated area of tissues and cells. Their character and resulting ratings are provided in Table 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 2018-2021 is provided in Table 18 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 variations are carried out where 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 119 inspections at sites of manufacturers of medicinal products and active substances or in control laboratories, five breaches of the Act on Pharmaceuticals were identified. Three proposals for fine imposition and two reports on failure to meet GMP requirements were issued. 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.

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

Tab. 17 **Inspections conducted in 2021 and their outcomes**

	Number of inspections					Inspection rating			
	Total	Initial	Follow-up	Targeted	Variation	Compliant[1]	Non -compliant	Breach of law	Proposed fine
Manufacturers of medicinal products	67	0	48	3	16	48	0	4	3
Manufacturers of active substances	33	2	21	1	9	23	0	1	0
Control laboratories	19	2	17	0	0	19	0	0	0
Active substance importers	4	3	1	0	0	4	0	0	0
Blood centres	77	3	58	1	15	61	0	0	0
Blood banks	3	0	3	0	0	3	0	0	0
GCP inspections – Ethics Committees	0	0	0	0	0	0	0	0	0
GCP inspections – others	19	0	0	19	0	0	0	0	0
TC, DC, DL, DIS inspections	59	4	50	2	3	54	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 2018–2021**

	2018		2019		2020		2021	
	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	58	9	59	2	56	1	67	4
Manufacturers of active substances	14	0	23	3	22	0	33	1
Control laboratories	8	0	17	0	10	0	19	0
Active substance importers	2	0	4	0	4	0	4	0
Blood centres	51	0	64	0	62	0	77	0
Blood banks	19	0	11	0	2	0	3	0
GCP inspections + ethics committees	34	1	33	1	21	0	19	0
Tissue centres, donation centres, diagnostic laboratories	101	0	59	0	53	0	59	0
Total	**286**	**10**	**270**	**6**	**230**	**0**	**281**	**1**

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

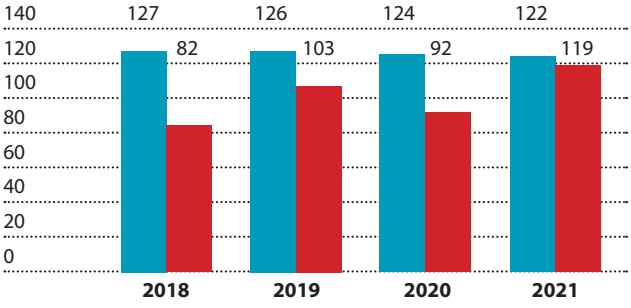
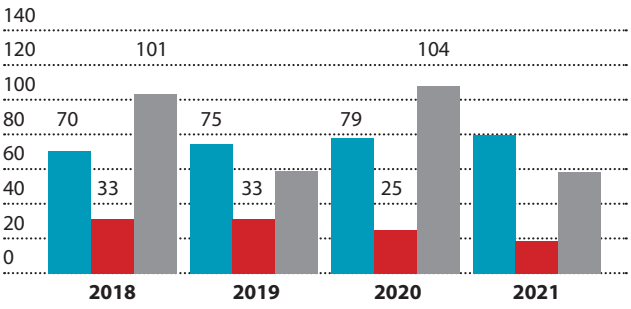


Fig. 8 **Overview of completed inspections in the area of blood centres + blood banks, GCP + EC, and HTC (tissue centres, diagnostic laboratories, donation centres) in the period of 2018–2021**



Haemovigilance

In 2021, 37 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 one report is still pending and in twelve cases, the suspected SAR was not confirmed. Of confirmed serious adverse reactions, six SARs involved blood or blood component donors and 18 SARs concerned post-transfusion reactions in transfusion product recipients (ten cases of anaphylaxis; three haemolytic reactions arising from AB0 system incompatibility; and one case of a transfusion-related acute lung injury (TRALI), one transfusion-associated circulatory overload (TACO), one transfusion-transmitted viral infection – hepatitis E, one transfusion-transmitted bacterial infection, and one graft-versus-host disease). In 16 cases, transfusion product recipients fully recovered from the transfusion product post-administration SARs (i.e., from the post-transfusion reaction); in one patient, the reaction resulted in mild consequences; and one patient died (unrelated to the transfusion). In all six cases, the donors of blood or blood components fully recovered from the SARs.

Furthermore, nine reports of suspected serious adverse events (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. Two cases did not constitute a SAE; one suspected SAE is still pending. Two cases constituted transfusion product confusion during dispensing; two cases dispensing of an incompatible transfusion product arising from confusion of the recipient´s blood sample in the department; one case was a mistake in the transfusion set installation; and one case constituted confusion of dispensed transfusion products in the 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.

Within the scope of its involvement in the European Rapid Alert System for Blood (RAB), in 2021, the Institute received four new reports and one complementary report from four countries. Three cases involved

an epidemiological situation (associated with the occurrence of the West Nile virus), one case a warning against defective apheresis plasma collection sets, and one case problems with the use of an infectious marker analyser.

Good Laboratory Practice (GLP)

In 2021, a total of twelve 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, six follow-up inspections were performed.

Good Clinical Practice (GCP)

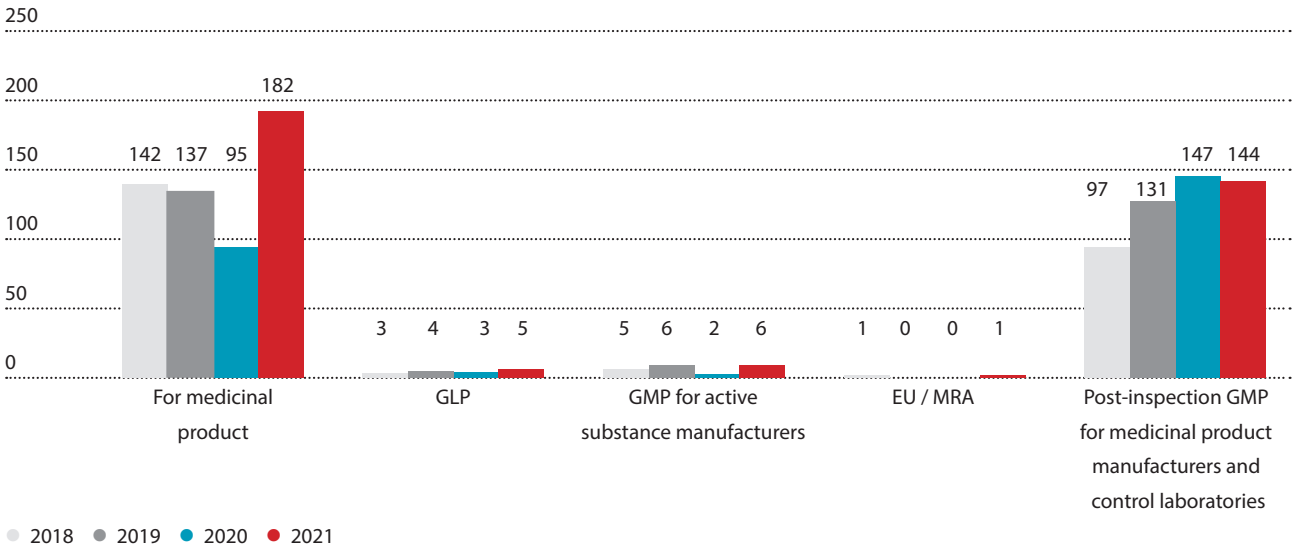
Due to the emergency measures associated with the COVID-19 pandemics, in 2021, the number of Good Clinical Practice inspections dropped compared to previous periods.

In the course of 2021, the total of 17 inspections of Good Clinical Practice were conducted. Of the said number, 15 concerned a targeted inspection of a clinical trial site (a GCP inspection at the investigator's site), 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 one was a targeted inspection of the sponsor.

Certification

In total, 338 various certificates were issued. Post-inspection Good Manufacturing Practice Certificates are entered in the EudraGMDP 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

The total of 1,329 cases were received (a 35-% increase compared to 2020); all of them were processed within predefined timelines.

Foreign Inspections

In 2021, three Good Manufacturing Practice inspections at foreign entities were conducted, of which one via distant assessment.

Tab. 19 **Foreign inspections**

	2018	2019	2020	2021
Number of inspections	4	7	2	3
Certificate issuance	1	4	1	3
Issued non-compliance	0	1	0	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 2021**

Quality defects	2014	2015	2016	2017	2018	2019	2020	2021
Reports received in total	345	333	420	443	496	497	496	**559**
Reports from the Czech Republic	181	181	243	277	286	284	304	**301**
Reports from abroad	164	152	177	166	210	213	192	**258**
Resulted in recall (in SÚKL codes)	60	79	72	79	89	59	47	**54**
Administrative procedure (since 04/2017)	-	-	-	20	33	81	55	**80**
Rapid Alert	6	11	17	22	6	15	1	**8**

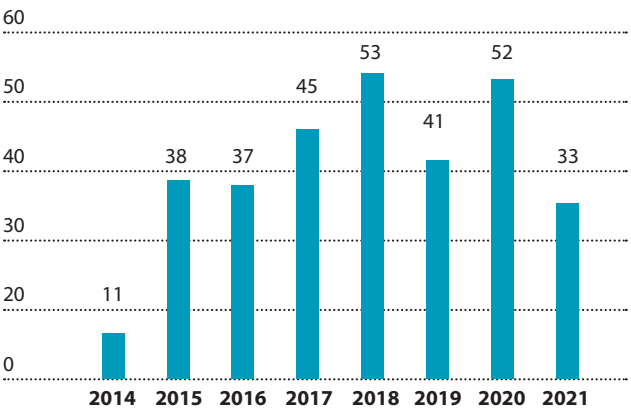
Explanatory notes: Rapid alert = a rapid alert notification sent by the Institute within the scope of the international Rapid Alert system.

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 2021, the complaints 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 258 reports on quality defects.

The Quality Defects Unit handles 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 2021, 83 administrative procedures were commenced and 80 final decisions were issued; these concerned 145 medicinal products (in SÚKL codes) and 335 batches of medicinal products.

The Quality Defects Unit addresses also reports concerning the presence of counterfeit medicinal products in the legal distribution chain or their theft. In 2021, the Quality Defects Unit addressed 33 such cases in total, of which two concerned theft of medicinal products from the legal distribution chain. An overview of addressed reports concerning the presence of counterfeit products is provided by Fig. 10:

Fig. 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 2021, the Quality Defects Unit received and evaluated 52 such reports in total.

Furthermore, the Quality Defects Unit monitored the recall of 16 medicinal products (in SÚKL codes) for marketing authorisation reasons (changed method of dispensing or change of shelf-life).

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

Tab. 21 **Measures implemented in 2021 (related to SÚKL codes)**

Implemented measures	Number
Recall from distributor level	0
Recall from healthcare facility level	54
Recall from patient level	0
Suspended distribution, dispensing and/or use	1
Released distribution, dispensing, and use	1
Permitted distribution, dispensing, marketing, and use in the provision of healthcare services through an administrative procedure	(number of batches: 335)145

Mutual exchange of information and cooperation with the Slovak drug authority, ŠÚKL in Bratislava, has been ongoing, and in 2021, the Quality Defects Unit cooperated with ŠÚKL in several cases.

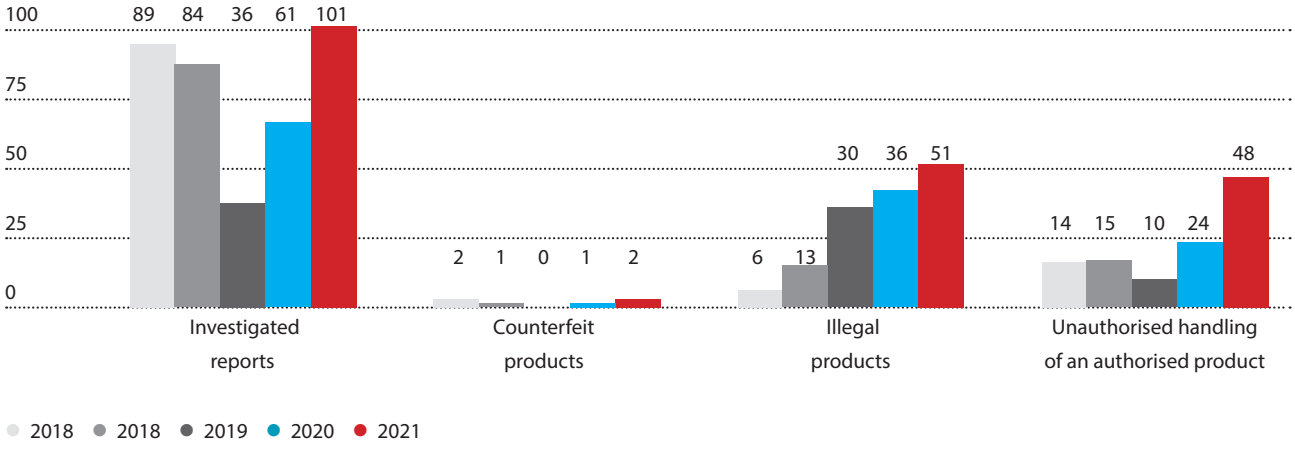
The Quality Defects Unit was involved in the preparation of implementation of Regulation 161/2016, supplementing Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use (hereinafter referred to as the "Safety Feature Regulation"). In the course of 2021, a web application for the submission of applications as referred to under Section 11(r) of the Act on Pharmaceuticals was created in cooperation between the Ministry of Health and IT, in order to accelerate the administrative procedure. The representatives of the Institute participated in the meetings of the expert group for safety features, in international teleconferences, and regular meetings with the National Organisation for Medicines Verification (Národní organizace pro ověřování pravosti léčiv).

For 2021, the Institute recorded the total of 36,486 reports on unsuccessful safety feature verification (for the entire period from 09 February 2019 to 31 December 2021, this number amounted to 1, 176,756 reports in total). In the course of the year, the Quality Defects Unit communicated with 23 marketing authorisation holders in respect of whose products a high number of such reports was identified. During 2021, the Unit issued favourable recommendations for the total of 24 medicinal products and 91 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 14 reports concerning suspected broken anti-tamper devices (ATDs), incl. other cases of non-compliance with Regulation No 2016/161.

4.10 Enforcement

In 2021, 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 of medicinal products 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 2017–2021**



In 2021, the total of 101 reports (either the Institute's own or received reports) were investigated. In 2021, the Institute was monitoring and detecting illegal offers of medicinal products in the internet environment and executed 29 control purchases. Fifty-one cases of handling of unauthorised medicinal products and 48 cases of unauthorised handling of authorised medicinal products were identified.

In 2021, the Institute prepared the total of 360 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 2021, the Institute investigated the total of 135 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 2021, the Institute completed twelve administrative procedures, which resulted in the imposition of 13 fines for breaches of the Act on Advertising Regulation in the aggregate amount of 1,330,000 CZK.

The subject of investigations into advertising was printed advertising matter (51 %), websites (32 %), and promotional samples of medicinal products (17 %).

Advertising for prescription-only medicines accounted for 31 % of the investigated cases, advertising for over-the-counter medicines represented 69 % of cases.

Pharmaceutical companies or their legal representatives filed 20 % of reports on suspected breaches of law, 2 % of reports were filed anonymously, 12 % were lodged by private individuals, and 66 % by SÚKL employees.

Tab. 22 **Overview of investigated reports of suspected breaches of the Act on Advertising Regulation in 2021**

	Reports brought forward from 2020	Newly received reports in 2021	Total
Number of reports	4	131	135
Investigation completed	4	125	129
Forwarded for commencement of administrative procedure	0	11	11
Completed administrative procedures	0	10	10
Number of finally imposed fines	0	11	11

Fig. 12 **Overview of investigated reports of suspected breaches of the Act on Advertising Regulation (2017–2021)**

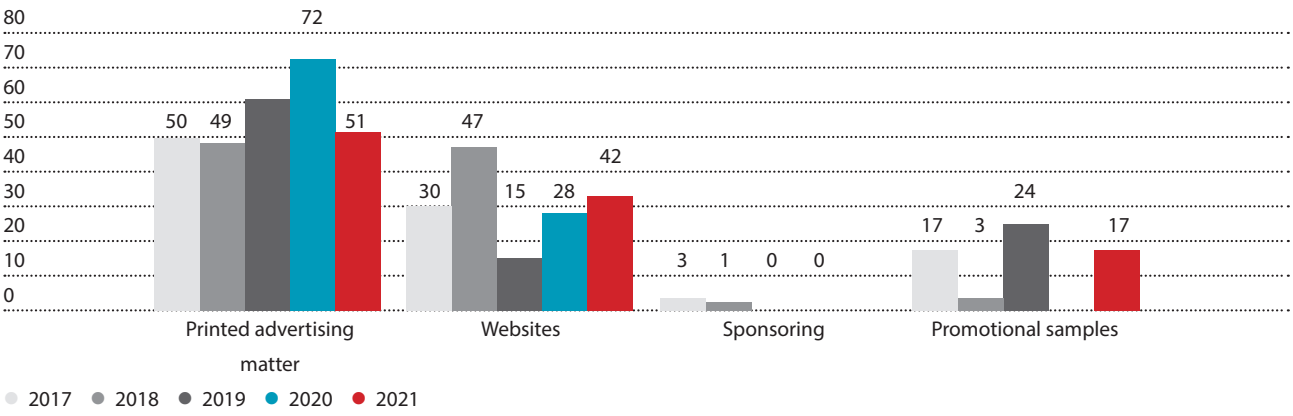
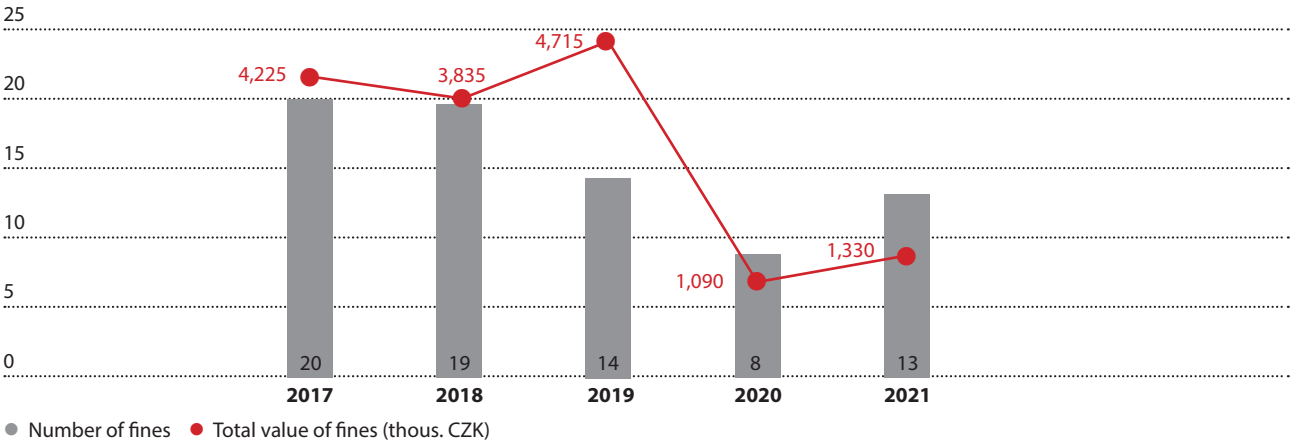


Fig. 13 **Overview of fines imposed for breaches of the Act on Advertising Regulation (2017–2021)**



Upon request, the Institute issued/provided 49 expert opinions/consultations on the issue of proposed advertising for medicinal products for human use.

The inspectors of the Advertising Regulation Unit completed 16 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 2021, the Institute commenced investigation into 103 cases of various products, most often dietary supplements and cosmetic products, for suspected classification as a medicinal product. In 32 cases, an administrative procedure regarding the nature of the product was initiated ex officio or upon request. In 2021, the Institute reclassified the total of 23 products to the group of medicinal products. Upon request, it provided three expert opinions on issues regarding product classification as a medicinal product or another product.

4.12 Standardisation and Pharmacopoeial Activities

In the first half of 2021, the Pharmacopoeia employees prepared for print the Fourth Supplement to Czech Pharmacopoeia 2017 – Supplement 2021 (hereinafter referred to as "Suppl. 2021"). In its European part, it contains the translations of three supplements to the Tenth Edition of European Pharmacopoeia (Ph. Eur. 10.0, Suppl. 10.3, 10.4, and 10.5).

Czech Pharmacopoeia 2017 – Supplement 2021 was published in cooperation with the Grada Publishing house in one volume as binding from 01 December 2021 and it is available also in electronic format (as a PDF file accessible via a paid link on Grada´s website). 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, Suppl. 2020, and Suppl. 2021.

The European part contains the total of 376 texts, of which the General Part includes 38 general texts (of which six are new ones), four revised general articles, and eight revised general articles concerning pharmaceutical forms (of which two are new ones). The Special Part contains 16 revised articles for vaccines for human use and five revised articles for vaccines for veterinary use, five articles for radiopharmaceuticals (of which four are new ones), 30 articles for herbal drugs (of which five are new ones), and four articles for homeopathic preparations. The number of chemical and biological monographs on active substances, excipients, and medicinal products is 266 (of which 19 are new ones).

The National Part of Suppl. 2021 contains 16 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, in Suppl. 2020 as well as in Suppl. 2021. Table XVI: *Storage and shelf-life of products prepared in pharmacies* was updated with regard to the results of the "Shelf-life of individually prepared medicinal products" project.

Furthermore, the General Part contains an overview of updated testing agents and reference substances used in national monographs.

It contains a new text *Alternative Methods of Radiopharmaceuticals Control* drafted on the basis of the WHO International Pharmacopoeia.

Tab. 23 **Number of texts in the European Part of Czech Pharmacopoeia 2017 – Suppl. 2021**

European Part	General Part	Special Part	Total
New	8	28	36
Revised	42	298	340
Total	**50**	**326**	**376**

Concurrently with the proof-reading and print preparation of Suppl. 2021, translations and revisions of three other European Pharmacopoeia supplements were under way (Suppl. 10.6, 10.7, and 10.8). The three European editions will form part of Czech Pharmacopoeia 2017 – Supplement 2022 (hereinafter referred to as "Suppl. 2022"). In the European Part, this concerns approximately 280 texts.

Furthermore, in the second half of 2021, works on the National Part of Suppl. 2022 began; also in this case, updated tables will be included.

The preparation and distribution of national reference substances was organised. It concerns the re-attestation of Suxamethonium-diiodide CRLN and distribution of reference substances for monograph Butamirati citras (five CRLNs in total), the interest in which increased.

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

The employees of the Unit regularly attended the EPC meetings and meetings of secretariats of national pharmacopoeial commissions (in 2021, these meetings were only virtual).

Information about the binding nature of individual Ph. Eur. editions was published in SÚKL's information media.

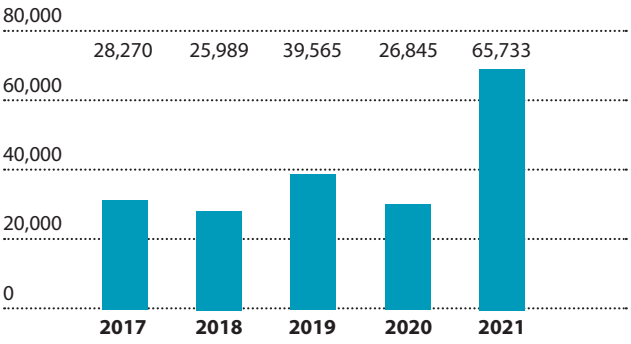
A proposal for a new concept of the Czech Pharmacopoeia concerning a reduced number of translations from the European Pharmacopoeia into the Czech language was prepared, discussed with the representatives of the Ministry of Health, and subsequently approved. This change will be applicable since Czech Pharmacopoeia 2023 and works on the preparation of lists and texts have started in late 2021.

4.13 Penalties Imposed in the Area of Pharmaceuticals and Medical Devices

Penalties in the Area of Pharmaceuticals and Human Tissues and Cells

Based on its ex-officio findings, particularly those identified during regular inspections of regulated entities, or findings from reports received from the Czech Police and other administrative bodies of the Czech Republic or from private individuals, 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 possibility 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 2021. 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 2021, in the area of penalties, the Institute continued also the imposition of penalties in the form of so-called aggregate fines for committed offences referred to by several laws according to which it is within the powers of the Institute to address offences, particularly in the sphere of medicinal product handling. As of 01 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. The Institute has been availing of this possibility since 2018. In 2021, the Institute imposed six admonitions in total. Furthermore, in 2021, the Institute imposed the first penalty of ban on operation upon a medicinal product distributor, who, contrary to a general measure of the Ministry of Health banning distribution of medicinal products listed therein to foreign countries, did distribute these medicinal products abroad. The penalty of the ban on operation was imposed for the period of one year. The possibility to impose a ban on operation for up to 2 years for this offence has been included in the Act on Pharmaceuticals since 01 December 2017.

Fig. 14 **Amount of finally imposed penalties in the area of pharmaceuticals and human tissues and cells in 2017–2021 (in thousands)**



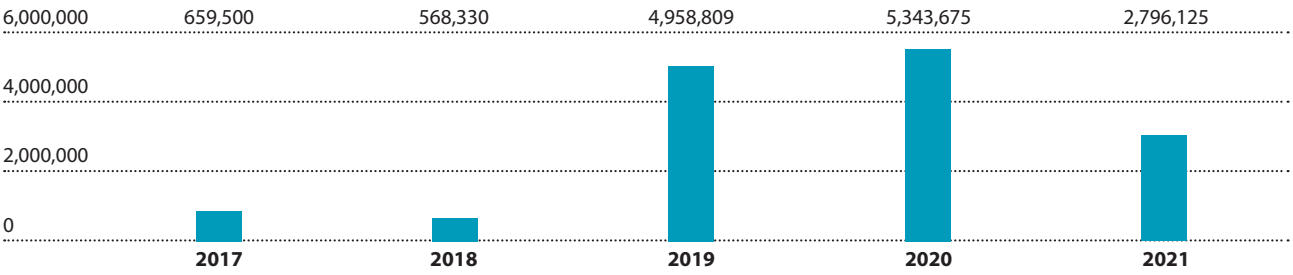
Tab. 24 **Amounts of penalties in the area of pharmaceuticals and human tissues and cells in 2017–2021**

Act	2017	2018	2019	2020	2021
	28,270,000 CZK	**25,989,000 CZK**	**39,565,000 CZK**	**26,845,000 CZK**	**65,733,000 CZK**
on Pharmaceuticals	21,088,000 CZK	19,514,000.00 CZK	29,079,000 CZK	24,559,000 CZK	62,237,000 CZK
on Drug Precursors	115,000 CZK	50,000.00 CZK	0 CZK	0 CZK	0 CZK
on Dependency-Producing Substances	647,000 CZK	110,000.00 CZK	263,000 CZK	250,000 CZK	160,000 CZK
on Prices	645,000 CZK	1,940,000.00 CZK	4,387,000 CZK	54,000 CZK	872,000 CZK
on Advertising Regulation	4,255,000 CZK	3,835,000.00 CZK	4,715,000 CZK	1,090,000 CZK	1,330,000 CZK
on Human Tissues and Cells	1,100,000 CZK	0.00 CZK	200,000 CZK	0 CZK	0 CZK
on Public Health Insurance	90,000 CZK	50,000.00 CZK	50,000 CZK	732,000 CZK	374,000 CZK
Code of Control Procedure	330,000 CZK	435,000.00 CZK	490,000 CZK	160,000 CZK	760,000 CZK
on Medical Devices	0 CZK	55,000.00 CZK	46,000 CZK	0 CZK	0 CZK
on Technical Requirements for Products	0 CZK	0 CZK	335,000 CZK	0 CZK	0 CZK

Penalties in the Area of Medical Devices

On the basis of ex officio findings of the Institute arising, in particular, from inspection activities conducted at regulated entities and on the basis of motions from private individuals, the Medical Device Legal Support Unit initiates administrative procedures concerning offences, within which penalties are imposed with a view to the severity of the identified breach as per the respective law. In 2021, the Institute continued to impose penalties on the basis of so-called order pursuant to the Code of Administrative procedure. In the area of penalties, in 2021, the Institute continued also to impose penalties in the form of so-called aggregate fines for committed offences referred to by several laws according to which it is within the powers of the Institute to address offences. As of 01 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. The Institute has been availing of this possibility since 2018. In 2021, the Institute imposed ten admonitions in total. With the coming into force of Act No 268/2014 Coll. (on 01 April 2015), since 2016, the Medical Device Legal Support unit has observed an increase in proposals to initiate administrative procedures for administrative offences as part of adverse event investigation monitoring, particularly breaches of the obligation stipulated by Section 75 of Act No 268/2014 Coll., i.e., to inform the Institute about established safety corrective actions and their termination. In association with the drafting of the new Act on Medical Devices, and the drafting of the Act on in Vitro Diagnostic Medical Devices that came into force on 26 May 2021, however, these merits of the case have been kept only in the Act on in Vitro Diagnostic Medical Devices.

Fig. 15 **Overall comparison of fines (CZK) in the area of medical devices in 2017–2021**



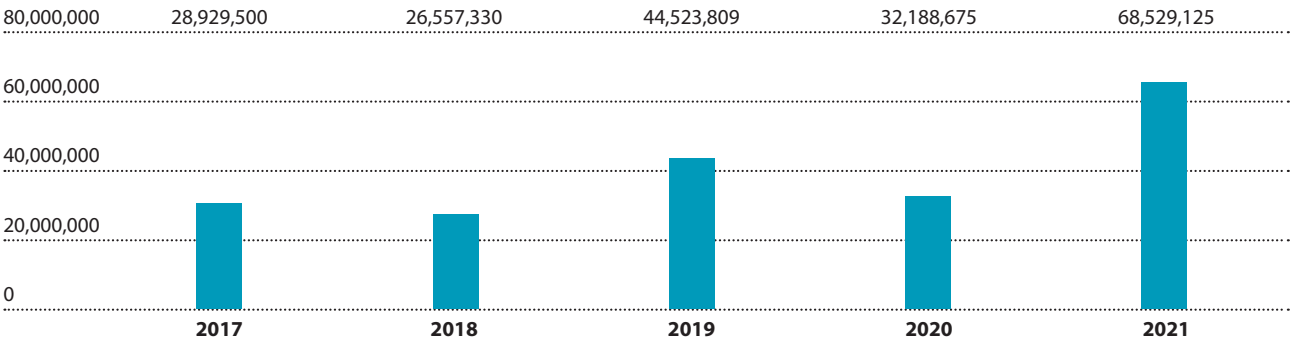
Tab. 25 **Comparison of fines in the area of medical devices in 2017–2021**

Act	2017	2018	2019	2020	2021
	659,500 CZK	**568,330 CZK**	**4,958,809 CZK**	**5,343,675 CZK**	**2 796,125 CZK**
Code of Control Procedure	0 CZK	0 CZK	0 CZK	0 CZK	50,000 CZK
on Medical Devices	559,500 CZK	568,330 CZK	3,210,058 CZK	3,723,125 CZK	1,320,000 CZK
on Technical Requirements for Products	100,000 CZK	0 CZK	1,748,751 CZK	1,620,550 CZK	1,426,125 CZK

Summary of Penalties Imposed by the Institute in 2021 (Pharmaceuticals and Medical Devices)

In 2021, the Institute imposed penalties in the overall amount of 68,529,125 CZK (Tab. 25 and 26 refer). With reference to Act No 250/2016 Coll., on Liability for Offences and Procedures Pertaining Thereto, as amended, in 2021, the Institute imposed the total of 16 admonitions instead of a financial sanction.

Fig. 16 **Total penalties imposed by the Institute (pharmaceuticals and medical devices)**



■ 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 principles of procedure transparency 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 2021, the Section continued in the initiation of in-depth reimbursement revisions in accordance with the schedule. For 2021, the initiation of 16 in-depth revisions was scheduled; eventually, 19 in-depth revisions (233 SÚKL codes) were commenced. The difference in the number of scheduled and initiated in-depth revisions reflects process and organisational & technical conditions at the time of in-depth revision initiation (such as pending previous in-depth revisions). 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 they were initiated on the basis of reports from healthcare payers.

For 2021, 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. 26 **Overview of administrative procedures in 2021**

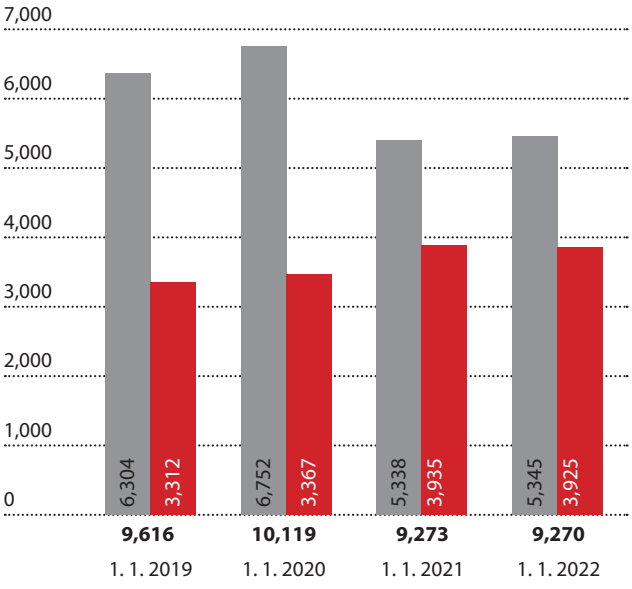
Applications for maximum ex-factory price determination	Number of SÚKL codes
Initiated	27
Decided	18
Appeal procedure pending	0
Became final	15
Applications for maximum ex-factory price change	
Initiated	207
Decided	190
Appeal procedure pending	0
Became final	181
Applications for maximum ex-factory price reduction – abbreviated procedure	
Initiated	66
Decided	66
Appeal procedure pending	3
Became final	63
Applications for maximum ex-factory price revocation	
Initiated	2
Decided	2
Appeal procedure pending	0
Became final	2
Maximum price in-depth revisions	
Initiated	1,147
Decided	1,147
Appeal procedure pending	0
Became final	1,147

The principal legislation governing the area of price regulation in 2021 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 the 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 01 January 2020 and the Price Decision with effect as of 01 March 2020; and due to the change in the Price Decision, the number of applications for maximum price determination increased in 2020. In 2021, the Price Decision was not amended, and the number of applications for maximum price determination hence substantially decreased compared to the previous year.

In 2021, 133 administrative procedures regarding the maximum ex-factory price change were commenced (compared to 134 administrative procedures in 2020); applications filed by marketing authorisation holders prevailed (three applications were filed by health insurance companies and 130 applications were filed by marketing authorisation holders).

With a view to the stability of the price regulation, the share of medicinal products regulated only by the profit margin remained almost unchanged compared to 2018. Compared to 2020, however, the share of products regulated only by profit margin apparently increased in 2021 (Fig. 17).

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



With a view to the structure of medicinal products, it may be stated that in the individual months of 2021, the numbers of medicinal products in most of the aforementioned maximum price zones were decreasing continuously throughout the year (Tab. 27). The most significant decrease occurred in the zone of More than 300 CZK up to 500 CZK incl. The number of medicinal products increased particularly in the zone of More than 50,000 CZK up to 100,000 CZK incl.

Tab. 27 **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	21	21	21	21	21	21	21	20	20	20
More than 20 CZK up to 50 CZK incl.	280	276	276	276	275	280	277	274	278	280	278	276
More than 50 CZK up to 100 CZK incl.	733	724	712	718	708	709	710	710	717	722	720	714
More than 100 CZK up to 200 CZK incl.	915	921	914	883	886	903	902	900	909	910	920	913
More than 200 CZK up to 300 CZK incl.	501	500	507	498	504	514	513	510	538	534	549	554
More than 300 CZK up to 500 CZK incl.	523	528	513	496	492	481	469	468	457	451	457	464
More than 500 CZK up to 1,000 CZK incl.	645	651	656	647	644	625	615	618	613	615	619	618
More than 1,000 CZK up to 2,000 CZK incl.	510	515	504	508	508	510	510	514	512	504	499	506
More than 2,000 CZK up to 3,000 CZK incl.	201	201	203	204	208	208	201	210	212	206	206	206
More than 3,000 CZK up to 5,000 CZK incl.	271	276	280	276	272	271	266	272	272	268	264	258
More than 5,000 CZK up to 10,000 CZK incl.	259	249	248	250	253	252	253	258	261	256	257	257
More than 10,000 CZK up to 20,000 CZK incl.	168	174	172	181	183	179	184	183	189	189	191	194
More than 20,000 CZK up to 30,000 CZK incl.	82	81	76	65	70	76	78	78	79	82	84	83
More than 30,000 CZK up to 50,000 CZK incl.	62	65	65	64	66	58	58	61	63	64	61	63
More than 50,000 CZK up to 100,000 CZK incl.	90	91	90	95	99	107	99	101	106	106	109	107
More than 100,000 CZK	77	80	74	70	69	69	71	69	76	80	77	77
Number of codes	**5,338**	**5,353**	**5,311**	**5,252**	**5,258**	**5,263**	**5,227**	**5,247**	**5,303**	**5,287**	**5,311**	**5,310**

Development of Average End-User Prices

In 2021, there was no change to the profit margins or to the VAT, the rate of which for medicinal products remained at 10 % also in 2021. 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 4.9 %. The highest increase of average prices occurred in the lowest price zone. The highest decrease occurred in the More than 2,500 CZK up to 5,000 CZK 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 5 %, with the highest increase in the More than 2,500 CZK up to 5,000 CZK price zone.

The highest decrease occurred in the More than 1,000 CZK up to 2,500 CZK incl. The situation in ex-factory price levels (ex. profit margin and VAT) focusing upon a more detailed comparison of the last quarters of 2020 and 2021 is illustrated by Fig. 18 and 19.

Fig. 18 **Prices of pharmaceuticals regulated by maximum price – comparison of average prices in Q4 2020 and Q4 2021 by price zones**

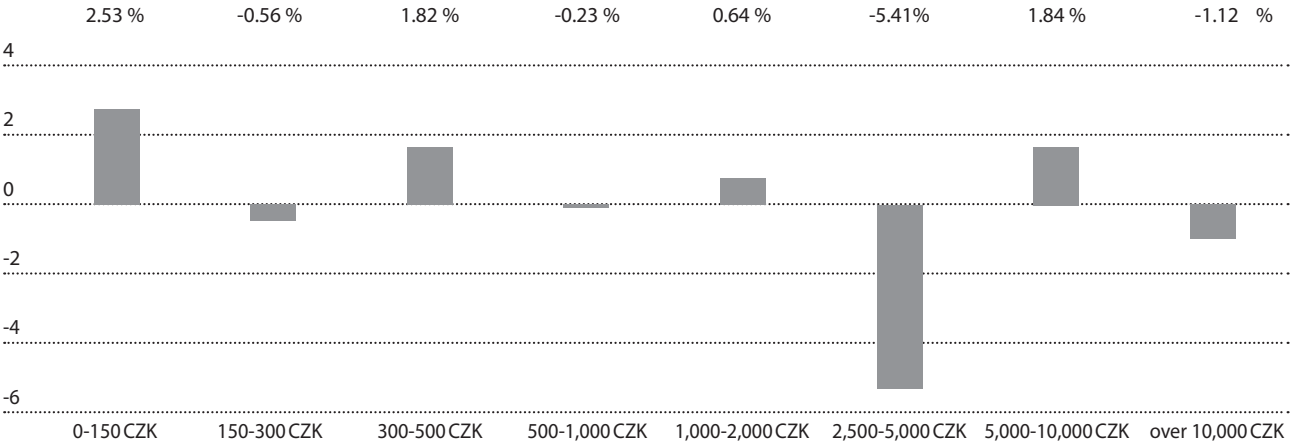
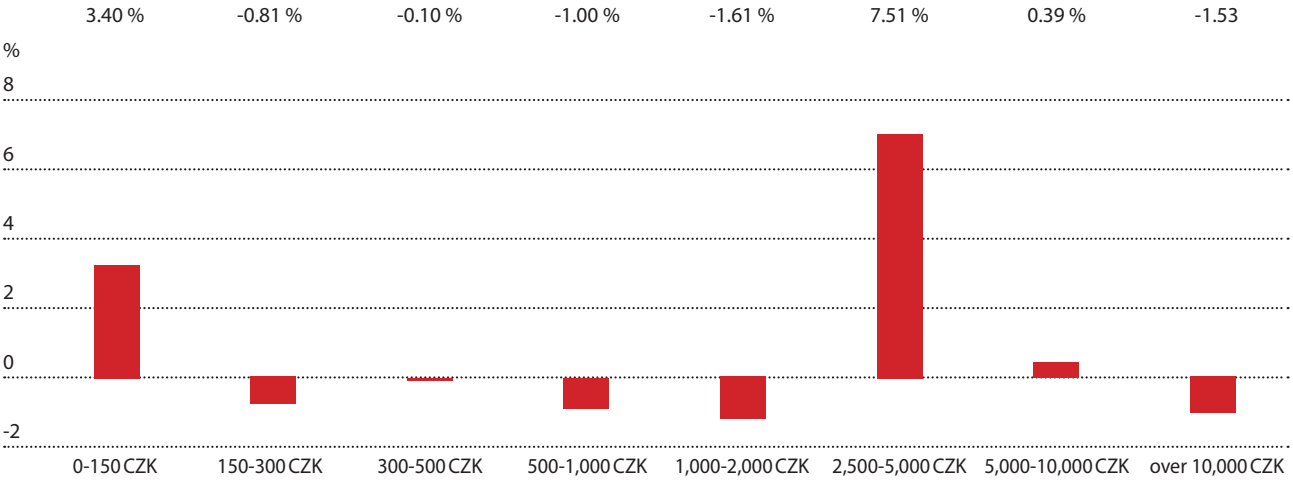


Fig. 19 **Prices of pharmaceuticals regulated by profit margin – comparison of average prices in Q4 2020 and Q4 2021 by price zones**



Overview of the Most Commonly Distributed Medicinal Products Whose Maximum Price 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 2021, the maximum prices both increased and decreased in the group of the most commonly distributed medicinal products whose maximum price changed. The biggest change in terms of maximum price increase occurred for medicinal product CONDROSULF (Tab. 28).

Tab. 28 **Ten most commonly distributed medicinal products by number of packages reported in compliance with DIS-13 Guideline whose maximum price changed**

Code	ATC	Name	Name supplement	No. of packages	Original maximum price (CZK)	New maximum price (CZK)	Change to maximum price (%)
0098219	C03CA01	FURON	40MG TBL NOB 50	1,060,856	53.38	47.74	-10.6
0200935	A12BA01	KALNORMIN	1G TBL PRO 30	894,750	39.97	37.07	-7.3
0233016	J01CF04	PROSTAPHLIN	1000MG INJ PLV SOL 1	745,295	49.18	94.83	92.8
0231956	R03AC02	VENTOLIN INHALER N	100MCG/DÁV INH SUS PSS 200/DÁV	635,447	44.71	39.80	-11.0
0131426	J07BB02	VAXIGRIP TETRA	INJ SUS ISP 1X0,5ML+J	624,565	329.82	219.49	-33.5
0014821	M01AX25	CONDROSULF	800MG TBL FLM 30	573,927	258.42	946.31	266.2
0002679	R03AL01	BERODUAL N	0,02MG/0,05MG/DÁV INH SOL PSS 200DÁV	544,945	142.,41	129.01	-9.4
0140192	A02BC01	OMEPRAZOL STADA	20MG CPS ETD 100	500,747	76.43	119.09	55.8
0243138	H03AA01	EUTHYROX	50MCG TBL NOB 100 II	500,690	54.47	49.35	-9.4
0187425	H03AA01	LETROX	50MCG TBL NOB 100	437,472	44.01	40.17	-8.7

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. 29).

Tab. 29 **Ten most commonly distributed medicinal products by financial volume in end-user prices reported in compliance with DIS-13 Guideline whose maximum price changed**

Code	ATC	Name	Name supplement	Financial volume in end-user price	Original maximum price (CZK)	New maximum price (CZK)	Change to maximum price (%)
0223046	L01FF01	OPDIVO	10MG/ML INF CNC SOL 1X24ML	1,061,497,612	86,496.60	68,391.16	-20.9
0168904	B01AF01	XARELTO	20MG TBL FLM 98 II	1,022,737,330	5,331.59	4,891.61	-8.3
0168462	L04AA27	GILENYA	0,5MG CPS DUR 28	902,989,627	40,890.19	34,426.01	-15.8
0222682	L04AA36	OCREVUS	300MG INF CNC SOL 1X10ML	785,843,539	137,084.65	128,731.74	-6.1
0222376	J05AP57	MAVIRET	100MG/40MG TBL FLM 84(4X21)	751,505,075	339,492.53	305,259.08	-10.1
0210187	L01EL01	IMBRUVICA	140MG CPS DUR 90	690,699,401	132,631.35	130,892.86	-1.3
0219085	L02BX03	ZYTIGA	500MG TBL FLM 60(5X12)	559,073,266	79,518.94	66,464.22	-16.4
0194569	S01LA04	LUCENTIS	10MG/ML INJ SOL 1X0,165ML	542,130,173	15,277.36	14,324.36	-6.2
0193805	J07AH09	BEXSERO	INJ SUS 1X0,5ML+J	538,339,783	2,252.80	1,884.15	-16.4
0193747	B01AF02	ELIQUIS	5MG TBL FLM 168	531,299,381	4,677.66	4,232.24	-9.5

Amounts and Conditions of Reimbursements from Health Insurance Funds

Tab. 30 **Overview of administrative procedures in 2021**

Applications for determination or change of the amount and conditions of reimbursement	Number of SÚKL codes
Initiated	653
Decided	163
Appeal procedure pending	39
Became final	101
Applications for determination or change of maximum price and the amount and conditions of reimbursement	
Initiated	244
Decided	89
Appeal procedure pending	9
Became final	124
Applications for reimbursement revocation	
Initiated	69
Decided	51
Appeal procedure pending	0
Became final	47
Applications for maximum price and reimbursement revocation	
Initiated	82
Decided	77
Appeal procedure pending	0
Became final	75
Ex officio initiated procedures	
Initiated	505
Decided	386
Appeal procedure pending	93
Became final	184
Procedures concerning similar products	
Initiated	939
Decided	866
Appeal procedure pending	45
Became final	704

In 2021, 31 applications for determination of reimbursement of highly innovative products were submitted.

Pursuant to the provisions of Section 39 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 2021, savings of public health insurance funds were generated both by in-depth and abbreviated revisions of reimbursements. The total savings arising from abbreviated revisions enforceable in 2021 are estimated at 1,356,373,520 CZK, and those arising from in-depth revisions at 1,771,167,648 CZK.

Tab. 31 **Overview of enforceable 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
01/2021	31	6	15,320,449 CZK
02/2021	46	7	132,998,095 CZK
03/2021	7	3	240,180,788 CZK
04/2021	41	4	925,564,707 CZK
05/2021	114	10	393,906,552 CZK
06/2021	12	1	- CZK
07/2021	79	8	15,648,792 CZK
08/2021	17	5	146,798,028 CZK
09/2021	13	5	58,745,101 CZK
10/2021	43	6	319,515,329 CZK
11/2021	50	7	241,109,638 CZK
12/2021	244	9	428,877,057 CZK

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

Tab. 32 **Overview of the number of codes of medicinal products/foods for special medical purposes in price zones according to the List of Prices and Reimbursements (SCAU) by month**

Reimbursement zone	01	02	03	04	05	06	07	08	09	10	11	12
Up to 20 CZK, incl.	160	160	157	148	149	153	150	151	151	150	151	148
More than 20 CZK up to 50 CZK, incl.	754	756	749	732	730	733	730	731	735	733	740	732
More than 50 CZK up to 100 CZK, incl.	1,283	1,278	1,260	1,236	1,229	1,251	1,239	1,237	1,253	1,255	1,249	1,239
More than 100 CZK up to 200 CZK, incl.	1,592	1,610	1,587	1,559	1,553	1,540	1,563	1,559	1,568	1,558	1,565	1,566
More than 200 CZK up to 300 CZK, incl.	794	814	804	791	802	784	761	768	769	773	775	794
More than 300 CZK up to 500 CZK, incl.	882	881	879	870	875	866	903	906	912	921	915	917
More than 500 CZK up to 1,000 CZK, incl.	1,066	1,058	1,056	1,052	1,047	1,048	1,017	1,049	1,045	1,039	1,039	1,040
More than 1,000 CZK up to 2,000 CZK, incl.	907	898	888	885	879	901	891	899	902	900	906	898
More than 2,000 CZK up to 3,000 CZK, incl.	382	390	388	389	388	383	381	381	381	378	377	376
More than 3,000 CZK up to 5,000 CZK, incl.	348	346	347	341	334	337	341	346	344	352	369	361
More than 5,000 CZK up to 10,000 CZK, incl.	429	428	429	434	440	448	440	444	447	442	436	434
More than 10,000 CZK up to 20,000 CZK, incl.	305	297	298	300	301	300	302	308	314	314	314	311
More than 20,000 CZK up to 30,000 CZK, incl.	108	105	105	105	107	113	114	112	113	113	113	111
More than 30,000 CZK up to 50,000 CZK, incl.	76	78	80	81	81	90	90	92	93	95	95	93
More than 50,000 CZK up to 100,000 CZK, incl.	99	100	96	99	102	105	105	105	112	112	113	113
More than 100,000 CZK	88	91	86	85	86	87	90	91	96	100	100	100
Number of codes	9,273	9,290	9,209	9,107	9,103	9,139	9,117	9,179	9,235	9,235	9,257	9,233

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 funds, there was a significant decrease in the reimbursement for individual packages of medicinal products. The highest reduction was seen in medicinal products TECFIDERA and AVASTIN (Tab. 33).

Tab. 33 **Ten most commonly distributed medicinal products by financial volume in end-user prices reported in compliance with DIS-13 Guideline, for which reimbursement was changed**

Code	ATC	Name	Name supplement	Financial volume in end-user prices	Original reimbursement (CZK)	New reimbursement (CZK)	Change in reimbursement (%)
0193747	B01AF02	ELIQUIS	5MG TBL FLM 168	531,299,381	3,833.94	3,823.20	-0.3
0193695	S01LA05	EYLEA	40MG/ML INJ SOL 1X0,09ML	501,559,554	22,283.04	16,258.18	-27.0
0028397	L01FG01	AVASTIN	25MG/ML INF CNC S OL 1X16ML	479,722,089	25,926.96	16,369.13	-36.9
0194319	L04AA31	AUBAGIO	14MG TBL FLM 28	414,989,583	18,060.85	12,724.71	-29.5
0028937	L04AX04	REVLIMID	10MG CPS DUR 21	413,537,399	90,159.34	78,195.06	-13.3
0193870	L01FD02	PERJETA	420MG INF CNC SOL 1X14ML	413,160,355	66,935.52	64,529.09	-3.6
0168373	B01AE07	PRADAXA	150MG CPS DUR 60X1 I	398,892,867	1,369.26	1,365.43	-0.3
0210773	L01FF01	OPDIVO	10MG/ML INF CNC SOL 1X10ML	356,895,608	29,454.43	27,737.16	-5.8
0167601	L04AC05	STELARA	90MG INJ SOL ISP 1X1ML	350,271,300	51,003.22	36,272.93	-28.9
0194769	L04AX07	TECFIDERA	240MG CPS ETD 56	300,485,045	36,175.21	22,673.97	-37.3

In the entire group of medicinal products for which reimbursement was changed and which were the most distributed ones, product reimbursements were decreased (Tab. 34).

Tab. 34 **Ten most commonly distributed medicinal products by number of packages reported in compliance with DIS-13 Guideline 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
0014821	M01AX25	CONDROSULF	800MG TBL FLM 30	273,491	159.71	220.75	289,564	
0030434	C03DA01	VEROSPIRON	25MG TBL NOB 100	248,359	130.57	169.24	247,522	
0168373	B01AE07	PRADAXA	150MG CPS DUR 60X1 I	112,310	1,369.26	1,365.43	135,577	
0216478	M01AX26	PIASCLEDINE	100MG/200MG CPS DUR 30	124,824	159.71	220.75	114,632	
0184377	R03AK08	COMBAIR	100MCG/6MCG/ DÁV INH SOL PSS 180DÁV	52,925	900.59	1,073.75	64,289	*/
0029740	A10BD08	EUCREAS	50MG/1000MG TBL FLM 60 I	108,356	891.23	740.08	108,080	
0200819	C10AA05	ATORVASTATIN RATIOPHARM GMBH	20MG TBL FLM 90	68,228	279.53	165.41	98,538	
0046755	C03DA01	VEROSPIRON	50MG CPS DUR 30	57,717	78.33	101.54	74,389	
0500140	A10BD07	JANUMET	50MG/1000MG TBL FLM 56	66,799	835.71	690.74	66,702	
0218110	R03BA02	MIFLONID BREEZHALER	400MCG INH PLV CPS DUR 60	30,758	188.46	300.12	27,679	*/

** – 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*

For majority of medicinal products whose reimbursement was changed and which were the most commonly distributed ones (by number of packages; DIS-13 reporting), reimbursements were increased in 2021.

Table 35 presents a list of essential changes to the reimbursement system in 2021, 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. 35 **Overview of newly reimbursed original pharmaceuticals and significant extensions of reimbursement with decisions issued in 2021**

Name of the medicinal product and active substance	Indication (clinical use)	Reimbursement effective from
BLINCYTO (blinatumomab)	Acute lymphoblastic leukaemia (ALL) in first complete remission following previous chemotherapy	March 2021
ATECTURA BREEZHALER (indacaterol + mometasone)	Persisting (complicated) forms of bronchial asthma	May 2021
ENERZAIR BREEZHALER (indacaterol + mometasone + glycopyrronium)	Persisting (complicated) forms of bronchial asthma	May 2021
REVLIMID (lenalidomide)	Treatment-naïve multiple myeloma (combination with bortezomib and dexamethasone)	April 2021
KADCYLA (trastuzumab emtansine)	Early HER2 positive breast carcinoma (adjuvant monotherapy)	March 2021
LYNPARZA (olaparib)	Advanced ovarian carcinoma, fallopian tube carcinoma or peritoneal carcinoma with BRCA mutation (providing treatment response to first-line platinum was achieved)	April 2021
ALUNBRIG (brigatinib)	First-line treatment of non-small-cell lung carcinoma	May 2021
IMBRUVICA (ibrutinib)	Mantle cell lymphoma in patients who have previously completed treatment with rituximab (and transplantation or are ineligible for transplantation)	May 2021
ALPROLIX (long-acting factor IX)	Previously untreated patients (PUPs) with haemophilia B	May 2021
BAVENCIO (avelumab)	Advanced renal carcinoma with favourable prognosis (in combination with axitinib)	April 2021
TRULICITY (dulaglutide)	Increased reimbursement for patients with diabetes and BMI 30-35	May 2021
PRADAXA (dabigatran)	First-line prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation	April 2021
KEYTRUDA (pembrolizumab)	Adjuvant treatment of malignant melanoma (in monotherapy)	March 2021
KEYTRUDA (pembrolizumab)	Non-small-cell non-squamous lung carcinoma (with PD-L1 expression greater than 50 %) in combination with chemotherapy	March 2021
FLEBOGAMMA, GAMMAGARD, KIOVIG, OCTAGAM, PRIVIGEN (intravenous immunoglobulins)	Clinically serious drug-induced hypogammaglobulinemia	May 2021
AVONEX, BETAFERON, COPAXONE, EXTAVIA, REBIF (interferons for the treatment of multiple sclerosis)	Reimbursement for a broader group of patients with attack-form of multiple sclerosis (2 relapses in 2 years). Furthermore, amendment to the conditions of reimbursement involving the possibility to switch the patient to another active substance for first-line therapy or multiple sclerosis (in case of intolerance, adverse drug reactions or lack of efficacy of interferon treatment).	May 2021
NEUPRO (rotigotine)	Restless legs syndrome	April 2021
OCALIVA (obeticholic acid)	Primary biliary cholangitis	May 2021
IBRANCE (palbociclib)	Locally advanced or metastatic breast carcinoma	June 2021
NUBEQA (darolutamide)	Non-metastatic, castration resistant prostate carcinoma with high risk of developing metastases	June 2021
AZACITIDIN(E) MYLAN /STADA/ ACCORD /BETAPHARM/, VIDAZA (azacitidine)	Prolongation of treatment with azacitidine (cancellation of the limitation of the total number of 14 reimbursed cycles) in patients with myelodysplastic syndrome, acute myeloid leukaemia, and chronic myelomonocytic leukaemia	July 2021
TAGRISSO (osimertinib)	First-line treatment of locally advanced or metastatic non-small-cell lung carcinoma with EGFR gene mutation	June 2021
KEYTRUDA (pembrolizumab)	First-line treatment of metastatic or nonresectable recurring squamous head and neck carcinoma	July 2021
XOSPATA (gilteritinib)	Acute myeloid leukaemia with FLT3 mutation (type FLT3-ITD or FLT3-TKD), in first relapse of the disease	June 2021
FLUCLOXACILINA AZEVEDOS (flucloxacillin)	Treatment of skin and soft tissue infections caused by Staphylococcus Aureus. Product in specific therapeutic programme.	July 2021
IMNOVID (pomalidomide)	Relapsing or refractory multiple myeloma (combination pomalidomide + bortezomib + dexamethasone)	July 2021

NINLARO (ixazomib)	Relapsing or refractory multiple myeloma (combination ixazomib + lenalidomide + dexamethasone)	July 2021
BRAFTOVI (encorafenib)	Combined treatment (encorafenib + cetuximab) of metastatic colorectal carcinoma in patients pre-treated with previous therapy including oxaliplatin.	August 2021
VENCLYXTO (venetoclax)	Combined treatment (venetoclax + obinutuzumab) of treatment-naïve chronic lymphocytic leukaemia	August 2021
TECFIDERA (dimethyl fumarate)	First-line treatment of relapsing-remitting multiple sclerosis with high disease activity	September 2021
ROZLYTREK (entrectinib)	Non-small-cell lung carcinoma in patients with a specific type of genetic mutation (ROS 1)	October 2021
DUPIXENT (dupilumab)	Severe form of atopic dermatitis in children aged 6-11 years	October 2021
DOPTELET (avatrombopag)	Severe platelet deficit in adult patients with chronic liver disease who are scheduled for invasive intervention	October 2021
POLIVY (polatuzumab)	Combined treatment (polatuzumab + bendamustine + rituximab) of relapsing/refractory diffuse large B cell lymphoma	September 2021
NATPAR (parathormone)	Chronic hypoparathyroidism in adult patients not adequately controlled by standard-of-care therapy	October 2021
KEYTRUDA (pembrolizumab)	Locally advanced or metastatic urothelial carcinoma in patients pre-treated with platinum-based chemotherapy	October 2021
FOTIVDA (tivozanib)	First-line treatment of clear-cell renal cell carcinoma with favourable prognosis	November 2021
HUMIRA (adalimumab)	First-line systemic treatment of psoriasis	December 2021
BAVENCIO (avelumab)	First-line maintenance treatment of urothelial carcinoma	November 2021
ELIQUIS (apixaban)	First-line prevention of stroke and systemic embolism in patients with nonvalvular atrial fibrillation	November 2021
OPDIVO (nivolumab)	First-line treatment of metastatic non-small-cell lung carcinoma with PD L1 expression of 0-49 % (combination OPDIVO + ipilimumab)	December 2021
OTEZLA (apremilast)	Moderate to severe psoriasis in pre-treated patients	January 2022
ILUMETRI (tildrakizumab)	Moderate to severe psoriasis in pre-treated patients	January 2022
OFEV (nintedanib)	Chronic fibrosing interstitial lung disease of progressive phenotype (i.e., conditions with aggravating breathing symptoms or increasing organic lung involvement)	December 2021
LYNPARZA (olaparib)	Locally advanced or metastatic breast carcinoma (HER2 negative, with BRCA mutation) in patients who have not been treated with chemotherapy for advanced disease.	December 2021
OCREVUS (ocrelizumab)	First-line rrMS + plus extension as part of lateral switch due to lack of efficacy	January 2022

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 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 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

In 2021, the total of 912 applications for determination/change or revocation of maximum price and/or conditions and amount of reimbursement of medicinal products/foods for special medical purposes were submitted.

Applications for determination of maximum price and/or the amount and conditions of reimbursement and applications for change of maximum price and/or the amount and conditions of reimbursement represented an equal share of the total number of submitted applications, i.e., approx. 45 %, and administrative procedures concerning the determination of the amount and conditions of reimbursement/maximum price and conditions of reimbursement following the process outlined under Section 39g(9) of the Act on Public Health Insurance (so called "similar products") accounted for 29 % of the overall number of procedures initiated upon request. The remaining approx. 10 % of the total number of submissions were applications for revocation of maximum price and/or the amount and conditions of reimbursement.

The trend of a mild increase in the number of applications submitted by health insurance companies has continued and in 2021, it accounted for approx. 18 % of the total number of applications.

Twenty-eight administrative procedures initiated upon request were suspended by resolution as early as during the control of the application in so-called validation phase. The most common cause of suspending the administrative procedure was an obstacle preventing the commencement of the procedure as per the provision of Section 48(1) of the Code of Administrative Procedure (lis pendens), which occurred in more than 50 % of these suspended administrative procedures.

In 2021, 23 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. 36 **Validation of applications for determination/change/ revocation of maximum prices and/or reimbursement amounts and conditions, for abbreviated revision of maximum price or reimbursement system – 2021**

Period	Submitted applications	Suspended due to defective submission and application shortcomings	Discontinued in the validation phase
January	108	1	1
February	89	0	3
March	104	1	5
April	72	0	3
May	82	1	5
June	58	0	1
July	57	0	1
August	86	1	3
September	71	0	2
October	43	3	2
November	65	2	1
December	77	2	1
Total	**912**	**11**	**28**

Individually Prepared Medicinal Products

Individually prepared medicinal products (hereinafter referred to as "IPLPs") are subjected to the conditions of material price regulation (hereinafter referred to as "VUC") set forth by the Price Regulation (effective for 2021). 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 "ATP").

The conditions for determination of the amount and conditions of reimbursement by means of general measures (hereinafter referred to as "OOP") are set forth by Act No 48/1997 Coll., on Public Health Insurance and on Amendments to Some related Acts, 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.

General Measures (OOPs)

In the course of 2021, five general measure procedures were initiated and properly completed.

As of 01 February 2021, OOP 08-20 for the group of radiopharmaceuticals, initiated in late 2020, became effective. By means of this OOP, a new radiopharmaceutical, 11C methionine, was included in the IPLP List. This diagnostic radiopharmaceutical is intended for the detection of gliomas and other malignant CNS tumours for patients in the age of 5-90 years. The Institute estimated an increase in public health insurance funds by 104 mil. CZK/year as a consequence of including the new radiopharmaceutical.

As of 01 March 2021, the following general measures were published: OOP 01-21 for DPV, 02-21 for TP, and 03-21 for RF. All of these OOPs were published in compliance with Government Regulation No 603/2020 Coll., amending Government Regulation No 341/2017 Coll., on salaries of public service and administration employees, as amended, and Government Regulation No 304/2014 Coll., on civil servant salaries, as amended, increasing the salaries of healthcare professionals by 10 % in the basic tariff. General measures OOP 02 21 TP and OOP 03-21 RF reflected the change in the minute performance rate in compliance with Decree No 563/2020 Coll., amending Decree No 134/1998 Coll., setting forth the list of healthcare procedures and their point values, as amended with effect from 01 January 2021. The overhead minute rate per minute of time performance was increased from the original value of 3.19 points to the new value of 3.28 points. In compliance with Decree No 428/2020 Coll., setting point values, reimbursement amounts for reimbursed services, and regulatory restrictions for 2021, the point value decreased from the original amount of 1.07 CZK per point to the new amount of 1.05 CZK per point. Furthermore, in OOP 03-21 RF, the Institute included in the IPLP list a new radiopharmaceutical code for 99mTc-DTPA (code RF 0002112), which is to be reported strictly with procedure 47197 (glomerular filtration determination by blood sample radioactivity measurement). Furthermore, RF 68Ga-PSMA-11, code 0002110 was excluded within the scope of a specific therapeutic programme, and an authorised radiopharmaceutical, 68Ga-PSMA-11, was included under code 0002113.

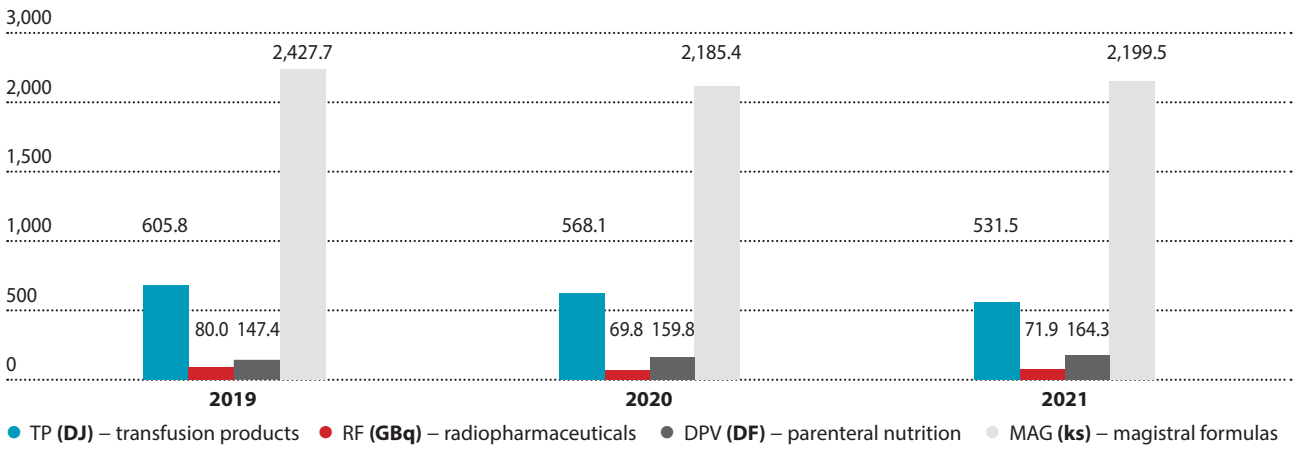
As at 01 June 2021, general measure OOP 04-21 for the RF subgroup came into force. It reflected the new price source materials and the €/CZK exchange rate on the basis of materials published by the Czech National Bank (ČNB). The said OOP reflected the revoked authorisation for product SODIUM CHROMATE (51CR) SOLUTION 37MBQ/ML INJ SOL 37MBQ (code 0137485) and as this was the only product from the radiopharmaceuticals group under codes 0002062 and 0002066, these codes were deleted from subgroup 13. Furthermore, marketing authorisation of product METASTRON 37MBQ/ML INJ SOL 1X4ML (code 0066455) was revoked, and thus the radiopharmaceutical under code 0002012 was taken out of subgroup 13.

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

The consumption of individually prepared medicinal products is evaluated in defined units (hereinafter referred to as "DU") by individual IPLP subgroups.

In case of the TP subgroup, in 2021, the consumption decreased, while in respect of the other subgroups, i.e., RF, DPV, and MAG, consumption slightly increased in comparison to the previous period. The values specified for the period of 2020 in the 2020 annual report were updated as of 04 February 2022. Data for the consumption of individually prepared medicinal products in 2021 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 2021 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 2019-2021 is shown in Fig. 20.

Fig. 20 **Overview of consumption of individually prepared medicinal products for the period of 2019–2021 in thous. DU**



In 2021, 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 3.19 points to the value of 3.28 points in compliance with Decree No 563/2020 Coll., amending Decree No 134/1998 Coll., setting forth the list of healthcare procedures and their point values, as amended with effect from 01 January 2021. In compliance with Decree No 428/2020 Coll., setting point values, reimbursement amounts for reimbursed services, and regulatory restrictions for 2021, the point value decreased from the original amount of 1.07 CZK per point to the new amount of 1.05 CZK per point. In compliance with Government Regulation No 304/2014 Coll., on civil servant salaries, as amended, the salaries of healthcare professionals were raised in the basic tariff by 10 %.

In 2021, a new item was included in the RF group of the IPLP List. With effect as of 01 February 2021, diagnostic radiopharmaceutical 11C methionine was included. As of 01 March 2020, a new code was included in the RF group – RF 99mTc-DTPA (code RF 0002112), which is reported strictly with procedure 47197 (glomerular filtration determination by blood sample radioactivity measurement). Furthermore, RF 68Ga-PSMA-11, code 0002110 was excluded within the scope of a specific therapeutic programme, and an authorised radiopharmaceutical, 68Ga-PSMA-11, was included under code 0002113.

The distribution of expenses in the IPLP group in 2021 by individual subgroups is illustrated by Fig. 21.

Fig. 21 **Distribution of total expenses in the IPLP group for 2021**

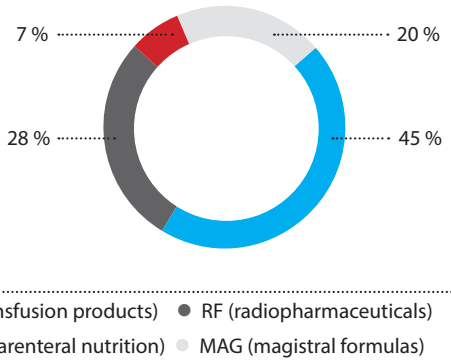
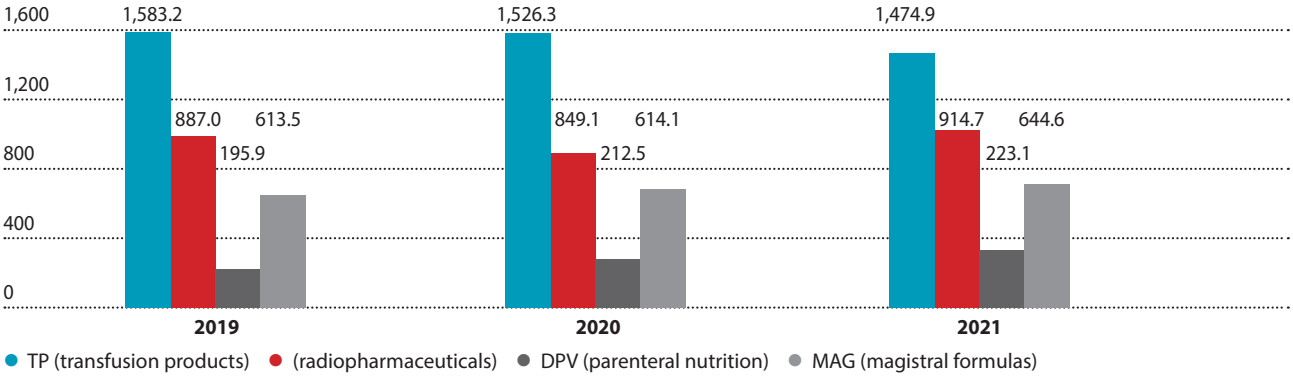


Fig. 22 illustrates also a comparison of expenses in the period of 2019-2021 for individual IPLP subgroups. Compared to 2020, an increase in the costs reimbursed from the public health insurance funds was seen in the DPV, RF, and MAG subgroups; only the TP subgroup exhibited a decrease, which corresponds also to the lower consumption of this subgroup.

Fig. 22 **Comparison of expenses by subgroups of individually prepared medicinal products for the period of 2019–2021 in mil. CZK**



The total expenses for the IPLP group reimbursed from public health insurance funds amounted to 3,202.0 mil. CZK in 2020; in 2021 this amount was 3,257.3 mil. CZK, which is an increase in expenses by 55,3 mil. CZK, i.e., 1.73 % compared to 2020.

MEDICAL DEVICES DEPARTMENT

In the area of medical device regulation, 2021 was the year of legislative changes. In May, Regulation (EU) 2017/745 of the European Parliament and of the Council on medical devices (hereinafter referred to as "MDR") along with the new Act No 89/2021 Coll., on Medical Devices (hereinafter referred to as the "Act on Medical Devices") took effect as well as the amended Act No 268/2014 Coll., that covers the area of in vitro diagnostic medical devices (hereinafter referred to as the "IVD

Act") until the coming into effect of Regulation (EU) 2017/746 of the European Parliament and of the Council on in vitro diagnostic medical devices (hereinafter referred to as the "IVD Regulation") in 2022. In this respect, it was necessary to cater for the development of the Registry of Medical Devices (hereinafter referred to as the "RZPRO"), which continues to be availed of on the basis of the IVD Act and, in some agendas, covers the role of the European Database of Medical Devices (EUDAMED) that represents the major process tool for both of the aforementioned Regulations. According to information from the European Commission, EUDAMED roll-out is to be postponed at least until 2023. At the same time, the staff of the Medical Devices Department were busy preparing new processes in compliance with the new legislation and tenders for a Medical Device Information System that, in compliance with the Act on Medical Devices, will serve as the new agenda system for the Medical Devices Department, covering all agendas, including medical device reimbursements. In the course of the year, works on the preparation of the new Act on Medical Devices were initiated in cooperation with the Ministry of Health; the Act is to come into force along with the IVD Regulation and it will merge the area of medical devices with the area of in vitro diagnostic medical devices. The staff of the Medical Devices Department 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.

4.15 Medical Device Control and Expert Opinion Unit (KOP)

Controls

The Institute´s surveillance activities over persons handling medical devices are stipulated by Regulation (EU) 2017/745 of the European Parliament and of the Council on medical devices (hereinafter referred to as "MDR") along with the new Act No 89/2021 Coll., on medical devices (hereinafter referred to as the "Medical Device Act") as well as by the amended Act No 268/2014 Coll., that covers the area of in vitro diagnostic medical devices (hereinafter referred to as the "IVD Act"), and Act No 22/1997 Coll., on Technical Requirements for Products and on Amendments to Some Acts, as amended. The regulated persons include healthcare service providers in the sphere of medical device use as well as medical device 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 and newly also surveillance over medical device advertising.

The objective of both scheduled and ad hoc inspections 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 2021, the inspectors of the Control Unit conducted the total of 109 inspections, of which 47 were inspections at providers of healthcare services (both state and non-state healthcare facilities) and 62 were inspections at medical device manufacturers, importers, distributors, and persons selling, dispensing or servicing medical devices. During these inspections, 236 medical devices were inspected. The tables below provide a more detailed statistics regarding the total number of inspected medical devices and persons.

Forty-seven 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, 62 inspections were conducted as part of market surveillance, in which compliance with the requirements of medical device supply to the market was checked. The number of shortcomings identified in respect of persons subjected to market surveillance was 98.

The Medical Device Inspection and Expert Opinion Unit forwarded the total of 71 motions to the Medical Device Legal Support Unit.

Tab. 37 **Overview of inspections conducted by KOP**

Number of inspections	109
Number of inspections instigated by a motion (of the total number of inspections)	54
Number of inspected medical devices	*236
Number of inspected Legally Controlled Measuring Instruments (of the total number of inspected medical devices)	0
Number of shortcomings identified in inspected medical devices	*98
Number of motions forwarded to the Medical Device Legal Support Unit (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. 38 **KOP inspection rating**

Entity	Number of inspections	*1	*2	*3
POS – providers	47	27	16	0
CEN – price control	0	0	0	0
DIS – distributors	33	10	5	15
DOV – importers	22	11	4	7
PRO – persons selling medical devices	10	9	1	0
SER – persons servicing medical devices	8	7	1	0
VYD – persons dispensing medical devices	4	4	0	0
VYR – manufacturers	21	1	13	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 Institute and in response to filed applications for medical device notification in the RZPRO. In 2021, the KOP Unit issued 97 expert opinions concerning the nature of a product or medical device classification. The aforementioned activities of the Unit in the processing of opinions regarding product nature or medical device classification are also shared with the Advertising Surveillance Unit in the sphere of pharmaceuticals. Of the aforementioned number, 31 opinions were issued on the basis of an external request and 66 opinions on the basis of requests from other units of the Institute.

4.16 Medical Device 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 and in the MDR, 36 individual applications for authorisation of CIMD conduct and 43 individual applications for variations to CIMD conditions were submitted to the Institute in 2021 via the RZPRO Clinical Investigations module.

With regard to the change of legal regulations, in compliance with the transitory provision of Section 72(1) of the Act on Medical Devices, three pending procedures regarding the authorisation of a medical device clinical investigation were stopped. In compliance with Section 9(h) of Act No 268/2014 Coll., on Medical Devices and on Amendment to Act No 634/2004 Coll., on Administrative Fees, as amended as at the last effective date, i.e., 25 May 2021, 14 favourable opinions authorising the conduct of CIMD were issued in administrative procedures. From 26 May 2021, 16 applications for authorisation of CIMD were granted for CIMDs designed in compliance with the requirements set forth by the MDR. Furthermore, in 2021, 36 applications for authorisation of variations to the conditions of CIMDs authorised and initiated pursuant to Act No 268/2014 Coll., on Medical Devices and on Amendment to Act No 634/2004 Coll., on Administrative Fees, as amended, were granted.
With regard to the COVID-19 pandemics and amendments to legal regulations, three inspections of the conduct of clinical investigations on medical devices at providers of healthcare services were carried out, in which one type of an investigational medical device was 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. An important aspect in the selection of the subject-matter of inspections in 2021 was the knowledge gained from previous official activity. During the on-site inspections, an improper procedure of the conduct of the clinical investigation was identified in all three cases and subsequently, it was proposed to initiate an administrative procedure with the sponsor.

In total, 290 serious adverse events (hereinafter referred to as "SAE") were individually reported from ongoing clinical investigations via the RZPRO Clinical Investigations module.

Within the scope of international cooperation in the sphere of clinical evaluations, in 2021, a representative of the Medical Device Clinical Trials Unit participated in regular web meetings of the medical device 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 MDR and upon exchange of information among the EU Member States. Due to the pandemic situation, all meetings were held online.

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

The coming into force of the MDR also drove changes to the entities´ obligations in the sphere of medical device vigilance regarding the reporting of adverse events, suspected adverse events, and field corrective actions. The changes concerned, in particular, the area of definitions, where the obligation to report to the competent authority now applies only to serious adverse events. The obligations of distributors, persons servicing medical devices, and healthcare service providers to report suspected adverse events was cancelled on the national level and now applies only to manufacturers and authorised representatives. Nevertheless, reporting of suspected adverse events by distributors, persons servicing medical devices, and healthcare service providers is supported and welcome so as to be able to ensure the safety of patients and users of medical devices.

As of the last effective date of Act No 268/2014 Coll., on Medical Devices and on Amendment to Act No 634/2004 Coll., on Administrative Fees, as amended, i.e., 25 May 2021, 376 adverse events considered to be associated with the use of medical devices in the provision of healthcare services within the territory of the Czech Republic were reported to the Institute. Since 26 May 2021, 760 SAEs and AEs considered to be associated with the use of medical devices and in vitro medical devices in the provision of healthcare services within the territory of the Czech Republic were reported to the Institute in compliance with MDR requirements. Furthermore, two adverse events arising outside the territory of the Czech Republic associated with medical devices of Czech manufacturers were notified in 2021. All of the cases were subjected to investigation. The development of the number of AE reports in 2013-2021 is illustrated by Fig. 23.

The total number of received reports on safety corrective actions regarding medical devices from competent national authorities, manufacturers or their authorised representatives, distributors or importers, as applicable, amounted to 859. Of the total number of received reports, 476 concerned medical devices distributed on the Czech market. The development of the number of reports on safety corrective actions in 2013-2021 is illustrated by Fig. 24.

In 2021, the Institute published 399 communications to users – Field Safety Notices (FSN) via the 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. Nevertheless, one unscheduled inspection of a healthcare service provider was carried out on the basis of evaluation of a suspected adverse event report received by the Institute´s non-stop service.

Thirty-two penalties were imposed for offences in the sphere covered by the Medical Device Clinical Trials and Vigilance Unit. The Medical Devices Legal Support Unit (PPZ) was forwarded 26 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, seven 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 2021, the inspectors of the Medical Device Clinical Trials and Vigilance Unit participated in regular meetings of the PMSV (Post Market Surveillance and Vigilance) Working Group of the Medical Device Coordination Group (MDCG) of the European Commission; they participated in three meetings and ten 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 the updated version of the Manufacturer Incident Report (MIR) form and a Design change in combination with

a corrective action, and provision of comments on the proposed new version of MIR, PMSV Work Programme 2021, and document Questions & Answers on Vigilance Terms and Concepts.

SÚKL updated the vigilance sections of its website – specifically the "Medical device (suspected) adverse event report", a section concerning the new version of the MIR form, including questions and answers on the implementation of this form. Information on medical device vigilance and in vitro diagnostic medical device vigilance was split.

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

Fig. 23 **Overview of notified adverse events in 2013–2021**

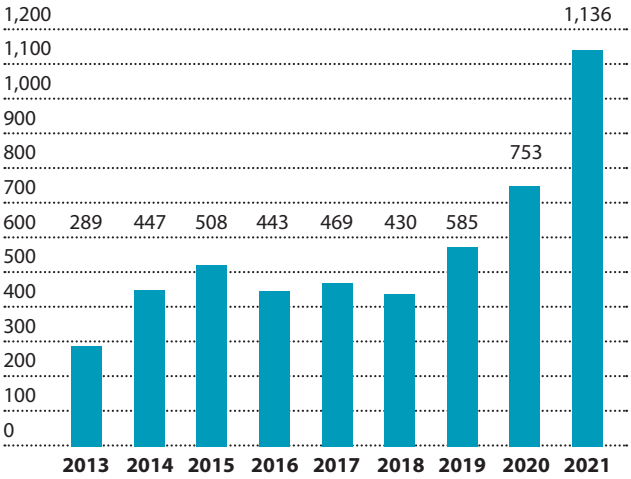
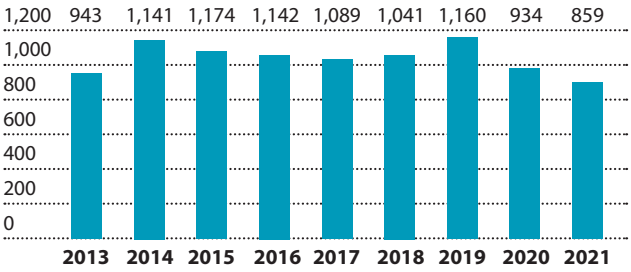


Fig. 24 **Overview of safety corrective actions for medical devices adopted in 2013–2021**



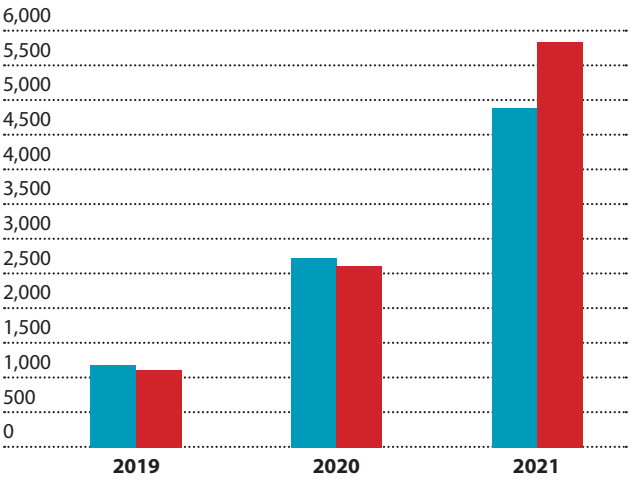
4.17 Registration and Notification Unit (RAN)

The Registration and Notification Unit (RAN) is in charge of registration of persons and associated activities, regulation in the area of medical device notifications and associated activities, and the issuance of certificates of free sale in compliance with the Act on Medical Devices, IVD Act, and MDR.

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

In total, during the past year, the Unit confirmed or asked for amendment of 5,734 notifications in the Persons module. In 2021, 4,849 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. 25.

Fig. 25 **Ratio of submitted and concluded notifications**



- **Notification of Person**
  In 2021, RAN concluded 1,909 submitted notifications of persons.

- **Notification of Activity**
  In 2021, 393 notifications regarding activities in general were completed – these concerned activities of manufacturers, distributors, importers, persons servicing medical devices, authorised representatives, and clinical investigation sponsors.

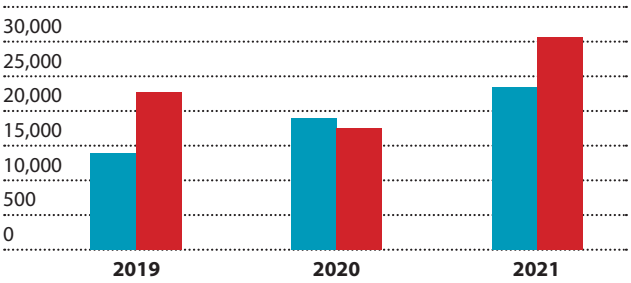
- **Notifications of changes to data**
  In total, 2,195 notifications of changes to data of a person were processed and completed.

- **Notification of deletion of a person**
  In 2021, the RAN Unit processed 70 notifications of deletion of a person.

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

In total, the Unit completed 25,373 applications in the Medical Device module in the last year. In 2021, 23,003 applications were entered in the Medical Device 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. 26.

Fig. 26 **Ratio 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 2021, the Unit completed 10,191 administrative procedures regarding applications for medical device notification.

- Applications for medical device notification renewal
  In total, 4,217 administrative procedures regarding applications for medical device notification renewal were completed.

- Applications for change to medical device data
  In total, 9,747 applications for change to medical device data were processed and completed.

- Applications for medical device deletion
  The Unit completed 884 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 2021, 341 applications were submitted, of which 340 were completed.

4.18 Medical Device Legal Support Unit (PPZ)

Decision-Making in the Area of Product Nature Determination and Proper Classification of the IVDs, Decision-Making on whether MDR Applies to a Product

In compliance with the Act on Medical Devices, since 2015, the Institute, as the first-instance administrative authority, had been involved in the agenda of decision-making in the area of product nature determination and proper classification of medical devices. Since the effective date of the Act on Medical Devices and the coming into existence of the IVD Act, 26 May 2021, this agenda has been split into decision-making about whether MDR applies to a product, and decision-making on the determination of the nature of an IVD device and its proper classification.

Until 25 May 2021, the following applied: if the Institute, in its assessment of applications for medical device notification, identified any justified doubt as to the proper risk class classification of the assessed medical device, or doubts as to whether the product met the definition of a medical device, it commenced an administrative procedure with the applicant. Since 26 May 2021, the Institute commences administrative procedures where it identifies any justified doubt as to whether the assessed product falls within the scope of the MDR and where it identifies any justified doubt as to the proper risk class classification of the assessed IVD or doubt as to whether the product meets the IVD definition.

In 2021, 34 proposals for the commencement of an administrative procedure on product nature and 39 proposals for the commencement of an administrative procedure on medical device classification were forwarded to the Medical Device Legal Support Unit.

In 2021, the Institute commenced 34 ex-officio administrative procedures on product nature and 39 ex-officio administrative procedures regarding medical device classification.

In 2021, the Institute received no application for decision regarding product nature or medical device classification.

In 2021, 17 decisions on medical device classification and 21 decisions on product nature were issued. Furthermore, the Institute issued 112 rulings on administrative procedure termination.

Fig. 27 **Overview of administrative procedures commenced in 2021**

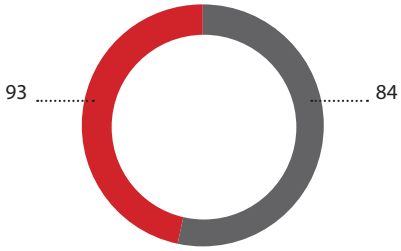
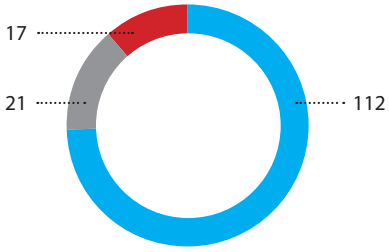
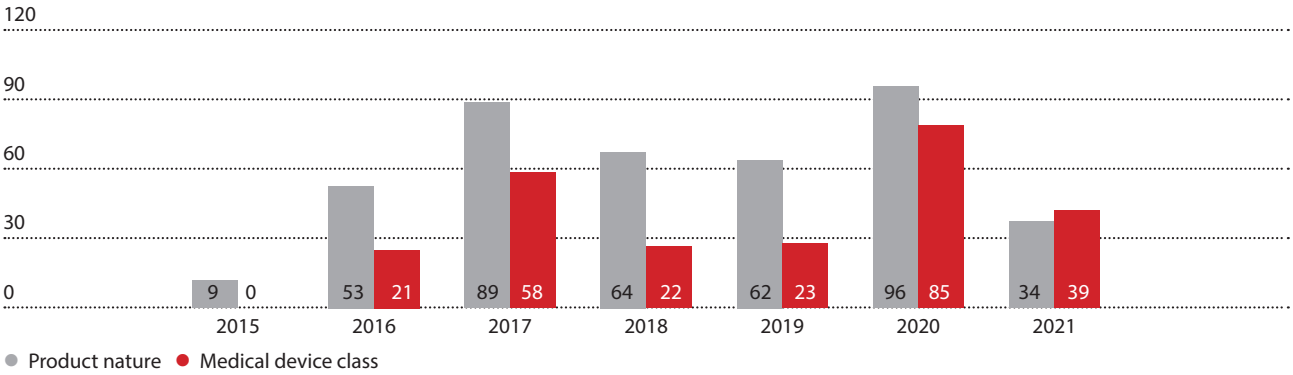


Fig. 29 **Overview of decisions issued in 2021**



Explanatory notes: AP – administrative procedure

Fig. 28 **Overview of forwarded proposals for the commencement of ex-officio administrative procedures in 2015–2021**



Offences

The Institute, as a first-instance administrative authority, commences administrative procedures regarding offences in case a breach of obligations imposed by the Act on Medical Devices, the IVD Act and the Act on Technical Requirements for Products is identified, particularly with reference to the inspection activity conducted at providers of healthcare services, medical device manufacturers, distributors, importers, authorised representatives, persons servicing, dispensing or prescribing medical devices, clinical investigation sponsors and investigators, both for medical devices and for IVDs.

In 2021, the Institute imposed fines for breach of the Act on Medical Devices, the IVD Act, and the Act on Technical Requirements for Products amounting to the total of 2,796,125 CZK. The highest proportion of fines imposed in 2021 for the breach of the Act on Medical Devices were fines imposed upon medical device distributors and healthcare service providers.

In 2021, 65 orders and 14 decisions were issued. Furthermore, the Institute issued three rulings regarding administrative procedure termination.

In compliance with the coming into effect of Act No 268/2014 Coll., (on 01 April 2015), the Medical Device Legal Support Unit has seen an increase in the proposals for commencement of an administrative procedure regarding administrative offences since 2016 within the scope of monitoring of adverse event investigations, particularly breach of the obligation laid down by Section 75 of Act No 268/2014 Coll., i.e., to inform the Institute of established safety corrective actions and their termination. With the coming into effect of the new Act on Medical devices and the IVD Act, since 26 May 2021, these merits of a case have remained only in the IVD Act.

Tab. 39 **Overview of forwarded motions for administrative procedure commencement in 2015–2021**

Overview for:	2015	2016	2017	2018	2019	2020	2021
Clinical Trials Unit	-	3	1	-	-	-	4
Vigilance Unit	2	47	79	88	185	65	21
Control Unit	22	69	64	20*	-*	116	71
Medical Device Notification Unit	-	-	-	-	6	-	1
Total	**24**	**119**	**144**	**108**	**191**	**181**	**97**

** In the period from 01 August 2018 to 31 December 2019, surveillance over the medical device market was the responsibility of SÚKL´s Surveillance Section.*

Appeals

In 2021, the Medical Device Legal Support Unit received the total of 65 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. 40 **Overview of appeals forwarded to the Ministry of Health of the Czech Republic in 2021**

Unit	No. of appeals	Returned for reconsideration	Granted	Declined	Withdrawn by applicant	Terminated administrative procedures
Legal Support Unit	40	1	-	2	-	24
Medical Device Reimbursement Unit	2	1	-	-	-	-
Medical Device Registration and Notification Unit	23	1	-	11	1	-
Total number of appeals for 2021	**65**	**3***	**6***	**4***	**1***	**-**

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

4.19 Medical Device 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 procedures. Manufacturers themselves notify the Institute of the classification of their medical device in a reimbursement group. 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 and out-of-pocket payment for the patient. In case a medical device is assigned to an improper reimbursement group, the Institute initiates an administrative procedure regarding non-inclusion in the reimbursement group or removal from a reimbursement group. Notifications of medical device reimbursements may be lodged at any time. The maximum amounts of reimbursement for individual reimbursement groups are 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 device prices.

The major output from the Unit´s operation is, in particular, the process of issuing the Medical Device Reimbursement and Price List for medical devices reimbursed on order, which is the main index for the realisation of reimbursements for medical devices reimbursed on order from the public health insurance funds. On 31 December 2021, the Medical Device Reimbursement and Price List contained 12,511 items in total.

Tab. 41 **Medical device reimbursement notifications in 2021**

Reimbursement notifications	Number
Total submissions	4,217
New notifications	1,063
Change notifications	889
Removal notifications	192
Year-to-year producer price increases	2,073

Tab. 42 **Overview of administrative procedures**

Administrative procedures	Number
Commenced	7
Concluded	10

Tab. 43 **Medical Device Reimbursement and Price List**

Medical Device Reimbursement and Price List	Number
Total	**12,511**
Included	804
Excluded	196

■ STATE AGENCY FOR MEDICAL CANNABIS

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

4.20 Unit of State Agency for Medical Cannabis

In 2021, 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 2021, the Institute took over and placed in distribution 42,570 grams of medical cannabis per the 2020 licence from the winner of the public contract for the supply of medical cannabis, Elkoplast Slušovice s.r.o.. By means of the second to fifth medical cannabis order (as per the 2020 licence), the Institute ordered the total of 31,000 grams of medical cannabis from the successful supplier, which ensured continuity of medical cannabis supplies onto the Czech market. The unit supervised the organisation of safe storage, transportation, and distribution of medical cannabis to pharmacies via the Institute´s contract distributor, Alliance Healthcare s.r.o. It also mediated the process of concluding framework contracts on the transfer of medical cannabis between pharmacy operators and the Institute. OSALK was preparing expert source materials for issues regarding medical cannabis for the Press and Information 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 2020, 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. In 2021, 312 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 96 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. 44 **Cannabis dispensing in 2021 by months**

Month	1	2	3	4	5	6	7	8	9	10	11	12
No. of issued e-prescriptions	1,402	1,308	1,613	1,614	1,573	1,751	1,301	1,689	1,690	1,833	1,976	1,691
No. of patients for whom medical cannabis was prescribed (unique)	1,173	1,106	1,324	1,346	1,335	1,402	1,129	1,449	1,470	1,568	1,665	1,496
Dispensed amount of medical cannabis (g)	7,273.63	6,967.49	8,856.16	8,591.22	8,734.74	9,868.55	7,741.00	9,816.11	10,049.50	13,325.18	11,139.45	9,804.32

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 provision 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 Jan Evangelista 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 2021:

- Suspended supplies: 1,853 reports (in 70 % of which supplies have already been restored);

- Terminated supplies: 744 reports;

- Restored supplies: 1,467 reports;

- Initiated supplies: 819 reports;

- Irreplaceable medicinal products: 123.

2. Addressing medicinal product unavailability

2.1 Addressing disrupted supplies of medicinal products within the Institute

- Checking/solving 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 the Czech.

- When assessing applications for the placement of individualbatchesof a medicinal product into circulation where the labelling is in a language other than the Czech, the Institute abides by the particulars stipulated by Section 3(6)(b) of Decree No 228/2008 Coll.

- In 2021, the Institute issued the total of 151 decisions allowing for the placement of a foreign-language batch into circulation, which is a 15-% increase compared to the previous year.

2.3 Identifying the possibilities of individual import of non-authorised medicinal products

- Pursuant to the provision of Section 8(3) of the Act on Pharmaceuticals, it is possible to prescribe or use a non-authorised medicinal product in cases when the authorised medicinal product is not available.

- KOČ employees check the database in compliance with Art. 57 (EMA database, Regulation [EC] no. 726/2004 of the European Parliament and of the Council) to see whether in the EU, medicinal products which could be used as a replacement for the unavailable medicinal products have been authorised. Furthermore, KOČ employees check guideline DIS-13 to see whether such medicinal products are imported to the Czech Republic, or, if applicable, they contact medicinal product distributors about possible import of unauthorised medicinal products.

- In the application of Section 77(1)(i) of Act No 378/2007 Coll., on Pharmaceuticals, and Section 46 of Decree No 229/2008 Coll., on Manufacture and Distribution, the Institute assesses and issues approvals of submitted applications for import of non-authorised medicinal products from third countries. In 2021, 96 approvals of import of non-authorised medicinal products from third countries were issued in total, which is 130 % 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 2021, three 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 2021, the Institute drafted opinions on 78 new applications.
  - In 2021, an electronic application form UST-20, incl. its English version, was put into live operation.

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 2021, the KOČ unit drafted two 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. Assessment of Medicinal Product Replaceability in Relation to the Activities of Other Units

- KOČ employees also assess medicinal product replaceability for the Quality Defects Unit and the Marketing Authorisation Section. In total, this concerned 36 replaceability assessments for the Quality Defects Unit and 44 assessments of exemptions from the sunset clause for the Marketing Authorisation Section in 2021.

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 a significant impact upon the provision of healthcare services, it notifies the Ministry of Health to this effect, providing source materials and information on the basis of which the Institute drew this conclusion. In 2021, KOČ submitted the total of 27 reports on jeopardised availability for 156 codes of medicinal products in total and six proposals for exclusion from the list for 93 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 2021, the Institute validated 1,444 applications for distribution of listed products abroad submitted by distributors, which represented a year-to-year growth of 73 %. 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 pursuant to 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 2021, KOČ submitted 36 motions suggesting prohibition of distribution abroad for the total of 46 medicinal products (SÚKL codes).**

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 2021, the Czech Republic was represented in the Supply Chain Disruptions Working Group by the KOČ Unit; the group prepared a specimen uniform format for the sharing of information about cases of unavailability affecting several EU countries, and was involved in the SPOC (Single Point of Contact) pilot project, where the representatives of national agencies share information on the availability of critical medicinal products with each other.

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 settings and medicinal oxygen. The scope of monitored medicinal products was based upon the lists of essential medicinal products of EMA and EC working groups.

7.2 For the Ministry of Health, the KOČ Unit drafted 14 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.

5 PROCESSING AND PROVISION OF INFORMATION

5.1 Information Technologies

In the area of information technologies, 2021 continued to be affected by the ongoing COVID-19 pandemics. In 2021, employees continued to be provided with mobile technical means allowing them to work in the home office mode.

In 2021, the preparation for the implementation of database infrastructure upgrades for some systems, inter alia the ePrescription system via Oracle Exadata C&C, took place. In 2021, a tender for the vendor of the aforementioned technology was organised and a contract awarded, and preparatory works for the launch of the new technologies in SÚKL´s environment were completed. In 2022, the physical assembly of the new equipment in the Institute´s environment will be carried out and data will be migrated from the existing data repositories. The new technology will allow to enhance operation as well as technical security of data in the operated systems. Furthermore, in association with the ePrescription system, environment and infrastructure for the operation of new functionalities, such as eVaccination, were under preparation. Moreover, adjustment of the infrastructure of the entire system was performed in order to enhance the performance and security of the operated systems. With regard to the growing number of cyber-security threats, several measures were implemented in 2021 in order to achieve a greater security of the operated systems. In the sphere of cyber-security, an inspection of selected systems by the National Cyber and Information Security Agency (NÚKIB) took place in the Institute in late 2021.

In 2021, two Olomouc and České Budějovice OKL branches moved to new premises. Also, new tenders were opened for several service agreements expiring in 2021. In the Institute´s infrastructure, new lines for connection to state administration systems were created via the public administration communication infrastructure system (KIVS) and the relevant Institute´s system using this communication were connected to this new line.

Project documentation was prepared for the reconstruction of back-up data centre scheduled for 2022. As part of the project documentation preparation, the required load-bearing capacity of floors in the individual rooms where IT technology is to be placed, was checked.

In August 2021, SÚKL´s Information Approach was updated and, with regard to the necessity of periodic attestation, the attestation procedure was carried out and resulted in obtaining the Protocol of Completed Testing as part of attestation of long-term public administration information system (ISVS) management from the certified attestation centre.

In early 2021, the complex documentation for the preparation of SÚKL´s electronisation project implementation was completed. The main objective of electronisation is to support major, auxiliary, communication, and management processes with electronic tools and systems and to ensure a more efficient conduct of working tasks and greater data robustness. Other objectives then include the conduct of all processes and their outputs in compliance with effective and drafted legislation of the Czech Republic and the European legislation (EU, EMA), and, last but not least, increasing SÚKL´s reputation thanks to more advanced outputs for the general public and professionals that may be used in a more effective manner. On the basis of requests from individual regulatory units of the Institute, almost twenty individual projects specifications for possible implementation were completed. On the basis of negotiations with individual regulatory units, source materials were processed and financial and staffing resources needed over time were estimated.

One of the important projects of SÚKL´s electronisation is also the planned replacement of the personnel information system which should improve the functioning of internal processes. The planned launch into production operation is January 2023, and for this reason, it was necessary to start working on the preparation of the tender dossier as early as in 2021.

Tender dossier was drafted also for another important project of SÚKL´s electronisation, an information system for administrative procedure management, which should provide a better support for process management in the course of administrative procedures.

On a continuous basis, the set of published open-source data was being extended and their quality enhanced. Selected data sets, such as data contained in the Registry of Medical Devices, were newly published also in the National catalogue of Open-Source Data.

Furthermore, in 2021, new automated search mechanisms, incl. an API interface, were created, and works on new form solutions were under way to cater for the replacement of the editing system and rebuilding of web portals of the Institute.

Last but not least, it is necessary to mention the works conducted on external identity adjustments to ensure the authentication of persons engaged in other healthcare professions, incl. the use of the National Identity Authority, in association with the planned launch of the eOrder. It may be stated that in 2021, the Information Technology Department continued to implement numerous measures to further increase the performance, availability, and security level of operated systems of the Institute in line with the global trends in this area and the growing risk of potential cyber-attacks aimed at the Institute´s systems.


E R E C E P T

ePrescription System

Electronic prescription 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-Security 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 2021, 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 insureds, which provides the former with a complete overview of dispensing. Since the launch of mandatory electronic prescription, applications for doctors, patients, and pharmacists have been also made available. In their application, doctors have the possibility to prescribe an ePrescription or make a record of applied vaccination outside their offices. The patient application allows patients to view a list of those ePrescriptions prescribed for them or applied vaccinations, 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. 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; in 2020, it was 28.5 million SMS messages and 840 thousand e-mail messages; and in 2021 the record amount of almost 34 million SMS messages and 688 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, medication record, vaccination record or the prepared electronic medical device order, 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.

In 2021, more than 76 million ePrescriptions were issued and almost 75 million were dispensed, which only confirms the routine operation and usage of the system.

Almost 50 thousand doctors and dentists, i.e., their vast majority, had SÚKL generate access data for them. In 2021, 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 2021, 46,651 doctors, 18,175 healthcare facilities, and 2,778 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. Since March 2021, the same certificate has been used also by the Reservatic system serving for the reservation of COVID-19 vaccination appointments. These are important positive steps taken in favour of professionals as healthcare staff may avail of the current authentication means for other systems implemented nationwide by the state administration.

The amendment to Act No 167/1998 Coll., on Dependency-Producing Substances, with implications for Act No 378/2007 Coll., on Pharmaceuticals, taking effect on 01 January 2022, and the amended Decree No 329/2019 Coll., on the prescribing of medicinal products, effective as of 23 December 2021, brought numerous changes relevant for the area of electronic prescription. In 2021, all of the changes were implemented in a manner allowing the schedule to fully observe the legislative timelines for the launch of the individual functionalities.

The first change is electronisation of so-called blue-stripe prescriptions, i.e., prescriptions for medicinal products containing highly addictive substances listed under Annex 1 or 5 to Government Regulation on the List of Dependency-Producing Substances. Until the end of 2021, these prescriptions were issued as paper-based prescriptions only; since 01 January 2022, however, they have been available in electronic format only. Their electronic format is mandatory, nevertheless, the same exemptions apply to them as those applicable to standard prescriptions in terms of the possibility to issue them in hard copies.

This change is associated also with the change in the prescribing of medical cannabis, which has been prescribed only on prescriptions with the highly-addictive-substance flag since 01 January 2022.

In order to facilitate control activities entrusted to regional authorities, since January 2022, SÚKL has provided regional authority employees with access to an application that allows them to retrieve and check ePrescriptions with the blue stripe/highly-addictive-substance flag issued in the concerned region.

Other currently prepared record is that of electronic vaccination. Since 01 January 2022, doctors have been obliged to make a vaccination record for all vaccinations applied – regular, special, extraordinary as well as voluntary ones, reimbursed and non-reimbursed ones, with the transient exception of vaccination against COVID-19. It will be possible to make a record of applied vaccination for patients whose identity has or has not been verified, but, like in the medication record, the record of the specific patient will display only those vaccinations for which the identity of the patient was verified during the record-taking. This record will become part of the medication record and hence will be accessible only to the patient whose identity was verified against the ROB registry during vaccination.

As of 01 December 2021, a functionality has been launched allowing citizens to express their disagreement with the viewing of their vaccination record. 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 or vaccination record. 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 or vaccination record of their children. The default set-up used as of 01 December 2021 for the viewing of the patient´s vaccination record was the set-up currently used by the patient for his/her medication record.

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.

For healthcare professionals, the conditions for viewing the vaccination record are identical to those governing the viewing of the medication record. Pursuant to the effective legislative provision, the initial viewing of the patient´s shared medication record 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 the patient is evidenced by the fact that this doctor prescribed an ePrescription for the patient in the past, which was then dispensed in a pharmacy, the presentation of the identification document is not required. The pharmacist may view the record only if the patient presents his/her identification document.

Pursuant to effective legislation, the vaccination record is accessible also to Regional Public Health Authorities and the Public Health Authority of the Capital City of Prague. On the basis of the legislative authorisation, such access to data within the stipulated scope has been provided by SÚKL since January 2022.

As of 01 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 01 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 epidemics 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 substantially contributed to safeguarding the protection of health for all citizens of the Czech Republic.

Fig. 30 **Number of prescribed and dispensed ePrescriptions in individual months of 2021 (mil.)**

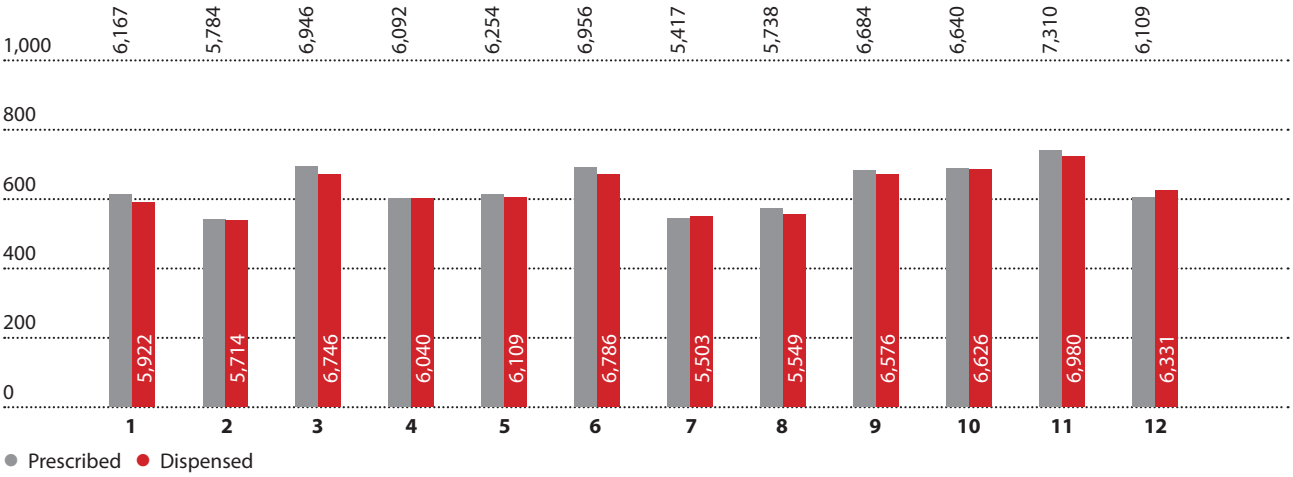
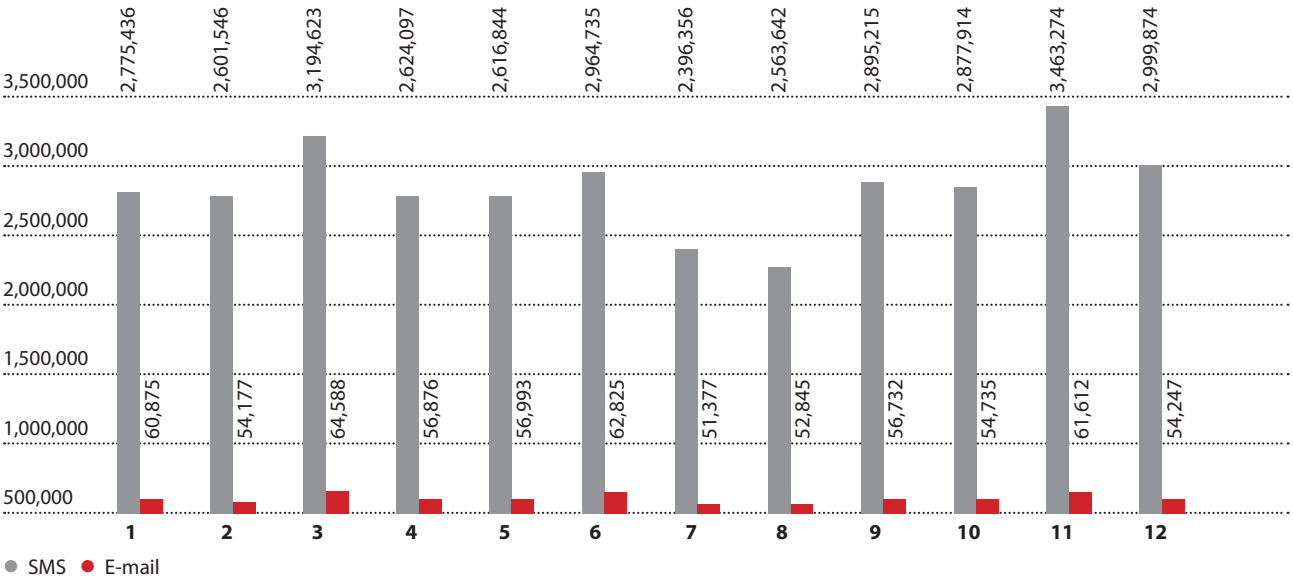


Fig. 31 **Number of e-mail and SMS messages sent in 2021**



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 19,496 components (incl. combined components). In 2021, 453 new components were entered.

- In 2021, an update of flagging of doping components and of products containing such substances in the DLP was carried out pursuant to The 2021 Prohibited List – The World Anti-Doping Code effective as of 01 January 2021. Thereafter, flagging was performed on a quarterly basis and in each quarter, a list of newly authorised medicinal products with doping was sent to the Antidoping Committee.

- A revision of substances labelled as doping by the Pharmazie.de database took place.

- New components were entered and components from revised and corrected monographs of the Czech Pharmacopoeia 2021 Supplement and of the European Pharmacopoeia supplements 10.5, 10.6 and 10.7 were amended.

- Components were piecemeal amended to be consistent with the new concept of the DLP Component Library (dedicated lines for certain literature sources).

- Components from the Proposed and Recommended INN WHO lists issued in 2021 were entered and amended.

- •Data about dependency-producing and psychotropic substances were updated in compliance with the new version of Government Regulation on the lists of dependency-producing substances.

- Data about substances with a doping effect were updated as per the new version of Government Regulation stipulating, for the purposes of the Criminal Code, the definition of substances with anabolic and other hormonal effects and their "larger quantity" and what was considered a method of increased oxygen transfer in the human body and other methods with a doping effect for the purposes of the Criminal Code.

- In respect of groups of components with a similarity in the language structure of their Czech names, unification pursuant to uniform rules was performed.

Registry of Medicinal Products

In 2021, the Institute granted 408 marketing authorisations (2,603 SÚKL codes). Authorisation was revoked for 381 marketing authorisation numbers, which corresponds to 3,599 codes. The authorisation was revoked either upon request of the marketing authorisation holder (293 marketing authorisation numbers), or due to the sunset clause (81 marketing authorisation numbers), or due to the fact that the holder did not apply for marketing authorisation renewal (seven marketing authorisation numbers). The validity of 5,645 codes in total expired (the period of the code final sale expired or marketing authorisation was revoked).

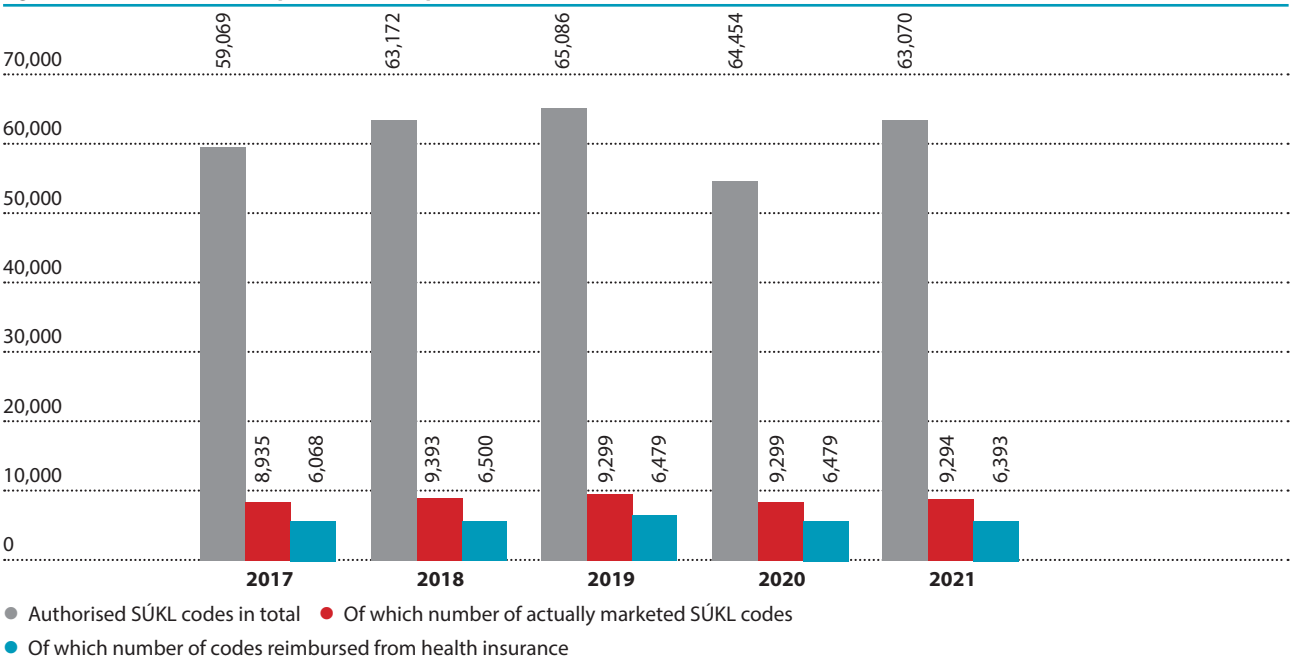
In the course of 2021, no distribution was reported for 53,776 codes (86 %) of medicinal products, excluding homeopathic preparations. Hence despite having a valid marketing authorisation, these products were not placed on the market.

Authorised medicinal products contained 2,799 various active substances in total.

Tab. 45 **Selected subgroups of authorised medicinal products recorded in the Institute´s database as of 31 December 2021**

	Total no. of marketing authorisation (MA) numbers / marketed MA numbers	Total no. of SÚKL codes / marketed SÚKL codes
Medicinal products in total (excl. homeopathic preparations)	**18,595/6,419**	**63,070/9,294**
Of which by MA numbers:		
MA numbers granted by the Institute	6,425/4,918	50,867/7,782
MA numbers of products authorised via Community Centralised Procedure	12,170/1,500	12,203/1,512
Of which by content:		
Single-component	14,908	50,658
Multi-component	3,690	12,398
Of which by type of dispensing:		
Prescription-only medicinal products	17,779/5,730	59,033/8,111
OTC medicinal products	865/699	3,934/1,167
Restricted OTC medicinal products	4/4	24/4
Restricted prescription-only medicinal products	7/7	79/9
Homeopathic preparations	275/274	892/390

Fig. 32 **Authorised medicinal products in the period of 2017–2021**



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.

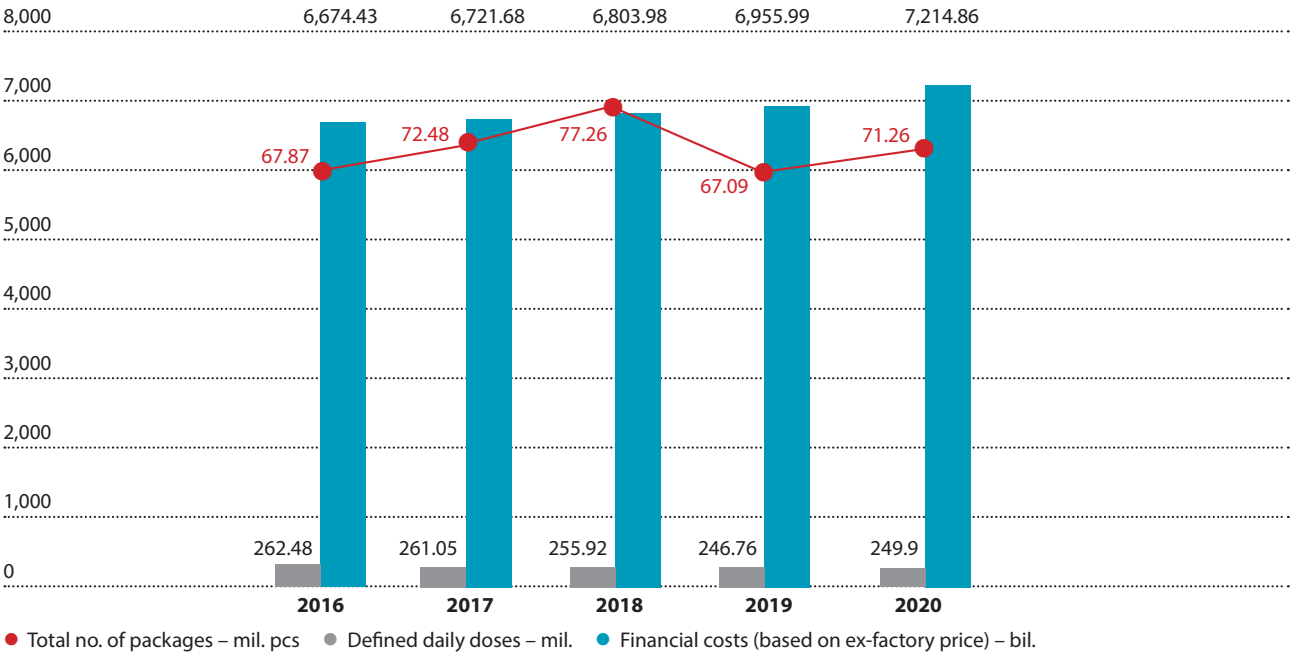
Evaluation of Deliveries of Distributed Medicinal Products

In 2021, 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 2021, 249.9 million packages of medicinal products were distributed, which corresponds to approx. 7,214.86 mil. DDD. The value of these deliveries amounted to 71.26 billion CZK (based on ex-factory price).

Fig. 33 **Deliveries of medicinal products in 2017–2021**



Tab. 46 **Deliveries of distributed medicinal products in 2021**

Medicinal products in total	**Number**
Deliveries to pharmacies and healthcare facilities (mil. packages)	249.903
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	71,257.832
Deliveries to pharmacies and healthcare facilities (mil. DDD)	7,214.865
DDD/1,000 inhabitants/day	1,848.407
Prescription-only medicinal products	
Deliveries to pharmacies and healthcare facilities (mil. packages)	174.781
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	70,987.806
Deliveries to pharmacies and healthcare facilities (mil. DDD)	6,587.120
DDD/1,000 inhabitants/day	1,687.583
OTC and selected pharmaceuticals	
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. packages)	74.960
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. CZK based on ex-factory price)	270.026
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. DDD)	627.681
DDD/1,000 inhabitants/day	160.808
Restricted OTCs	
Deliveries to pharmacies and healthcare facilities (mil. packages)	0.163
Deliveries to pharmacies and healthcare facilities (mil. DDD)	0.064
DDD/1,000 inhabitants/day	0.016
Homeopathic preparations	
Deliveries to pharmacies (mil. packages)	1.698

During 2021, the Data Analysis Unit processed the total of 5,870 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.

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 and the information portal for the public www.olecich.cz, administered by Tio and serving both professionals and the general public. TIO is also in charge of social networks (Facebook, Twitter, Instagram) through which it communicates important topics addressed by SÚKL.

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, through 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 127 patient questions. In 2021, the largest proportion of the questions concerned drug interactions and COVID-19 vaccines.

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

In 2021, TIO organised two public opinion surveys. The survey "Resources and utilisation of information in the sphere of pharmaceuticals" was a follow-up to previously implemented surveys and it mapped the shift in public opinion since 2018, when it was last conducted. The survey focused upon the general public, doctors, and pharmacists. Its results have been published on the website and described in press releases. The other implemented survey concerned the use of antibiotics and it targeted the answers from the general public. Its results were presented on a press conference held as part of the European Antibiotic Day and they are also available from SÚKL´s website.

In 2021, TIO answered 4,425 inquiries from the general public and from professionals which were sent via e-mail or post. Approximately 2,903 more inquiries were handled through the infoline.

Via e-mail, the Unit answered 637 questions from the media and other questions were answered by phone. In this area, TIO has noted a significant increase in the agenda (in 2020, 230 questions were answered by e-mail). More often than in previous years, the representatives of the Institute provided regular statements for radio or TV broadcasting. Ninety-eight press releases were published on the Institute´s website.

6 FINANCIAL AND MATERIAL RESOURCES OF THE INSTITUTE

6.1 The 2021 Income and Expenditure Account

Income

In 2021, extra-budgetary income in the total amount of 594,694 thous. CZK was achieved. The major part of this income was generated by the reimbursement of costs of expert activities that were conducted by SÚKL upon request from manufacturers, distributors, vendors, and other legal entities as well as natural persons. The major part of the overall volume was represented by income from applications in the sphere of marketing authorisations of medicinal products and in the sphere of maintenance payments. 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, Act No 268/2014 Coll., on in Vitro Diagnostic Medical Devices, as amended, and Act No 89/2021 Coll., on Medical Devices, as amended for the funding of payroll, operating and investment expenditures not covered by allocated financial resources from the state budget. In 2021, the total amount of 528,174 thous. CZK was used in this manner through permissible excess expenditure. Of this amount, 511,270 thous. CZK were used for non-investment expenditure and 16,904 thous. CZK for the financing of investment needs.

In addition to income from the reimbursement of costs of expert activities, another portion of income came from the revenues of the state budget, such as collected administrative fees for submitted applications amounting to 35,679 thous. CZK, income from imposed fines amounting to 2,524 thous. CZK, income from lease in the amount of 302 thous. CZK, income from the sale of goods (medical cannabis) amounting to 6,398 thous. CZK, refunds of excess advance payments made, related fully to the previous budgetary years, and other compensations amounting to 919 thous. CZK, etc. the Transfers from the reserve fund line shows the volume of extra-budgetary income used for the funding of expenditures in 2021. An overview of the reported budget income as of 31 December 2021 is provided in Tab. 47.

Tab. 47 **State budget income (thous. CZK)**

Item	Approved budget	Actual amount
Administrative fees	24,800	35,679
Received penalty payments	4,000	2,524
Income from lease	0	302
Income from the sale of goods	0	6,398
Other income	0	11
Received non-capital contributions and compensation	0	919
Transfers from the reserve fund	0	528,174
TOTAL	**28,800**	**574,007**

Expenditure

Data concerning expenditures incurred in 2021 broken down by individual categories are provided in **Table 48.**

The total investment expenditure from extra-budgetary resources amounted to 16,893 thous. CZK. Investment resources were used to finance the procurement of laboratory instruments in the total amount of 8,158 thous. CZK (centrifuge with cooling, electrophoresis, pre-weights with a printer, biohazard box, biological incubator, washer, UV-VIS spectrophotometer, HPLC, capillary electrophoresis apparatus). The costs of procured licences amounted to 522 thous. CZK, the costs of technical upgrades of applications and SW to 4,783 thous. CZK (ERP, eSSL Athena, and others), the purchase and replacement of HW cost 606 thous. CZK, and the costs of the Business Trip Report System and business trips amounted to 1,218 thous. CZK. A fire protection measure in Building no. 24 was implemented and cost 158 thous. CZK; the preparation of documentation for planned construction works amounted to the total of 1,448 thous. CZK (in particular, preparation of reconstruction of roof of Building no. 24 and data centre reconstruction). Non-investment expenditures were utilised in the total amount of 667,449 thous. CZK, of which 156,308 thous. CZK came from the state budget and 511,141 thous. CZK were taken from extra-budgetary resources. Extra-budgetary resources included resources from abroad provided for the EURIPID project (utilised amount: 21 thous. CZK) and the EUnetHTA project (utilised amount: 20 thous. CZK).

Tab. 48 **Expenditures (thous. CZK)**

Indicator	Approved budget	Final budget	Actual amount
Employee salaries	24,155	51,180	51,180
Civil servant salaries	91,783	301,294	301,282
Other payments for completed work, severance pay, surrenders	3,603	15,130	15,128
Mandatory insurance premium	40,405	122,437	122,429
Contribution to the Fund of Social and Cultural Needs	2,319	7,080	7,080
Operating acquisitions and related expenditure	967	170,657	170,350
Acquisition of long-term tangible and intangible fixed assets	0	16,904	16,893
TOTAL	**163,232**	**684,682**	**684,342**
Of which: operating expenditure	163,232	667,778	667,449
capital expenditure	0	16,904	16,893

Expenditures for International Projects within the EU

The EURIPID project has been under way since 2008. It concerns a voluntary association of competent authorities in charge of the pricing and reimbursements of medicinal products. The association was established for the purposes of setting up a joint database of reimbursed medicinal product prices. At present, 26 countries are involved in the project. 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 medical devices are under way. In 2021, 21 thous. CZK from foreign funds were utilised for payroll and statutory deductions in the project.

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 term of the project was extended until the end of May 2021. 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, SÚKL, in cooperation with the Ministry of Health, is so called associated partner. In total, more than 78 organisations from 29 countries are involved in the project. This joint action is co-funded by the European Commission and the Member States, with the EC covering 60 % of the project costs. In 2021, 20 thous. CZK were utilised for the project from foreign funds (payroll, incl. statutory deductions).

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 the previous year 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, which was then implemented in 2021. The Institute, along with The Netherlands, acted as the educational institution in this pilot project, providing training in the sphere of requirements governing the conduct of clinical trials for three aforementioned selected countries. In the final year, 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 2021, no funds were utilised for the project.

As early as in 2018, the Institute, along with the main project partner – the Vysočina Region – became involved in the Deployment of Cross Border Services in the Czech Republic (NIX-ZD.CZ II) project. The objective of this project is to create, test, and deploy a cross-border ePrescription service. The total duration of project implementation has been scheduled from 01 July 2018 until 30 June 2022. Of the total project costs, 75 % will be covered by the CEF TELECOM European subsidy. During 2021, the project focal point was the testing of the data exchange between the Czech Republic and other Member States and the successful completion of pre-audit tests. Another equally essential activity was the gradual preparation of audit documentation and subsequent submission of an application for the audit process which is to be conducted by an external audit agency appointed by the European Commission for this superstructure module. On the basis of the results of all tests of interaction with other Member States, the Czech cross-border exchange interface was continuously modified as necessary. In the second half of the year, SÚKL intensified

communication with pharmacy software vendors with regard to the preparation of the new service at end-users´ (pharmacists) as such. In the following year 2022, SÚKL´s utmost priority will be, in particular, the successful completion of the audit process so as to be able to roll-out this superstructure module into production environment. In 2021, project expenditures amounted to 1,792,956 CZK (extra-budgetary funds of the Institute).

Other

A total of 60,783.14 CZK were utilised for foreign activities. The conduct of foreign business trips was strongly limited due to the COVID-19 pandemics. In 2021, only four foreign business trips of employees took place, of which two concerned inspections in pharmaceutical companies, one concerned an education event, and one was organised by the Office of Government.

Assets

The total assets as of 31 December 2021 amounted to 1,340,799 thous. CZK, of which fixed assets represented the volume of 365,078 thous. CZK and current assets 975,721 thous. CZK. Of the total liabilities of 1,340,799 thous. CZK, equity amounted to 1,293,610 thous. CZK and borrowed capital to 47,189 thous. CZK. Selected types of assets and liabilities are listed in Tab. 49.

Tab. 49 **Overview of selected types of assets and liabilities of the organisation (thous. CZK)**

Item	Past period 2020	Current period 2021
ASSETS	**1,298,284**	**1,340,799**
A. Total fixed assets	**388,522**	**365,078**
of which:		
I. Long-term intangible fixed assets – total	93,085	80,872
II. Long-term tangible fixed assets – total	295,437	284,206
of which:		
Lots	4,530	4,530
Buildings	231,920	226,986
Separate tangible movables and sets of tangible movables	54,416	46,671
Unfinished tangible fixed assets	4,571	6,019
B. Total current assets	**909,762**	**975,721**
of which:		
I. Inventory - total	905	1,727
II. Short-term receivables - total	14,193	11,738
III. Short-term financial assets - total	894,664	962,706
LIABILITIES	**1,298,284**	**1,340,799**
C. Equity	**1,255,740**	**1,293,610**
of which:		
I Assets of the accounting entity and adjustments	226,626	226,542
II. Funds of the accounting entity	858,661	925,357
Fund for Cultural and Social Needs	1,873	1,990
Reserve Fund	856,788	923,367
III. Economic result	–866,683	-1,005,761
Economic result for the current accounting period	–137,040	-139,078
Economic result for the previous accounting periods	–729,643	-866,683
IV. Income and expenditure account of the budget management	1,037,136	1,147,472
D. Total borrowed capital	**42,544**	**47,189**
of which:		
I. Total long-term liabilities	0	0
II. Total short-term liabilities	42,544	47,189

Auditing

In 2021, no audits conducted by public administration bodies pursuant to the Act on Financial Audits or by the Supreme Audit Office took place.

7 FOCUS UPON EMPLOYEES

7.1 Personnel Issues

Organisational Structure

In compliance with the Institute´s systemisation approved for 2021 pursuant to Act No 234/2014 Coll., on Civil Service, as of 01 January 2021, the number of systemised positions was 572, of which 463 were civil service positions and 109 employment positions.

As part of the organisational changes associated with the Institute´s systemisation effective as of 01 January 2021, compared to 2020, the number of civil service and employment positions changed, yet overall, an increase of only one systemised position took place. More substantial changes concerned the Marketing Authorisation Section, where two units were cancelled and, at the same time, one department was created, where the systemised positions from the cancelled units were transferred to. The reason for this change is implied by the situation in which the number of assessed centralised procedures increased of up to 100 % due to Brexit. The objective of the proposed change was to ensure a more effective work coordination, as previously, one manager managed the total of 22 employees whose activities differed in many cases.

In the course of 2021, several other systemisation modifications were implemented with effect as at 01 March 2021, 15 April 2021, 01 July 2021, and 01 October 2021; these modifications concerned service position changes and amendments in the appointment of managerial staff permanent substitutes.

The number of physical employees on the Institute´s payroll as of 31 December 2021 was 542 persons, of which 423 were women (i.e., 78 %) and 119 were men (i.e., 22 %).

As part of the Personal and Working Life Harmonisation Policy support, as of 31 December 2021, the total of 71 employees of the Institute (of which 69 were women), i.e., 13.1 % of the total number of employees, worked part-time.

Age Structure of Employees

Average age: females 43.7 years; males 42.3 years. The overall average age of all employees is 43 years.

Tab. 50 **Numbers of employees at local workplaces**

Brno	33
České Budějovice	5
Hradec Králové	7
Olomouc	5
Ostrava	4
Pilsen	2
Prague	480

Tab. 51 **Age structure of employees as of 31 December 2021**

Year	% of employees under 35 years	of employees aged 36 to 55 years	% employees older than 55 years
2019	31.5	50.7	17.8
2020	28.9	53	18.1
2021	**27.1**	**53.3**	**19.6**

Qualification Structure of Employees

Tab. 52 **Qualification structure of employees by achieved level of education as of 31 December 2021**

Highest	Primary	Secondary	Technical colleges	University – bachelor´s degree	University – master´s degree	Postgraduate
Number of employees	2	98	4	11	386	35
% of the total number of employees	0.4	18.3	0.7	2.1	72.0	6.5

Staff Turnover

The overall staff turnover taking into account all start-ups and departures, amounted to 9.6 %, which was a slight decrease compared to 2020.

In total, 223 tenders for vacancies were opened during 2021, on the basis of which the total of 83 employees and civil servants were admitted (see Tab. 53).

Tab. 53 **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	**131**	**54**	**92**	**29**

In 2021, the total of 52 employees terminated their employment or civil service.

Tab. 54 **Overview of employment and civil service terminations in 2021 by reason of employment/civil service termination**

	Employment	Civil service
Cancellation of employment/civil service in probationary period	8	4
Agreed time expiry	6	1
Termination by agreement (Section 49 of the Labour Code)	3	0
Notices given by employees/termination of civil service upon request of the civil servant	4	19
Notices given due to organisational reasons/by decision of the civil service authority	0	4
Termination of civil service performance in SÚKL due to transfer of the civil servant to another civil service authority	-	0
Retirement	2	1
TOTAL	23	29

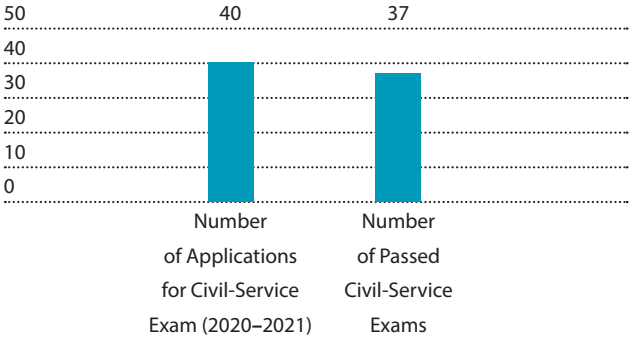
Civil-Service Exam

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).

Twenty-two applications were brought forward from 2020 to the next calendar year and in the course of 2021, 18 applications lodged by the employees of the Institute were newly registered, which amounts to 40 applications in total. Of the total number, in 2021, 37 employees successfully passed both parts of the civil-service exam. The remaining three employees will take the exam in 2022 (within 12 months of their recruitment as civil servants, as stipulated by the Act on Civil Service).

Of the total number of civil-service exams taken, only one employee did not succeed on the first attempt (in the specialised part of the civil-service exam). The employee successfully passed the exam on a second attempt.

Obr. 34 **Civil-service exams in 2021**



7.2 Employee Education

In 2021 (as in the previous year 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) by the organisers, depending on the currently effective government regulations and measures associated therewith (such as limited number of attendees, cancelled events, etc.). 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 of men and women, 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 the need for continuous deepening and increasing of qualification and knowledge of our staff in individual fields. There were practically no foreign educational events, as the global epidemiological situation did not allow for their organisation.

Both in 2020 and in 2021, due to the COVID-19 disease, management training of managerial staff was organised within the necessary scope in the form of online education. When the measures were lifted, management training took place in the strictly necessary scope and it focused upon the development of personal talents and management skills.

The epidemiological situation hindered also language education, which was organised primarily in online format during 2021. 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.

For selected employees who will be actively involved in the Czech Presidency of the Council of the EU (CZ PRES) in the second half of 2022, an educational session in the English language called Training in Communication Skills was organised; the training focused particularly on the development of communication, negotiation, and presentation skills in the area of health law, and it assumed a group learning form. The employees involved in CZ PRES will directly participate in the negotiations about legislation in the Council of the EU or act as co-chairs, and present and prepare background materials for the organised events.

In 2021, the Information Security (Cybersecurity) Manager and the Data Protection Officer organised a mandatory training for all employees of the Institute in issues concerning cybersecurity, personal data protection, and internal management regulations of the Institute. The training focused upon essential implications of Decree No 82/2018 Coll., on Cybersecurity, and of Act No 110/2019 Coll., on Personal Data Processing.

The total volume of funds incurred for all types of educational activities amounted **1,511,000 CZK.**

Tab. 55 **Overview of educational activities in 2021 – follow-up education**

Type of event	Number of events	Number of hours	Number of attendees
Specialised courses & training; language courses	1,606	4,151	531
Mandatory training	94	196	690
Foreign specialised training	4	80	4

8 FOCUS UPON QUALITY

SÚKL has an established and certified quality management system compliant with the requirements of the ČSN EN ISO 9001:2016 standard. In October 2021, the LL-C (Certification) Czech Republic s.r.o. certification body conducted a review of some of the Institute´s certified processes as part of a surveillance audit and noted that the Institute´s quality management system continued to meet the requirements of this standard.

The Laboratory Control Department has developed a management system compliant with the ČSN EN ISO/IEC 17025:2018 standard. In November 2021, a successful compliance check of the established 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, 20 such internal audits took place in 2021.

In order to fulfil its mission and achieve its vision, a new "Strategic Plan of the State Institute for Drug Control for 2021–2025" was issued by SÚKL. The Plan stipulates the Institute´s strategic goals for the next five years.

In 2021, as part of the quality management system, the Institute focused upon improvements in obtaining feed-back from clients and stakeholders and steps towards more successful feed-back monitoring were taken.

The valuable stimuli from the obtained feed-back gave rise to relevant measures ensuring a greater effectiveness of the Institute´s activities.

9 INFORMATION SECURITY MANAGEMENT POLICY AND CYBERSECURITY

Also in 2021, SÚKL had to respond to trends in the area of cybersecurity that had started to emerge in previous years.

This concerned, in particular, further extension of obligations in the protection of information and information systems arising from other legal regulations issued by the competent state authorities. For example, as an implication of Decree No 360/2020 Coll., amending Decree No 317/2014 Coll., on Important Information Systems and Their Determining Criteria, SÚKL performed an evaluation of all of the used information systems. As a result, the number of important systems grew from five to 15.

This fact has been – and will continue to be – demanding in terms of compliance with the requirements set forth by Decree No 82/2018 Coll., and the system changes will surely extend to next periods.

As in the year before, in 2021, we also noted an increased number of cybersecurity events, attempted attacks on information systems. None of these attempts was successful which, however, does not mean that we can drop our guard in the area of increasing the security measures and processed data protection.

In May 2021, the Institute successfully passed a surveillance 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 14 years.

10 OUTLOOK FOR 2022

This year, the Czech Republic will stand at the head of the European Union, holding its second presidency of the Council of the EU. The presidency is one of the most important rights and most demanding tasks implied by the EU membership. It works on a rotational principle and Member States rotate every six months in a predefined order. Our presidency will hence be taken over from the French presidency as of 01 July 2022 and on 01 January 2023, it will be passed onto Sweden. The Czech Republic enters its second presidency with more than 18 years of experience with work on all levels and in all bodies and institutions of the EU.

SÚKL will be involved in the presidency on two levels: as part of the presidency team in the negotiations of the new European legislation in the Council of the EU and as a host of informal committee and workgroup meetings traditionally held by the presiding country.

The employees of the Institute represent the Czech Republic in agendas that SÚKL is in charge of during negotiations concerning new legislative proposals and non-legislative documents on the working level of the Council of the EU and they provide expert support for all levels of negotiations, including the meetings of Ministers for Employment Social Policy, Health and Consumer Affairs (EPSCO). SÚKL as the responsible authority drafts the framework position, which is approved by the government and which establishes the basic position of the Czech Republic and essential limits that cannot be passed, so called red lines. During negotiations, SÚKL then prepares instructions and takes part in negotiations with other Member States, striving to achieve a common approach of the Council and to find a general compromise also in the next stage of trialogues with the European Parliament and with the European Commission.

We expect that during our presidency, the main attention in the sphere of SÚKL´s powers will focus on the negotiations concerning a revision of legislation on blood, human tissues and cells as well as a revision of the Regulation on fees payable to the European Medicines Agency (EMA). In late 2022, the Commission should present a draft revision of the paediatric regulation and regulation on orphan medicinal products and probably also draft revision of general pharmaceutical legislation, i.e., Regulation (EU) 726/2004 and Directive 2001/83/EC. The other part of our role in the course of the presidency will be the presentation of the Czech Republic and of SÚKL as the host of presidency events in the sphere of regulation of pharmaceuticals and medical devices.

SÚKL will be involved in the presidency events as the host of eight face-to-face meetings in Prague and three virtual meetings. These are, in particular, a meeting of the Heads of Medicines Agencies (HMA), informal meetings of EMA´s scientific committees and regular meetings of the European Medicines Regulatory Network (EMRN) working groups. For capacity reasons, we are not able to organise all usual meetings; nevertheless, SÚKL´s presidency calendar is still busy: in September, the first meeting of HMA and the EMACOLEX lawyer group will take place; in October, it will be an informal meeting of the CHMP and PRAC committees, the CMDh coordinating group, and competent authorities for medical devices (CAMD); for November, the schedule includes a meeting of the Paediatric Committee and three virtual meetings: HMA 2, IT Directors, and WGQM. The presidency events will be concluded in December with the Working Group of Communication Professionals (WGCP) meeting. In addition to these events, hosted by SÚKL, we will be involved also in the organisation of meetings of national competent authorities for pricing and reimbursements (NCAPR) as well as a wealth of other meetings where our representatives will assume the role of co-chairs or presenters of priorities of the Czech presidency.

In 2022, the State Institute for Drug Control will continue to be intensively involved in the agenda associated with the COVID-19 disease. Via its representatives in EMA´s committees, the Institute has been actively involved in the process of approval of vaccines against this infection, the recording, processing, and evaluation of reported suspected adverse reactions to these vaccines, and it has been also in charge of the agenda of administrative release of vaccines to the Czech Republic.

In the sphere of marketing authorisation of pharmaceuticals, an increase in the requests for abbreviated schedules and regulatory flexibility for medicinal products needed for supportive treatment of COVID-19 may still be anticipated as well as a greater involvement in centralised marketing authorisations of drugs intended directly for the treatment or prevention of COVID-19 (monoclonal antibodies, vaccines).

In the area of pharmacovigilance, an increased interest of the general public and professionals regarding reporting of suspected adverse reactions to COVID-19 vaccines still persists. Requirements for abbreviated timelines will affect also the Clinical Trials Department, where clinical trials on drugs for the treatment or prevention of COVID-19 are being assessed in an abbreviated schedule. Furthermore, we expect an increased interest in consultations in the area of new drugs against COVID-19.

The current priority in the area of medicinal product availability is to safeguard drugs for intensive care which are being monitored by the Institute on a continuous basis in relation 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. The monitoring of availability of medicinal products within the EU has become one of the cornerstones of the EU pharmaceutical strategy for the coming period.

In 2022, the Medical Devices Department will continue its intensive control of vendors of antigen tests and face masks, focused, in particular, upon the labelling and storage of these devices. In 2021, Regulation (EU) 745/2017 on medical devices (MDR) took effect and in

2022, Regulation (EU) 746/2017 on in vitro diagnostic medical devices (IVDR) that will bring substantial changes to the method of conducting controls and which, at the same time, increases the demands for the sharing of information about the surveillance activities performed by competent authorities on the EU level is to come into force. The new Act on Medical Devices, the draft of which newly incorporates surveillance over advertising into the surveillance agenda, is a call for extending and strengthening the Institute´s control mechanisms.

The prepared new administrative procedure management system of the Pricing and Reimbursement Regulation Section will meet the requirements of a modern agenda system. This system should lift the administrative burden through automation and simplify the managerial leadership of the Section. In compliance with the new provisions of Act No 48/1997 Coll., on Public Health Insurance, effective as of 01 January 2022, SÚKL will safeguard regulatory mechanisms for the determination of maximum prices and the amount and conditions of reimbursements of medicinal products in a new mode. We are well prepared for the roll-out of new processes and we expect a smooth run.

In the Surveillance Section, we have prepared a new approach to the licencing procedure for the granting of licences for the growing of medical cannabis for the coming year in compliance with amended Act No 167/1998 Coll., on Dependency-Producing Substances.

In 2022, new legislation came into force which introduced more e-healthcare instruments, specifically electronic medical device order and electronic vaccination card. Another news is the introduction of prescribing of medicinal products containing dependency-producing substances of Groups 1 and 5 of Government Regulation No 463/2013 Coll., on Dependency-Producing Substances, on electronic prescription. In 2022, the Institute will also focus on enhancing the electronisation of its internal procedures and planning and implementation of projects of a new website that will become a modern platform for the presentation of information in line with the current trends and demands for the availability of information, its straightforward presentation, visual layout, and search options.

In this year, the Institute will continue to promote its activities (e.g., on social networks) and will keep bringing the latest information about events in EMA (particularly in association with COVID-19).

11 LIST OF ABBREVIATIONS

ALL	Active lymphoblastic leukaemia
AMR	Antimicrobial resistance
API	Application Programming Interface
ASR-WS	Assessment Safety Report Worksharing
ATC	Anatomical Therapeutic Chemical
ATD	anti-tampering device
CAP	Centrally Authorised Product
CAU	Pricing and Reimbursement Regulation Section
CAT	Committee for Advanced Therapies
CDNÚ	Central Database of Adverse Drug Reactions
CKS	End-user price
CMS	Concerned Member State
CNS	Central nervous system
CRO	Contract Research Organization
CRS	Chemical Reference Substance
CRLN	National chemical reference substances
CTEG	Clinical Trial Expert Group
CTFG	Clinical Trials Facilitation Group
CTIS	Clinical Trial Information System
CÚEO	Central Repository of Vaccination Records
CÚEP	Central Repository of Electronic Orders
CÚER	Central Repository of Electronic Prescriptions
Cz.Ph.	Czech Pharmacopoeia
ČSN	Czech technical standard
ČSSZ	Czech Social Security Administration
DCP	Decentralised Procedure for marketing authorisations
DDD	Daily defined dose
DIS	Distributor of tissues and cells
DU	Defined unit
DL	Diagnostic laboratory
DLL	Active substance importers
DLP	Database od medicinal products
DPV	Parenteral nutrition products for home therapy
DSUR	Development Safety Update Report
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EC	Ethics committee
EPC	European Pharmacopoeia Commission
EMA	European Medicines Agency
EC	European Communities
EUDAMED	European database of medicinal products
EudraGMP	European Community of Manufacturing Authorisations and of Certificates of Good Manufacturing Practice
EUnetHTA	European Commission and Council of Ministers targeted Health Technology Assessment
EV EWG	EudraVigilance Expert Working Group
FIH	First-in-human
FSCA	Field Safety Corrective Action
FSN	Field Safety Notice
PV	Pharmacovigilance
HARP	Harmonisation of risk management plans
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
INN WHO	International Non-proprietary Name
IPLP	Individually prepared medicinal product
ISDB	International Society of Drug Bulletins
ISMS	Information Security Management System
ISVS	Public administration information systems
IVD	In-vitro Diagnostic
KB	Blood bank
CT	Clinical trial
KHV	Clinical trials and Vigilance Unit
KLP	Cannabis for medical use
KIVS	Public administration communication infrastructures
CIMD	Clinical investigation of medical devices
LMS	Lead Member State
MP	Medicinal Product
ATMP	Advanced therapy medicinal products
LTB	Human tissues and cells
MAG	Magistral formulas
MAH	Marketing Authorisation Holder
MC	Maximum price
MDCG	Medical Devices Coordination Group
MDR	Medical Device Regulation
MIR	Manufacturer Incident Report
MJA	Mutual Joint Audit
MRA	Medicine Regulatory Authority
MRP	Mutual Recognition Procedure
MZ ČR	Ministry of Health of the Czech Republic
NCAR	National Competent Authority Report (medical devices)
AE	Adverse event
ADR	Adverse drug reaction
NÚKIB	National Cyber and Information Security Agency
OCABR	Official Control Authority Batch Release
OECD	Organisation for Economic Co-operation and Development
OKL	Drug Control Unit
OLZP	Department of Pharmaceuticals and Medical Devices
OMCL	Official Medicines Control Laboratories
ONM	Nuclear Medicine Department
OOP	General Measure
OOVL	Detached pharmaceuticals dispensing unit
OP	Profit margin
OSALK	Unit of the State Agency for Medical Cannabis
OZ	Donation Centre
PČR	Czech Police
PhV	Pharmacovigilance
PhV BT	Pharmacovigilance Business Team
PhV IWG	Pharmacovigilance Inspectors Working Group
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PMSV	Post-Market Surveillance and Vigilance Working Group

PPZ	Medical Device Legal Support Unit
PRAC	Pharmacovigilance Risk Assessment Committee
PSMF	Pharmacovigilance System Master File
PSUR	Periodic Safety Update Report
PSUSA	Periodic Safety Update Single Assessment
PTS	Proficiency Testing Study
PZLÚ	Foods for special medical purposes
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
ROB	Registry of inhabitants
RZPRO	Registry of Medical Devices
SAE	Serious Adverse Event
SAKL	State Agency for Medical Cannabis
GDP	Good Distribution Practice
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
SpLP	Specific therapeutic programme
SPOC	Single point of contact
AP	Administrative Procedure
STARS	Strengthening Training of Academia in Regulatory Science
SÚKL	State Institute for Drug Control
SUP	Suspected Unknown Product
SUSAR	Suspected Unexpected Serious Adverse Reaction
GMP	Good Manufacturing Practice
SZPI	Czech Agriculture and Food Inspection Authority (CAFIA)
ŠÚKL	Slovak State Institute for Drug Control
TIO	Press and Information Unit
TP	Transfusion products
TZ	Tissue centres
UHR	Reimbursement
ÚZIS	Institute of Health Information and Statistics of the Czech Republic (IHIS CR)
VHP	Voluntary Harmonization Procedure
VUC	Materially regulated price
WHO	World Health Organisation
SAR	Serious adverse reaction
SAE	Serious adverse event
ZoRR	Acton Advertising Regulation
ZoZP	Act on Medical Devices
ZP	Health insurance
ZP	Medical device
ZTS	Blood centre

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