ANNUAL REPORT 2022

SÚKL

STATE INSTITUTE
FOR DRUG CONTROL

CONTENTS

1. INTRODUCTION

For the State Institute for Drug Control (hereinafter referred to as the "Institute" or "SÚKL"), 2022 was an exceptional year due to the Czech Presidency of the EU Council. This important event was reflected in the activities particularly in the second half of 2022, although preparations had commenced as early as in 2019.

Within the scope of the Presidency, the Institute organised eight face-to-face and two on-line meetings of working groups and committees; six more meetings were organised by other EU medicines agencies under the auspices of the Czech Minister of European Affairs. Face-to-face meetings were attended by more than 350 foreign delegates, mostly from partner medicine and medical devices agencies from EU Member States, but also from the European Commission, the European Medicines Agency, the European Directorate for the Quality of Medicines and Health Care of the Council of Europe, and, last but not least, by representatives of patients, the academia as well as the pharmaceutical industry. More details on the Institute's activities at the time of the Czech Presidency are provided in chapter 3.4 hereof.

In 2022, the Institute 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.

Since the start of 2022, the Institute, in cooperation with the Ministry of Health, continued preparatory works on the new Act on Pharmaceuticals, specifically splitting the existing Act into the human and veterinary parts. Furthermore, the Institute, as the regulator in the sphere of medicinal products, has been involved in the preparation of the new text of the basic standard for medicinal products. In the course of 2022, joint meetings with the Ministry of Health, the purpose of which was such preparation of the new legislative regulation, were held and the work is to continue also in 2023.

As further detailed herein, the Institute contributed to legislative amendments concerning the marketing authorisation of medicinal products, clinical trials on medicinal products, and medical devices. In addition to direct legislative works, the Institute was also involved in the assessment of individual proposed amendments to the concerned Chamber documents discussed by the Chamber of Deputies of the Parliament of the Czech Republic. The Institute also commented on other proposed legal regulations governing areas that were also of relevance for the Institute's operation, inter alia, issues concerning consumer protection. In this respect, the Institute held negotiations with the Ministry of Industry and Trade as the lead body in charge of amendment to Act No 634/1992 Coll., on Consumer Protection, because this amendment gives new powers to the Institute. In this area, the Institute, moreover, cooperated with the Czech Trade Inspection.

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

In 2022, the Institute continued to cooperate with the Institute for State Control of Veterinary Biologicals and Medicines in Brno; in the sphere of regulating the pharmaceuticals market, it cooperated with the Office for the Protection of Competition. In the area of market surveillance, the Institute's partners included primarily the Czech Agriculture and Food Inspection Authority (CAFIA) and the Customs Administration. The Institute, however, cooperated also with the law enforcement authorities, where we have seen a significantly increasing trend of sharing information and data from the information systems administered by the Institute, particularly the ePrescription system, with almost treble the volume compared to 2021.

Cooperation also continues on the international level. The Institute has been actively involved in international cooperation in more than 100 workgroups, subgroups, and committees. These are, in particular, the bodies of the EU Council, 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 and Health Care (EDQM) or the Organisation for Economic Cooperation and Development (OECD). One of the high priorities in the field of drug regulation is primarily the membership of the Institute's experts in EMA scientific committees which address issues associated e.g., with the safety of medicinal products on the EU market or the approval of new pharmaceuticals. The Institute has been also 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. One of the most important 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, the role of which has been significantly enhanced due to the COVID-19 pandemic.

Following successful validation, the total of 601 applications were submitted for expert assessment to the Marketing Authorisation Section. In 2022, 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 107 in 2021 to 139 in 2022. Furthermore, 345 applications for the revocation of marketing authorisation were processed, which is a slight increase compared to 2021.

In 2022, the numbers of SMS and e-mail messages with ePrescription identifier broke records. Specifically, they amounted to more than 41 million SMS messages and 700 thous. e-mail messages.

2022 saw the coming into force of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use and the related launch of the EU portal, i.e., the Clinical Trials Information System (hereinafter referred to as the "CTIS"). As of 31 January 2022, the transition period commenced during which sponsors have been able to choose the method of submitting their applications for the authorisation of clinical trials either nationally, as had been done to date, or via the CTIS with joint assessment of the application by all of the concerned Member States. In 2022, the total of 415 applications for clinical trial authorisation were submitted; 351 applications for clinical trial authorisation/notification were submitted nationally and 64 applications were submitted via the CTIS. In total, 326 national decisions were issued. Most of the applications concerned phase III international, multicentric, randomised, blinded, placebo- or active-controlled clinical trials conducted by foreign sponsors.

In 2022, the Institute received 5,702 suspected adverse drug reaction (ADR) reports. This number of received reports is significantly higher than those in 2010-2020 (on average, approx. 3,000 reports annually). 2021 brought an extreme increase in the number of reports (the total of 13,759), which was caused primarily by the unprecedented interest in the safety of the COVID-19 vaccines – in total, there were 10,631 submitted reports of suspected ADRs to these vaccines in 2021. Compared to this, in 2022, almost five times less suspected ADRs to COVID-19 vaccines were reported, specifically, 2,260 reports were received.

The Laboratory Control Department completed 617 sample analyses. The number of samples rated as non-compliant slightly decreased compared to the previous year (to 2.6 %). Quality defects were confirmed primarily in pharmacy samples. Otherwise, the quality of proprietary medicinal products available on the Czech market is very good.

As at the end of 2022, the Institute registered the total of 2,480 pharmacies and 3,494 vendors of selected human medicinal products, 42 nuclear medicine departments of healthcare facilities, 387 medicinal product distributors, and 53 brokers of medicinal products for human use. In 2022, the inspectors of the Pharmacy and Distribution Department completed the total of 731 inspections of pharmacy care facilities – pharmacies, of which 30 concerned hospital pharmacies of inpatient care providers. In 2022, the inspections of vendors of selected medicinal products involved 109 shops in total; furthermore, distributors were subjected to 277 inspections and brokers to eleven inspections.

In 2022, the Inspection Department conducted the total of 256 inspections as part of its surveillance activities in the sphere of manufacture of pharmaceuticals (incl. the manufacture of transfusion products and raw materials for further manufacture of pharmaceuticals), of which 73 were inspections focused upon the regulated area of tissues and cells.

In 2022, the Quality Defects Unit that deals with cases concerning the occurrence of counterfeit medicinal products in the legal distribution chain or theft of medicinal products addressed the total of 66 such cases, of which three were cases of theft of medicinal products from the legal distribution chain.

In 2022, the Institute addressed the total of 143 instigations concerning a breach of Act No 40/1995 Coll., on Advertising Regulation, as amended. Thirteen administrative procedures were completed and as a result thereof, 14 penalties amounting to the total of 2,380,000 CZK 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.

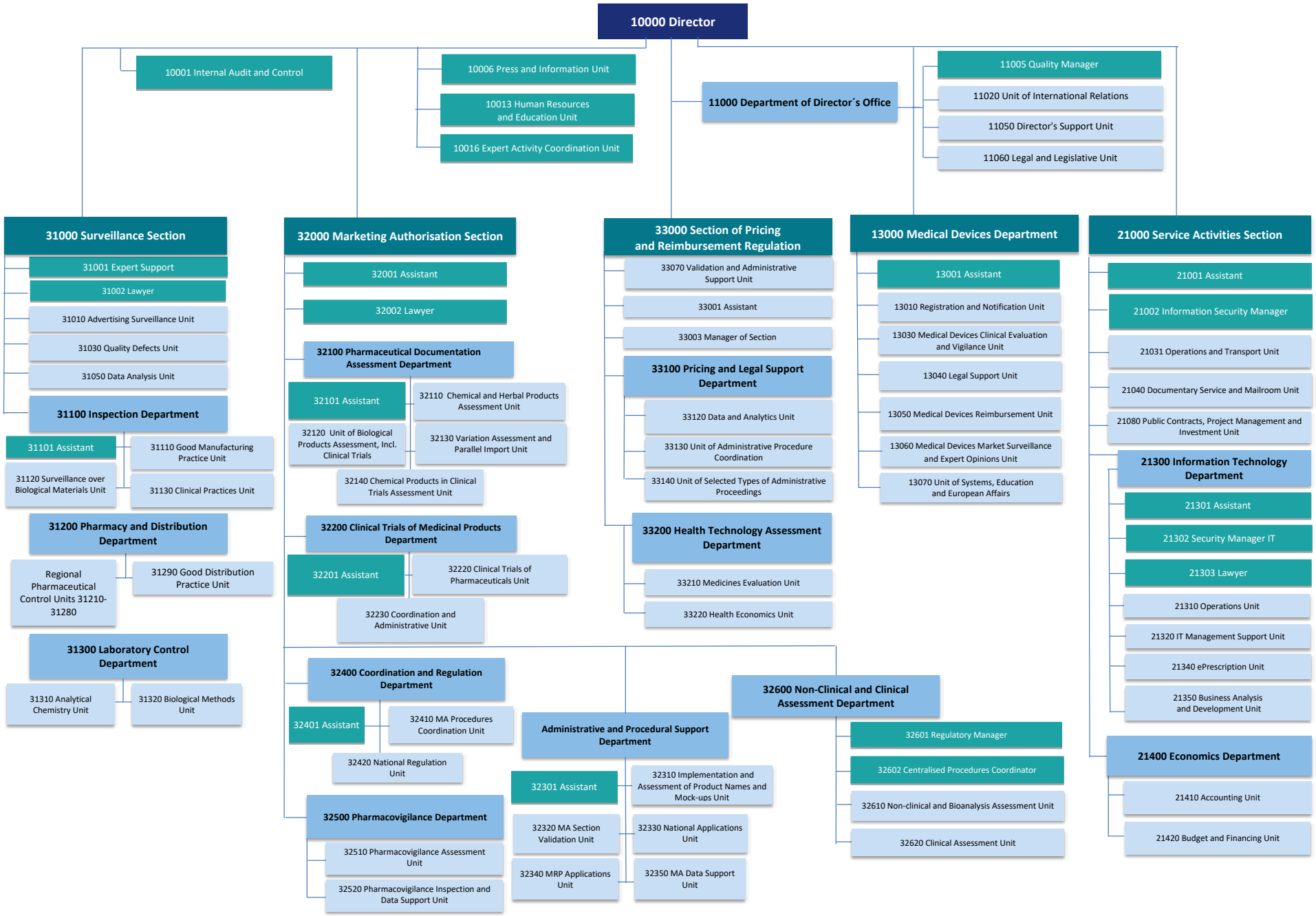
The objective of both scheduled and ad hoc inspections conducted by the Institute is to make sure that medical devices that are made available on the market in the Czech Republic are safe and functional and that health care is provided using appropriate, safe, and effective medical devices in a manner preventing any damage to the health of users or patients in the proper use of the devices for their intended purposes. In 2022, the inspectors of the Control Unit conducted the total of 167 inspections, of which 92 were inspections at providers of healthcare services (both state and non-state healthcare facilities) and 75 were inspections at medical devices manufacturers, importers, distributors, and persons dispensing or servicing medical devices.

In the course of 2022, the Section of Pricing and Reimbursement Regulation continued to commence in-depth reimbursement revisions as planned. The plan for 2022 included the commencement of 18 in-depth revisions that were also commenced (457 SÚKL codes). In 2022, 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 2022 are estimated at 2,442,359,091 CZK, and at 810,751,508 CZK, respectively.

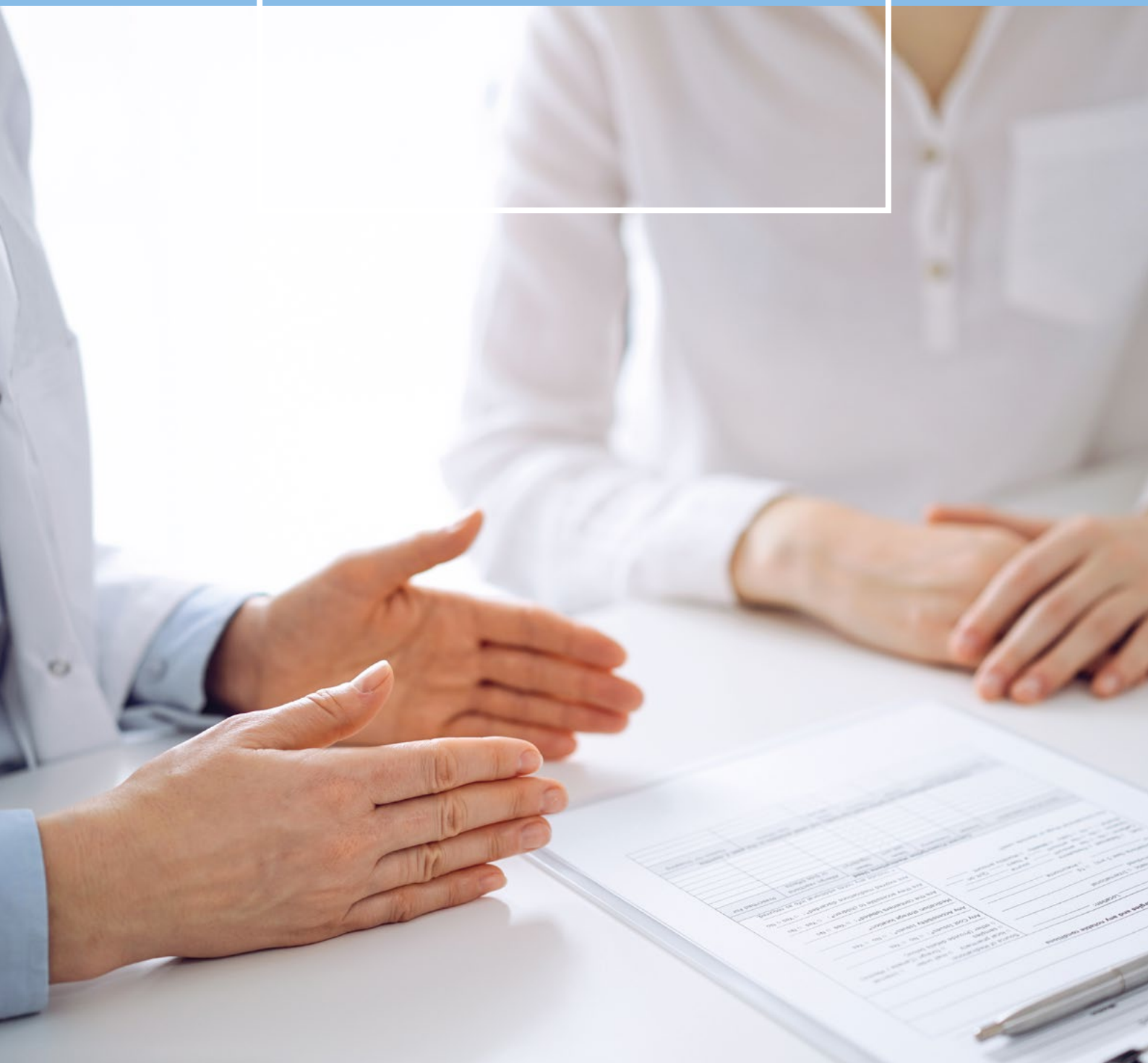
The ePrescription system keeps bringing a wealth of benefits, particularly for the patients. Last year, two new modules – eVaccination and eVoucher – were successfully launched. Also, a new functionality allowing for the use of citizen's identity also by healthcare professionals, was implemented. The electronic delivery of the ePrescription identifier – via SMS or e-mail messages – has been gaining an ever-growing popularity. Their numbers in 2022 grew to the record amount of more than 41 million SMS messages and 700 thousand e-mail messages. In 2022, the last steps to launch the cross-border ePrescription were completed and the system is expected to go live in 2023.

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, epreskripce.cz, and the OSALK website www.sakl.cz. The Press and Information Unit also coordinates 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


10000 Director
10001 Internal Audit and Control
10006 Press and Information Unit
10013 Human Resources and Education Unit
10016 Expert Activity Coordination Unit
11000 Department of Director´s Office
11005 Quality Manager
11020 Unit of International Relations
11050 Director's Support Unit
11060 Legal and Legislative Unit
31000 Surveillance Section
31001 Expert Support
31002 Lawyer
31010 Advertising Surveillance Unit
31030 Quality Defects Unit
31050 Data Analysis Unit
31100 Inspection Department
31101 Assistant
31110 Good Manufacturing Practice Unit
31120 Surveillance over Biological Materials Unit
31130 Clinical Practices Unit
31200 Pharmacy and Distribution Department
Regional Pharmaceutical Control Units 31210-31280
31290 Good Distribution Practice Unit
31300 Laboratory Control Department
31310 Analytical Chemistry Unit
31320 Biological Methods Unit
32000 Marketing Authorisation Section
32001 Assistant
32002 Lawyer
32100 Pharmaceutical Documentation Assessment Department
32101 Assistant
32110 Chemical and Herbal Products Assessment Unit
32120 Unit of Biological Products Assessment, Incl. Clinical Trials
32130 Variation Assessment and Parallel Import Unit
32140 Chemical Products in Clinical Trials Assessment Unit
32200 Clinical Trials of Medicinal Products Department
32201 Assistant
32220 Clinical Trials of Pharmaceuticals Unit
32230 Coordination and Administrative Unit
32400 Coordination and Regulation Department
32401 Assistant
32410 MA Procedures Coordination Unit
32420 National Regulation Unit
32500 Pharmacovigilance Department
32510 Pharmacovigilance Assessment Unit
32520 Pharmacovigilance Inspection and Data Support Unit
Administrative and Procedural Support Department
32301 Assistant
32310 Implementation and Assessment of Product Names and Mock-ups Unit
32320 MA Section Validation Unit
32330 National Applications Unit
32340 MRP Applications Unit
32350 MA Data Support Unit
32600 Non-Clinical and Clinical Assessment Department
32601 Regulatory Manager
32602 Centralised Procedures Coordinator
32610 Non-clinical and Bioanalysis Assessment Unit
32620 Clinical Assessment Unit
33000 Section of Pricing and Reimbursement Regulation
33070 Validation and Administrative Support Unit
33001 Assistant
33003 Manager of Section
33100 Pricing and Legal Support Department
33120 Data and Analytics Unit
33130 Unit of Administrative Procedure Coordination
33140 Unit of Selected Types of Administrative Proceedings
33200 Health Technology Assessment Department
33210 Medicines Evaluation Unit
33220 Health Economics Unit
13000 Medical Devices Department
13001 Assistant
13010 Registration and Notification Unit
13030 Medical Devices Clinical Evaluation and Vigilance Unit
13040 Legal Support Unit
13050 Medical Devices Reimbursement Unit
13060 Medical Devices Market Surveillance and Expert Opinions Unit
13070 Unit of Systems, Education and European Affairs
21000 Service Activities Section
21001 Assistant
21002 Information Security Manager
21031 Operations and Transport Unit
21040 Documentary Service and Mailroom Unit
21080 Public Contracts, Project Management and Investment Unit
21300 Information Technology Department
21301 Assistant
21302 Security Manager IT
21303 Lawyer
21310 Operations Unit
21320 IT Management Support Unit
21340 ePrescription Unit
21350 Business Analysis and Development Unit
21400 Economics Department
21410 Accounting Unit
21420 Budget and Financing 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 2022, the Institute continued its intensive cooperation with the Ministry of Health of the Czech Republic, particularly in the implementation of EU regulations governing the sphere of pharmaceuticals and medical devices, as well as in the legislative process of adoption of new legal regulations or amendments to existing legislation 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, continued the 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. Following agreement between the Ministry of Health and the Ministry of Agriculture, it was decided to prepare a new act due to the need for the actual division of regulation of pharmaceuticals 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 is rather extensive in itself.

In this respect, the Institute, as the regulator in the area of medicinal products, has been significantly involved in the drafting of the new wording of the basic standard governing medicinal products. In the course of 2022, joint meetings with the Ministry of Health, the purpose of which was the very preparation of the new legal regulation, continued. All SÚKL's units concerned with the agenda of medicinal products have been actively involved in this preparatory process.

The legislative amendments concerned also the marketing authorisation of medicinal products. As early as in 2021, the Institute, in cooperation with the Ministry of Health of the Czech Republic, 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 legal 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 2022, the legislative process for this Decree was successfully completed and on 08 March 2022, the Decree was successfully published in the Collection of Acts as Decree No 27/2022 Coll., amending Decree 228/2008 Coll., on marketing authorisation of medicinal products, as amended.

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 draft of 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, implemented 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.

The Institute was also involved in the drafting of those implementing legal regulations whose legislative process was completed in 2022 – Decree No 53/2022 Coll., stipulating the amounts of reimbursement of costs of expert activities conducted by the Institute pursuant to the Act on Dependency-Producing Substances; Decree No 168/2022 Coll., amending Decree No 85/2008 Coll., on the list of active substances and excipients that may be used for the preparation of medicinal products, as amended by Decree No 270/2013 Coll.; Decree No 219/2022 Coll., amending Decree No 236/2015 Coll., stipulating the conditions for the prescribing, preparation, distribution, dispensing, and use of magistral formulas containing medical cannabis, as amended by Decree No 307/2020 Coll., as well as Decree No 235/2022 Coll., on the growing and processing of medical cannabis plants.

Last but not least, in 2022, in the area of medicinal products, the Institute effectively contributed to the drafting of the amended Act on Pharmaceuticals and amended Act on Medical Devices in terms of implementation of Regulation (EU) 2022/123 of the European Parliament and of the Council of 25 January 2022 on a reinforced role for the European Medicines Agency in crisis preparedness and management for medicinal products and medical devices. The objective is to safeguard a high degree of human health protection through an enhanced ability of the Union to manage emergencies in the sphere of public health with consequences for medicinal products and medical devices and to respond to such emergencies. Another objective is to contribute to the safeguarding of a flawless operation of the internal market with these products during emergencies in the area of public health. In 2023, the legislative process concerning this legislative draft amendment is expected to progress further.

The Institute also closely cooperated with the Ministry of Health in the implementation of Regulation (EU) 2021/2282 of the European Parliament and of the Council of 15 December 2021 on health technology assessment and amending Directive

2011/24/EU. Health technology assessment (HTA) is a multidisciplinary process, which collects and evaluates information on medical, social, economic, and ethical consequences arising from the usage of health technologies. It aims to enhance the effective capacity of the healthcare system and to maximise value that may be derived from limited resources. For the purposes of the implementation, the Institute has prepared the first draft of amended Act on Public Health Insurance which will undergo further legislative process in 2023.

With reference to the powers defined by the provision of Section 29(6) of Act No 89/2021 Coll., in 2021, the Institute prepared a draft of a new decree governing the area of eVoucher. The eVoucher allows for electronic prescription of medical devices and, in principle, it is an analogy to the well-established electronic prescription of medicinal products via the ePrescription system. The legislative process concerning this Decree was completed in early 2022 when, initially, on 15 March 2022, a Communication from the Ministry of Health on Launching the Central Repository of Electronic Vouchers was published under no. 54/2022 Coll., and, thereafter, the Decree as such was published on 29 April 2022 as Decree No 97/2022 Coll., implementing some provisions of the Act on Medical Devices concerning electronic vouchers.

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"). Following the preparation of the draft of a new Act on Medical Devices, as a suitable adaptation of the Medical Device Regulation, in the course of 2019, it was also necessary to commence works on the preparation of another new draft act 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 into effect on 26 May 2021, in line with the effective date of the MDR.

In 2022, the Institute continued its cooperation with the Ministry of Health of the Czech Republic and 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 easier to apply in practice. The draft joint act covers the adaptation provisions of both Regulations as well as areas not explicitly covered by the Regulations, such as medical device servicing. In association with the legal order adaptation to the Regulations, amendments to other legal regulations were also drafted, specifically those to Act No 40/1995 Coll., on Advertising Regulation, and Act No 634/2004 Coll., on Administrative Fees. The purpose of the aforementioned Regulations is to safeguard a smooth working of the internal market concerning 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. This Act was published on 07 December 2022 in the collection of Act as Act No 375/2022 Coll., on Medical Devices and in Vitro Medical Devices, along with so called amendment Act No 376/2022 Coll., amending some acts in association with the adoption of the Act on Medical Devices and on in Vitro Diagnostic Medical Devices.

In respect of the aforementioned joint act, the Institute was also involved in the drafting of implementing legal regulations which, in terms of their structure, draw on previously adopted decrees. Also in this case, the legislative process was completed in 2022, specifically in December. It concerned the following implementing legal regulations: Decree No 377/2022 Coll., implementing some provisions of the Act on Medical Devices and in Vitro Diagnostic Medical Devices; Decree No 378/2022 Coll., on specimen ID card of inspectors of the State Institute for Drug Control pursuant to the Act on Medical Devices and in Vitro Diagnostic Medical Devices; Decree No 379/2022 Coll., stipulating the amounts of reimbursement of costs of expert activities conducted by the State Institute for Drug Control pursuant to the Act on Medical Devices and in Vitro Diagnostic Medical Devices.

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.

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

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

As in the previous years, cooperation with the Ministry of Health of the Czech Republic in drafting of opinions of the Czech Republic on preliminary questions raised with the European Court of Justice regarding the areas of competence 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 area of pharmaceutical market regulation, it cooperated with the Office for the Protection of Competition. 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. As in the previous years, in 2022, the Institute continued its highly 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 significantly growing trend in the transfer of information and data from information systems administered by the Institute, particularly the ePrescription system (approx. treble increase cf. 2021) has been obvious.

In total, this involved 260 queries, of which 203 were raised by the Czech Police, eight by courts of justice, two by a public prosecution office, 27 by the Customs Administration of the Czech Republic, two by tax authorities, six by the General Police Inspectorate (GIBS), three by an insolvency administrator, one by the Czech Trade Inspection, one by the Ministry of Health of the Czech Republic, one by the National Cyber and Information Security Agency, one by the ombudsman, one by the National Security Authority, and one by the Military Police.

The Institute, in cooperation with the Ministry of Health and the Ministry of Interior, continued its active 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 through its participation in the activities of 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). The membership of the Institute's employees in EMA scientific committees that address e.g., issues associated with medicinal product safety on the EU market or the approval of new pharmaceuticals, has been considered a matter of particular importance from the perspective of regulation of pharmaceuticals. The Institute has been also 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. One of the most important groups 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 whose role has been much enhanced due to the COVID-19 pandemic.

The Institute is a member of HMA working groups as well as their management structures and it has been 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. Relevant strategic information from these groups is forwarded via membership in sectoral and cross-sectoral bodies also down to the national level. One of the key problems being addressed on the global international level is e.g., the area of medicinal product availability or the issue of antimicrobial resistance (AMR).

Also in 2022, the Institute continued 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 for the purposes of enhancing qualification of the employees of medicines agencies of the EU Member States.

On the EU level, the Institute is also involved in the process of adoption of new European legislation and in discussions on non-legislative proposals in the EU Council falling under the Institute's responsibility. In 2022, for instance, discussions on the draft regulation on the standards of quality and safety of substances of human origin began; the regulation is to revise the current EU legislation governing the standards of quality and safety of human blood and the determination of quality and safety standards for human tissues and cells.

BUSINESS TRIPS ABROAD

Due to the continued COVID-19 pandemic, in early 2022, the absolute majority of international meetings were organised in the on-line mode. In March, the situation changed, the pandemic was subsiding and, gradually, restrictions were being lifted. Conditions for travel became favourable again and the number of business trips abroad started to grow slowly. In total, 146 business trips abroad took place in 2022, of which 50 were partially or fully reimbursed by the organising institutions (the European Commission, EU Council, EMA, EDQM, etc.). Of the total number of completed trips, 13 were educational events, 14 were trips within the scope of expert projects, 14 trips were undertaken to conduct foreign inspections (particularly in India), and 105 were routine business trips abroad. The Institute's employees travelled mostly to Brussels and Amsterdam, where they participated in events held in European institutions.

3.4 CZECH PRESIDENCY OF THE EU COUNCIL

An important event in the international sphere in 2022 was the Czech Presidency of the EU Council in the second half of 2022, which also significantly influenced the work of the Institute. Preparations had started as early as in 2019. The representatives of the Institute were involved in the activities of the Central Coordinating Group for the Preparation of the Presidency of the Office of the Government as well as in the Coordinating Group of the Ministry of Health for the Preparation of the 2022 Czech Presidency of the EU Council. Within the scope of the Presidency, the Institute organised eight face-to-face meetings and two on-line meetings of working groups and committees. Six other meetings were organised by other EU medicines agencies under the auspices of the Czech Minister for European Affairs.

Face-to-face meetings were attended by more than 350 foreign delegates, mostly from partner agencies for medicinal products and medical devices from the EU Member States, but also from the European Commission, the European Medicines Agency, the European Directorate for the Quality of Medicines and Health Care (EDQM) of the Council of Europe and, last but not least, representatives of patients, the academia as well as the pharmaceutical industry. These meetings were mostly meetings of working groups of the medicines regulatory network and committees and working groups of the European Medicines Agency (so called "strategic review and learning meetings" [SRLM]). Specifically, Prague hosted a meeting of the European Medicines Agencies Co-operation of Legal and Legislative Issues (EMACOLEX) working group, a Working Group of Communications Professionals (WGCP) meeting, the Competent Authorities for Medical Devices (CAMD) committee meeting, a Heads of Medicines Agencies (HMA) meeting, a SRLM of the Committee for Medicinal Products for Human Use (CHMP), a joint SRLM of the Pharmacovigilance Risk Assessment Committee (PRAC) and the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh), and a SRLM of the Paediatric Committee (PDCO). Some of the meetings held under the auspices of the Czech Presidency were organised by other EU medicines agencies: a SRLM of the Committee for Orphan Medicinal Products (COMP) in Germany (BfarM), a SRLM of the Committee for Advanced Therapies (CAT) in France (ANSM), a SRLM of the Committee on Herbal Medicinal Products (HMPC) in Malta (MMA), a meeting of the Homeopathic Medicinal Products Working Group (HMPWG) in Italy (AIFA), a meeting of the Clinical Trials Coordination Group (CTCG) in Belgium (AFMPS), and a meeting of the Working Group of Enforcement Officers (WGEO) in Portugal (INFARMED). Other meetings availed of the opportunity of on-line organisation. The Institute organised an on-line HMA meeting and a meeting of IT Directors, which is a working group of directors in charge of IT issues. At the time of the Czech Presidency, moreover, one on-line and one face-to-face meeting of competent authorities in the sphere of pricing and reimbursement regulation took place, with organisational contribution from the European Commission. SÚKL employees contributed to these events not only in terms of organisation, but also by preparing the agenda and, in many cases, they also presented current topics within their powers. SÚKL representatives in the respective working groups and committees chaired or co-chaired the meetings and were involved in the drafting their outputs. The importance of the events and the care given thereto by the Institute were emphasised by the personal presence of the Institute's Director, Mgr. Irena Storová, MHA, at meetings whenever possible, and regular monitoring of the preparation and progress of events by the top management of the Institute. Positive feed-back from foreign delegates evidenced that the Institute's efforts to present the Czech Republic as best as possible and careful preparation as well as the commitment of anyone involved in the events contributed to the success of the Czech Presidency.

The Institute, inter alia, was involved in updating sector agendas, further detailing the planned priorities of the Czech Republic as the EU Council presiding country in the concerned period. Within the scope of the agendas entrusted thereto, SÚKL was also involved in the work of Presidency teams in the preparation of source materials and discussions on legislative drafts in the EU Council, e.g., the aforementioned regulation on the standards of quality and safety for substances of human origin or the regulation on the European Health Data Space (EHDS).

EUROPEAN MEDICINES AGENCIES CO-OPERATION OF LEGAL AND LEGISLATIVE ISSUES (EMACOLEX)

In the area of legal collaboration represented by the European Medicines Agencies Co-operation of Legal and Legislative Issues (EMACOLEX) group, collaboration of medicines agencies became enhanced during the Czech Presidency, as after two years of on-line meetings, it was possible to organise a face-to-face meeting of the EMACOLEX group, which was much appreciated by the attendees. The benefit of the Prague meeting was, in particular, the harmonisation of interpretations of disputable legal issues arising from the new EU pharmaceutical legislation and judicature concerning pharmaceuticals, legal comparative studies in individual national approaches, e.g., during the implementation of EU directives and regulations, and enhanced and deepened cooperation among the Member States represented in the group. The Czech Republic, as the presiding country, much appreciates also attendance by EMA representatives. At the time of the Czech Presidency, the group was also completing tasks assigned by HMA.

HEADS OF MEDICINES AGENCIES (HMA)

The face-to-face meeting of EU Heads of Medicines Agencies, attended, inter alia, also by the representatives of the European Medicines Agency, the European Commission, or the European Directorate for the Quality of Medicines and Health Care of the Council of Europe, was held in a highly friendly atmosphere since the very beginning. The agenda of the meeting, which was prepared in cooperation with colleagues from the Institute for State Control of Veterinary Biologicals and Medicines (ÚSKVBL), was much varied and included, inter alia, sharing of current information on the activities of the EC or EMA or information on the preparation and implementation of a joint action for the support of enhanced capacities of the European regulatory network within the scope of the EU4Health 2022 programme. Issues associated with the implementation of the Clinical Trials Regulation were also discussed, specifically, in association with the CTIS portal, through which it will become mandatory to submit applications for new clinical trials as of 31 January 2023. The Institute's Director gave a presentation on

the ePrescription system as part of the eHealth under development. Furthermore, outputs from a meeting with stakeholders held just before the HMA meeting were also presented, and space was given also to the medical device agenda. Part of the second day of the meeting then focused on veterinary issues, because HMA covers also the sphere of veterinary medicines regulation; in the Czech Republic, the ÚSKVBL is in charge of this area.

HMA MEETING WITH STAKEHOLDERS

During the Czech Presidency, SÚKL organised also a meeting with stakeholders (as part of the Heads of Medicines Agencies meeting), to discuss electronisation of package leaflets of medicinal products. The representatives of medicines agencies, EMA, the pharmaceutical industry, patients, distributors, healthcare professionals and pharmacists together discussed the pros, risks, and possible benefits of implementing this approach to sharing the package leaflet. Conclusions from this meeting may be used in the drafting of revised European pharmaceutical legislation.

SRLM OF THE PAEDIATRIC COMMITTEE (PDCO)

The PDCO SRLM took place on 5-7 October 2022. The essential topics discussed were personalised clinical studies not only in the field of paediatric oncology, the issues of real-world evidence (RWE) utilisation, and a potentially new method of paediatric investigation plans (PIP) submission that would flexibly reflect state-of-the art knowledge about the disease and active substance in question. The expert topic focused on the treatment of spinal muscular atrophy and possibilities of newborn screening.

SRLM OF THE PHARMACOVIGILANCE RISK ASSESSMENT COMMITTEE (PRAC) AND THE COORDINATION GROUP FOR MUTUAL RECOGNITION AND DECENTRALISED PROCEDURES - HUMAN (CMDH)

The Joint meeting of the Pharmacovigilance Risk Assessment Committee (PRAC) and the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh) was held on 18-19 October 2022. The meeting was split into two sections. On day one, separate meetings were held; these meetings discussed topics solely within the agenda of the individual groups. On day two, a joint PRAC and CMDh meeting was held, which discussed overlapping topics relevant for both groups, such as transparency of publication of conclusions from major safety variations to marketing authorisations or the possibilities of utilising advanced technologies in the sphere of risk minimisation measures.

The agenda of the separate PRAC meeting consisted of three main topics, presented from various perspectives and broadly discussed. The first topic concerned the use of pharmaceuticals in pregnancy and lactation, focusing on best ways to present these topics in the product information. The second topic was the quality of individual reports of suspected adverse drug reactions, as the overall quality of the pharmacovigilance signal assessment and subsequently adopted regulatory measures depend on the report quality. The third topic followed up on the second one – it focused upon patient reports, with emphasis on best ways to use them in further safety evaluation. All of the topics provoked a huge interest, which was apparent from a rich discussion and an interest in establishing action points where these topics are to continue to be addressed.

The separate CMDh meeting addressed, in particular, topics associated with the issues of human resource capacities, which is a problem currently faced by majority of the national regulatory authorities, and a European Commission project addressing this topic was presented. Furthermore, the meeting addressed possible ways to simplify marketing authorisation of critical medicinal products (both in terms of medicinal product shortage on the market in small countries in particular, and from the perspective of marketing authorisation of needed medicinal products, such as antibiotics). All of the topics were concluded with specific proposals for amendments to the processes set up in the area of European marketing authorisations of medicinal products, which were then forwarded to the CMDh plenary session for official discussion and approval.

COMPETENT AUTHORITIES FOR MEDICAL DEVICES (CAMD)

As part of the Czech Presidency, the Medical Device Department (OZP) hosted a two-day meeting of the Competent Authorities for Medical Devices (CAMD) in October 2022 – including a one-day meeting of the CEG steering committee. The meeting agenda comprised primarily of topics associated with the implementation of European regulations that principally change the regulatory framework in the area of medical devices and in vitro diagnostic devices. OZP representatives focused part of the agenda upon expert issues and presented their own experience from the concerned areas, comparing it to the findings they gained from other Member States from an interview survey carried out prior to the CAMD meeting. Along with other participants, the meeting was attended also by representatives of the European Commission, HMA Core Group members and NBCG (notified body) representatives. The agenda included also a panel discussion, with active involvement of the representatives of all represented bodies, who brought various insights into the regulation implementation issues. The meeting gained a favourable evaluation by all participants and contributed to better understanding and strengthening of CAMD position within bodies involved in activities associated with medical device regulation.

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

The CHMP SRLM took place on 14-16 November 2022. The topics discussed included lectures on EMA activities (Raw data pilot, capacity building a future regulatory landscape in EU) on one hand, and a programme focused on the work of CHMP and improvement of the harmonised assessment among Member States (wording of section 5.1 of the SmPC, CHMP learnings, enhancement of assessment report clarity, and exchange of experience with co-rapp critique) on the other hand. The expert topic was covered by an external lecturer specialising in the development of medicinal products in academic environment, mostly in the area of antineoplastic therapy.

WORKING GROUP OF COMMUNICATIONS PROFESSIONALS (WGCP)

The meeting of the Working Group of Communications Professionals (WGCP) was held on 01-02 December. The delegates were representatives of regulatory authorities from European Union Member States and representatives from the European Medicines Agency (EMA). The primary purpose of the Communication Professionals meeting was to share experience from crisis communication across the European Union, to keep a common communication line in the area of medicinal products and medical devices across the EU, and to share experience gained from various situations in communication with the media and the general public as well as professionals. Along with the sharing of so called best practices, the meeting also brought information about the CTIS project, the delegates discussed the success of the MedSafetyWeek campaign, of which SÚKL was a regular active participant, just like tens of countries from all over the world. The agenda included also a workshop on ways to approach so called trolls on social networks.

IT DIRECTORS

The on-line meeting was organised for the representatives of IT Directors; the Institute's Director delivered the opening speech and a presentation on the ePrescription system as part of the currently developed eHealth. This meeting offered information about IT projects managed by EMA as well as discussions on hot topics regarding big data processing in health care and cyber-security. The meeting received a highly favourable feed-back and EMA representatives expressed their cordial thanks to the Institute for excellent organisation, technical preparation as well as active involvement in the drafting of the agenda and the content of individual presentations and other contributions.

HEADS OF MEDICINES AGENCIES (HMA II)

The second meeting of the Heads of Medicines Agencies during the 2022 Czech Presidency was organised on-line, again in cooperation with colleagues from the ÚSKVBL. Its main topics included, inter alia, issues concerning medicinal product shortages within the EU or the implementation of the Clinical Trial Regulation, and the status of the prepared CTIS portal. Other discussions focused upon the Benchmarking projects of EU medicines agencies (BEMA) and cooperation with the WHO; again, space was given also to medical devices and the veterinary area.

NATIONAL COMPETENT AUTHORITIES ON DRUG PRICING AND REIMBURSEMENT

On 12 October and on 12 December 2022, the regular plenary sessions of the Network of Competent Authorities on Pricing and Reimbursement (NCAPR) of the EU Member States took place. For the Czech Presidency, both meetings were prepared, together with Commission representatives, also by the employees of SÚKL's Pricing and Reimbursement Regulation Section and the employees of the Ministry of Health of the Czech Republic.

SÚKL also co-chaired both meetings. The topics discussed included, inter alia, the issues of the approach of countries to budgetary impact of newly reimbursed health technologies on the entry of products into the reimbursement system and reimbursement regulation for orphan medicinal products. Although there are traditionally significant differences among the systems and processes of pricing and reimbursement regulation in various EU Member States, the Member States face the same challenges (i.e., across the EU, there is an apparently increasing pressure on health insurance budgets or the trend of growing expenditures for orphan medicinal products). This platform enabled to share experience in looking for solutions and ways to overcome these challenges.

Both the technical and organisational coverage of all events organised by the Institute within the scope of the Czech Presidency was of a very high standard and feed-back from delegates on this aspect was highly favourable, as well as that on the agenda content of all meetings, which strived to include many important topics in the area of medicinal product and medical device regulation.

4. REGULATORY ACTIVITIES OF SÚKL

4.1 RECORD SYSTEM

In 2022, the electronic record system of the Institute, incl. its regional workplaces, registered 92,515 delivered documents and 71,700 dispatched documents (Tab. 1). The decrease in the number of received documents was due to the fulfilment of the registration and notification obligation of entities and changing legislation in the sphere of medical devices, where some of the obligations carried out via the Medical Devices Registry cease to exist. The priority channel for official document delivery are data mailboxes (Tab. 2).

Tab. 1 Registration of documents in 2020–2022

	2020	2021	2022
Received documents	97,748	102,484	92,515
Dispatched documents	65,101	77,488	71,700

Tab. 2 Overview of communication channels in 2022

	Mailroom	E-mail messages	Data messages	Medical device reimbursement notifications	Total
Received documents	25,799	52,451	10,871	3,394	**92,515**

	Dispatch room	E-mail messages	Data messages	Electronic notice board	Total
Dispatched documents	4,349	9,227	50,907	7,217	**71,700**

MARKETING AUTHORISATION SECTION

Prior to their placement onto the market in the Czech Republic, most proprietary medicinal products are 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.

The product therapeutic indications, contraindications, 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 [Periodic Safety Update Report] 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 concerning exceptions from the subset 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 ensuring the safety of medicinal products and conducting the evaluation of their risk/benefit ratios. The pharmacovigilance activities comprise 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.), evaluation of any available data on potential risks, implementation of regulatory measures intended for risk minimisation, and of communicating new safety information both to professionals and to the general public.

4.2 MARKETING AUTHORISATION OF MEDICINAL PRODUCTS

APPLICATIONS FOR NEW MARKETING AUTHORISATION

In 2022, 601 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 slightly decreased from 642 applications in 2021 to 603 applications in 2022. 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 2022, the number of received applications for DCP marketing authorisation with the Czech Republic acting as the Reference Member State increased from 107 applications in 2021 to 139 applications in 2022.

601

applications for new marketing authorisation were forwarded for expert assessment following successful validation.

MARKETING AUTHORISATION RENEWALS

In 2022, the total of 316 applications were forwarded for expert assessment following successful validation. Most of them were applications for MRP/DCP marketing authorisation renewals; in 2022, the total number of received applications for marketing authorisation renewal was slightly higher than in 2021.

VARIATIONS TO MARKETING AUTHORISATIONS

In 2022, the number of received applications for variations to MRP/DCP marketing authorisations was similar to the previous year, but the number of received applications for variations to national marketing authorisations slightly decreased. The total number of received applications hence slightly dropped. At the same time, the number of submitted applications for transfers of national marketing authorisations as well as MRP/DCP marketing authorisation transfers slightly decreased.

PARALLEL IMPORT

In 2022, the number of submitted applications for parallel import authorisation significantly decreased, specifically from 57 applications in 2021 to 32 applications in 2022. At the same time, however, the number of submitted applications for variations to parallel import authorisations increased from 77 applications in 2021 to 108 applications in 2022.

MARKETING AUTHORISATION REVOCATIONS

In 2022, 345 applications for revocation of marketing authorisation were decided, which is a slight increase compared to 2021.

Tab. 3 Marketing authorisation (MA) applications agenda

Process of marketing authorisation of medicinal products	Submitted in 2022	Decided in total in 2022	Total pending as of 31 December 2022
New marketing authorisations	**603**	**601**	**927**
- of which national	14	29	68
- of which MRP-RMS	22	14	55
- of which DCP-RMS	139	122	168
- of which CMS (MRP and DCP)	428	436	636
MA renewals	**330**	**390**	**282**
- of which national	17	32	61
- of which RMS	53	90	25
- of which CMS	260	280	196
National variations to MAs	**1,881**	**1,996**	**326**
- of which MA transfers	116	114	11
- of which PIL and labelling	70	58	20
- of which bulk MRP-RMS variations	1,695	1,824	295
MRP-RMS variations	**817**	**903**	**149**
- of which MA transfers	17	16	0
- of which PIL and labelling	28	35	0
- of which bulk MRP-RMS variations	772	852	149

Process of marketing authorisation of medicinal products	Submitted in 2022	Decided in total in 2022	Total pending as of 31 December 2022
MRP-CMS variations	**4,275**	**4,401**	**1,156**
- of which MA transfers	91	78	13
- of which PIL and labelling	130	149	23
- of which bulk MRP-CMS variations	4,054	4,174	1,120
MA revocations	**335**	**345**	**0**
Parallel import	**32**	**54**	**19**
Parallel import variations	**108**	**99**	**16**
Parallel import renewals	**13**	**19**	**3**
Parallel import revocations	**6**	**6**	**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 2022, the Institute conducted 147 administrative procedures concerning the granting of an exemption from the sunset clause (marketing authorisation expiry for products not placed on the market for the period of three years).

In the course of 2022, the sunset clause as referred to under Section 34a of the Act on Pharmaceuticals applied to 80 MA numbers and the marketing authorisation of these medicinal products was terminated.

Tab. 4 Applications for exemption from the sunset clause

	Conducted in 2022
Administrative procedures for exemption from the sunset clause	**147**
- of which: submitted applications	147
- of which: ex officio initiated administrative procedures	0
- granted	113
- declined	9
- suspended as undue	24
- suspended as unjustified	0
- suspended for failure to provide amendment	1
- 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 2022, we gave 19 oral consultations (including consultations held in the form of teleconferences) and issued 19 written opinions on process-regulation and expert requests for consultations.

In 2022, we issued 15 written opinions on requests for consultations concerning medicinal product names.

In June 2022, two one-day seminars of the Marketing Authorisation Section concerning the area of marketing authorisation of medicinal products were held.

4.3 COOPERATION WITH THE EUROPEAN MEDICINES AGENCY AND CHMP

In 2022, as part of its 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:

- eight times as the rapporteur/co-rapporteur;
- 23 times it assessed type I and II variations to centralised marketing authorisations;
- once it assessed a referral;
- 26 times it assessed pharmaceutical documentation for scientific advice procedures.

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 and was actively involved in the preparation of expert events held during the Czech Presidency of the EU Council.

4.4 CLINICAL TRIALS

2022 saw the coming into force of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC and the associated launch of the EU portal CTIS. 31 January 2022 was the start of the transitional period during which sponsors have had the possibility to choose whether they wish to submit their application for clinical trial authorisation either nationally, as in the past, or via the CTIS portal with joint assessment of the application by all concerned Member States. This is, moreover, associated with the effect of two versions of the Act on Pharmaceuticals and its implementing legal regulations that govern the individual methods of application submission. The transitional period will end in 2025, until which it is necessary to maintain also two systems of ethics committees.

415

submitted applications for clinical trial authorisation

With the coming into force of Regulation (EU) No 536/2014, SÚKL's ethics committee commenced its operation. The Committee assesses applications for clinical trial authorisation submitted via CTIS. In the course of 2022, the amended Act on Pharmaceuticals was drafted and adopted, allowing for the involvement of existing multicentric ethics committees in the process of assessment of applications for clinical trial authorisation submitted via CTIS since the end of 2022. In the second half of the year, three meetings with the representatives of these ethics committees were organised in order to set up the coordination of the process and the possible involvement of the ethics committees. Regular working meetings will continue also in the next year.

In 2022, the total of 415 applications for clinical trial approval were submitted, of which 351 applications for clinical trial authorisation/notification were submitted nationally and 64 applications were submitted via the CTIS. In total, 326 national decisions were issued. Most applications concern phase III studies, international, multicentric, randomized, blinded placebo- or active substance-controlled clinical trials conducted by foreign sponsors. Of the total number of 326 nationally decided applications for clinical trial authorisation/notification, 19 were for clinical trials submitted by non-commercial entities (academic research), 43 applications concerned orphan drugs (medicinal products for rare diseases), 43 were applications for clinical trials enrolling also children or intended directly for the paediatric population (paediatric clinical trials), four applications concerned clinical trials on advanced therapy products (three gene therapies and one tissue engineering therapy), and ten applications were for first-in-human (FIH) trials. In the course of the assessment process, 34 applications in total were withdrawn (14 applications for clinical trial authorisation and 20 clinical trial notifications); no application was declined.

Of the 64 applications for clinical trial authorisation submitted via CTIS, 13 applications were approved, seven applications were withdrawn, three were declined, and three lapsed for failure to comply with timelines.

Tab. 5 Clinical trials in 2022

Tab. 5.1 Applications submitted via CTIS

Submitted applications for CT authorisation			
New applications – Czech Republic as RMS	New applications – Czech Republic as CMS	Resubmission	Transition trial = CT transferred to the new CTIS
2	43	4	12

Substantial amendments		Added Member State (AM)	
Czech Republic as the RMS	Czech Republic as the CMS	Czech Republic as the RMS	Czech Republic as the CMS
0	8	0	3

Withdrawn applications	Authorised CTs Authorised/authorised with condition		Declined CTs		Lapsed applications
	New CTs	Transferred CTs	RMS	CMS	
7	8	5	2	1	3

Tab. 5.2 Applications submitted nationally pursuant to the Act on Pharmaceuticals

	Pending from the previous period	Applications received in 2022	Number of decisions issued in 2022	Of which declined	Of which withdrawn
Applications for CT authorisation	36	351	135	0	14
CT notifications	55		191	0	20
Notifications of amendments to CTs	---	3,784	3,689	---	---

Tab. 6 Numbers of applications submitted nationally in 2022 by clinical trial phase

	Applications received in 2022	Applications assessed in 2022
Phase I	18	20
Phase II	101	88
Phase III	200	182
Phase IV	17	18
Bioequivalence studies	15	18

Tab. 7 Indication groups of clinical trials submitted nationally and assessed in 2022

Indication group	Number
Oncology	102
Metabolic disorders + endocrinology	3
Healthy volunteers	15
Neurology	27
Cardiovascular system	25
Respiratory + allergology	22
Infectious	8
Dermatology	13
Rheumatology	24
Haematology	11
Psychiatry	7
GIT	11
Urogenital diseases	7

Indication group	Number
ENT	2
Gynaecology	7
Ophthalmology	8
Paediatrics	6
Internal medicine	7
Transplantations	0
Anaesthesiology and resuscitation	0
Investigations	0
Diabetology	5
Other	2
Pain	1
Vaccination	2
Pharmacokinetics	11

Also in this year, we took active part in the activities of the EMA working group; the topic discussed coherently during all meetings was the current situation of CTIS. We were addressing outages and errors of the system, looking for and fine-tuning solutions of situations not covered by Regulation (EU) No 536/2014, arising in the course of the year. We were involved in the provision of comments on and updating EMA's Q&A document on the requirements for submitted documents, with particular focus on clinical trials transferred into the mode governed by Regulation (EU) No 536/2014. We took active part in the meetings of international groups; the Clinical Trials Coordination Group (CTCG) held 32 meetings, the Clinical Trial Expert Group (CTEG) four meetings, the Clinical Trials Advisory Group (CTAG) five meetings, and the Clinical Trial Information System – Working Group 21 meetings addressing the aforementioned issues. In the course of the year, the regular on-line meetings of representatives of medicines agencies, EMA, and the European Commission on problems with CTIS on the basis of submitted specific questions, so called assessor's round table, was commenced.

We have been also involved in the operation of the Committee for Advanced Therapies (CAT), where we attended 16 meetings, of which two in person and the rest via on-line connection.

In 2022, we were involved in two international projects. It was the EU4Health CT CURE for accelerated assessment of clinical trials focused upon the treatment of the COVID-19 disease. In this project, we were involved in the assessment of two clinical trials. The other project was the EU4Health SAFE-CT, focusing upon joint assessment of safety data in clinical trials. The activities in this project concentrated particularly on the set-up of a harmonised procedure for the assessment of safety reports from clinical trials.

We attended two meetings of the Ethics Committee Forum. During the spring meeting, we informed ethics committee members about the current situation with CTIS, shared our initial experience with the assessment of applications submitted via CTIS, advised about requirements for grant projects and their assessment, and provided information about implemented measures allowing to transfer Ukrainian patients to clinical trials in the Czech Republic in the context of the war in Ukraine. During the autumn meeting, we presented information on SÚKL's approach to the assessment of applications for clinical trials concerning the diagnosis of multiple sclerosis, on the current situation with ethics committees and the two systems of ethics committees for the transitional period, and our colleagues from the Medical Device Department had a presentation on the new legislation governing medical devices.

In 2022, we organised three working meetings with the representatives of multicentric ethics committees, the major topic of all of them being the coming into force of Regulation (EU) No 536/2014, the launch of CTIS, and the situation with ethics committees. The members also had the opportunity to attend our seminars. Furthermore, two meetings with the representatives from the Association of Innovative Pharmaceutical Industry (AIFP), the Association of Clinical Research Organisations (ACRO), Czech Association of Pharmaceutical Companies (ČAFF), and the Czech Clinical Research Infrastructure Network (CZECRIN) were held.

In 2022, we organised seven seminars for sponsors, CROs, monitors, and contact persons on the CTIS portal and the coming into force of Regulation (EU) No 536/2014, three lectures in the university hospital for academic researchers, two lectures for university students (Pharmaceutical Faculty Hradec Králové and University of Chemistry and Technology Prague), one lecture for a pharmacist course and one lecture for qualified persons at the Institute for Postgraduate Medical Education (IPVZ), one lecture for sponsors and CROs and one lecture as part of the Good Clinical Practice course for investigators, one lecture on GMOs for a meeting held by the Ministry of Environment. Newly, we organised seven workshops for CZECRIN coordinators with practical lessons in the submission of applications for clinical trial authorisation via CTIS, in order to help academia switch to the new system of application submission via CTIS. In 2022, we gave 20 consultations to twelve pharmaceutical companies and 80 to non-commercial entities (the academia, researchers, representatives of healthcare providers), 16 by means of an oral consultation and four in the form of a written opinion issued upon request. Furthermore, we issued 33 written opinions upon request for project distinction to advise whether a particular project is a clinical trial on a medicinal product or not.

The receding COVID-19 pandemic and improving situation allowed to lift the emergency measures for new or ongoing clinical trials and for priority assessment of clinical trials on COVID-19 therapies or prophylaxis as at 23 May 2022. The new increase in COVID-19 cases required re-introduction of the measures, albeit less strict, in August 2022. The introduced emergency measures enhanced the sponsors' effort for so called decentralised clinical trials, when parts of the clinical trial are conducted outside the trial site. Therefore, in 2022, discussions on the possibilities of decentralised clinical trials in European working groups continued and are going to continue also in the next year.

4.5 PHARMACOVIGILANCE

In compliance with the Act on Pharmaceuticals, SÚKL's Pharmacovigilance Department (OFV) operates a system of spontaneous reports of suspected adverse drug reactions (ADR) from the Czech Republic. In 2022, SÚKL received the total of 5,702 reports (the figure may slightly vary with a view to the data cut-off for the Annual Report, as the report duplicity and validity checks continue to be performed on an ongoing basis). This number of received reports is significantly higher than figures from the period of 2010–2020 (on average, approx. 3,000 reports annually). Nevertheless, 2021 brought an extreme increase in the number of reports (13,759 in total), which was caused particularly by an unprecedented interest in the safety of COVID-19 vaccines. In total, there were 10,631 reports of suspected ADRs to these vaccines in 2021. In 2022, the number of suspected ADR reports concerning COVID-19 vaccines dropped almost five times, specifically to 2,260 reports. Of the total number of reports received in 2022, 1,846 reports were from medicinal product marketing authorisation holders (pharmaceutical companies) and 3,856 were reports sent to SÚKL directly by healthcare professionals and patients (of which 1,573 were reports from healthcare professionals and 2,285 reports from patients – two reports were sent by the healthcare professional and the patient in parallel).

5,702

suspected adverse drug reaction reports

Of the total number of 5,702 received reports, 2,662 concerned COVID-19 vaccines. In respect of all other medicinal products, 3,040 reports were received. 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. 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. In 2022, we contacted the reporter 409 times to obtain important additional information concerning the report (so called follow-up), which is more than in the years preceding the COVID-19 pandemic. 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, at the same time, 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 83 active substances on the pan-European level. In 2022, the Pharmacovigilance Assessment Unit assessed 948 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 enhancing its involvement in international pharmacovigilance procedures. In the sphere of Periodic Safety Update Reports (PSURs) for individual products, the Institute assessed the total of 25 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 2022. The Institute acts as the PSUSA LMS for the total of 60 substances, 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 completed the assessment of seven new marketing authorisations of these medicinal products and performed the assessment of 20 more procedures concerning centrally authorised products in total during 2022. In total, we have been appointed the PRAC rapporteur for 20 centrally authorised medicinal products.

SÚKL's Pharmacovigilance keep enhancing their involvement in pharmacovigilance activities on the European level on a continuous basis. We actively participated in eleven regular meetings of the PRAC pharmacovigilance committee in the European Medicines Agency (EMA); due to the pandemic, most of these meetings assumed a remote form. Furthermore, ten one-day teleconference meetings of the PRAC committee took place. Our active involvement assumes the form of thorough monitoring of and provision of comments on ongoing procedures held by other countries. In the course of 2022, we sent written comments on procedures held by other countries 127 times in total and at meetings, we presented seven procedures held by us. In addition to regular PRAC meetings, there were two extraordinary meetings organised under the auspices of the state presiding the EU Council. We actively participated in the first meeting held in Paris, where we gave two presentations. The other meeting was a meeting that we organised ourselves in Prague under the auspices of the Czech EU Council Presidency. We prepared

a high-quality agenda for the two-day meeting – on the first day, the joint PRAC and CMDh meeting took place; on the second day, both bodies held separate meetings. The meeting was highly successful, and we received extensive favourable feed-back.

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. Of the 15 assessment reports of this group published in 2022, our member drafted seven. We are also actively represented in the PRAC working group for follow-up questionnaires, i.e., questionnaires used to obtain additional important information on reported suspected ADRs, and in a group focused upon the treatment of pregnant and lactating women with multiple sclerosis.

In cooperation with other units of the Marketing Authorisation Section, conclusions adopted by CHMP and the PRAC pharmacovigilance committee were being transferred to Czech clinical practice on an ongoing basis. On its website, the Institute published ten communications intended for healthcare professionals or for the general public on medicinal product safety. In cooperation with marketing authorisation holders, the Institute published educational materials on the safer use of 80 active substances and 20 letters to healthcare professionals focused upon increased safety of medicinal product use. Assessors from the Pharmacovigilance Assessment Unit were involved in the assessment of marketing authorisation dossiers where they looked at the pharmacovigilance section; in 2022, they prepared 1,896 reports on pharmacovigilance documentation in total.

The Pharmacovigilance Department continues to issue the Adverse Drug Reactions Bulletin (Nežádoucí účinky léčiv). In 2022, 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. Sixty-eight notifications (of commencement, termination, or update) of post-marketing safety studies conducted in the Czech Republic were processed.

In 2022, the Pharmacovigilance Inspection and Data Support Unit carried out the total of 14 inspections of pharmacovigilance systems of marketing authorisation holders. One inspection was brought forward from 2021 due to the epidemiologic situation; twelve inspections were scheduled, one was conducted in addition to the plan, in parallel to the inspection of another marketing authorisation holder in the same pharmacovigilance system.

Of the completed inspections, six were inspections of the complete pharmacovigilance system, where the marketing authorisation holder's PSMF is stored in the Czech Republic (two of them were conducted as inspections requested by CHMP). Eight inspections focused upon the pharmacovigilance activities of MA holder's local representation in the Czech Republic.

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 two marketing authorisation holders.

The Pharmacovigilance Department communicates with the public, it answers questions from healthcare professionals, the general public as well as pharmaceutical companies. In 2022, we answered 630 questions in writing or by phone. As part of dissemination of information on the safety of pharmaceuticals and also to increase suspected adverse drug reaction reporting, the employees of the Pharmacovigilance Department gave seven presentations at 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 still ongoing pandemic. The Institute also focuses upon the education of pharmaceutical companies in the proper conduct of pharmacovigilance. In 2022, we continued the tradition of organising two one-day seminars for companies on news in pharmacovigilance from the previous year and furthermore, we gave two presentations at a seminar organised by another SÚKL section.

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 conduct 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 governing 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, moreover, carries out 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 conducted 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 sphere of manufacture of pharmaceuticals, good clinical and laboratory practices, and issuance 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 aimed at eliminating a potential jeopardy caused by a pharmaceutical or an excipient of inadequate quality, including assessments of the measures proposed/adopted by the regulated entities. It is also in charge of issues of counterfeit and 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 submitted as per 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 safeguarded by the Advertising Regulation Unit. The Unit carries out investigations into complaints pertaining to inappropriate advertising for HMPs and provides expert opinions on advertising materials and on advertising regulation issues. The Unit is, moreover, involved in enforcement in those cases where illegal situation has been identified – i.e., illegal handling of pharmaceuticals, and also in decision-making on whether a specific product is a medicinal product or not.

4.6 LABORATORY CONTROL

Laboratory control is carried out by the Laboratory Control Department both within the scope of requirements set forth by the Act on Pharmaceuticals, i.e., the Department controls the quality of pharmaceuticals in circulation pursuant to predefined projects and releases batches of predefined medicinal products, and on the basis of internally submitted requests (requirements from 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 2022 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 2022

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
3/2021 Pharmacy samples	86	220	212	8	0
1/2021 Control of Braille on medicinal product labelling	68	68	68	0	0
8/2019 Medicinal products with implemented MA variation	6	11	11	0	0
4/2021 Medicinal products containing atomoxetine	14	28	28	0	0
BIO/3/2021 Comparison of BET assay methods	5	11	11	0	0
Expiry period of individually prepared medicinal products	7	21	15	6	3 (pharmacopoeial monographs)
Total	**186**	**359**	**345**	**14**	**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 2023, works on the following projects have been under way: control of medicinal products containing quetiapine fumarate, lisinopril and captopril, metamizole, levetiracetam, allopurinol, and verification of the microbiological quality of herbal teas. New projects have been under preparation, specifically control of medicinal products containing betahistine dihydrochloride, aripiprazole, sertraline, nimesulide, celecoxib, meloxicam, budesonide, gabapentin, and donepezil. 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. Analytical control of influenza vaccines and verification of the method of monoclonal antibody analysis by capillary electrophoresis are being planned.

Tab. 9 Batch release of predefined medicinal products

Product type	No. of medicinal products	No. of batch reports	Released on the basis of certificate	Released after lab. control	Total number of released batches	Not released	Completed within timeline
Blood derivatives	52	747	742	5	747	0	747
Vaccines	38	449	437	11	448	1*	448**

** Not released due to discontinued parallel testing by MA holder.*
*** The delay was not caused by the laboratory; adequate documentation was not provided.*

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	28	26	2
Suspected counterfeit, illegal samples*	45	-	-
International OMCL studies *	18	16	2
Internal quality control of purified water	128	128	0
Verification of quality of a reference substance for Ph. Eur.	2	2	0
Other analyses **	20	20	0
Total	**241**	**192**	**4**

** Sample compliance cannot be evaluated.*
*** E.g., requested microbiological controls, other requested analyses, etc.*

The tables above indicate that in the Laboratory Control Department, 617 sample analyses were completed. Compared to the last year, the number of samples rated as non-compliant (ex. counterfeit and illegal products) slightly decreased to 2.6 % (vs. 3.0 % in 2021; 3.2 % in 2020; 4.2 % in 2019; 5.8 % in 2018; 3.9 % in 2017). Quality defects were confirmed particularly for pharmacy samples. Otherwise, the quality of proprietary medicinal products available on the Czech market has been very good.

To the extent 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. Fig. 3 illustrates the number of released batches of blood derivatives and vaccines; for some blood derivatives, an internationally recognised certificates (OCABR – Official Control Authority Batch Release) were issued after laboratory testing.

Fig. 1 Number of sample analyses in 2017–2022

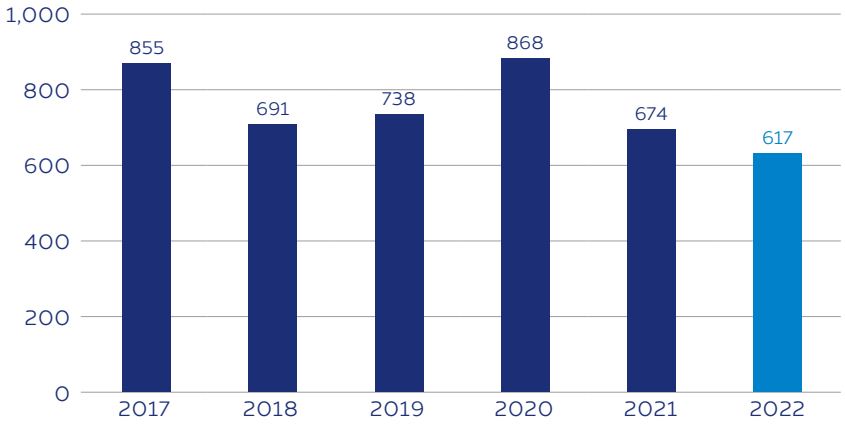


Fig. 2 Development in the number of non-compliant samples in 2017–2022 (%)

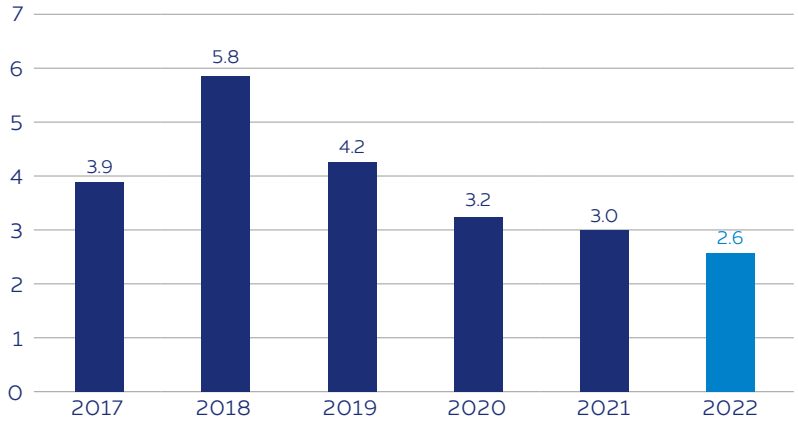
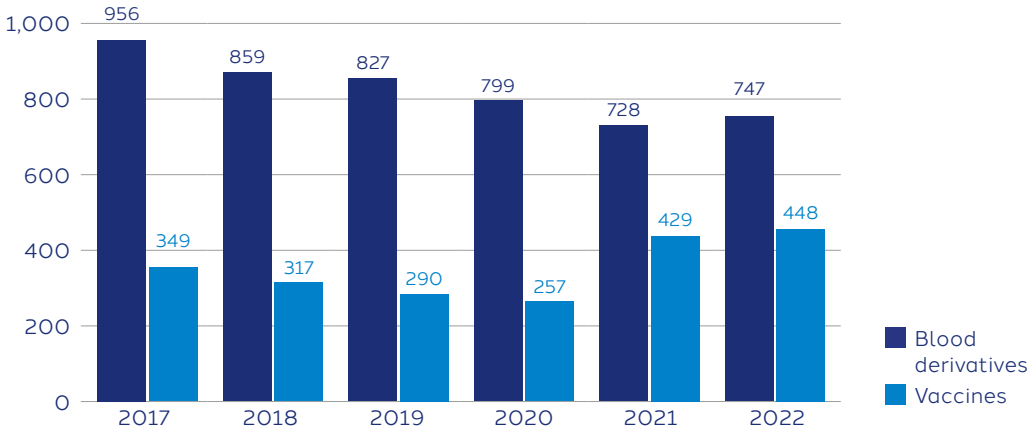


Fig. 3 Number of released batches in 2017–2022



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 the 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 2022, the Laboratory Control Department participated in collaborative international studies listed in Table 11.

Tab. 11 Participation in international studies

Study	Study name	Rating
PTS 219	Dissolution	good
PTS 225	Optical Rotation	corrective action
PTS 226	Liquid Chromatography	good
PTS 228	Refractive Index	good
CRS	Nicotine Ditartrate	good
CRS	Sodium Alendronate	good
SUP 011	Suspected Unknown Product	good
MSS 060	Olanzapine	good

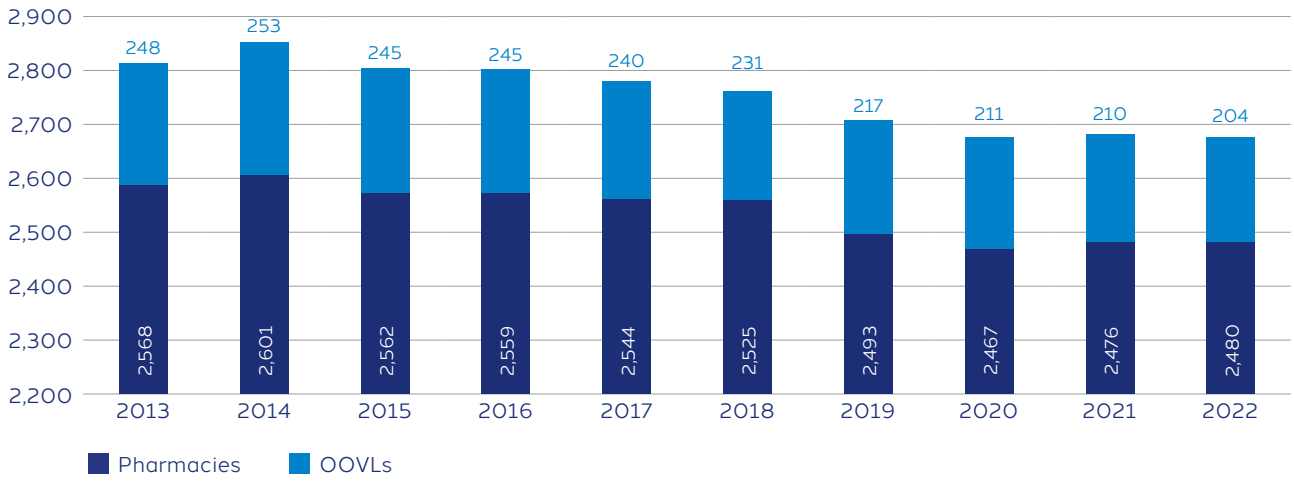
Legend to abbreviations:
PTS – Proficiency Testing Study. Quality control of the work of the laboratory; EDQM provides the samples, reference substances, and method. Once the results are sent back to EDQM, they are statistically processed, and the laboratory obtains the rating of the study.
CRS – Verification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

Supervision in the area of medicinal product handling is one of the principal activities of the Pharmacy and Distribution Department. 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 2022, the Institute kept a record on 2,480 pharmacies in total, of which four were within the scope of powers of the Ministry of Defence of the Czech Republic; moreover, the Institute kept a record on 204 detached pharmaceutical and medical device dispensing units (hereinafter referred to as "OOVL"), 3,494 vendors of selected medicinal products for human use, 42 nuclear medicine departments of healthcare facilities, 387 wholesale distributors and 53 brokers of medicinal products for human use. Compared to 2021, the total number of pharmacies increased by four entities and the number of OOVLs decreased by six units (Fig. 4).

Fig. 4 Number of pharmacies and OOVLs in the last 10 years (as of 31 December 2022)



In 2022, the inspectors of the Pharmacy and Distribution Department conducted the total of 731 inspections in pharmaceutical care facilities – pharmacies, of which 30 were hospital pharmacies of inpatient care providers. Of the total number of completed inspections, 15 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 388 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 59 final decisions on imposition of a fine for breach of obligations stipulated by the Act on Pharmaceuticals in the total amount of 17,835,000 CZK, incl. aggregate fines (see below), and on finalised administrative procedures based on inspections carried out in the previous period, and two admonitions were adopted in respect of pharmacy operators. Nine fines in the total amount of 880,000 CZK were imposed for failure to cooperate during the inspection. In three cases, the preparation of medicinal products was suspended for a pharmacy due to unverified equipment (weights used during preparation, laminar box).

The main reasons for the issuance of a decision imposing an administrative penalty included very serious shortcomings in the proper record-keeping and archival of the medicinal products received, stocked, and dispensed; dispensing of medicinal products with a quality defect for which they should have been recalled; dispensing of medicinal products without medical prescription or on invalid prescriptions, dispensing by unauthorised staff; and 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 2022, identification of major breaches of the Act on Dependency-Producing Substances resulted in the total of eleven final decisions on fine imposition upon pharmacy operators, of which the fines for offences referred to under this Act amounted to the total of 60,000 CZK. In other cases, pharmacy operators committed offences referred to also under the Act on Pharmaceuticals, and for this reason, an aggregate fine was imposed thereupon.

In the case of control of handling precursors, the total of four final decisions on fine imposition pursuant to the Act on Precursors amounting in total to 45,000 CZK was issued in 2022; in two cases, an aggregate fine was imposed.

The main reasons for the issuance of the decision on fine imposition included serious and multiple breaches of the Act on Dependency-Producing Substances in terms of record-keeping and documentation of dependency-producing substances and products, including the storage of 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.

Completed inspections focusing on compliance with price regulation rules in pharmacies identified a breach of price regulations in 39 cases. In 2022, 16 decisions on administrative penalty imposition in total became final, of which seven cases involved financial sanctions amounting to 76,000 CZK in total; in one case, an aggregate fine was imposed; and the other eight 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, two breaches 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 2022; one decision on fine imposition for the breach of the Act on Pharmaceuticals and Act on Public Health Insurance identified in the previous period became final; the fine amounted to 37,500 CZK (aggregate fine).

In 2022, moreover, 234 inspections of the handling of medicinal products in healthcare facilities were conducted. The inspections took place in three inpatient departments of healthcare service providers and in 231 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, seven targeted inspections were carried out. In total, eight final decisions on fine imposition in the total amount of 1, 140,000 CZK were issued for the identified breaches of the Act on Pharmaceuticals (this includes also finalised administrative procedures based on inspections conducted in the previous period).

The major reasons for the 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; handling of medicinal products 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, particularly incorrect storage of medicinal products or failure to keep the required regulatory documentation and documentary records.

In 2022, inspections of vendors of selected medicinal products involved 109 outlets in total. Seventeen final decisions on fine imposition in the total amount of 254,000 CZK for breach of the obligations implied by the Act on Pharmaceuticals were issued.

In other healthcare facilities authorised to prepare medicinal products (Nuclear Medicine Departments [ONM] and workplaces preparing autogenous vaccines for human use [HAV]), 18 inspections in total were carried out; the findings from the inspections resulted in the proposition of imposition of two administrative penalties (a fine and an admonition).

Summary results from inspections completed in 2022 are provided in Table 12.

Tab. 12 Inspection surveillance over pharmacies, nuclear medicine departments, healthcare facilities, and vendors of selected medicinal products in 2022

Inspected entity	Inspection type	Number	Classification of defects						Penalties		
			1	%	2	%	3	%	A	B	C
Pharmacies	Regular inspections	731	450	61.6	178	24.4	103	14.0	3	-	70
	Price controls	100	Not rated by classification of defects						-	-	16
	Inspections of dependency-producing substances and precursors	388	314	80.9	59	15.2	15	3.9	-	-	15
ONMs		13	7	53.8	5	38.5	1	7.7	-	-	0
HAVs		3	1	33.3	2	66.7	-	-	-	-	0
Healthcare facilities		234	173	69.7	47	25.2	14	5.1	-	-	8
Vendors of selected medicinal products		109	80	73.4	11	10.1	18	16.5	-	-	17

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 2022, inspectors from the Pharmacy and Distribution Department took a total of 221 samples of medicinal products during inspections in pharmacies, of which 72 were samples of pharmaceutical products intended for the preparation of magistral formulas in the pharmacy. Out of 149 pharmacy samples (medicinal products prepared in pharmacies), only two were out-of-specification: in one case, the defect was out-of-specification content of the active substance; the other concerned the presence of an undeclared antimicrobial ingredient. 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 2022, the total of 200 requests for issuance of an opinion were received from pharmacy operators and 204 favourable binding opinions were issued.

In 108 cases, the issuance of the binding opinion was associated with an inspection in the pharmacy (on-the-spot check of technical and material equipment) and in five cases, with an inspection of the OOVL (Table 13 refers). Furthermore, in this context, 113 consultations on the technical equipment of existing pharmacies or the construction of new pharmacies, and 416 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 Další činnost Odboru lékárenství a distribuce

Initial pharmacy inspection	Establishment of a new pharmacy/ OOVL	Defunct pharmacies/OOVLs
108	77/7	73/13
Initial OOVL inspection	**Consultations on material and technical equipment**	**Other consultations**
5	113	416

DISTRIBUTION OF MEDICINAL PRODUCTS

In 2022, the number of distributors exhibited a year-to-year increase by two entities to the total of 387 medicinal product distribution authorisation holders. Of the total number of authorised distributors, 94 entities were both a distribution authorisation holder and a pharmacy operator.

In 2022, 21 new distribution authorisations and 129 decisions on variations to distribution authorisations were issued, and 19 authorisations were revoked upon request of their holders. The distribution authorisations were not expired as per Section 76(4) of the Act on Pharmaceuticals and in one case the authorisation was revoked by the decision of the Institute pursuant to Section 76(3) of the Act on Pharmaceuticals.

The total of 15 entities applied for entry into, variation to entry in, or deletion from the Registry of Brokers of Human Medicinal Products in 2022; as of 31 December 2022, the Registry included 53 brokers in total.

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

Tab. 14 Distribution and brokerage of pharmaceuticals in 2022

	Received applications	Decisions issued/Registry entries made
Application for distribution authorisation		
Application for variation to distribution authorisation	124	129
Application for revocation of distribution authorisation	17	19
Application for entry in the Registry /variation to entry in the Registry/deletion from the Registry	15	13

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

In 2022, the total of 277 inspections of distributors and eleven inspections of brokers were conducted, of which eight were targeted inspections carried out on the basis of internal and external reports. In total, twelve reports on the operation of distributors were received, in respect of which no serious shortcoming in the observance of Good Distribution Practice (GDP) was identified.

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 distribution and export, and control of compliance with the distributor's obligations associated with the verification and checks of safety features in respect of those medicinal products that bear such features.

Of the total number of 225 rated inspections of distributors (follow-up and targeted inspections), 75.5 % were rated with grade 1 (good), 19.5 % with grade 2 (satisfactory), and 5 % with grade 3 (not satisfactory). On the basis of identified facts, in 23 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 179 post-inspection Good Distribution Practice Certificates were issued, of which eleven Certificates were of limited validity or scope (for two years in six cases; five were with restricted storage scope). 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 64 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).

75.5 %

inspections of distributors were rated with grade 1 (good)

In 2022, 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 carried out. A breach of pricing regulations was identified in two cases and they consisted of 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 and application as required by the pricing authority pursuant to Section 5(5) of the Act on Prices. In 2022, three fines in the total amount of 9,065,000 CZK were finally imposed upon distributors for committed pricing offences.

In 2022, on the basis of facts identified during the completed inspections, distributors were imposed the total of 21 final decisions on fines for breaches of obligations set forth by the Act on Pharmaceuticals and its implementing regulations amounting to 6,060,000 CZK in total (incl. also finalised administrative procedures based on inspections conducted in the previous period). One final decision on imposition of a fine in the amount of 50,000 CZK was 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 distribution of medicinal products outside the territory of the Czech Republic contrary to a measure issued by 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; as well as failure to file an application for variation to the distribution authorisation in case of changes concerning the distributor; and failure to verify safety features of medicinal product labelling along with failure to comply with the obligation to notify SÚKL of suspected counterfeit medicinal products.

In one case, the distribution authorisation was suspended and declaration of non-conformity with GDP rules was issued due to serious breaches of the obligations implied by the Act on Pharmaceuticals and conditions of Good Distribution Practice; this were entered in the EudraGMDP database.

The results of inspections at distributors in 2022 are shown in Table 15.

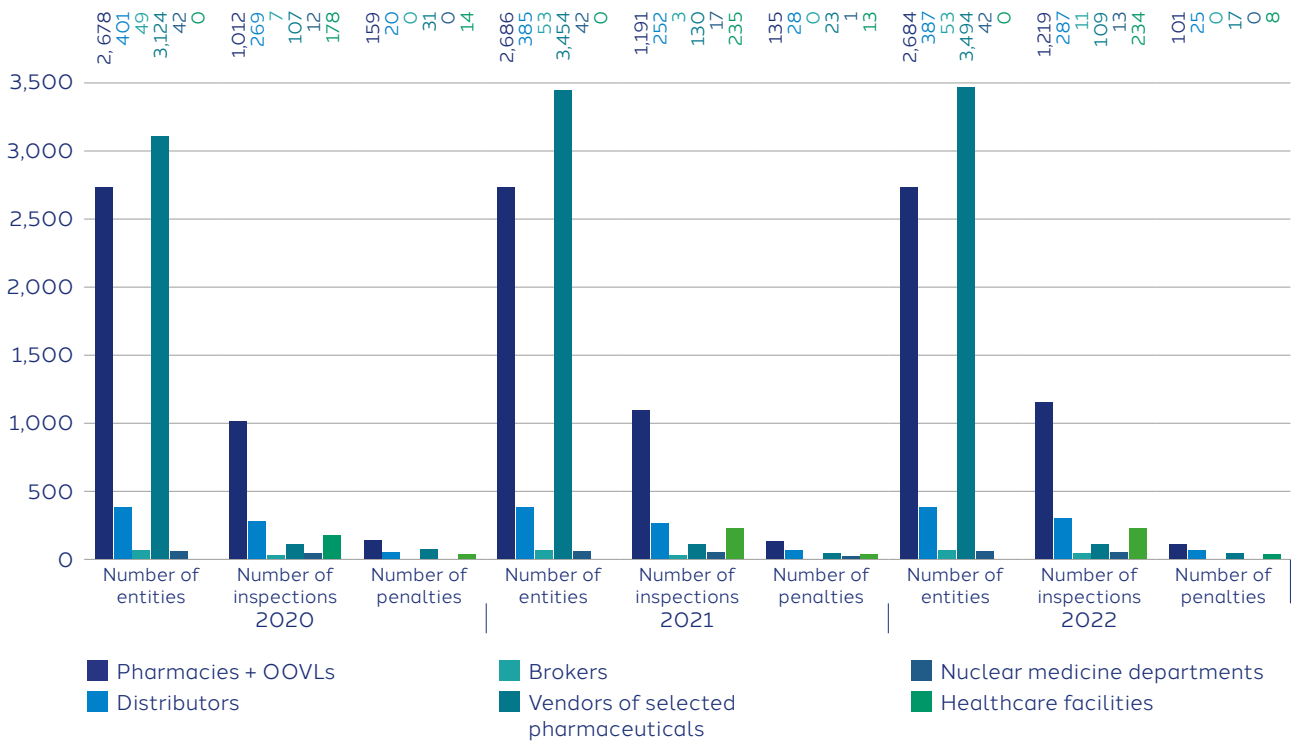
Tab. 15 Inspection surveillance over distributors

Number of inspections					Inspection rating			Measures	
Total	Initial	Follow-up	Targeted	Variation	1	2	3	NCR	Proposed fine
277	21	217	8	31	170	44	11	1	23

Inspection Rating
Inspections are rated on the basis of the identified shortcomings and their severity, and according to the achieved point score, the overall level of com pliance with the principles of Good Distribution Practice is expressed by the following rating:
1 – Good; 2 – Satisfactory; 3 – Not satisfactory.

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

Fig. 5 Information on surveillance activities in 2020–2022



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. The Department also conducts 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 on the Institute's website.

In the sphere of manufacturers (incl. blood centres), the total of 112 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.

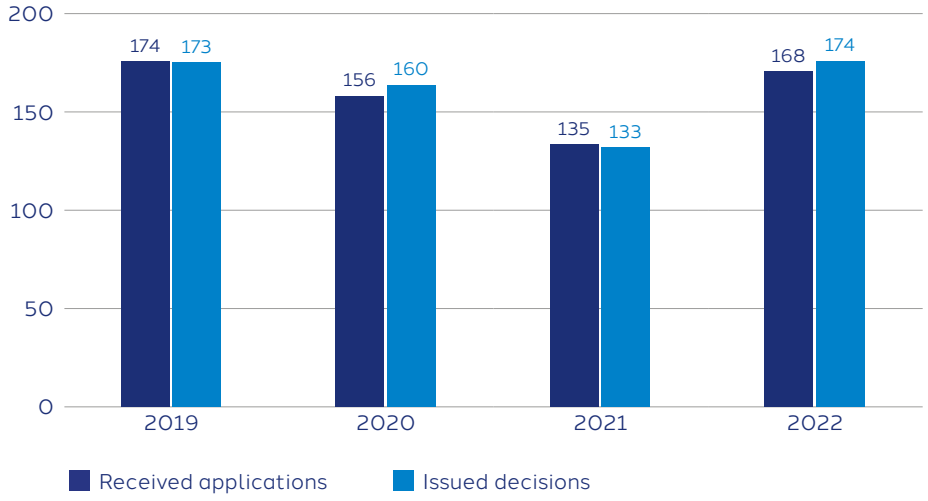
In 2022, 48 applications for authorisation to engage in an operation and applications for variations thereto were received.

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

Application type		2019		2020		2021		2022	
		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	2	4	4	1	0	3	2
	Control laboratories	1	3	0	0	1	1	1	1
	Blood centres	3	3	1	1	3	3	3	3
Application for variation to manufacturing authorisation	Manufacturers of medicinal products	59	60	53	52	53	53	52	55
	Control laboratories	1	1	5	5	2	2	6	6
	Blood centres	45	44	49	47	39	43	47	46
Application for manufacturing authorisation revocation	Manufacturers of medicinal products	4	5	6	6	2	2	3	3
	Control laboratories	1	1	0	0	1	1	0	0
	Blood centres	0	0	0	0	0	0	1	1
Application for operating authorisation for:	Tissue centre	1	1	1	3	0	1	2	2
	Distribution of tissues and cells	1	1	1	1	0	0	0	0
	Donation centre	0	0	0	0	0	0	0	0
	Diagnostic laboratory	1	0	0	1	1	1	1	1

Application type		2019		2020		2021		2022	
		Received applications	Issued decisions	Received applications	Issued decisions	Received applications	Issued decisions	Received applications	Issued decisions
Application for variation to operation of:	Tissue centre	43	38	27	32	29	24	41	46
	Distribution of tissues and cells	0	1	0	0	0	0	0	0
	Donation centre	0	0	0	0	0	0	2	2
	Diagnostic laboratory	9	9	7	7	2	2	4	4
Application for revocation of operation of:	Tissue centre	0	1	1	1	0	0	0	0
	Distribution of tissues and cells	0	0	0	0	0	0	1	1
	Donation centre	2	2	1	1	0	0	0	0
	Diagnostic laboratory	1	1	0	0	0	0	1	1
Total		**174**	**173**	**156**	**160**	**135**	**133**	**168**	**174**

Fig. 6 Numbers of received and decided applications



In 2022, 256 inspections in total were conducted, of which 73 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 2019-2022 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 performed 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 98 inspections at manufacturers of medicinal products and active substances or in control laboratories, no breach of law was identified. The GMP standard in blood centres was rated mostly as good and 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 2022 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	**48**	2	39	1	6	48	0	0	0
Manufacturers of investigational medicinal products	**14**	2	9	1	2	14	0	0	0
Manufacturers of active substances	**17**	5	9	0	3	17	0	0	0
Control laboratories	**12**	1	11	0	0	12	0	0	0
Control laboratories for investigational medicinal products	**2**	0	2	0	0	2	0	0	0
Active substance importers	**5**	1	4	0	0	5	0	0	0
Blood centres	**52**	1	42	0	9	52	0	0	0
Blood banks	**12**	0	12	0	0	12	0	0	0
GCP inspections – Ethics Committees	**1**	0	0	1	0	0	0	0	0
GCP inspections – others	**20**	0	0	20	0	20	0	1	1
TC, DC, DL, DIS inspections	**73**	3	62	1	7	71	2	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 2019–2022

	2019		2020		2021		2022	
	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	59	2	56	1	67	4	62	0
Manufacturers of active substances	23	3	22	0	33	1	17	0
Control laboratories	17	0	10	0	19	0	14	0
Active substance importers	4	0	4	0	4	0	5	0
Blood centres	64	0	62	0	77	0	52	0
Blood banks	11	0	2	0	3	0	12	0
GCP inspections + ethics committees	33	1	21	0	19	0	21	1
Tissue centres, donation centres, diagnostic laboratories	59	0	53	0	59	0	73	0
Total	**270**	**6**	**230**	**0**	**281**	**1**	**256**	**1**

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

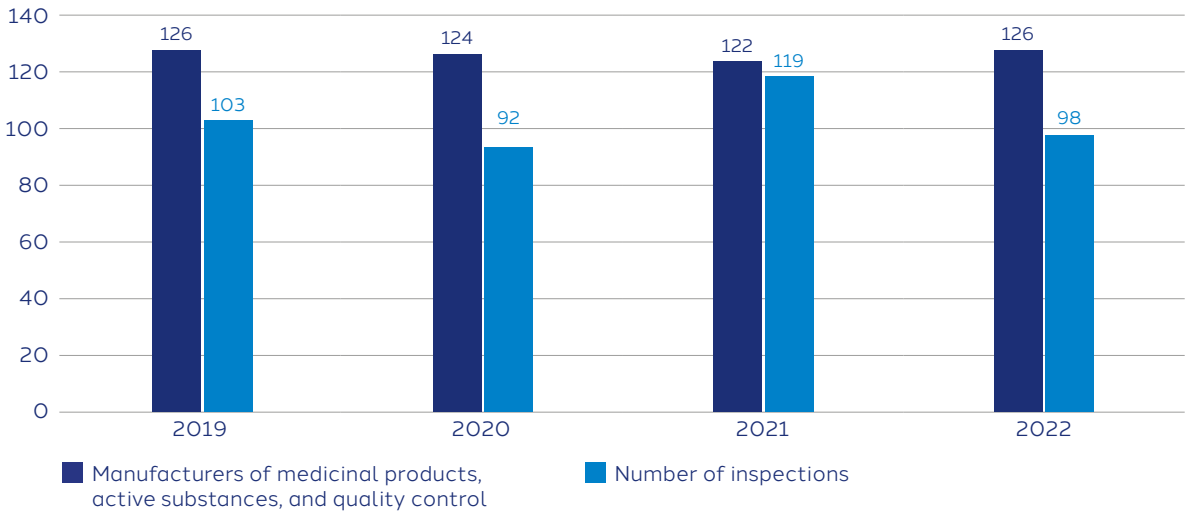
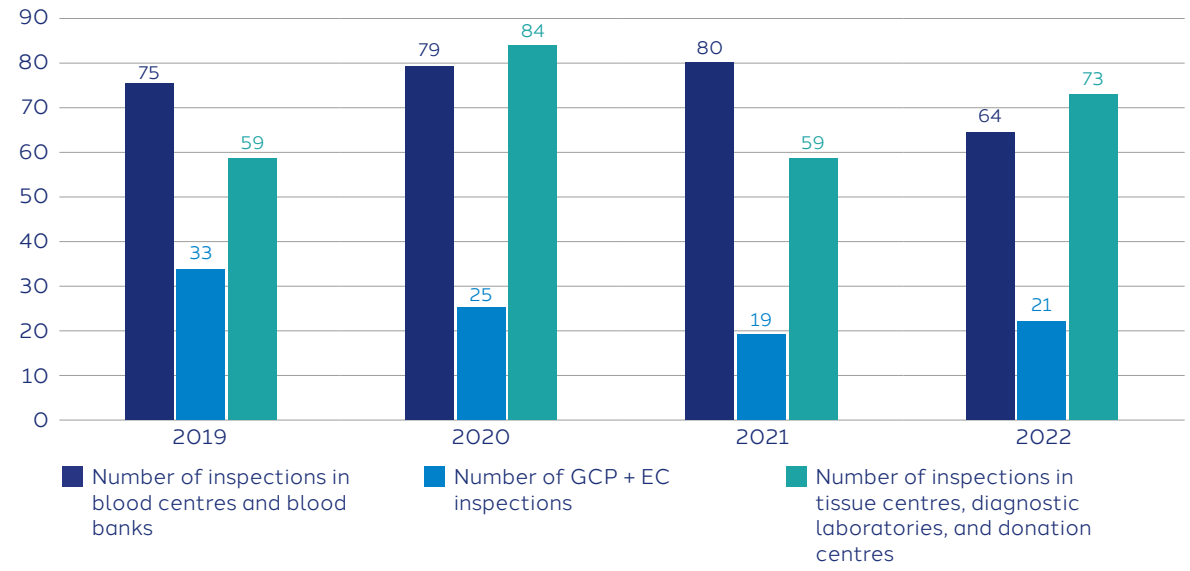


Fig. 8 Overview of conducted inspections in the area of blood centres + blood banks, GCP + EC, and HTC (tissue centres, diagnostic laboratories, donation centres) in the period of 2019–2022



HAEMOVIGILANCE

In 2022, 35 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 four reports are still pending and in five cases, the suspected SAR was not confirmed. Ten SARs involved blood or blood component donors (two investigations are still pending) and 25 SARs concerned post-transfusion reactions in transfusion product recipients, of which, two investigations are still pending; the investigations concern nine cases of anaphylaxis; four cases of transfusion-associated circulatory overload (TACO), one of them still pending; four cases of haemolytic reactions arising from ABO system incompatibility, one of them still pending; two cases of transfusion-related acute lung injury (TRALI), one case of febrile non-haemolytic reaction, and five cases of suspected HBV transmission due to occult hepatitis of the donor (in two cases, HBV was not transmitted to the patient; in three cases, it was not possible to re-examine the TP donor). In all of the concluded SARs concerning blood or blood component donors, full recovery of the donor was confirmed; of the concluded SARs concerning TP recipients, one SAR resulted in mild consequences for the TP recipient, five recipients died but their death was not related to the transfusion; all other SARs resulted in full recovery.

Furthermore, 13 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. Six cases did not constitute a SAE; of the confirmed SAEs, one case concerned detected occult hepatitis B of the donor, two cases confirmed anti-HBc positivity of the donor (incl. previous donations), two cases identified non-sterility of manufactured TPs, and two cases constituted TP confusion at a clinical 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 2022, the Institute received the total of eleven reports from six countries. Eight cases concerned an epidemiological situation (five were associated with the occurrence of the West Nile virus fever, two were associated with the occurrence of monkeypox, and one was associated with the occurrence of the dengue fever); two cases concerned information about the arrangement of measures during the occurrence of the West Nile virus fever and one case a warning against technical problems (defective collection sets).

21

conducted Good Clinical Practice inspections

GOOD LABORATORY PRACTICE (GLP)

In 2022, 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, seven follow-up inspections were carried out.

GOOD CLINICAL PRACTICE (GCP)

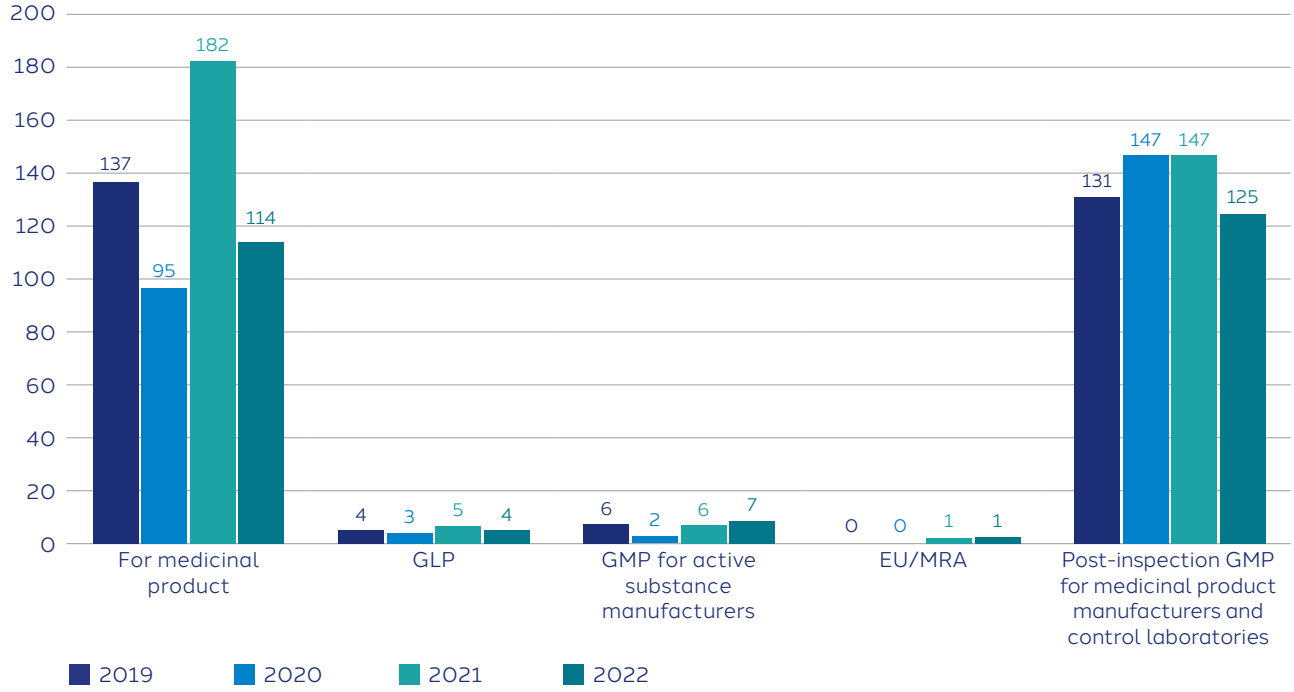
Due to the emergency measures associated with the COVID-19 pandemic, in 2022, the number of Good Clinical Practice inspections was reduced compared to previous periods.

In the course of 2022, the total of 21 Good Clinical Practice inspections were conducted. Of the said number, 18 concerned a targeted inspection of a clinical trial site (a GCP inspection at the investigator's site), one was an inspection of compliance with the obligations of an ethics committee, and two were inspections on the basis of an application for the issue of a Good Clinical Practice Certificate carried out at a healthcare service provider where a first-in-human (FIH) clinical trial is conducted.

CERTIFICATION

In total, 251 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 1,048 cases were received; all of them were processed within predefined timelines.

FOREIGN INSPECTIONS

In 2022, six Good Manufacturing Practice inspections at foreign entities were conducted, of which one via remote assessment, and two Good Clinical Practice inspections of foreign entities took place.

Tab. 19 Foreign inspections

	2019	2020	2021	2022
Number of inspections	7	2	3	6
Certificate issuance	4	1	3	6
Issued non-compliance	1	0	0	0

MEDICAL CANNABIS

As of 01 January 2022, the amended Act on Dependency-Producing Substances has been effective; it stipulates new provisions on the licencing of medical cannabis growing. In the Institute, it is the GMP Unit of the Inspection Department who is in charge of this agenda. In 2022, the Institute granted five licenses for medical cannabis growing.

Until March 2022, the Inspection Department was also involved in activities aimed at ensuring availability of the medical cannabis active substance from a Czech grower for Czech patients. In 2022, the Institute took over and placed into distribution the last delivery of 920 grams of medical cannabis based on contract VZ31/2019 from the winner of the public contract for medical cannabis supply, Elkoplast Slušovice s.r.o. Furthermore, until March 2022, the Institute supervised the arrangements for safe storage, transport, and distribution of medical cannabis to pharmacies via the Institute's contract distributor, Alliance Healthcare, s. r. o. It also safeguarded the pricing of medical cannabis for pharmaceutical care facility operators and the administration of published medical cannabis pricelist. The Inspection Department was drafting expert source materials on medical cannabis issues for the Press and Information Unit, other regulatory units and the Management of the Institute.

Furthermore, the Inspection Department was in charge of ensuring compliance with the Institute's information and notification obligations in respect of the Czech Police and the Ministry of Health of the Czech Republic, as required by Act No 167/1998 Coll., on Dependency-Producing Substances. Current information on legislative amendments and monthly statistics of medical cannabis dispensing in the Czech Republic were regularly published on the www.sakl.cz website.

Tab. 20 Cannabis dispensing in 2022 by month

	January	February	March	April	May	June
No. of issued e-prescriptions	2,055	1,872	2,275	2,088	2,401	2,347
No- of patients prescribed medical cannabis (unique)	1,721	1,580	1,816	1,743	1,973	1,961
Dispensed medical cannabis amounts (g)	11,607.63	10,526.19	12,362.23	11,620.87	13,202.40	13,758.58

	July	August	September	October	November	December
No. of issued e-prescriptions	1,959	2,221	2,364	2,311	2,591	2,394
No- of patients prescribed medical cannabis (unique)	1,694	1,886	1,985	1,993	2,194	2,117
Dispensed medical cannabis amounts (g)	12,391.75	13,282.76	14,236.64	13,606.73	16,004.46	14,847.56

4.9 QUALITY DEFECTS OF PHARMACEUTICALS AND COUNTERFEIT PRODUCTS IN THE LEGAL DISTRIBUTION CHAIN

Since 2015, the number of reports in the area of quality defects of pharmaceuticals has been increasing (Table 21 refers). A major increase in the number of reports was seen in 2022; this included both reports received from the Czech Republic and from foreign countries (Fig. 10 refers). This is, inter alia, due to the increased field awareness to report quality defects and the new possibility to avail of electronic forms that make reporting easier. The growing number of reports from abroad is given by a higher involvement of non-European regulatory authorities in the information system via which quality defect reports are being received.

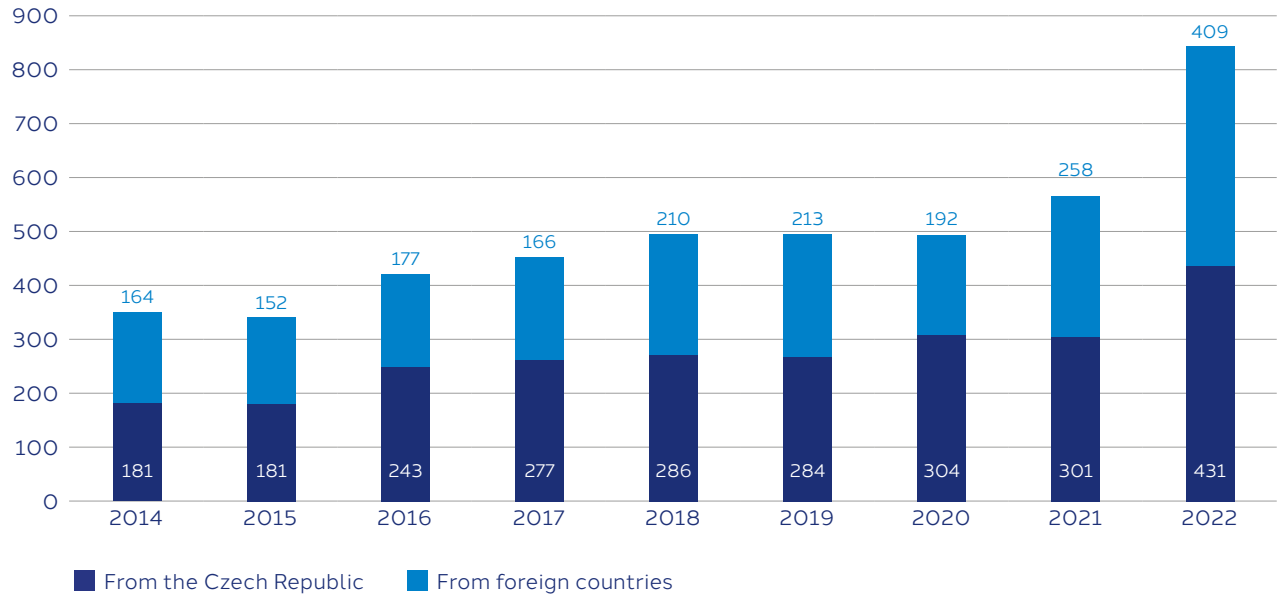
Tab. 21 Number of reports received in 2022

Quality defects	2014	2015	2016	2017	2018	2019	2020	2021	2022
Reports received in total	345	333	420	443	496	497	496	559	840
Reports from the Czech Republic	181	181	243	277	286	284	304	301	431
Reports from abroad	164	152	177	166	210	213	192	258	409
Resulted in recall (in SÚKL codes)	60	79	72	79	89	59	47	54	38
Administrative procedure (since 04/2017)	-	-	-	20	33	81	55	80	99
Rapid Alert	6	11	17	22	6	15	1	8	10

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

As part of addressing quality defects, effective actions have been taken to reduce the impact of quality defects of pharmaceuticals upon patient health. Just like in previous years, in 2022, 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 manufacture of medicinal products and for the preparation of medicinal products in pharmacies. Through the international Rapid Alert System involving the EU, MRA, and PIC/S Member States, the Institute received and evaluated the total of 409 reports on quality defects. The proportion of received Czech and foreign reports is illustrated by Fig. 10.

Fig. 10 Number of received reports from 2014 to 2022

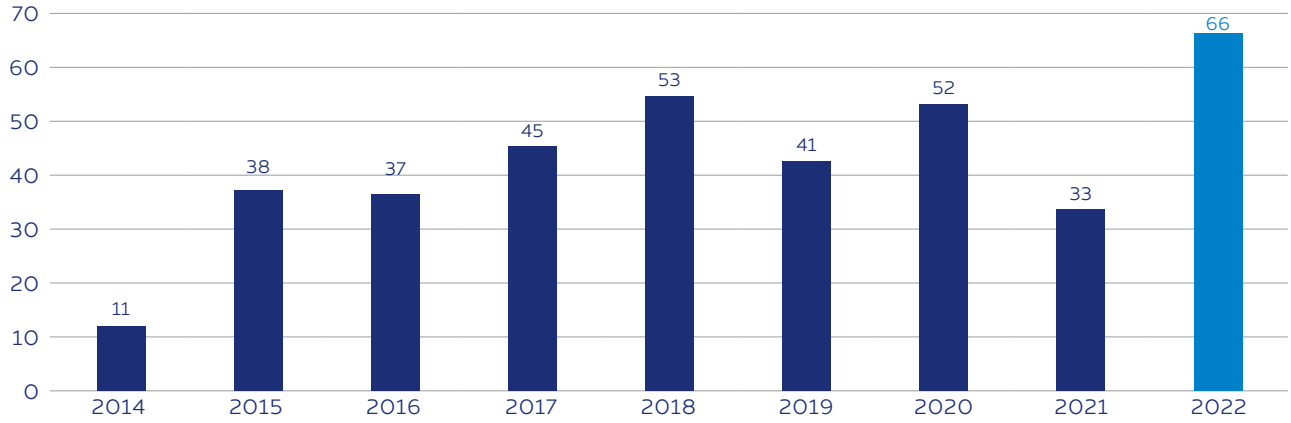


In case of a quality defect of a pharmaceutical not constituting a jeopardy to the life or health of people, the Quality Defects Unit issues a decision on allowing the distribution, dispensing, placement into circulation, and use of such pharmaceutical or its particular batch in the provision of healthcare services. In 2022, 99 administrative procedures in total were commenced and 99 final decisions were issued; these concerned 530 batches of medicinal products (283 SÚKL codes).

Since May 2022, the Quality Defects Unit has been publishing information letters for operators specifying the quality defect for which a decision on keeping the pharmaceutical on the market or a warning of a quality defect of a pharmaceutical or a condition that could be considered defective has been issued. In 2022, ten information letters were published.

The Quality Defects Unit addresses also reports concerning the presence of counterfeit medicinal products in the legal distribution chain or their theft. In 2022, the Quality Defects Unit addressed 66 such cases in total, of which three concerned thefts of medicinal products from the legal distribution chain. An overview of addressed reports concerning the presence of counterfeit products and stolen medicinal products is provided in Fig. 11.

Fig. 11 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 pharmaceutical. In 2022, the Quality Defects Unit received and evaluated 156 such reports in total.

Furthermore, the Quality Defects Unit monitored the recall of two medicinal products (in SÚKL codes) for marketing authorisation reasons (reduced shelf-life).

An overview of measures implemented in 2022 for individual medicinal products (in SÚKL codes) is provided in Table 22. All of these cases concerned measures taken by the marketing authorisation holders or operators themselves; the Institute was only monitoring or adjusting their actions.

Tab. 22 Measures implemented in 2022 (related to SÚKL codes)

Implemented measures	**Počet**
Recall from distributor level	0
Recall from healthcare facility level	34
Recall from patient level	4
Suspended distribution, dispensing and/or use	11
Released distribution, dispensing, and use	4
Permitted distribution, dispensing, marketing, and use in the provision of healthcare services through an administrative procedure	283 (number of batches: 530)

The Quality Defects Unit was involved in the adaptation of Regulation 161/2016, supplementing Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use (hereinafter referred to as the "Safety Feature Regulation"). In the course of 2022, the first inspection of the repository of the National Organisation for Medicines Verification (Národní organizace pro ověřování pravosti léčiv, z. s.; NOOL) was conducted. The representatives of the Institute participated in the meetings of the expert group for safety features, in international teleconferences, and regular meetings with NOOL.

During 2022, the Institute recorded the total of 16,248 reports on unsuccessful safety feature verification (for the entire period from 09 February 2019 to 31 December 2022, this number amounted to 1, 191,610 reports in total). In the course of the year, the Quality Defects Unit communicated with 28 marketing authorisation holders in respect of whose products a high number of such reports was identified. In the course of 2022, the Unit issued favourable recommendations for the total of nine medicinal products and twelve 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 15 reports concerning suspected broken anti-tamper devices (ATDs), incl. other cases of non-compliances with Regulation No 2016/161.

4.10 ENFORCEMENT

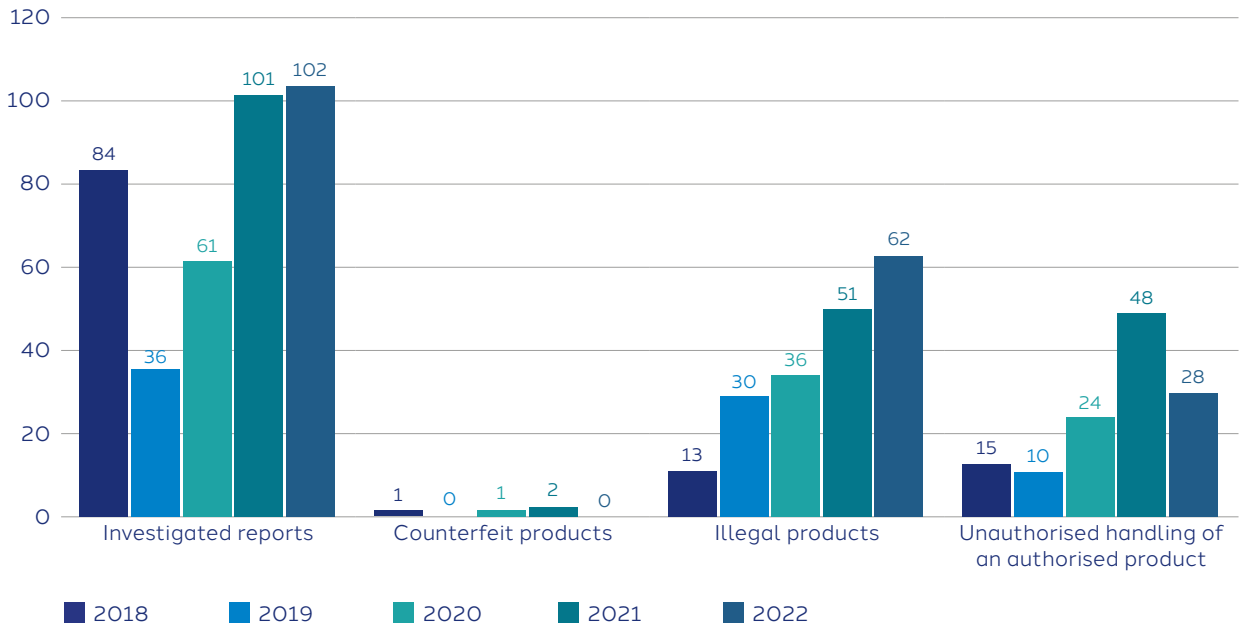
In 2022, active surveillance in the area of illegal handling of medicinal products focused particularly upon the identification, investigation, and penalisation of cases of distribution and sales of medicinal products by unauthorised persons and upon monitoring of the internet environment, where illegal 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 of potentially international impact.

In 2022, the total of 102 reports (either the Institute's own or received reports) were investigated. In 2022, the Institute was monitoring and detecting illegal offers of medicinal products in the internet environment and executed 28 control purchases. Sixty-two cases of handling of unauthorised medicinal products and 40 cases of unauthorised handling of authorised medicinal products were identified.

62 cases of handling unauthorised medicinal products

and **40** cases of unauthorised handling of authorised medicinal products.

Fig. 12 Control activities in the period of 2018–2022



In 2022, the Institute prepared the total of 424 opinions on shipments from third countries for the customs authorities for the purposes of release or 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 in 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).

In accordance with its new power pursuant to the provision of Section 13(3)(s) of Act No 378/2007 Coll., on Pharmaceuticals and on Amendments to Some Related Acts (the Act on Pharmaceuticals), since 01 January 2022, the Institute has been keeping a list of websites offering medicinal products contrary to this Act (hereinafter referred to as the "list of websites with illegal medicinal product offer"); the list is being published by the Institute on its website. In 2022, the Institute investigated 155 cases of websites with illegal medicinal products offer and listed 140 websites.

4.11 SURVEILLANCE IN THE AREA OF REGULATION OF ADVERTISING FOR MEDICINAL PRODUCTS

In 2022, the Institute investigated the total of 143 reports of suspected breaches of Act No. 40/1995 Coll., on Advertising Regulation, as amended (hereinafter referred to as the "Act on Advertising Regulation"); the Institute completed 13 administrative procedures, which resulted in the imposition of 14 fines for breaches of the Act on Advertising Regulation in the aggregate amount of 2,380,000 CZK.

Tab. 23 Overview of investigated reports of suspected breaches of the Act on Advertising Regulation in 2022

	Reports brought forward from 2021	Newly received reports in 2022	Total
Number of reports	5	138	143
Investigation completed	5	100	105
Forwarded for commencement of administrative procedure	0	22	11
Completed administrative procedures	0	2	2
Number of finally imposed fines	0	2	2

The subject of investigations into advertising was printed advertising matter (56 %) and websites (44 %).

Advertising for prescription-only medicines accounted for 67 % of the investigated cases, advertising for over-the-counter medicines represented 33 % of cases.

Pharmaceutical companies or their legal representatives filed 20 % of reports on suspected breaches of law, 20 % of reports were lodged by private individuals, 1 % by state administration authorities, and 59 % by SÚKL employees.

Fig. 13 Overview of investigated reports of suspected breaches of the Act on Advertising Regulation (2018–2022) (%)

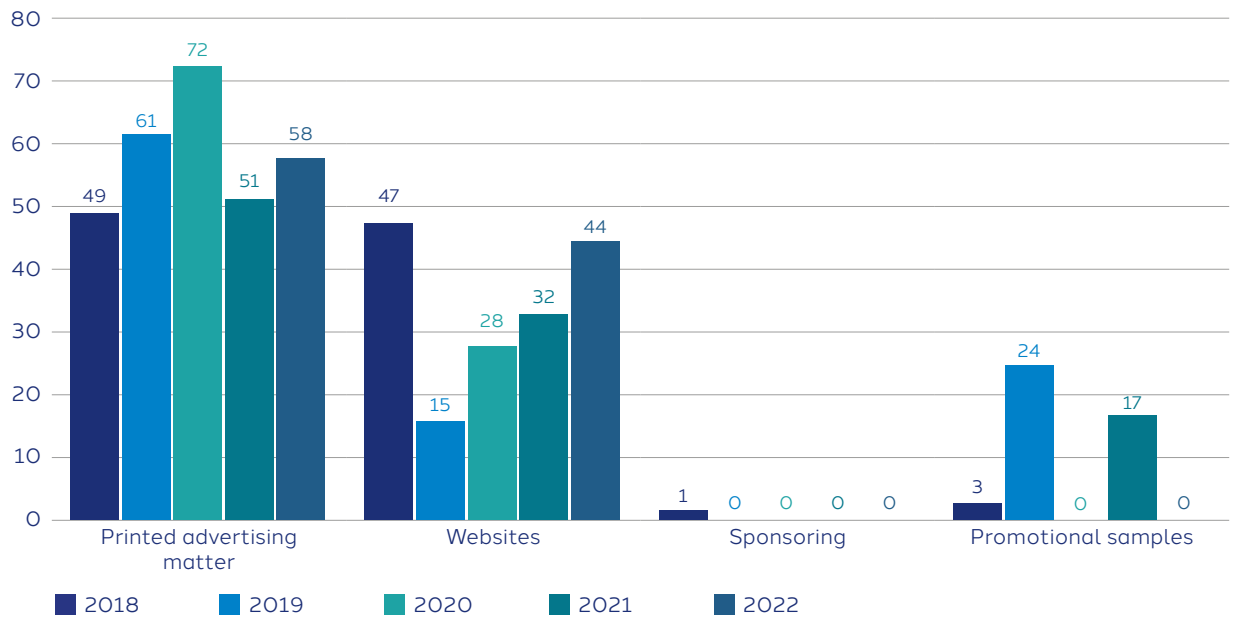
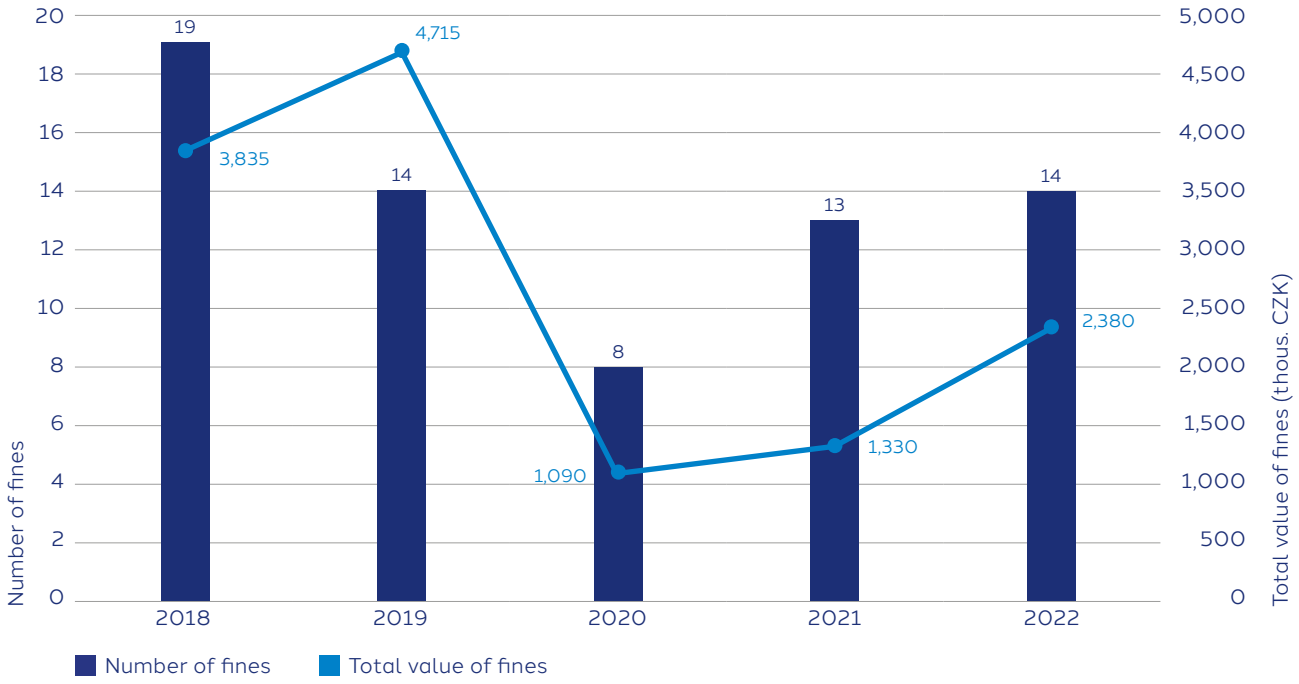


Fig. 14 Overview of fines imposed for breaches of the Act on Advertising Regulation (2018–2022)



Upon request, the Institute issued/provided 37 expert opinions/consultations on the issue of proposed advertising for medicinal products for human use.

The inspectors of the Advertising Regulation Unit completed 23 inspections of compliance with the Act on Advertising Regulation and the Act on Pharmaceuticals.

SURVEILLANCE IN THE AREA OF DECISION-MAKING ABOUT PRODUCT CLASSIFICATION

In 2022, the Institute commenced investigation into 96 cases of various products, most often dietary supplements and cosmetic products, for suspected classification as a medicinal product. In 22 cases, an administrative procedure regarding product classification was initiated ex officio or upon request. In 2022, the Institute reclassified the total of 40 products to the group of medicinal products. Upon request, it provided one expert opinion on issues regarding product classification as a medicinal product or another product.

4.12 STANDARDISATION AND PHARMACOPOEIAL ACTIVITIES

In the first half of 2022, the Pharmacopoeia employees prepared for print the Fifth Supplement to Czech Pharmacopoeia 2017 – Supplement 2022 (hereinafter referred to as "Suppl. 2022"). In its European part, it contains the translations of three supplements to the Tenth Edition of European Pharmacopoeia (Ph. Eur. 10.0, Suppl. 10.6, 10.7, and 10.8).

Czech Pharmacopoeia 2017 – Supplement 2022 was published in cooperation with the Grada Publishing house in one volume as binding from 01 December 2022 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 cumulative and it contains all unrevised texts of Czech Pharmacopoeia 2017 along with new and revised texts of Suppl. 2018, Suppl. 2019, Suppl. 2020, Suppl. 2021, and Suppl. 2022.

The European part of Czech Pharmacopoeia contains the total of 275 texts, of which the General Part includes 25 general texts (of which five are new ones), eight revised general articles, and five revised general articles concerning pharmaceutical forms. The Special Part contains 30 revised articles for vaccines for human use and four articles for vaccines for veterinary use (of which one is new), seven revised articles for radiopharmaceuticals, 25 articles for herbal drugs (of which ten are new ones), three articles for homeopathic preparations (of which two are new ones), and 167 chemical and biological articles for active substances, excipients, and medicinal products (of which seven are new ones).

The National Part of Czech Pharmacopoeia – Suppl. 2022 contains ten texts in total.

Its General Part includes the full version of Tables II, III, IV, V, VI, X, and XII, which contain active substances included in Czech Pharmacopoeia 2017, in Suppl. 2018, Suppl. 2019, Suppl. 2020, Suppl. 2021 as well as this Supplement. The General Part contains an overview of updated testing agents and reference substances used in national monographs.

The Special Part contains revised articles Althaeae sirupus, Cremor refrigerans, and Sulfuris suspensio.

Tab. 24 Number of texts in the European Part of Czech Pharmacopoeia 2017 – Suppl. 2022

European Part	General Part	Special Part	Total
New	5	20	25
Revised	34	216	250
Total	39	236	275

Along with the proof-reading and print preparation of Suppl. 2022, translations and revisions of articles from the new, 11th edition of European Pharmacopoeia (Ph. Eur. 11), which will form part of the new edition of Czech Pharmacopoeia 2023 (hereinafter referred to as Ph. Cz. 2023) were being prepared in line with the new concept of Czech Pharmacopoeia publishing which relies on reduced number of translations.

Ph. Cz. users had the option to send a request for inclusion of translation of a particular Ph. Eur. article in the Czech Pharmacopoeia. For this purpose, a list of all articles from the Special Part of European Pharmacopoeia was published on SÚKL's website (Pharmacopoeia).

Translations of all articles from the General Part of Ph. Eur. (including those without revision in edition 11), were included in the European Part of Czech Pharmacopoeia 2023. To date, approx. 450 European articles were included in the Special Part. The European Part will contain approx. 900 texts.

In cooperation with laboratories and the Pharmacy Section of the Pharmacopoeial Commission, project "Shelf-life of individually prepared medicinal products V" was carried out. It concerned the following products: Ergotamini tartras trituratus, Homatropini hydrobromidi oculoguttae, Homatropini hydrobromidi oculoguttae euacida, Atropini sulfatis oculoguttae, and Tetracaini hydrochloridi oculoguttae – and, for all of them, focused upon the possibilities of storage at room temperature. The project was completed in late 2022 and its results will be incorporated in Table XVI – Storage and shelf-life of products prepared in pharmacies – and in the relevant monographs.

In the second half of 2022, works on the National Part of Ph. Cz. 2023 commenced; the National Part will be published in full scale.

The distribution of national reference pharmacopoeial substances for national monograph Butamirati citras (five CRLN reference substances in total) and Suxamethonium-dijodid CRLN was organised.

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 regularly attended the EPC meetings and meetings of secretariats of national pharmacopoeial commissions (in 2022, these meetings were virtual).

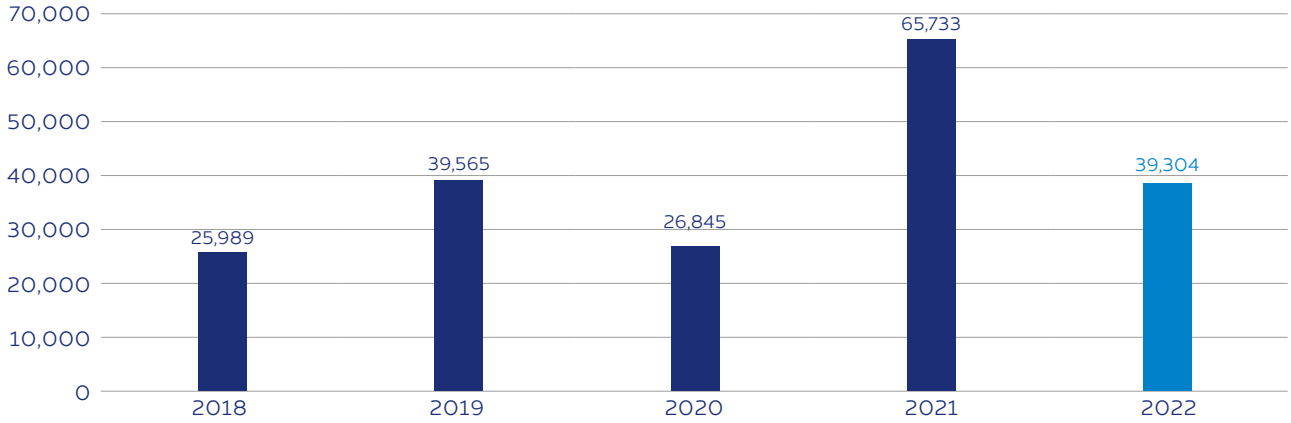
Information about the binding nature of individual Ph. Eur. editions was published in SÚKL's information media.

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 or legal entities, 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 2022. Since January 2015, the Institute has been imposing also penalties for committed offences referred to by the Act on Public Health Insurance regarding the provision of unauthorised bonuses in the dispensing of prescription-only medicinal products. In 2022, in the area of penalties, the Institute also continued 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 consider 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 2022, the Institute imposed eleven admonitions in total and 185 fines in the total amount of 39,303,500 CZK. Most often, the penalties were imposed for breaches of the Act on Pharmaceuticals (135 fines and three admonitions), the Act on Prices (eleven fines and eight admonitions) or for the breach of the Act on Advertising Regulation (13 fines).

Fig. 15 Amount of finally imposed penalties in the area of pharmaceuticals and human tissues and cells in the period of 2018–2022 (thous. CZK)



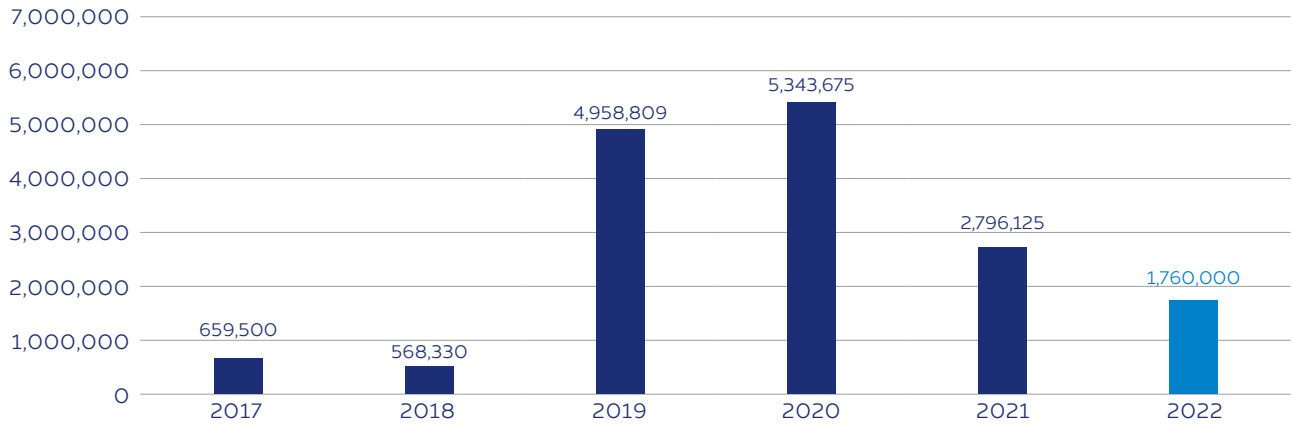
Tab. 25 Amounts of penalties in the area of pharmaceuticals and human tissues and cells in 2018–2022

Act	2018	2019	2020	2021	2022
	25,989,000 CZK	**39,565,000 CZK**	**26,845,000 CZK**	**65,733,000 CZK**	**39,303,500 CZK**
on Pharmaceuticals	19,514,000 CZK	29,079,000 CZK	24,559,000 CZK	62,237,000 CZK	26,757,500 CZK
on Drug Precursors	50,000 CZK	0 CZK	0 CZK	0 CZK	45,000 CZK
on Dependency-Producing Substances	110,000 CZK	263,000 CZK	250,000 CZK	160,000 CZK	60,000 CZK
on Prices	1,940,000 CZK	4,387,000 CZK	54,000 CZK	872,000 CZK	9,141,000 CZK
on Advertising Regulation	3,835,000 CZK	4,715,000 CZK	1,090,000 CZK	1,330,000 CZK	2,370,000 CZK
on Human Tissues and Cells	0 CZK	200,000 CZK	0 CZK	0 CZK	0 CZK
on Public Health Insurance	50,000 CZK	50,000 CZK	732,000 CZK	374,000 CZK	0 CZK
Code of Control Procedure	435,000 CZK	490,000 CZK	160,000 CZK	760,000 CZK	930,000 CZK
on Medical Devices	55,000 CZK	46,000 CZK	0 CZK	0 CZK	0 CZK
on Technical Requirements for Products	0 CZK	335,000 CZK	0 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 reports 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 act. Also in 2022, 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 2022, the Institute, moreover, continued to impose penalties in the form of so-called aggregate fines for committed offences referred to by several acts according to which it is within the powers of the Institute to consider 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 2022, the Institute imposed three 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 new Act on Medical Devices and 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. 16 Overall comparison of fines in the area of medical devices in the period of 2017–2022 (CZK)



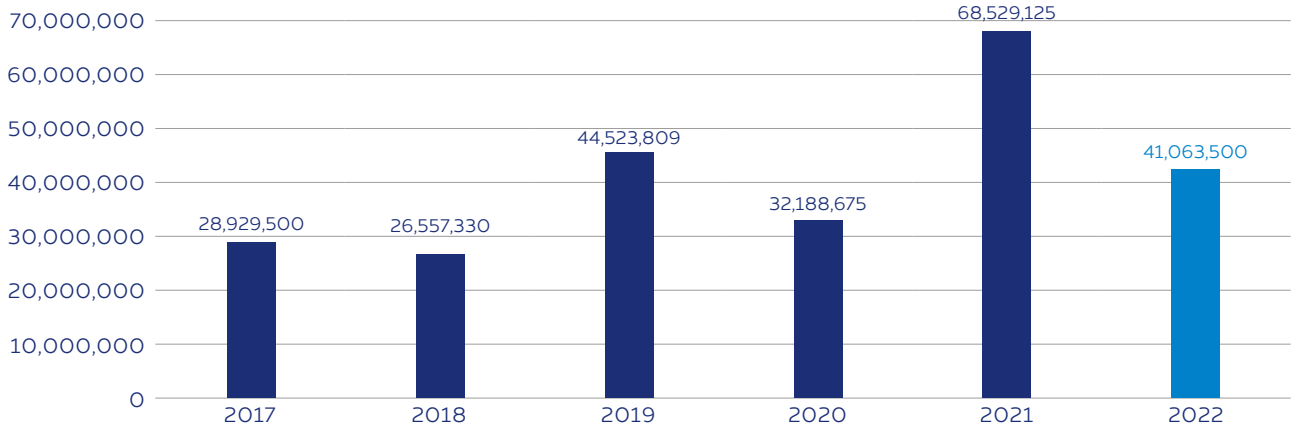
Tab. 26 Comparison of fines in the area of medical devices in the period of 2017–2022

Act	2017	2018	2019	2020	2021	2022
	659,500 CZK	**568,330 CZK**	**4,958 809 CZK**	**5,343 675 CZK**	**2,796,125 CZK**	**1,760,000 CZK**
Code of Control Procedure	0 CZK	0 CZK	0 CZK	0 CZK	50,000 CZK	250,000 CZK
on Medical Devices	559,500 CZK	568,330 CZK	3 210,058 CZK	3,723, 125 CZK	1,320,000 CZK	1,095,000 CZK
on Technical Requirements for Products	100,000 CZK	0 CZK	1,748 751 CZK	1,620 550 CZK	1,426,125 CZK	415,000 CZK

SUMMARY OF PENALTIES IMPOSED BY THE INSTITUTE IN 2022 (PHARMACEUTICALS AND MEDICAL DEVICES)

In 2022, the Institute imposed penalties in the overall amount of 41,063,500 CZK (Tab. 25 and 26 refer). In accordance with Act No 250/2016 Coll., on Liability for Offences and Procedures Pertaining Thereto, as amended, in 2022, the Institute imposed the total of 14 admonitions instead of a financial penalty.

Fig. 17 Total penalties imposed by the Institute (pharmaceuticals and medical devices) (CZK)



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 stipulated 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 initiation of an ex-officio administrative procedure may be submitted by any person.

4.14 PRICING AND REIMBURSEMENTS

In 2022, the pricing and reimbursement regulation of medicinal products and foods for special medical purposes was influenced by the adoption of Act No 371/2021 Coll., amending Act No 48/1997 Coll., on Public Health Insurance and Amendments to Some Related Acts, as amended, and some other acts. This amendment had, inter alia, a major impact upon the types of administrative procedures conducted by the Institute, as it introduced another way for orphan medicinal products to enter the reimbursement system. Specifically, this concerns a special administrative procedure for orphan products. Furthermore, the nature of administrative procedures concerning highly innovative medicinal products was substantially modified. The amendment also cancelled the instrument of maximum price in-depth revision and replaced it with an abbreviated revision.

MAXIMUM EX-FACTORY PRICES

Tab. 27 Overview of administrative procedures in 2022

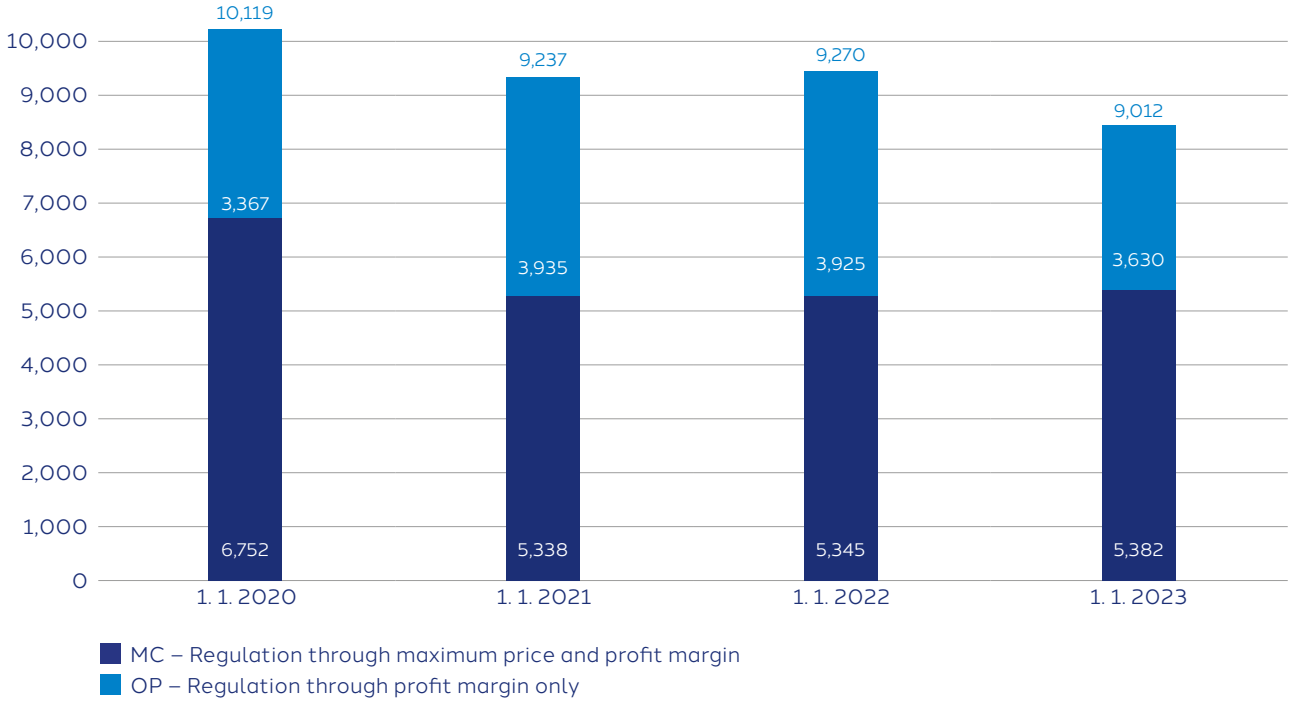
Applications for maximum ex-factory price determination	Number of SÚKL codes
Initiated	39
Decided	39
Appeal procedure pending	0
Became final	39
Applications for maximum ex-factory price change	
Initiated	81
Decided	74
Appeal procedure pending	3
Became final	68
Applications for maximum ex-factory price reduction – abbreviated procedure	
Initiated	2
Decided	2
Appeal procedure pending	0
Became final	2

The principal legislation governing the area of price regulation in 2022 continued to be 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"). On 30 November 2022, the Ministry of Health issued a new Price Regulation No 2/2023/OLZP, effective as of 01 January 2023. With regard to its effective date, however, this Regulation did not impact regulation of prices in 2022.

In 2022, 29 administrative procedures regarding maximum price determination were initiated (cf. two administrative procedures in 2021). For maximum price change, 63 administrative procedures were commenced (compared to 133 administrative procedures in 2021); applications filed by marketing authorisation holders prevailed (19 applications were filed by health insurance companies and 44 applications were filed by marketing authorisation holders).

The last three years have seen an obvious stability in the number of reimbursed medicinal products subjected to price regulation. In the last period, there was only a mild decrease in the number of products regulated by profit margin (Fig. 18).

Fig. 18 Structure of reimbursed products by the type of price regulation (no. of codes of medicinal products/foods for special medical purposes)



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

Price regulation zone	01	02	03	04	05	06	07	08	09	10	11	12
Up to 20 CZK incl.	20	20	20	20	20	20	20	18	10	9	9	9
More than 20 CZK up to 50 CZK incl.	279	288	285	282	278	276	273	253	247	242	236	237
More than 50 CZK up to 100 CZK incl.	720	714	706	707	700	700	702	663	649	650	653	654
More than 100 CZK up to 200 CZK incl.	922	921	911	914	899	897	896	869	852	850	857	855
More than 200 CZK up to 300 CZK incl.	552	538	533	528	522	519	517	495	479	477	476	482
More than 300 CZK up to 500 CZK incl.	460	453	452	450	449	450	453	443	433	443	445	443
More than 500 CZK up to 1,000 CZK incl.	620	615	615	613	614	618	615	605	592	612	633	644
More than 1,000 CZK up to 2,000 CZK incl.	511	511	503	506	512	516	519	527	526	527	527	531
More than 2,000 CZK up to 3,000 CZK incl.	206	207	209	210	212	212	213	208	205	211	222	223
More than 3,000 CZK up to 5,000 CZK incl.	262	262	261	264	263	268	272	266	263	264	262	268
More than 5,000 CZK up to 10,000 CZK incl.	258	257	257	257	258	257	263	256	251	252	255	254
More than 10,000 CZK up to 20,000 CZK incl.	199	198	196	202	205	208	212	209	206	208	212	217
More than 20,000 CZK up to 30,000 CZK incl.	85	91	94	96	98	98	98	96	97	97	105	109
More than 30,000 CZK up to 50,000 CZK incl.	66	66	67	69	73	77	78	77	79	81	84	95
More than 50,000 CZK up to 100,000 CZK incl.	110	119	153	161	163	170	176	170	173	181	189	193
More than 100,000 CZK	75	81	92	93	92	94	97	94	95	95	96	96
Number of codes	**5,345**	**5,341**	**5,354**	**5,372**	**5,358**	**5,380**	**5,404**	**5,249**	**5,157**	**5,199**	**5,261**	**5,310**

With a view to the structure of medicinal products (Tab. 28), it may be stated that in the individual months of 2022, the numbers of medicinal products in the aforementioned maximum price zones were decreasing more in the lower zones. The most significant decrease in the number of codes occurred in the zone of "More than 300 CZK up to 500 CZK incl." In the higher zones where an increase in the number of codes occurred, the highest increase in the number of medicinal products was seen in the zone of "More than 50,000 CZK up to 100,000 CZK incl."

DEVELOPMENT OF AVERAGE END-USER PRICES

In 2022, there was no change to the profit margins or to the VAT, the rate of which for medicinal products remained at 10 % also in 2022. 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 8.4 %. The highest increase of average prices occurred in the "More than 10,000 CZK" price zone. The biggest 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 decreased by 1.9 %, with the highest increase seen in the "More than 10,000 CZK" price zone.

The biggest decrease occurred in the "More than 500 CZK up to 1,000 CZK incl." price zone. The situation in ex-factory price levels (ex. profit margin and VAT) focusing upon a more detailed comparison of the last quarters of 2021 and 2022 is illustrated by Fig. 19 and 20.

Fig. 19 Prices of pharmaceuticals regulated by maximum price – comparison of average prices in Q4 2021 and Q4 2022 by price zones (%)

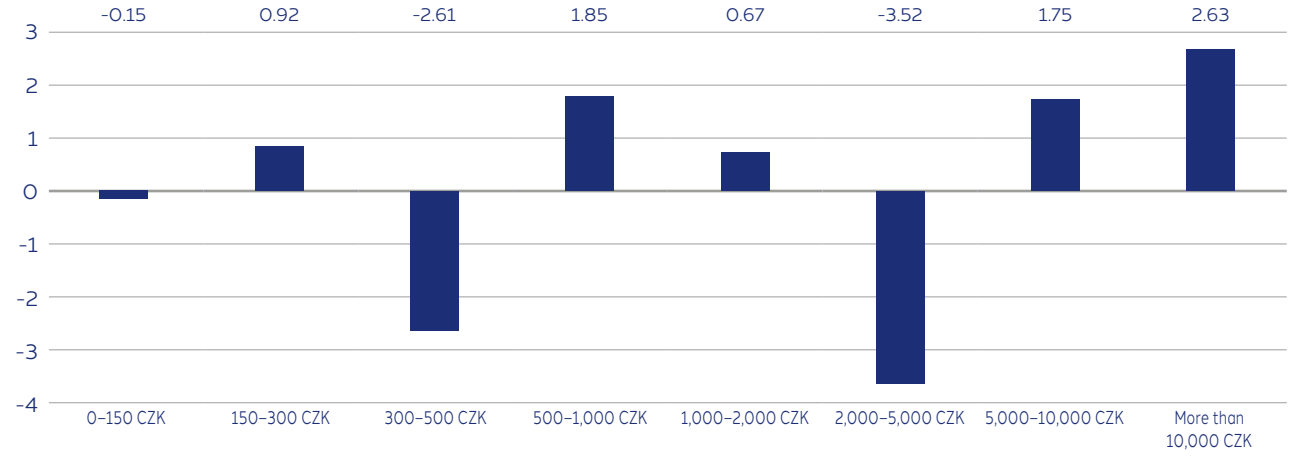
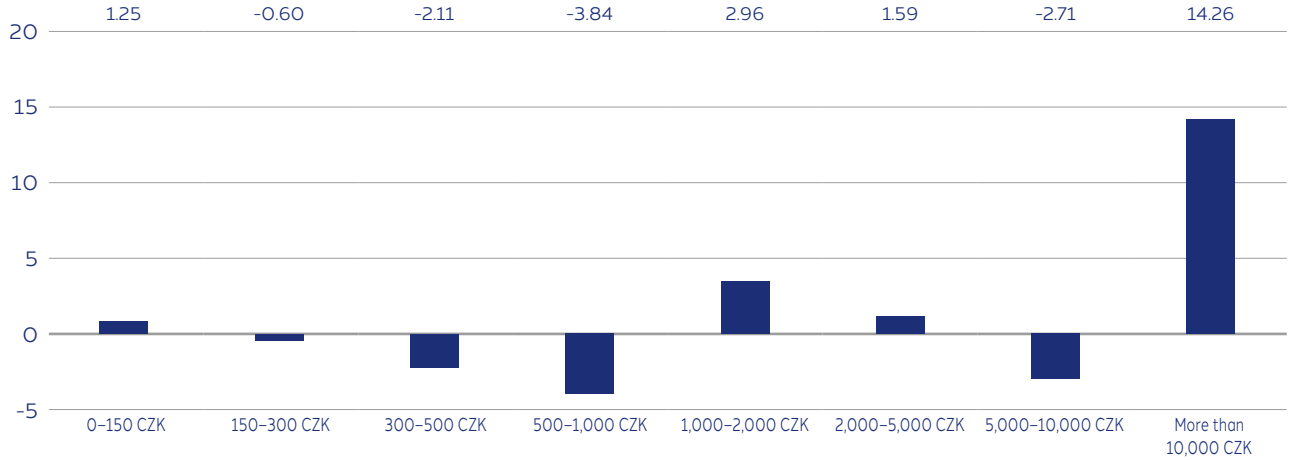


Fig. 20 Prices of pharmaceuticals regulated by profit margin – comparison of average prices in Q4 2021 and Q4 2022 by price zones (%)



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 2022, 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 BELOGENT (Tab. 29).

Tab. 29 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 (%)
0201970	D06AX	PAMYCON	33000IU/2500IU DRM PLV SOL 1	835,606	59.66	69.72	16.9
0176954	A03DA02	ALGIFEN NEO	500MG/ML+5MG/ ML POR GTT SOL 1X50ML	771,271	84.88	101.98	20.1
0131426	J07BB02	VAXIGRIP TETRA	INJ SUS ISP 1X0,5ML+J	487,702	219.49	229.02	4.3
0191922	A10BA02	SIOFOR	1000MG TBL FLM 60	386,847	62.82	72.24	15.0
0019577	A10BA02	STADAMET	1000MG TBL FLM 60 I	319,896	54.38	49.30	– 9.3
0149868	J07AL02	PREVENAR 13	INJ SUS 1X0,5ML+1SJ	266,606	1,062.62	1,013.14	– 4.7
0002429	N05AA02	TISERCIN	25MG TBL FLM 50	241,601	42.72	75.98	77.9
0096087	A10BA02	METFORMIN TEVA	500MG TBL FLM 60	219,212	61.22	29.34	– 52.1
0017170	D07CC01	BELOGENT	0,5MG/G+1MG/G CRM 30G	189,864	65.00	208.39	220.6
0100103	A10BA02	STADAMET	500MG TBL FLM 120	166,812	57.35	49.30	– 14.0

Medicinal products with the highest financial volume are in the lower price zones, except for medicinal product LYNPARZA. For most medicinal products, the maximum price was increased, except for medicinal products PREVENAR 13 and LYNPARZA. The most significant increase occurred with medicinal product SALOFALK (Tab. 30).

Tab. 30 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 (%)
0149868	J07AL02	PREVENAR 13	INJ SUS 1X0,5ML+1SJ	383,044,686	1,062.62	1,013.14	– 4.7
0222937	L01XK01	LYNPARZA	150MG TBL FLM 56	248,131,872	62,196.83	55,971.10	– 10.0
0131426	J07BB02	VAXIGRIP TETRA	INJ SUS ISP 1X0,5ML+J	159,779,241	219.49	229.02	4.3
0119539	A07EC02	PENTASA SACHET	2G GRA PRO 60	117,839,364	1,573.32	1,685.63	7.1
0226453	A05AA02	URSOSAN FORTE	500MG TBL FLM 100	112,669,779	1,290.31	1,396.93	8.3
0176954	A03DA02	ALGIFEN NEO	500MG/ML+5MG/ ML POR GTT SOL 1X50ML	111,870,851	84.88	101.98	20.1
0201970	D06AX	PAMYCON	33000IU/2500IU DRM PLV SOL 1	77,163,191	59.66	69.72	16.9
0195911	A07EC02	SALOFALK	3000MG GRA ENP 60	48,428,667	2,230.68	2,893.40	29.7
0119654	B03AE10	SORBIFER DURULES	320MG/60MG TBL MRL 100	46,279,536	219.63	248.19	13.0
0213250	A07EC02	PENTASA SACHET	4G GRA PRO SCC 30	44,483,838	1,573.32	1,685.63	7.1

AMOUNTS AND CONDITIONS OF REIMBURSEMENTS FROM HEALTH INSURANCE FUNDS

Tab. 31 Overview of administrative procedures in 2022

Applications for determination or change of the amount and conditions of reimbursement	Number of SÚKL codes
Initiated	269
Decided	196
Appeal procedure pending	16
Became final	156
Applications for determination or change of maximum price and the amount and conditions of reimbursement	
Initiated	197
Decided	123
Appeal procedure pending	25
Became final	80
Applications for reimbursement revocation	
Initiated	168
Decided	146
Appeal procedure pending	0
Became final	137
Applications for maximum price and reimbursement revocation	
Initiated	44
Decided	32
Appeal procedure pending	0
Became final	32
Ex officio initiated procedures	
Initiated	1,477
Decided	987
Appeal procedure pending	143
Became final	744
Procedures concerning similar products	
Initiated	747
Decided	747
Appeal procedure pending	6
Became final	692

In 2022, 29 applications for determination of reimbursement of highly innovative products were submitted.

In the course of 2022, the Section continued to initiate in-depth reimbursement revisions according to the schedule. Eighteen in-depth revisions (457 SÚKL codes) were scheduled for and also initiated in 2022.

Pursuant to the provisions of Section 39 of the Act on Public Health Insurance, the Institute is obliged, inter alia, to assess and, where applicable, change the amount of the basic reimbursement, the consistency of the amounts of reimbursements for all principally therapeutically interchangeable medicinal products or foods for special medical purposes with the basic reimbursement, the uniformity and effectiveness of the determined conditions of reimbursement, and compliance of the determined amounts and conditions of reimbursement of medicinal products and foods for special medical purposes with the law, particularly meeting the expected results and reasons for pharmacotherapy and cost-effectiveness. 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 2022, 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 2022 are estimated at 2,442,359,091 CZK, and those arising from in-depth revisions at 810,751,508 CZK.

Tab. 32 Overview of enforceable decisions on reimbursement revisions and the impact on public health insurance funds

Effective date	Number of SÚKL codes	Number of administrative procedures	Impact on health insurance funds
01/2022	31	6	326,696,035 CZK
02/2022	46	7	552,770,642 CZK
03/2022	7	3	38,827,892 CZK
04/2022	0	0	572,737,749 CZK
05/2022	44	7	163,711,831 CZK
06/2022	53	1	39,575,815 CZK
07/2022	40	5	80,943,010 CZK
08/2022	41	3	107,988,004 CZK
09/2022	130	3	211,411,475 CZK
10/2022	112	5	790,206,998 CZK
11/2022	30	4	269,765,367 CZK
12/2022	117	2	98,475,781 CZK

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

The overview of the number of medicinal product codes in the SCAU reimbursement price zones indicates that most often, medicinal products fall into the lower price zones, i.e., 3–7, in the reimbursement range of 50–1,000 CZK (Tab. 33). The value distribution in 2022 is almost identical to that of 2021, with minimum deviations only.

Tab. 33 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.	149	149	147	141	141	141	139	162	167	165	166	163
More than 20 CZK up to 50 CZK, incl.	739	740	725	721	709	702	709	688	688	685	687	690
More than 50 CZK up to 100 CZK, incl.	1,247	1,249	1,226	1,215	1,210	1,210	1,196	1,162	1,084	1,081	1,081	1,079
More than 100 CZK up to 200 CZK, incl.	1,563	1,553	1,558	1,563	1,543	1,543	1,537	1,498	1,482	1,477	1,473	1,473
More than 200 CZK up to 300 CZK, incl.	798	814	802	796	788	797	799	768	757	751	758	760
More than 300 CZK up to 500 CZK, incl.	910	890	874	862	861	868	912	915	926	890	885	892
More than 500 CZK up to 1,000 CZK, incl.	1,045	1,047	1,032	1,027	1,026	1,010	1,005	988	983	997	1,012	1,010
More than 1,000 CZK up to 2,000 CZK, incl.	919	865	862	862	852	829	793	792	787	811	816	823
More than 2,000 CZK up to 3,000 CZK, incl.	368	362	362	365	364	360	357	350	347	354	362	362
More than 3,000 CZK up to 5,000 CZK, incl.	358	352	347	342	342	342	336	334	330	330	329	332
More than 5,000 CZK up to 10,000 CZK, incl.	435	438	440	442	442	447	464	459	465	480	482	484
More than 10,000 CZK up to 20,000 CZK, incl.	314	318	321	328	330	330	336	326	309	329	338	345
More than 20,000 CZK up to 30,000 CZK, incl.	116	119	129	130	130	134	142	146	146	146	147	153
More than 30,000 CZK up to 50,000 CZK, incl.	99	106	117	117	122	128	132	124	128	135	143	150
More than 50,000 CZK up to 100,000 CZK, incl.	112	124	139	143	144	149	155	152	156	125	130	135
More than 100,000 CZK	98	94	97	99	98	98	99	96	97	97	98	98
Number of codes	**9,270**	**9,220**	**9,178**	**9,153**	**9,102**	**9,088**	**9,111**	**8,960**	**8,852**	**8,853**	**8,907**	**8,949**

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 medicinal products with the highest financial volume in end-user prices, there was a less significant decrease in the reimbursement for individual packages of medicinal products. The highest reduction of reimbursement occurred for medicinal products TRESIBA a REMICADE; a pronounced increase of reimbursement occurred for one medicinal product (STELARA) only (Tab. 34).

Tab. 34 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)
0209484	L01FF02	KEYTRUDA	25MG/ML INF CNC SOL 1X4ML	1,590,176,449	73,377.95	69,734.19
0168904	B01AF01	XARELTO	20MG TBL FLM 98 II	1,256,223,130	4,472.93	4,265.29
0223046	L01FF01	OPDIVO	10MG/ML INF CNC SOL 1X24ML	1,142,218,582	70,829.68	66,620.15
0210187	L01EL01	IMBRUVICA	140MG CPS DUR 90	644,856,520	137,507.53	135,399.37
0193747	B01AF02	ELIQUIS	5MG TBL FLM 168	635,915,936	3,823.20	3,655.96
0193826	A10AE06	TRESIBA	200U/ML INJ SOL 3X3ML	517,276,718	1,542.96	1,234.37
0027283	L04AB02	REMICADE	100MG INF PLV CSL 1	481,152,799	5,862.11	5,137.25
0168373	B01AE07	PRADAXA	150MG CPS DUR 60X1 I	430,442,851	1,365.43	1,305.70
0167601	L04AC05	STELARA	90MG INJ SOL ISP 1X1ML	427,444,336	36,272.93	51,003.22
0168899	B01AF01	XARELTO	15MG TBL FLM 98 II	370,955,812	3,354.70	3,198.97

The group of medicinal products for which reimbursement changed and which were distributed in the highest volumes, includes particularly relatively inexpensive medicinal products. In 2022, reimbursements of the aforementioned products were being both reduced and increased. In respect of medicinal product ATORIS, a significant increase in its reimbursement occurred, which was subsequently reflected also in the growing volume of its supplies (Tab. 35).

Tab. 35 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
0049009	C10AA05	ATORIS	20MG TBL FLM 90	85,094	165.41	279.53	91,661	*/
0148675	R06AX29	XADOS	20MG TBL NOB 50	78,593	97.96	83.26	67,670	*/
0168373	B01AE07	PRADAXA	150MG CPS DUR 60X1 I	75,654	1,365.43	1,305.70	84,242	*/
0193826	A10AE06	TRESIBA	200U/ML INJ SOL 3X3ML		1,542.96	1,234.37		x/
0204682	C10AA05	TORVACARD NEO	20MG TBL FLM 90	61,873	165.41	279.53	79,575	*/
0168904	B01AF01	XARELTO	20MG TBL FLM 98 II	63,562	4,472.93	4,265.29	76,797	*/
0210402	A10AE04	TOUJEO	300U/ML INJ SOL 3X1,5ML SOLOSTAR		1,157.22	925.78		x/
0184409	C10AA07	SORVASTA	10MG TBL FLM 30X1	114,025	93.18	55.14	145,036	
0049006	C10AA05	ATORIS	10MG TBL FLM 90	60,043	82.70	139.77	66,493	*/
0015378	C08CA01	AGEN	5MG TBL NOB 90 I	68,039	93.27	49.52	54,738	*/

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

Table 36 presents a list of essential changes to the reimbursement system in 2022, 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. The new type of administrative procedure concerning the determination of the amount and conditions of reimbursement of an orphan medicinal product is represented by medicinal product SPINRAZA, which entered the reimbursement system in November 2022.

Tab. 36 Overview of newly reimbursed original pharmaceuticals and significant extensions of reimbursement with decisions issued in 2022

Name of the medicinal product and active substance	Indication (clinical use)	Reimbursement effective from
OPDIVO (nivolumab)	Advanced oesophageal carcinoma (monotherapy, in pre-treated patients)	March 2022
VENCLYXTO (venetoclax)	Chronic lymphocytic leukaemia (monotherapy, following failure of previous treatment with B-cell receptor inhibitors)	April 2022
PHESGO (combined pertuzumab + trastuzumab)	Breast carcinoma (early-stage carcinoma: adjuvant treatment in combination with taxane chemotherapy / metastatic carcinoma: combined treatment with docetaxel)	March 2022
ZEJULA (niraparib)	Carcinoma of the ovaries, fallopian tubes or primary peritoneal carcinoma (maintenance therapy for responders to previous platinum chemotherapy)	March 2022
PREVYMIS (letermovir)	Prevention of cytomegalovirus (CMV) disease development in adult recipients (with CMV seropositivity) undergoing allogenic haematopoietic stem cell transplantation	April 2022
FORXIGA (dapagliflozin)	Chronic heart failure (in patients with persistent NYHA II and NYHA III symptomatology despite standard-of-care therapy)	March 2022
ONGENTYS (opicapone)	Parkinson's disease (treatment of advanced mobility complications in combination with s levodopa)	April 2022
KINERET (anakinra)	Cryopyrin-associated periodic syndrome and Still's disease (in children and in adults)	April 2022
DOPTELET (avatrombopag)	Primary chronic immune thrombocytopenia (cITP) in adult patients refractory to other treatments (such as corticosteroids, immunoglobulins)	April 2022
RYALTRIS (mometasone/ olopatadine)	Moderate to severe allergic rhinitis with inadequate effect of current therapy (intranasal corticosteroids)	May 2022
LORVIQUA (lorlatinib)	Monotherapy of advanced, ALK-positive non-small-cell lung carcinoma (NSCLC) in adult patients who progressed following previous therapy with alectinib or ceritinib in first-line ALK TKI treatment or with crizotinib and at least one more ALK TKI	April 2022
OPDIVO (nivolumab)	Advanced (non-resectable or metastatic) melanoma in adults treated with previous systemic therapy for inoperable, advanced or metastatic disease	May 2022
KESIMPTA (ofatumumab)	Relapsing-remitting multiple sclerosis (first- and second-line therapy)	April 2022
POTELIGEO (mogamulizumab)	Treatment of adult patients with mycosis fungoides (MF) or Sézary syndrome (SS), who underwent at least one previous systemic therapy	May 2022
REVLIMID (lenalidomide)	Newly diagnosed multiple myeloma (maintenance treatment) in patients, who have had autologous bone marrow transplantation	June 2022
OCALIVA (obeticholic acid)	Primary biliary cholangitis in combination with UDCA in patients with inadequate response to UDCA or as monotherapy in patients not tolerating UDCA	May 2022
ERLEADA (apalutamide)	Treatment of adult males with metastatic hormone-sensitive prostate carcinoma in combination with androgen deprivation therapy	May 2022
FLUCLOXACILLIN FRESENIUS KABI (infection flucloxacillin)	Treatment of skin or soft tissue infections caused by flucloxacillin-sensitive pathogens	June 2022
BYANNLI (paliperidone, 6-month)	Maintenance therapy of adult patients with schizophrenia, clinically stable, with good prognosis	July 2022
ADCETRIS (brentuximab vedotin)	Hodgkin's lymphoma with high risk of relapse after high-dose chemotherapy with subsequent stem cell transplantation	July 2022
ADCETRIS (brentuximab vedotin)	Relapsing-refractory Hodgkin's lymphoma after stem cell transplantation	June 2022

Name of the medicinal product and active substance	Indication (clinical use)	Reimbursement effective from
HUMIRA (adalimumab)	Treatment of adult patients with non-infectious intermediary and posterior uveitis and panuveitis	July 2022
INVOKANA (canagliflozin)	Diabetic kidney disease in patients with Type 2 diabetes	July 2022
DARZALEX (daratumumab)	In combination with lenalidomide and dexamethasone in the indication of multiple myeloma in patients who have had at least one previous therapy	July 2022
TECENTRIQ (atezolizumab)	First-line therapy of metastatic non-small-cell lung carcinoma (with the presence of PD-L1 molecule in at least 50 % of tumour cells)	July 2022
TECENTRIQ (atezolizumab)	Advanced or inoperable liver carcinoma (combination atezolizumab + bevacizumab)	July 2022
ALUNBRIG (brigatinib)	Monotherapy of advanced non-small-cell lung carcinoma in patients pre-treated with crizotinib	August 2022
VUMERITY (diroximel-fumarate)	First- and second-line treatment of relapsing-remitting multiple sclerosis (RRMS) + rapidly progressing RRMS	August 2022
OPDIVO (nivolumab)	First-line treatment of malign tumour of the pleura (in combination with ipilimumab)	August 2022
PONVORY (ponesimod)	Relapsing-remitting multiple sclerosis (2 attacks / 2 years + 1 attack / 1 year)	August 2022
OPDIVO (nivolumab)	In combination with ipilimumab for the treatment of metastatic colorectal carcinoma with mismatch repair deficiency or high microsatellite instability following previous combined fluoropyrimidine-based chemotherapy	August 2022
KEYTRUDA (pembrolizumab)	In combination with chemotherapy in first-line treatment of metastatic non-small-cell lung carcinoma (in the population of adult patients with squamous or non-squamous type)	August 2022
KEYTRUDA (pembrolizumab)	Monotherapy of patients with treatment-naïve metastatic carcinoma of the colon (with specific gene mutation type)	September 2022
IMBRUVICA (ibrutinib)	Mantle-cell lymphoma in pre-treated patients (with early relapse following rituximab therapy, who have had transplantation or who are not suitable candidates for transplantation)	September 2022
OPDIVO (nivolumab)	Adjuvant treatment of carcinoma of the oesophagus or gastroesophageal junction with residual disease following previous complete tumour removal	September 2022
ILUVIEN (fluocinolone acetonide)	Prevention of non-infectious uveitis relapse	October 2022
REBLOZYL (luspatercept)	Second-line treatment of transfusion-dependent anaemia secondary to myelodysplastic syndrome (MDS) and treatment of transfusion-dependent anaemia secondary to beta-thalassemia	October 2022
NGENLA (somatrogon)	Treatment of growth disorders caused by inadequate growth hormone secretion	October 2022
EVRENZO (roxadustat)	Treatment of anaemia (lack of red blood cells) in non-dialysed patients with chronic kidney disease and in patients included in a dialysis programme	October 2022
JINARC (tolvaptan)	Polycystic kidney disease in patients with stage 3 CKD (chronic kidney disease)	November 2022
IMFINZI (durvalumab)	First-line treatment of small-cell lung carcinoma (in combination with etoposide and platinum)	November 2022
BIMZELX (bimekizumab)	First- and second-line biological treatment of moderate psoriasis	November 2022
XELJANZ (tofacitinib)	First, second, and further lines of biological/targeted therapy of polyarticular juvenile idiopathic arthritis	November 2022
CIBINQO (abrocitinib)	Severe form of atopic dermatitis following failure (inadequate efficacy) of at least one of the conventional systemic immunosuppressive therapies (except for corticosteroids), or in patients who cannot be treated with systemic therapy due to intolerance or contraindication	November 2022
VERQUVO (vericiguat)	Patients with symptomatic chronic heart failure with reduced ejection fraction (HFrEF) in a stabilised condition following a recent decompensation episode	November 2022

Name of the medicinal product and active substance	Indication (clinical use)	Reimbursement effective from
SPINRAZA (nusinersen)	Spinal muscular atrophy; types I, II, and III	November 2022
RAVICTI (glycerol-phenylbutyrate)	Treatment of hyperammonemia (in patients with hereditary urea and glutamine metabolic disorder)	December 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 the determination of reimbursement for a new active substance, application for determination of reimbursement for a new indication, application for substantial variation to the conditions of reimbursement), the Institute has been publishing so called Assessment Report Summary on its website on an ongoing basis since 2020. The Institute has been publishing such Summaries for individual pharmaceuticals/procedures on its website in order to facilitate access of the general public to basic data and information about the assessed pharmaceuticals.

VALIDATION OF APPLICATIONS

In 2022, the total of 781 applications for determination, change or revocation of maximum price and/or conditions and amount of reimbursement of medicinal products/foods for special medical purposes or for abbreviated reimbursement revision were submitted.

781

applications for determination, change or revocation of maximum price and/or conditions and amount of reimbursement of medicinal products/ foods for special medical purposes or for abbreviated reimbursement revision.

In 2022, there was a significant increase in the number of applications for the amount and conditions of reimbursement / for determination of maximum price and the amount and conditions of reimbursement on the basis of which administrative procedures conducted as per the provisions of Section 39g(9) of the Act on Public Health Insurance (so called “similar products”) were initiated. These submissions accounted for 46 % of the overall number of procedures initiated upon request. The amended Act on Public Health Insurance, effective as at 01 January 2022, introduced a new type of administrative procedure for orphan medicinal products, specifically determination of reimbursement pursuant to the provisions of Section 39da. In total, there were 15 submitted applications, in which the marketing authorisation holder chose this procedure for the determination of reimbursement for the orphan medicinal product.

In its Section 39f(13), the amended Act on Public Health Insurance, effective as at 01 January 2022, moreover, introduced the applicant’s obligation to pay to the Institute the reimbursement of costs of the conduct of expert activities and, along with the submission of the application, to submit a proof of payment thereof pursuant to Section 39f(5)(j), as failure to reimburse the costs had been a common cause of issuance of calls for elimination of shortcomings of the application and required a resolution suspending the administrative procedure.

The total of 24 administrative procedures initiated upon request were suspended by resolution as early as during the control of the application in so-called validation phase. The resolution to suspend administrative procedure due to an obstacle preventing the commencement of the procedure as per the provision of Section 48(1) of the Code of Administrative Procedure (lis pendens) represented a mere third of the issued resolutions, which is a decrease compared to the previous years. Other causes of suspending the administrative procedure in the validation phase included, inter alia, withdrawal of the application by the submitter and an obvious legal inadmissibility of the application due to a non-authorised medicinal product, lack of authorisation on the part of the applicant, failure to eliminate shortcomings within timeline, etc.

In 2022, 39 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 medicinal product code.

Tab. 37 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 2022

Period	Submitted applications	Suspended due to defective submission and application shortcomings	Discontinued in the validation phase
January	36	1	3
February	43	0	2
March	60	3	2
April	62	2	2
May	46	5	1
June	78	3	1
July	92	1	4
August	73	1	1
September	95	0	4
October	65	1	4
November	81	4	0
December	50	1	0
Total	**781**	**22**	**24**

INDIVIDUALLY PREPARED MEDICINAL PRODUCTS (IPLP) AND OTHER PRODUCTS FOR WHICH REIMBURSEMENT IS DETERMINED BY MEANS OF GENERAL MEASURES

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 2022). 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"). From 2022, the Institute has been determining reimbursement by means of general measures also for the group of tissues and cells which, however, is not subjected to price regulation.

The conditions for the determination of the amount and conditions of reimbursement by means of general measures (hereinafter referred to as "OOP") are set forth by the Act on Public Health Insurance, specifically its Section 15(5). The drafting of general measures and the method of their publication are also 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 2022, six general measure procedures in total were initiated and properly completed.

As of 01 March 2022, the following general measures were issued: OOP 01-22 for TPs; OOP 02-22 for RFs; and OOP 03-22 for DPVs (for the group of radiopharmaceuticals, parenteral nutrition for home care, and transfusion products). All of these OOPs were issued in compliance with Government Regulation No 531/2021 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, and Government Regulation No 420/2021 Coll., amending Government Regulation No 341/2017 Coll., on salaries of public service and administration employees, as amended, Government Regulation No 304/2014 Coll., on civil servant salaries, as amended, and Government Regulation No 347/2021 Coll., amending Government Regulation No 304/2014 Coll., on civil servant salaries, as amended, increasing the salaries of healthcare professionals, which was reflected in the source materials for the calculation of reimbursement. General measures OOP 01 22 TP and OOP 02-22 RF also reflected the change in the minute performance rate in compliance with Decree No 482/2021 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 2022. The overhead minute rate per minute of time performance was increased from the original value of 3.28 points to the new value of 3.38 points. In compliance with Decree No 396/2021 Coll., setting point values, reimbursement amounts for reimbursed services, and regulatory restrictions for 2022, the point value was increased from the original amount of 1.05 CZK per point to the new amount of 1.08 CZK per point. Furthermore, in OOP 02-22, the Institute excluded radiopharmaceutical 18F fluoromisonidazole (code RF 0002107), whose specific therapeutic program expired on 30 July 2021, from the list of individually prepared medicinal products (IPLP) and other products the reimbursement of which is determined by means of a general measure (hereinafter referred to as the "IPLP List").

As at 01 April 2022, supplementary general measure OOP 04-22 for the RF group became effective; in this OOP, the Institute re-included the radiopharmaceutical 18F fluoromisonidazole (code RF 0002107) in the IPLP List on the basis of received approval of continued specific therapeutic programme using medicinal product 18F-FMISO issued by the Ministry of Health.

As at 01 June 2022, another general measure for subgroup RF 06-22 became effective; this measure reflected the new price source materials and the €/CZK exchange rate on the basis of materials published by the Czech National Bank (ČNB). This OOP, moreover, included a new code in the IPLP List: radiopharmaceutical 75Se tauroselcholic acid cps. (code RF 0002114), in a specific therapeutic programme, under subgroup 13.

As at 01 November 2022, general measure for the magistral formula subgroup, OOP 05-22, became effective in response to the stimulus received from the Association of Czech Health Insurance Companies (SZP ČR). The stimulus proposed the inclusion of autologous eye serum drops among non-reimbursed IPLPs (which the Institute declined) and, furthermore, an amendment to the wording of exemptions listed under section 5(e) of OOP 02-20.

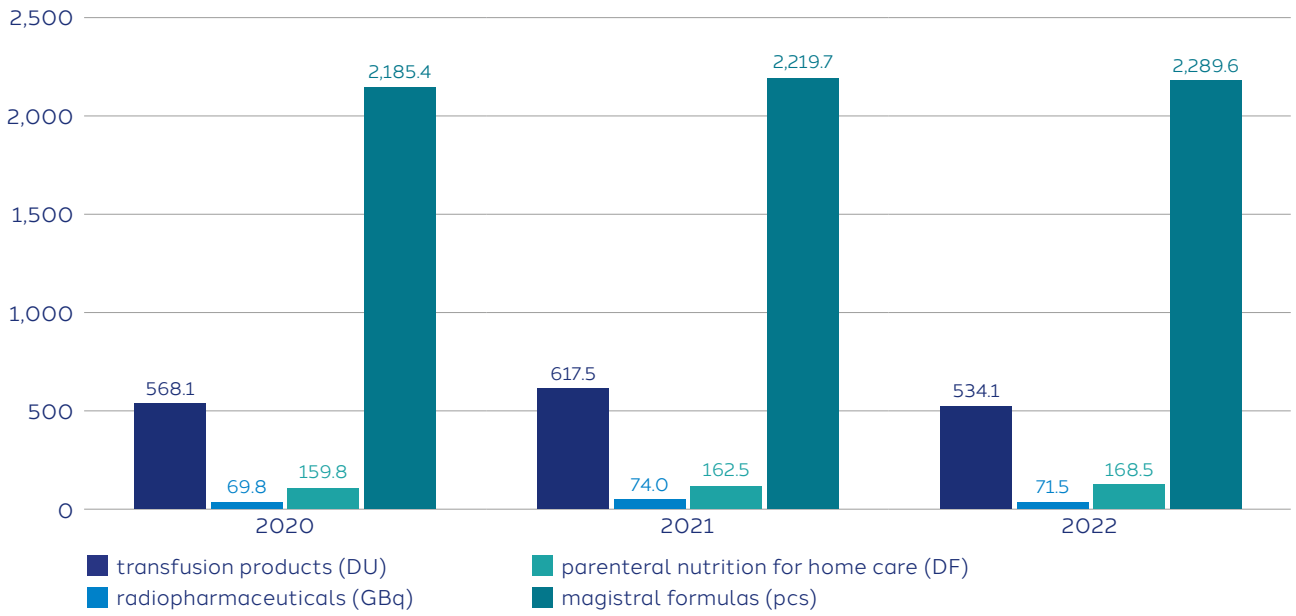
On 16 December 2022, the first general measure for the tissues and cells group was published. It was OOP 07-22, taking effect as at 01 January 2023, in which the Institute newly included the tissues and cells subgroup into the IPLP List.

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 and RF subgroups, in 2022, the consumption decreased, while in respect of the other subgroups, i.e., DPV and MAG, consumption slightly increased in comparison to the previous period. The values specified for the period of 2021 in the 2021 annual report were updated as of 18 January 2023. Data for the consumption of individually prepared medicinal products in 2022 are available only as at 01 October 2022, 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, Q4 2022 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 2020-2022 is shown in Fig. 21.

Fig. 21 Overview of consumption of individually prepared medicinal products for the period of 2020-2022 in thous. DU



In 2022, expenses incurred for individual IPLP subgroups were influenced by amendments to the Government Regulations mentioned above.

The distribution of expenses in the IPLP group in 2022 by individual subgroups is illustrated by Fig. 22.

Fig. 23 illustrates also a comparison of expenses in the period of 2020-2022 for individual IPLP subgroups. Compared to 2021, an increase in the expenses incurred by the public health insurance funds was seen in the DPV, RF, and MAG subgroups; only the TP subgroup exhibited a decrease compared to 2021, which corresponds also to the lower consumption in this subgroup.

Fig. 22 Distribution of total expenses in the IPLP group in 2022

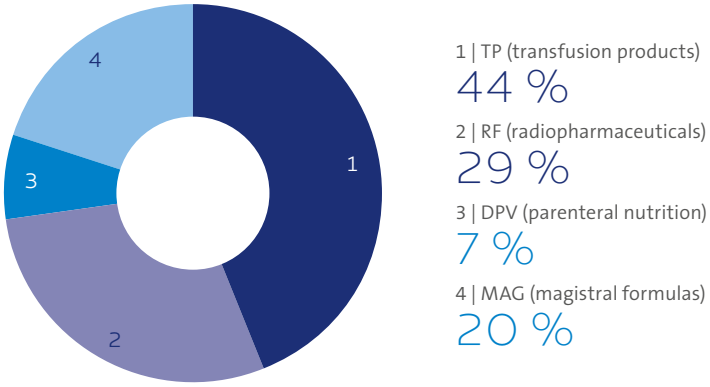
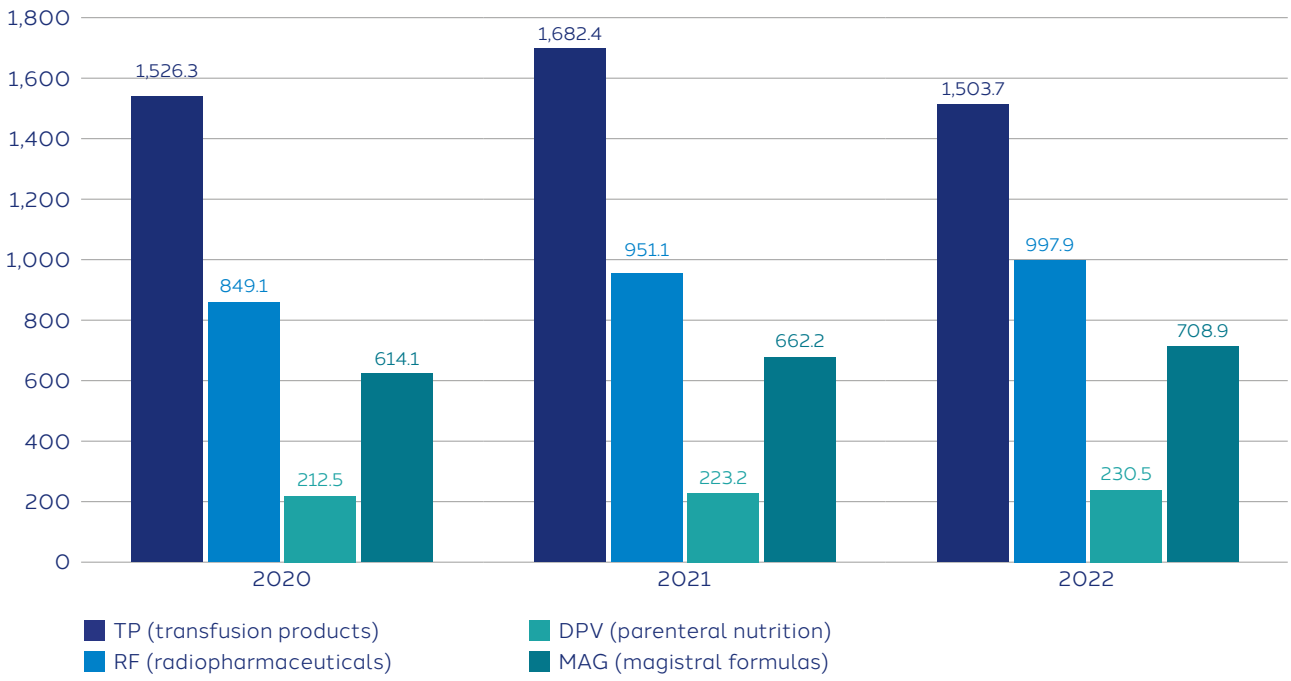


Fig. 23 Comparison of expenses by IPLP subgroup in the period of 2020–2022 in mil. CZK



The total expenses for the IPLP group reimbursed from public health insurance funds amounted to 3,518.9 mil. CZK in 2021; in 2022 this amount was 3,441.0 mil. CZK, which is a decrease in expenses by 77.9 mil. CZK, i.e., by 2.21 % compared to 2021.

MEDICAL DEVICE DEPARTMENT

In the area of medical device regulation, 2022 was again a year of legislative changes. In May, Regulation (EU) 2017/746 of the European Parliament and of the Council on in vitro diagnostic medical devices (hereinafter referred to as "IVDR") took effect, and, on 22 December 2022, the new Act No 375/2022 Coll., on Medical Devices and on in Vitro Diagnostic Medical Devices (hereinafter referred to as the "Medical Device Act") became effective. With a view to the aforementioned, 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 transitory provisions of the Medical Device 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 the information received from the European Commission, EUDAMED roll-out is to be postponed at least until the end of 2024.

At the same time, the staff of the Medical Device Department were busy preparing new processes in compliance with the new legislation and continued their work on the project of the Medical Device Information System that, in compliance with the Medical Device Act, will serve as the new agenda system covering all agendas in the sphere of medical device regulation on the national level, including medical device reimbursements. In the second half of 2022, the Medical Device Department staff concentrated, inter alia, on the organisation and preparation of the 51st Competent Authorities for Medical Devices (CAMD) plenary session, which was held on 20–21 October 2022 in Prague as part of the Czech Presidency of the EU Council. The employees of the Medical Device Department also participated in the meetings of various expert working groups of the European Commission focusing, in particular, on the set-up and harmonisation of individual processes in the medical device internal market and the specification of functionalities in the EUDAMED database.

4.15 MEDICAL DEVICE CONTROL AND EXPERT OPINION UNIT (KOP)

CONTROLS

The Institute's surveillance activities over persons handling medical devices was, in 2022, stipulated by Regulation (EU) 2017/745 of the European Parliament and of the Council on medical devices (hereinafter referred to as "MDR") along with Act No 89/2021 Coll., on Medical Devices (hereinafter referred to as the "Act on Medical Devices") 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, importers, distributors, persons servicing medical devices, and persons dispensing medical devices. This surveillance activity includes also the agenda of assessments of proper placement of medical devices on the market and newly also surveillance over advertising for medical devices.

167
conducted inspections

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 was 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 2022, the inspectors of the Control Unit conducted the total of 167 inspections, of which 92 were inspections at providers of healthcare services (both state and non-state healthcare facilities) and 75 were inspections at medical device manufacturers, importers, distributors, persons dispensing medical devices, and in servicing organisations. The tables below provide a more detailed statistics regarding the total number of inspected persons.

Ninety-two inspections were conducted 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,

75 inspections were conducted as part of market surveillance, in which compliance with the requirements governing medical device supply to the market was checked.

The Medical Device Inspection and Expert Opinion Unit forwarded the total of 58 motions to the Medical Device Legal Support Unit.

Tab. 38 Overview of inspections conducted by KOP

Number of inspections	167
Number of inspections instigated by a motion (of the total number of inspections)	41
Number of inspected medical devices	498*
Number of inspected Legally Controlled Measuring Instruments (of the total number of inspected medical devices)	0
Number of motions forwarded to the Medical Device Legal Support Unit (proposals for administrative procedure initiation)	58

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

Tab. 39 KOP inspection rating

Entity	Number of inspections	1*	2*	3*
POS – providers	92	38	56	1
CEN – price control	10	4	5	0
DIS – distributors	50	22	16	2
DOV – importers	40	15	13	3
SER – persons servicing medical devices	7	5	2	0
VYD – persons dispensing medical devices	7	3	4	0
VYR – manufacturers	7	1	2	2
Miscellaneous	0	0	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 rating 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 motions from other units of the Institute and in response to filed applications for medical device notification in the RZPRO. In 2022, the KOP Unit issued 75 expert opinions concerning the nature of a product or medical device classification. In the conduct of the aforementioned activities, when processing opinions regarding product nature or medical device classification, the Unit cooperates also with the Advertising Surveillance Unit in the sphere of pharmaceuticals. Of the aforementioned number, 66 opinions were issued on the basis of an external request and nine 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 imposed upon the sponsors of clinical investigations on medical devices (hereinafter referred to as "CIMD") by the Act on Medical Devices and in the MDR, 32 individual applications for authorisation of CIMD conduct and 40 individual applications for variations to CIMD conditions were submitted to the Institute in 2022 via the RZPRO Clinical Investigations module.

In compliance with the newly implemented Regulation (EU) 2017/746, on in vitro diagnostic medical devices, four applications for authorisation of the conduct of a performance study and one notification of the conduct of a performance study were submitted.

Twenty-three decisions authorising the conduct of clinical investigation were issued; eight procedures were stopped; and one application was declined.

Thirty-nine decisions authorising variations to clinical investigation were issued; two procedures were stopped.

Four authorisations of the conduct of a performance study were issued and, at the same time, one notification of the conduct of a performance study was assessed.

In total, 231 serious incidents were individually reported from ongoing clinical investigations via the RZPRO Clinical Investigations module.

With regard to the coming into effect of Regulation (EU) 2017/746 on 25 May 2022, a completely new agenda and operating procedures in the sphere of diagnostic medical device performance studies were being intensively implemented.

Within the scope of international cooperation in the sphere of clinical evaluations, in 2022, 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, furthermore, upon exchange of information among the EU Member States. Due to the pandemic situation, all meetings were held online. At the same time, intensive international cooperation in the implementation of Regulation (EU) 2017/746 was under way.

MEDICAL DEVICE VIGILANCE – MONITORING OF INVESTIGATIONS INTO SERIOUS INCIDENTS AND MONITORING OF FIELD SAFETY CORRECTIVE ACTION IMPLEMENTATION

The Act on Medical Devices and Act on in Vitro Medical Devices and the coming into force of the Regulation 2017/746, on in vitro diagnostic devices, also drove major changes, particularly in the area of IVDs. The obligation of distributors, persons servicing medical devices, and healthcare service providers to report suspected serious incidents was cancelled on the national level. Nevertheless, reporting of suspected serious incidents 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.

On the basis of effective legislation of the Czech Republic, 1,518 serious incidents considered 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. In all of the cases, monitoring was initiated. The development of the number of serious incident reports in 2013-2022 is illustrated by Fig. 24.

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 745. Of the total number of received reports, 379 concerned medical devices made available on the Czech market. The development of the number of reports on safety corrective actions in 2013-2022 is illustrated by Fig. 25.

In 2022, the Institute published 345 communications to medical device 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).

One inspection at a medical device manufacturer was conducted as part of monitoring the implementation of a safety corrective action within the territory of the Czech Republic. Four proposals to impose an administrative penalty for offences committed by healthcare service providers, manufacturers, persons servicing medical devices or medical device distributors were forwarded to the Medical Devices Legal Support Unit (PPZ).

As part of monitoring of a safety corrective action adopted 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 2022, the inspectors of the Medical Device Clinical Trials and Vigilance Unit participated in meetings of the PMSV (Post Market Surveillance and Vigilance) Working Group of the Medical Device Coordination Group (MDCG) of the European Commission; the signal detection and vigilance including data driven vigilance working group, and 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.

Fig. 24 Overview of notified incidents in 2013–2022

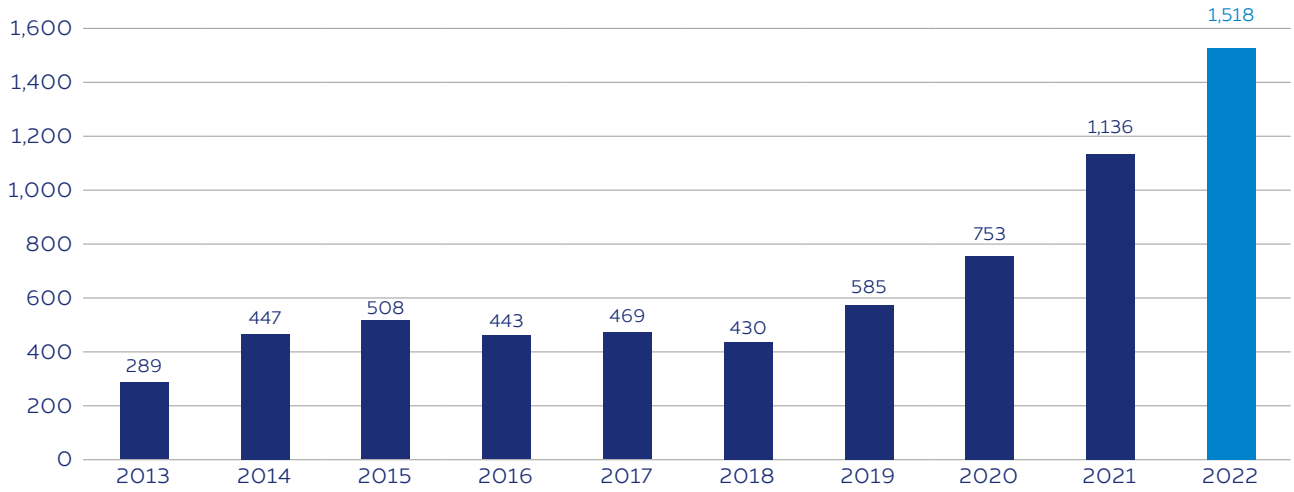
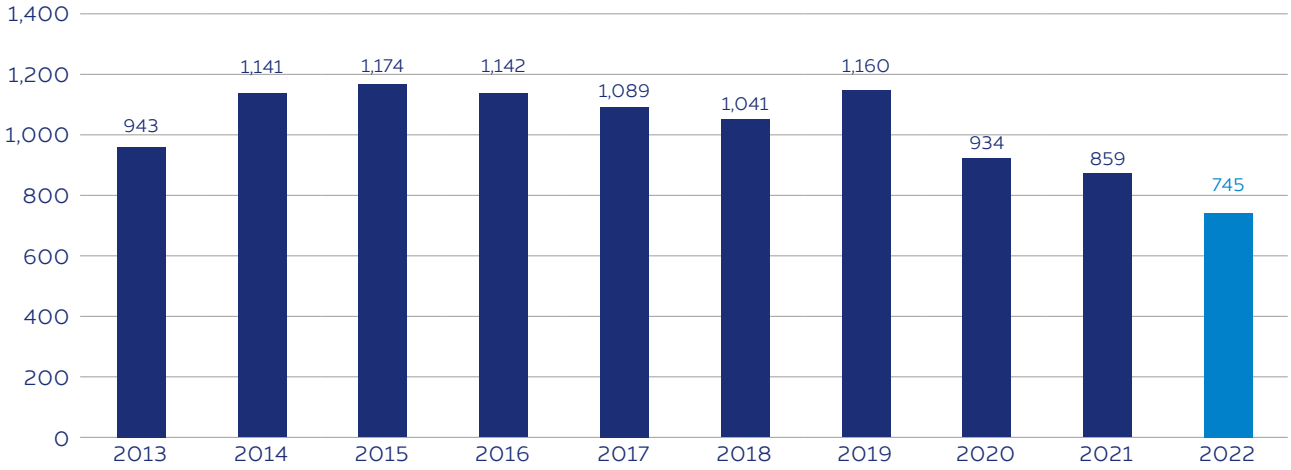


Fig. 25 Overview of safety corrective actions for medical devices adopted in 2013–2022



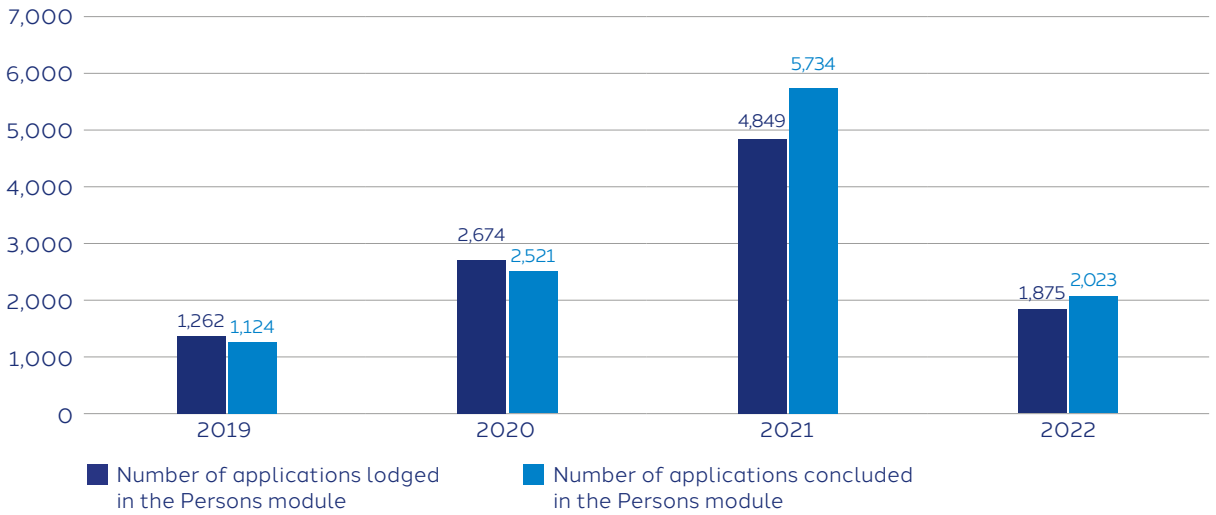
4.17 REGISTRATION AND NOTIFICATION UNIT (RAN)

The Registration and Notification Unit (RAN) focuses upon registration of persons and associated activities, on medical device notifications and associated activities, and the issuance of certificates of free sale in compliance with the Act on Medical Devices, the IVD Act, and the IVDR.

REGISTRATION OF PERSONS HANDLING MEDICAL DEVICES

In total, during the past year, the RAN Unit confirmed or asked for amendment of 2,338 notifications in the Persons module. In 2022, 1,875 notifications were lodged and 2,023 were completed. 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. 26.

Fig. 26 Ratio of submitted and concluded notifications in the Persons module



- **Notification of a person**

In 2022, the RAN Unit concluded 362 submitted notifications of persons.

- **Notification of an activity**

In 2022, 119 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, 1,394 notifications of changes to data of a person were processed and completed.

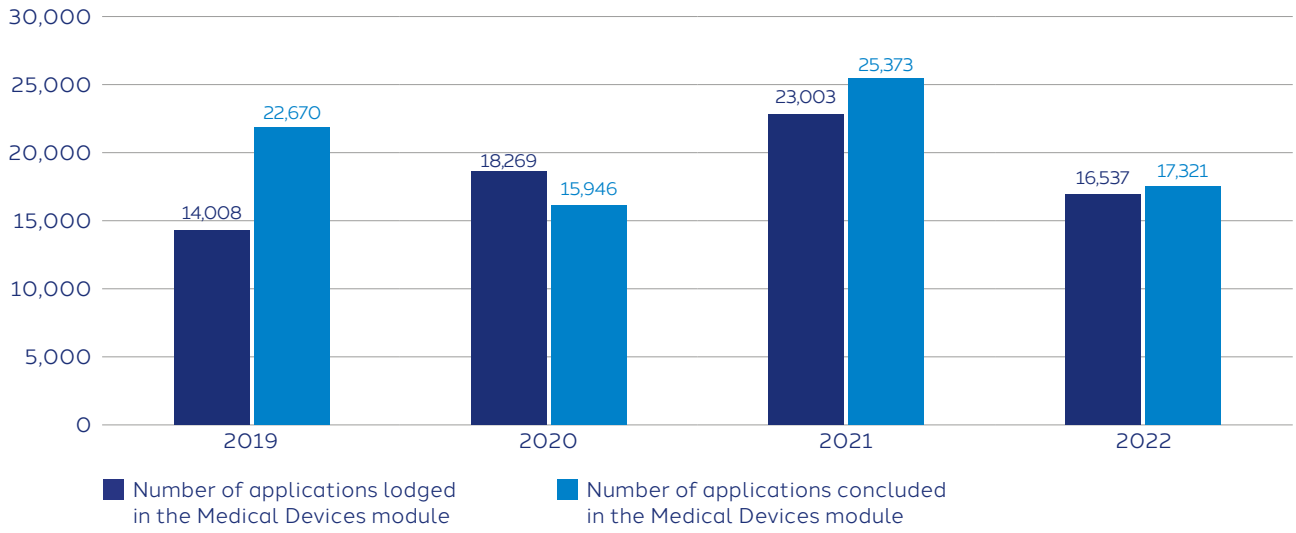
- **Notification of deletion of a person**

In 2022, the RAN Unit processed all of the 22 notifications of deletion of a person.

MEDICAL DEVICE NOTIFICATIONS

In total, the RAN Unit issued 18,954 documents, incl. invitations for amendment, in the Medical Devices module in the last year. In 2022, 16,537 applications were submitted in the Medical Devices module. A comparison of submitted and concluded applications (completed procedures governed by Act No 500/2004 Coll., the Code of Administrative Procedure) is illustrated by Fig. 27.

Fig. 27 Ratio of submitted and concluded applications



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

- **Applications for medical device notification**

In 2022, the Unit completed 9,791 administrative procedures regarding applications for medical device notification.

- **Applications for medical device notification renewal**

In total, 1,412 administrative procedures regarding applications for medical device notification renewal were completed.

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

In total, 8,151 applications for change to medical device data were processed and completed.

- **Applications for medical device deletion**

The Unit completed 967 applications for medical device deletion.

CERTIFICATES OF FREE SALE

- **Applications for certificates of free sale**

In 2022, 215 applications were submitted, of which 193 were concluded. Furthermore, twelve applications from 2021 and one application from 2020 were concluded.

4.18 MEDICAL DEVICES LEGAL SUPPORT UNIT (PPZ)

DECISION-MAKING IN THE AREA OF PRODUCT NATURE DETERMINATION AND PROPER CLASSIFICATION OF THE IVDS; DECISION-MAKING ON WHETHER A PRODUCT IS GOVERNED BY MDR

In compliance with Act No 268/2014 Coll., on Medical Devices, effective until 25 May 2021 (hereinafter referred to as "Act No 268/2014 Coll.), 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, i.e., since 26 May 2021, this agenda has been split into decision-making about whether a product is governed by the MDR, 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 devices 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, in its assessment of the application for medical device notification, it identifies any justified doubt as to whether the assessed product is governed by 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.

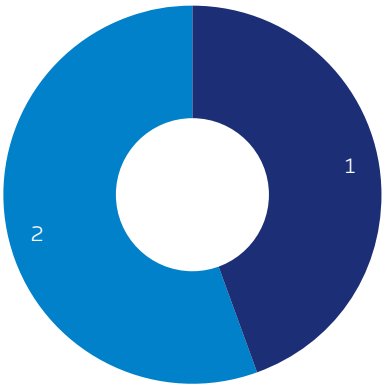
In 2022, 15 proposals for the commencement of an administrative procedure on whether a product was governed by the MDR, were forwarded to the Medical Devices Legal Support Unit.

In 2022, the Institute commenced 15 ex-officio administrative procedures on whether a product was governed by the MDR.

In 2022, the Institute received no application for a decision on whether a product was governed by the MDR or whether a product was an in vitro diagnostic device.

In 2022, five decisions stating that a product was governed by the MDR were issued. Furthermore, the Institute issued four rulings on termination of such administrative procedures.

Fig. 29 Overview of decisions issued in 2022

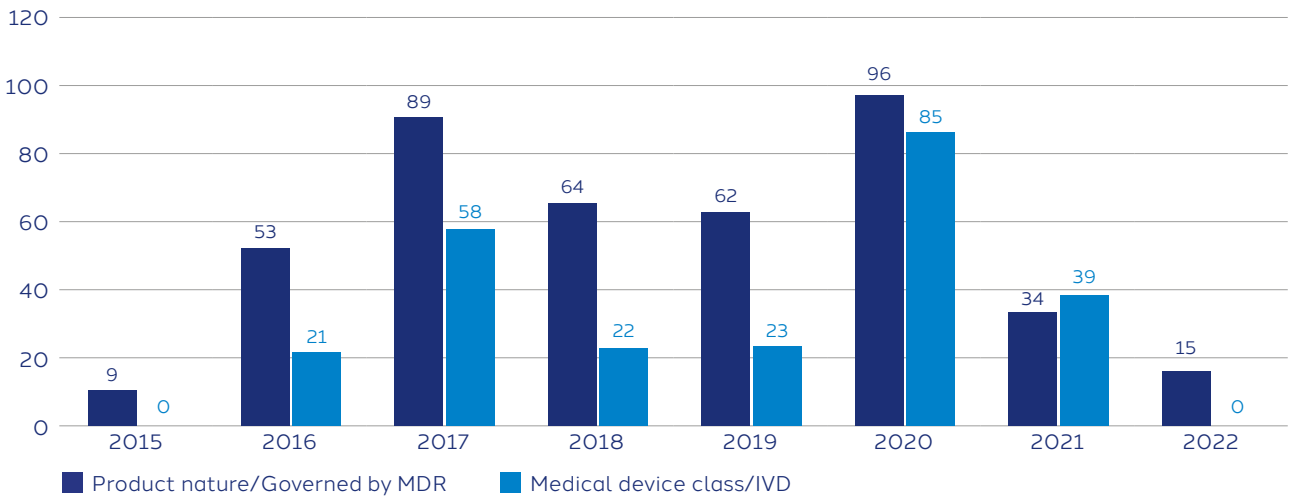


1 | Decision
4

2 | Ruling on AP termination
5

Explanatory notes:
AP – administrative procedure

Fig. 28 Overview of forwarded proposals for the commencement of ex-officio administrative procedures in 2015–2022



OFFENCES

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

In 2022, 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 1,760,000 CZK. The highest proportion of fines imposed in 2022 for the breach of the Act on Medical Devices were fines imposed upon medical device distributors and healthcare service providers.

In 2022, 25 orders and eight decisions were issued. Furthermore, the Institute issued five rulings on the termination of administrative procedures regarding offences.

In compliance with the coming into effect of Act No 268/2014 Coll., (on 01 April 2015), the Medical Devices Legal Support Unit has seen an increase in the proposals for commencement of an administrative procedure regarding offences since 2016 within the scope of monitoring of investigations into incidents, particularly breach of the obligation laid down by Section 75 of Act No 268/2014 Coll., i.e., to inform the Institute of adopted 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.

1.76 mil. CZK

This is the amount of fines imposed for breaches of the Act on Medical Devices, the IVD Act and the Act on Technical Requirements for Products.

Tab. 40 Overview of forwarded motions for administrative procedure commencement in 2015–2022

Overview for year:	2015	2016	2017	2018	2019	2020	2021	2022
Clinical Trials Unit	-	3	1	-	-	-	4	-
Vigilance Unit	2	47	79	88	185	65	21	4
Control Unit	22	69	64	20*	-*	116	71	58
Medical Devices Notification Unit	-	-	-	-	6	-	1	1
Total	**24**	**119**	**144**	**108**	**191**	**181**	**97**	**63**

** 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 2022, the Medical Devices Legal Support Unit received the total of 19 appeals to be addressed. In compliance with Section 88 of Act No 500/2004 Coll., the Code of Administrative Procedure, as amended, these appeals were forwarded via the Institute to the Ministry of Health of the Czech Republic as the appellate body.

Tab. 41 Overview of appeals forwarded to the Ministry of Health of the Czech Republic in 2022

Unit	No. of appeals	Returned for reconsideration	Granted	Declined	Withdrawn by applicant	Terminated administrative procedures
Legal Support Unit	17	5	-	8	1	1
Medical Devices Registration and Notification Unit	2	1	-	7	1	
Total number of appeals in 2022	**19**	**6***	**0***	**15***	**2***	**2***

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

4.19 MEDICAL DEVICES REIMBURSEMENT UNIT (UZP)

The reimbursement regulation has been based on a notification principle. Decisions on the inclusion of a specific medical device into a particular reimbursement group are primarily not taken via administrative procedures. Manufacturers themselves notify the Institute of their inclusion of their medical device in a reimbursement group. It is possible to notify of a new inclusion, 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 notification of a medical device inclusion in an improper reimbursement group is received, the Institute initiates an administrative procedure regarding non-inclusion in the reimbursement group or removal from a reimbursement group. Notifications of medical devices reimbursements may be lodged at any time. The maximum amounts of reimbursement for individual reimbursement groups are stipulated by the Act on Public Health Insurance.

A major part of the UZP Unit's operation represents a year-to-year producer price increase, which is implemented in compliance with Price Regulation 2/2022/OLZP of 07 January 2022, amending Price Regulation 1/2019/CAU of 22 May 2019, regulating medical devices prices.

The major output from the UZP Unit's operation is, in particular, the process of issuing the Medical Devices Reimbursement and Price List for medical devices reimbursed on voucher (hereinafter referred to as the "Medical Device Price List"), which is the main index for the realisation of reimbursements for medical devices reimbursed on voucher from the public health insurance funds. As at 31 December 2022, the Medical Device Price List contained 13,090 items in total.

Tab. 42 Medical device reimbursement notifications in 2022

Reimbursement notifications	Number
Total submissions	9,185
New notifications	1,298
Change notifications	569
Removal notifications	608
Year-to-year producer price increases	6,710

Tab. 43 Overview of administrative procedures

Administrative procedures	Number
Commenced	0
Concluded	0

Tab. 44 Medical Device Price List

Medical Device Price List	Number
Total	13,090
Included	1,034
Excluded	455

4.20 SYSTEMS, EDUCATION, AND EUROPEAN AFFAIRS UNIT (SYS)

As part of adopted systemisation, in 2022, the Systems, Education, and European Affairs Unit (SYS) was established in order to safeguard the administration and development of information systems used in the Medical Devices Department. In compliance with the new legislation, the medical devices regulation activities avail of the RZPRO registry, which needs to be updated to reflect legislative amendments; a Medical Devices Information System (ISZP) is being developed; and, at the same time, the EUDAMED European database, to which the ISZP is to be connected, is in development. Furthermore, the SYS Unit is in charge of organising expert seminars of the Medical Devices Department and it actively participates in European agendas in the sphere of medical devices regulation.

COORDINATION OF EXPERT ACTIVITIES

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 in creating conditions allowing to secure availability of medicinal products important for the provision of healthcare services is that of the Ministry of Health (MoH) 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, in cooperation with the Pharmaceuticals and Medical Devices Unit of the Ministry of Health of the Czech Republic, prepared a methodological guideline on addressing the availability of pharmaceuticals in document "ENSURING THE AVAILABILITY OF MEDICINAL PRODUCTS – COMMON MoH AND SÚKL METHODOLOGY".

4.21 EXPERT ACTIVITY COORDINATION UNIT

1. Market Report Administration – 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, moreover, are in charge of 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 for the Market Report in 2022:

- Suspended supplies: 2,826 reports (in 70 % of which supplies have already been restored);
- Terminated supplies: 939 reports;
- Restored supplies: 2,005 reports;
- Initiated supplies: 1,116 reports;
- Irreplaceable medicinal products: 131.

2. Addressing medicinal product unavailability

2.1 Addressing disrupted supplies of medicinal products within the Institute

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

2.2. Allowing for the placement of a foreign-language batch of a medicinal product onto the market

- 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 individual batches of a medicinal product the labelling of which is in a language other than the Czech onto the market, the Institute abides by the particulars stipulated by Section 3(6)(b) of Decree No 228/2008 Coll.
- In 2022, the Institute issued the total of 188 decisions allowing for the placement of a foreign-language batch onto the market, which is a 25-% 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 non-authorised medicinal products.
- In the application of Section 77(1)(i) of Act No 378/2007 Coll., on Pharmaceuticals, and Section 46 of Decree No 229/2008 Coll., on manufacture and distribution, the KOČ unit assesses and issues approvals of submitted applications for import of non-authorised medicinal products from third countries. In 2022, 146 approvals of import of non-authorised medicinal products from third countries were issued in total, which is 55 % 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 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 2022, the Institute drafted opinions on 59 new applications.

2.5. Identifying the possibility of individual preparation of medicinal products (hereinafter referred to as "individually prepared medicinal products" or "IPLP") in pharmacies

- IPLPs 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 2022, the KOČ unit drafted two assessments 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 (hereinafter referred to as "ZJ") and the Marketing Authorisation Section (hereinafter referred to as "REG"). In total, this concerned 30 replaceability assessments for the Quality Defects Unit and 60 assessments of exemptions from the sunset clause for the Marketing Authorisation Section in 2022.

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. Where the Institute, having regard to the evaluation of the stated facts, 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 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 also background materials and information on the basis of which the Institute drew this conclusion. In 2022, the KOČ unit submitted the total of 28 reports on jeopardised availability for 86 codes of medicinal products in total and one proposal for exclusion from the list for 18 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 2022, the Institute validated 2,300 applications from distributors intending to distribute listed products abroad, which represented a year-to-year growth by 59 %. 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, by means of which the Ministry of Health would prohibit the distribution of the concerned medicinal product(s) abroad. In 2022, the KOČ unit submitted 32 motions suggesting prohibition of distribution abroad for the total of 27 medicinal products (SÚKL codes).

6. Preparation, Sharing, Communication, and Addressing of Availability on the European Level

6.1. In 2022, the Czech Republic was actively represented by the Institute's Director and the KOČ unit in the implementation of the new Regulation (EU) 2022/123, 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. The Unit, inter alia, participated in the creation of processes of two newly established working groups – the Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG) and the Single Point of Contact Working Party (SPOC WP), where the representatives of national agencies mutually share information on the availability of critical pharmaceuticals.

6.2. In the course of the CZ PRES, as part of the meeting of the Heads of Medicines Agencies, SÚKL organised also a meeting with stakeholders addressing the topic of electronization of medicinal product package leaflet (chapter 3.4 refers).

5. PROCESSING AND PROVISION OF INFORMATION

5.1 INFORMATION TECHNOLOGIES

In the area of information technologies, 2022 was no longer that much affected by the COVID-19 pandemic. Home-office style of work became part of normal routine. The employees availed of mobile technologies to a great extent and, moreover, rules for their use were stabilised.

In 2022, several projects in the area of information technologies were completed. On the infrastructure level, a successful upgrade of the database infrastructure of selected systems, inter alia the ePrescription system, to Oracle Exadata C&C was successfully implemented. This upgrade allowed for a higher operating and technical security of data within the operated systems. One of the positive effects was reduction in the costs of licence support by approx. 40 %.

In the ePrescription system, two new modules – eVaccination and eVoucher– were launched successfully. At the same time, a new option of using Citizen's Identity also for healthcare professionals was implemented.

In 2022, the number of cyber-security threats kept growing, particularly in association with the overall geopolitical situation and the Ukraine war. Several measures were adopted to increase the security of the operated systems. In the sphere of cyber-security, the Institute implemented all of the corrective actions implied by the inspection of selected systems conducted by the National Cyber and Information Security Agency (NÚKIB) in late 2021.

The plan for 2023 includes reconstruction of the back-up data centre, for which project documentation has been drawn and a public contract is under way. Due to the location of some technologies, this project is coordinated with the main building roof reconstruction project.

In 2022, several projects included under the Institute's global electronization were being implemented. The main objective of electronization 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.

Of the completed projects, it is worth mentioning the replacement of the personnel information system, which should improve the functioning of internal processes in the area of personnel and payroll management. The system was successfully implemented; data were migrated; and since January 2023, the system has been running in production environment.

Another completed project is the database of clinical trials, which is linked to the pan-European clinical trial portal. This project was completed by the end of 2022 and has been also routinely used since January 2023.

The selection of vendor for the information system for the conduct and processing of administrative procedures, which should better support the process management in the course of an administrative procedure, was not successful in 2022. Finally, the vendor was selected only in early 2023 and this project will be one of the major projects in 2023.

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, have been published also in the National Catalogue of Open-Source Data.

It may be stated that in 2022, 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. Also, the efforts to increase the electronization of processing both expert and operational agendas have been successful.

ePRESCRIPTION SYSTEM

Electronic prescription and the establishment of the ePrescription information system are legislatively based on Act No 378/2007 Coll., on Pharmaceuticals, as amended. By means of the ePrescription system, the doctor issues an electronic prescription (ePrescription) for the patient; on the basis of this prescription, the pharmacy dispenses the medicinal product. The Central Repository of Electronic Prescriptions, as one of the components of the ePrescription system, collects and stores all ePrescriptions under conditions stipulated 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.

With a view to the requirement for mandatory electronic prescription, the process of modernisation of the entire system, also with regard to its inclusion in the 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 in the

critical infrastructure of the state, and hence has been governed by the tightest security measures as referred to by the Act on Cyber-Security and related legal regulations.

An ongoing system support has been established and on the basis of suggestions submitted 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. In an open tender held 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 Central Repository of Electronic Prescriptions (CÚER), the Central Repository of Electronic Vouchers (CÚEP), the Central Repository of Vaccination Records (CÚEO), the Registry of Restricted Medicinal Products ("RLPO"), the medication record, consent administration, and other specified components.

Since 01 January 2018, the system has been operated in the mode of mandatory electronic prescription. Throughout 2022, as well as in the previous years, its operation was not hindered by 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 patients and healthcare professionals have been also made available.

In their application, doctors have the possibility to prescribe an ePrescription, eVoucher or make a record of applied vaccination also outside their offices. The eVoucher prescription module is available in the application also to other healthcare professionals authorised to conduct this activity. Pharmacists and other persons dispensing medical devices may use the application to record the dispensing of a medical device on eVoucher. In the application, doctors and pharmacists may also view the patient's medication record, i.e., information on prescribed medicinal products or recorded vaccinations until 30 November 2022, if they are authorised to access these data. For pharmacists, moreover, there is a special application allowing pharmacists to gain information about an ePrescription in case functional standard communication with the ePrescription system is not available.

The patient application allows patients to view the list of ePrescriptions and eVouchers prescribed for them or applied vaccinations completed prior to 30 November 2022, in which the individual patient was clearly identified in the Registry of Inhabitants (ROB). Furthermore, parents have the option to view ePrescriptions and eVouchers issued for their underage children and their vaccination records completed prior to 30 November 2022. In the application, the patient may set up his/her consent or disagreement with the viewing of his/her medication record (list of ePrescriptions and vaccination records) or the medication record of his/her underage children. Furthermore, the complete history of accesses to his/her data, i.e., when a particular doctor or pharmacist viewed the lists of the patient's data, is available to the patient.

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 three 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; in 2021, almost 34 million SMS messages and 688 thousand e-mail messages; and in 2022, the figures reached the record amount of more than 41 million SMS messages and 700 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 electronic medical device voucher, and other news from the sphere of eHealth.

As part of the electronic prescription system operation, 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, safeguards 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 made available 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 more than a 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 utility of the system.

In 2022, more than 81 million ePrescriptions were issued and almost 80 million were dispensed, which have been the highest figures since 2018 to date. In February 2022, the borderline of 300 million ePrescriptions issued since the start of mandatory electronic prescription was overcome. The ePrescription system has hence become an essential instrument in the area of healthcare service provision.

81
million issued ePrescriptions

Almost 50 thousand doctors and dentists, i.e., their vast majority, had SÚKL generate access data for them. In 2022, application verifications with all professional chambers was flawlessly 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 2022, 46,903 doctors, 18,080 healthcare facilities, and 2,745 pharmacies were actively involved. At the moment, variations in the numbers of active entities and healthcare professionals reflect only common changes in the field, i.e., retiring individuals, arrivals of new graduates, establishment or dissolution of healthcare service providers.

On 01 January 2020, the Ministry of Labour and Social Affairs and the Czech Social Security Administration (ČSSZ) launched an electronic sick note system. Also in 2022, 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 Reservation system serving for the reservation of COVID-19 vaccination appointments. This is an important positive step taken in favour of professionals as healthcare staff may avail of the current authentication means for other systems implemented nationwide by the state administration.

Since 01 April 2020, 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. Since 01 January 2022, citizens of the Czech Republic may also apply for an excerpt from the list of vaccinations applied thereto. The data that may be required in the excerpt are limited to the period from 01 January 2022 to 30 November 2022. The scope of the data to be provided is defined by the relevant legislation.

Since 01 June 2020, the patient has had, moreover, the 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 presented patient's document, the pharmacist can retrieve the list of all ePrescriptions issued for the patient. The medicinal product dispensing proper is then carried out in a standard manner on the basis of the obtained ePrescription identifiers.

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.

On 01 January 2022, mandatory electronic format 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 was launched as required by law. Prior to the end of 2021, these prescriptions had been issued in paper format only; since 01 January 2022, however, they have been issued in electronic format. 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 the prescription in paper format. This extension was associated also with the change in prescribing medical cannabis which has been prescribed only on prescriptions with the highly-addictive-substance flag.

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.

Another record-keeping system is that of electronic vaccination records. 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 has been 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 displays only those vaccinations for which the identity of the patient was verified during the record-taking.

This record has become part of the medication record and is accessible only to the patient whose identity was verified against the ROB registry during vaccination. The amendment to Act No 378/2007 Coll., on Pharmaceuticals, terminated the recording of applied vaccinations in the ePrescription system as at 30 November 2022.

As of 01 December 2021, a functionality has been launched allowing citizens to express their possible 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 the 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 entered consents or disagreements with the viewing of the vaccination record are applicable solely to the data entered in the ePrescription system, i.e., data for the period from 01 January 2022 to 30 November 2022.

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 or vaccination 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 for 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. Available are data recorded in the period from 01 January 2022 to 30 November 2022.

On the basis of Act No 89/2021 Coll., on Medical Devices, electronization of medical device vouchers (eVouchers) was launched as one of the components of the ePrescription system. This Act came into effect on 26 May 2021 and, in compliance with Communication No 54/2022 Coll., of 08 March 2022, on putting the central repository of electronic vouchers into operation, the eVoucher was launched as of 01 May 2022. On 29 April 2022, Decree No 97/2022 Coll., of 22 April 2022, implementing some provisions of the Act on Medical Devices concerning electronic vouchers was published in the Collection of Acts. The Decree has been effective since 01 May 2022. At the moment, eVoucher record-keeping is optional.

With its functionality, the eVoucher replaces paper vouchers for medical devices. The intention in the development of the eVoucher module was to avail of the existing ePrescription system functionalities as much as possible to make the prescribing and issuance of eVouchers as simple as practicable. Vouchers may be issued electronically for all types of medical devices, i.e., those for sight correction, for patients with a hearing impairment as well as any others. The major processes covered by the ePrescription system include also the approval of eVouchers by health insurance companies where required by the nature of the prescribed medical device. The eVoucher module also allows for mail-order dispensing of the medical device where the requirements for remote sale stipulated by the MDR have been met.

In association with the launch of eVoucher, also the number of user roles that may access the ePrescription system has been extended. In addition to the previously established roles of the doctor and pharmacist, eVouchers may be prescribed also by other healthcare professionals and they may be dispensed also by pharmaceutical assistants, orthotics, prosthetics, optometrists, opticians, and other persons dispensing medical devices. Since May 2022, all users of the ePrescription system can access the ePrescription system also by means of NIA, i.e., login via e.g., bank identity, mobile eGovernment key or identity card with an activated electronic chip. Initially, this option was available only to patients using their patient application.

Since May 2022, almost 158 thous. eVouchers were issued, approx. 133 thous. were dispensed. The www.epreskripce.cz website publishes current information about active dispensaries where eVouchers may be used for dispensing. Their number is now close to three thousand.

Since as early as 2018, SÚKL, along with the main project partner – the Vysočina Region – has been involved in the Deployment of Cross Border Services in the Czech Republic (ePrescription/eDispensation) NIX-ZD.CZ II. project. The project focuses upon cross-border exchange of ePrescriptions and information about dispensed medicinal products, which, as a result, offers increased safety and quality of provided health care and patient comfort.

Cross-border exchange of electronic prescriptions will provide access to the ePrescription to a pharmacist in another participating EU Member State than the state where the ePrescription was issued. The Czech patient will be able to collect his/her medicine in any other EU Member State involved in the production environment of this cross-border exchange of electronic prescriptions. And, on the other hand, patients from those European countries that will be operating in the production environment, will be able to collect their prescriptions in Czech pharmacies.

In 2022, the last steps towards launching the cross-border ePrescription were conducted. Following successful European testing, the final audit conducted by the European Commission was also successfully completed. At the moment, we are awaiting only the formal and administrative permission to enter the production environment, which is expected to come in early 2023.

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. The importance of the ePrescription system may be evidenced also by numerous awards gained thereby since 2018. In 2022, ePrescription was pronounced the most beneficial project in the sphere of eHealth and digitisation of Czech health care and won an award on the INMED conference organised by EEZY Publishing, s. r. o.

The significance of the ePrescription system was also obvious during the second half of 2022, in association with the Czech Presidency of the EU Council. Presentations regarding the functionalities of the ePrescription system, its benefits and importance for Czech and potentially, in future, European patients were given during many expert and formal meetings while discussing healthcare.

Fig. 30 Number of prescribed and dispensed ePrescriptions in individual months of 2022 (mil.)

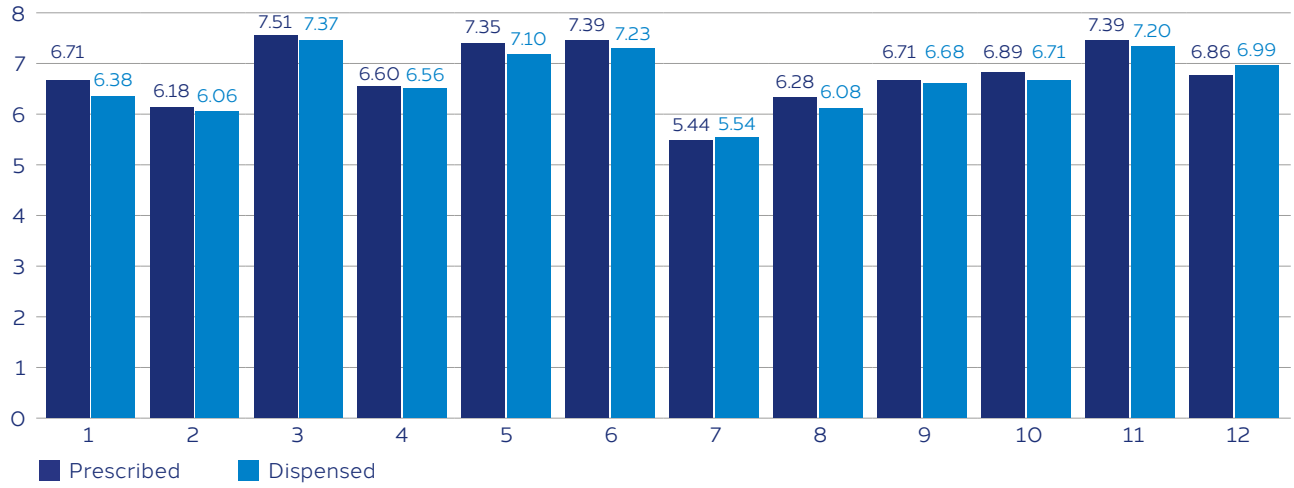
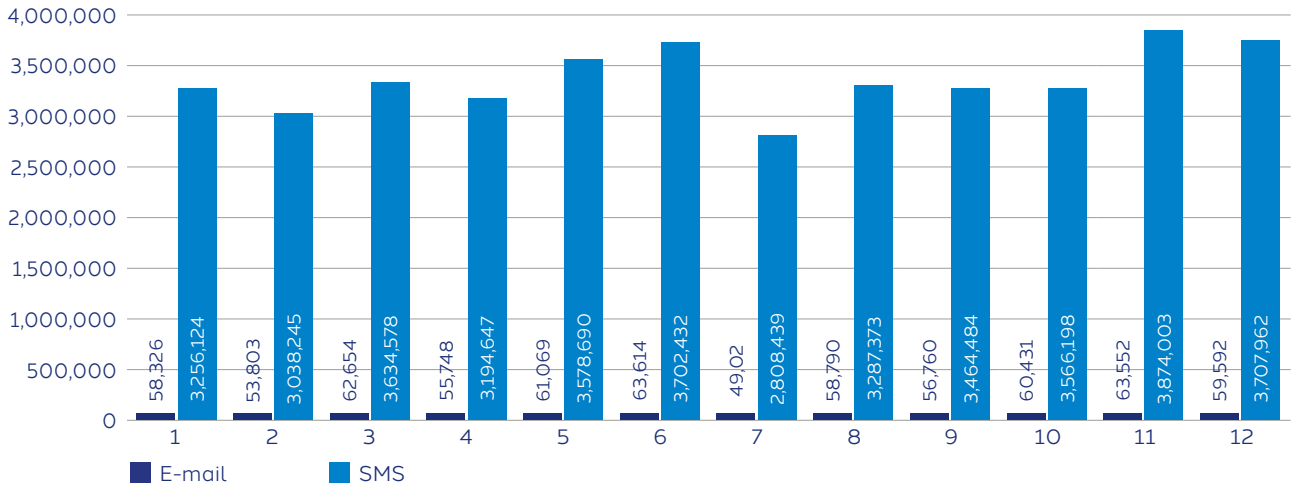


Fig. 31 Number of e-mail and SMS messages sent in individual months of 2022



5.2 DATABASE OF MEDICINAL PRODUCTS AND MONITORING OF SUPPLIES TO PHARMACIES

On the basis of the obligation stipulated by the Act on Pharmaceuticals, the Institute keeps a registry of authorised medicinal products and arranges for the publication of selected information in its information media. For the purposes of this registry, an internal database of medicinal products (DLP) is used; this registry is updated on an ongoing basis. The mandatory disclosure information from DLP is displayed in the database of medicinal products on SÚKL's website.

REGISTRY OF ACTIVE SUBSTANCES

At present, the DLP Component Library contains 19,967 components (incl. combined components). In 2022, 519 new components were entered.

- In 2022, an update of flagging of doping components and of products containing such substances in the DLP was carried out pursuant to "The 2022 Prohibited List – The World Anti-Doping Code" effective as of 01 January 2022. Thereafter, flagging was performed on a quarterly basis and in each quarter, the list of newly authorised medicinal products with doping components was sent to the Czech Antidoping Committee.
- A revision of substances labelled as doping by the Pharmazie.de database was carried out.
- New components were entered and components from revised and corrected monographs of the Czech Pharmacopoeia 2022 Supplement and of the European Pharmacopoeia supplements 10.8 and 11. 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 2022 were entered and amended.
- Data about dependency-producing and psychotropic substances were updated in compliance with the new version of Government Regulation No 463/2013, on the lists of dependency-producing substances.

REGISTRY OF MEDICINAL PRODUCTS

In 2022, the Institute granted 472 marketing authorisations (3,256 SÚKL codes). Authorisation was revoked for 438 marketing authorisation numbers, which corresponds to 5,215 codes. The authorisation was revoked either upon request of the marketing authorisation holder (345 marketing authorisation numbers), or due to the sunset clause (80 marketing authorisation numbers), or due to the fact that the holder did not apply for marketing authorisation renewal (13 marketing authorisation numbers). The validity of 7,591 codes in total expired (the period of the code final sale expired or marketing authorisation was revoked).

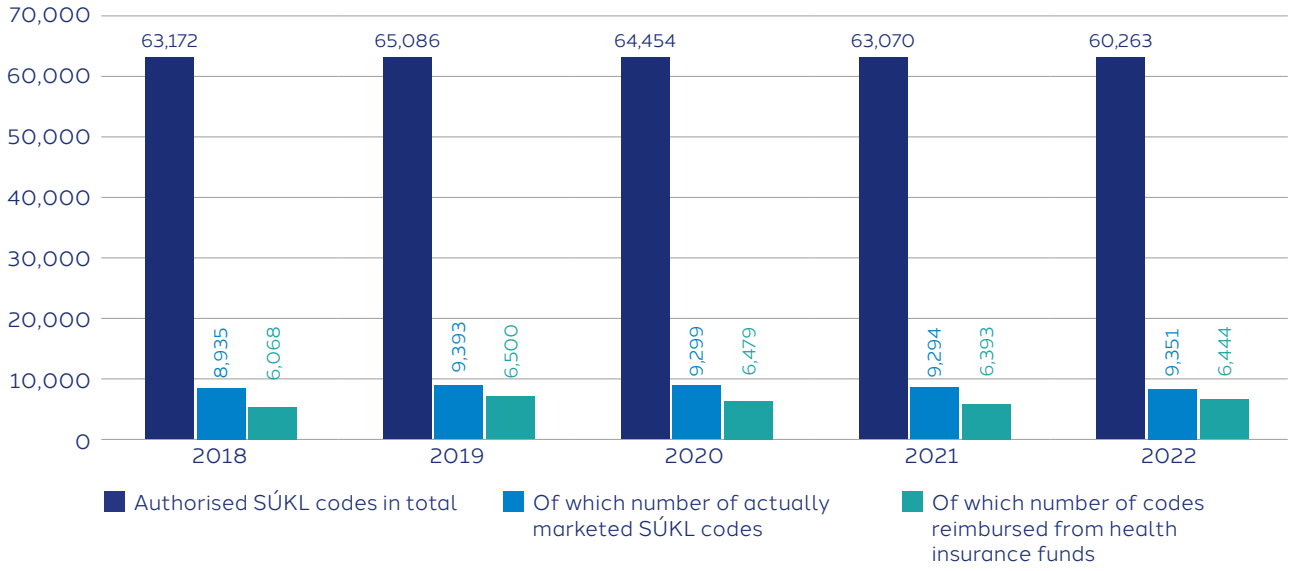
In the course of 2022, no distribution was reported for 50,912 codes (84 %) of medicinal products, excluding homeopathic preparations. Hence despite having a valid marketing authorisation, these products were not placed on the market.

Authorised medicinal products contain 2,651 various active substances in total.

Tab. 45 Selected subgroups of authorised medicinal products recorded in the Institute's database as of 31 December 2022

	Total no. of MA numbers / marketed MA numbers	Total no. of SÚKL codes / marketed SÚKL codes
Medicinal products in total (excl. homeopathic preparations)	**18,848/6,545**	**60,263/9,351**
Of which by MA numbers:		
MA numbers granted by the Institute	6,491/4,931	47,869/7,725
MA numbers of products authorised via Community Centralised Procedure	12,357/1,613	12,390/1,625
Of which by content:		
Single-component	15,166	48,638
Multi-component	3,683	11,608
Of which by type of dispensing:		
Prescription-only medicinal products	18,045/5,870	56,441/8,193
OTC medicinal products	861/687	3,728/1,141
Restricted OTC medicinal products	4/4	22/7
Restricted prescription-only medicinal products	7/6	69/8
Homeopathic preparations	274/274	756/391

Fig. 32 Authorised medicinal products in the period of 2018–2022



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. The List 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 placements 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.

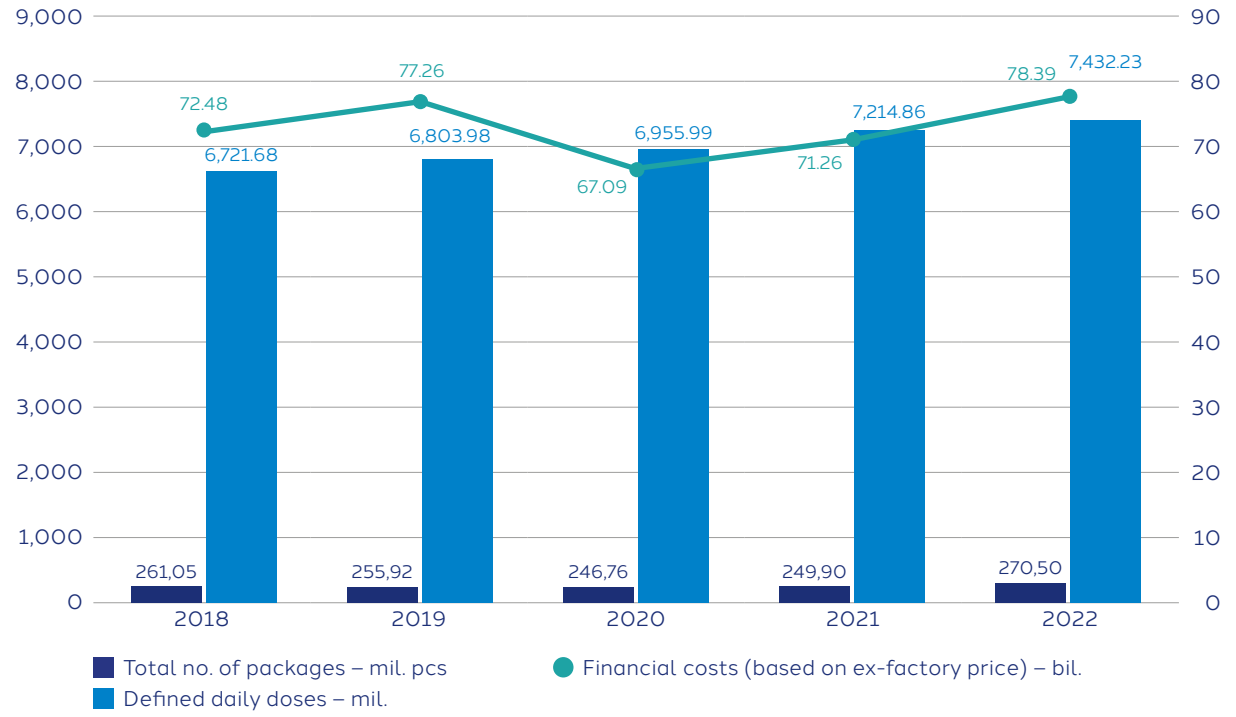
EVALUATION OF DELIVERIES OF DISTRIBUTED MEDICINAL PRODUCTS

In 2022, 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 both 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 evaluated.

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 the financial cost values over the years, data on financial costs are provided in producer prices, i.e., in 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 publishes summary information from monthly reports of entities authorised to distribute medicinal products in the Czech Republic on its website.

In 2022, 270.53 million packages of medicinal products were distributed, which corresponds to approx. 7,432.23 mil. DDD. The value of these deliveries amounted to 78.39 billion CZK (based on ex-factory price).

Fig. 33 Deliveries of medicinal products in the period of 2018–2022



Tab. 46 Deliveries of distributed medicinal products in 2022

Medicinal products in total	**Number**
Deliveries to pharmacies and healthcare facilities (mil. packages)	270.531
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	78,388.985
Deliveries to pharmacies and healthcare facilities (mil. DDD)	7,432.234
DDD/1,000 inhabitants/day	1,934.302
Prescription-only medicinal products	
Deliveries to pharmacies and healthcare facilities (mil. packages)	182.124
Deliveries to pharmacies and healthcare facilities (mil. CZK based on ex-factory price)	78,141.937
Deliveries to pharmacies and healthcare facilities (mil. DDD)	6,744.239
DDD/1,000 inhabitants/day	1,755.246
OTC and selected pharmaceuticals	
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. packages)	88.155
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. CZK based on ex-factory price)	247.048
Deliveries to pharmacies, healthcare facilities and vendors of selected pharmaceuticals (mil. DDD)	687.901
DDD/1,000 inhabitants/day	179.032
Restricted OTCs	
Deliveries to pharmacies and healthcare facilities (mil. packages)	0.250
Deliveries to pharmacies and healthcare facilities (mil. DDD)	0.093
DDD/1,000 inhabitants/day	0.024
Homeopathic preparations	
Deliveries to pharmacies (mil. packages)	1.911

During 2022, the Data Analysis Unit processed the total of 5,620 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 carried out 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 the activities of the Institute 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 of the aforementioned groups. TIO is also in charge of social networks (Facebook, Twitter, Instagram, LinkedIn), 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. Furthermore, a vaccination schedule with essential information regarding both mandatory and optional vaccination, incl. relevant vaccines, is available. For several years now, the general public may avail of the "Ask Us" service, through which doctors and pharmacists answer questions from 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 87 patient questions.

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 the second half of 2022, TIO was busy preparing the Czech Presidency of the EU Council. One of the meetings held as part of the Czech Presidency was a meeting of the Working Group of Communications Professionals (WGCP), which took place in early December in Prague (chapter 3.4 refers).

In 2022, TIO answered 2,643 inquiries from the general public and from professionals which were sent via e-mail or post. Approximately 2,289 more inquiries were handled by the infoline.

Via e-mail, the Unit answered 394 questions from the media and other questions were answered by phone. In this area, TIO has noted a decrease in the agenda (in 2021, 637 questions were answered by e-mail; in 2020, it was 230 questions). More often than in previous years, the representatives of the Institute also provided regular statements for radio or TV broadcasting. Thirty-seven press releases were published on the Institute's website.

6. FINANCIAL AND MATERIAL RESOURCES OF THE INSTITUTE

6.1 THE 2022 INCOME AND EXPENDITURE ACCOUNT

INCOME

In 2022, extra-budgetary income in the total amount of 589,375 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 requests lodged by 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 48/1997 Coll., on Public Health Insurance, as amended, Act No 167/1998 Coll., on Dependency-Producing Substances, as amended, and Act No 375/2022 Coll., on Medical Devices and on in Vitro Diagnostic Medical Devices, as amended, for the funding of payroll, operating, and investment expenditures not covered by allocated financial resources from the state budget. In 2022, the total amount of 574,739 thous. CZK was used in this manner through permissible excess expenditure. Of this amount, 550,596 thous. CZK were used for non-investment expenditure and 24,143 thous. CZK for the financing of investment needs.

In addition to income from the reimbursement of costs of expert activities, another part of income came from the revenues of the state budget, such as collected administrative fees for submitted applications amounting to 21,127 thous. CZK, income from imposed fines amounting to 4,008 thous. CZK, income from lease in the amount of 267 thous. CZK, income from the sale of goods (medical cannabis) amounting to 1,870 thous. CZK, compensations of administrative procedure costs and refunds of excess advance payments made, related fully to the previous budgetary years, amounting to 1,205 thous. CZK, etc. The Transfers from the reserve fund line shows the volume of extra-budgetary income used for the funding of expenditures in 2022. An overview of the budget income as of 31 December 2022 is provided in Table 47.

Tab. 47 State budget income (thous. CZK)

Item	Approved budget	Actual amount
Administrative fees	24,800	21,127
Received penalty payments	4,000	4,008
Income from lease	0	267
Income from the sale of goods	0	1,870
Income from service provision	0	73
Received non-capital contributions and compensation	0	1,205
Transfers from the reserve fund	0	574,739
Total	**28,800**	**603,289**

EXPENDITURE

Data concerning expenditures incurred in 2022 broken down by individual categories are provided in Table 48.

The total investment expenditure from extra-budgetary resources amounted to 24,133 thous. CZK. Investment resources were used to finance the procurement of laboratory instruments in the total amount of 1,066 thous. CZK (ultra-pure-water delivery system, ultra-microweights, a SDS PAGE set), logos for SÚKL buildings in the amount of 230 thous. CZK, technical equipment of a meeting room in the amount of 72 thous. CZK, and a promotion video in the amount of 254 thous. CZK. The costs of procured licences amounted to 160 thous. CZK, the costs of technical upgrades of applications and SW (ERP, eSSL Athena, and others) to 17,544 thous. CZK, the costs of HW purchase and replacement to 2,371 thous. CZK, the costs of procurement of a personnel information system to 1,196 thous. CZK, and the costs of a new agenda system (ISZP) to 617 thous. CZK. A superstructure upgrade of the JBS security system was implemented (224 thous. CZK) as well as a security system and a data network for OKL České Budějovice (110 thous. CZK). The preparation of documentation for planned construction works amounted to the total of 289 thous. CZK (in particular, preparation of reconstruction of roof of Building no. 24, data centre reconstruction, and the development of a temporary parking lot).

Non-investment expenditures were utilised in the total amount of 710,751 thous. CZK, of which 160,400 thous. CZK came from the state budget and 550,351 thous. CZK were taken from extra-budgetary resources. Extra-budgetary resources included resources from abroad provided for the EURIPID project (utilised amount: 93 thous. CZK) and the STARS project (utilised amount: 12 thous. CZK).

Tab. 48 Expenditures (thous. CZK)

Indicator	Approved budget	Final budget	Actual amount
Employee salaries	24,155	53,771	53,771
Civil servant salaries	91,783	310,645	310,644
Other payments for completed work, severance pay, surrenders	3,603	15,003	15,001
Mandatory insurance premium	40,405	126,955	126,950
Fund of Social and Cultural Needs contribution	2,319	7,272	7,272
Operating acquisitions and related expenditure	967	198,108	197,113
Acquisition of long-term tangible and intangible fixed assets	0	24,143	24,133
TOTAL	**163,232**	**735,897**	**734,884**
of which: operating expenditure	163,232	711,754	710,751
capital expenditure	0	24,143	24,133

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 aimed at enhancing 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 and to provide additional functionalities and analytical tools for the database are under way. In 2022, 103 thous. CZK were utilised for payroll including statutory deductions and travel expenditures in the project (of which, 93 thous. came from foreign funds). SÚKL will continue to act as an ordinary project member.

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 project was successfully completed in June 2022. It was a European project receiving the Horizon 2020 grant support. The objective of the project was 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 and establish support for the academia in the form of consultations. In 2020, on the basis of a survey carried out in the previous year at 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. In this pilot project, the Institute, along with The Netherlands, provided training in the sphere of requirements governing the conduct of clinical trials for three aforementioned selected countries. In 2022, a complex list of existing support activities for regulatory scientific advice in Europe was created; an analysis of the aforementioned educational pilot project was performed; and a specific plan of training in support of academic staff was prepared. The main output from the project was the "STARS Common Strategy Regulatory Support and Advice for Academia" publication. In 2022, 12,000 CZK were utilised for travel expenses within the scope of the project (source: funds from abroad).

Since 2018, the Institute, along with the main project partner – the Vysočina Region – has been involved in the Deployment of Cross Border Services in the Czech Republic (NIX-ZD.CZ II) project. The objective of this project is to create, test, and deploy a cross-border ePrescription service. The total duration of project implementation has been scheduled from 01 July 2018 until 30 June 2022. Of the total project costs, 75 % will be covered by the CEF TELECOM European subsidy. In the course of 2022, the project focal point was the testing of the data exchange between the Czech Republic and other Member States, successful completion of audit tests, completion of the audit, and the drawing of financial report upon project completion. In late 2022, formal steps for the roll-out of cross-border e-prescription in the production environment were being addressed, i.e., specifically, application submission, application approval by the European Commission, determination of timeline for production verification. At the moment, it is expected that the new cross-border e-prescription service will be launched in early 2023. In the following year 2023, SÚKL's utmost priority will be, in particular, the successful roll-out, marketing, and promotion of the new module of the ePrescription system and its further development. In 2022, project expenditures amounted to the total of 1,974 thous. CZK (extra-budgetary funds of SÚKL).

OTHER

In 2022, the total of 2,049,888.94 CZK was utilised for foreign business trips. As the COVID-19 pandemic still lasted in early 2022, the vast majority of international meetings were held on-line. In March, the situation changed, the pandemic began to subside, and gradually, restrictions were being lifted. Conditions became again favourable for travel, and the number of foreign trips started to increase slowly. In 2022, the total of 146 foreign business trips took place, of which 50 were fully or partially refunded by the organising institutions (European Commission, EMA, EDQM, etc.). Of the total number of conducted trips, 13 were educational events, 14 trips took place within the scope of expert projects, 14 trips were aimed at the conduct of foreign inspections (particularly in India), and 105 were routine foreign business trips. The employees travelled mostly to Brussels and Amsterdam, where they attended events at the European institutions.

ASSETS

The total assets as of 31 December 2022 amounted to 1,357,291 thous. CZK, of which fixed assets represented the volume of 355,819 thous. CZK and current assets 1,001,472 thous. CZK. Of the total liabilities of 1,357,291 thous. CZK, equity amounted to 1,304,425 thous. CZK and borrowed capital to 52,866 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 2021	Current period 2022
ASSETS	**1,340,799**	**1,357,291**
A. Total fixed assets	**365,078**	**355,819**
of which:		
I. Long-term intangible fixed assets – total	80,872	87,310
II. Long-term tangible fixed assets – total	284,206	268,509
of which:		
Lots	4,530	4,530
Buildings	226,986	221,985
Separate tangible movables and sets of tangible movables	46,671	
Unfinished tangible fixed assets	35,654	6 340
B. Total current assets	**6,019**	**6,340**
of which:		
I. Inventory - total	1,727	153
II. Short-term receivables - total	11,738	17,476
III. Short-term financial assets - total	962,706	983,843
LIABILITIES	**1,340,799**	**1,357,291**
C. Equity	**1,293,610**	**1,304,425**
of which:		
I Assets of the accounting entity and adjustments	226,542	226,531
II. Funds of the accounting entity	925,357	941,425
Fund for Cultural and Social Needs	1,990	2,238
Reserve Fund	923,367	939,187
III. Economic result	–1,005,761	–1,142,598
Economic result for the current accounting period	–139,078	–136,837
Economic result for the previous accounting periods	–866,683	–1,005,761
IV. Income and expenditure account of the budget management	1,147,472	1,279,067
D. Total borrowed capital	**47,189**	**52,866**
of which:		
I. Total long-term liabilities	0	0
II. Total short-term liabilities	47,189	52,866

AUDITING

In 2022, no public administration audits conducted by control bodies pursuant to the Act on Financial Audits took place.

7. FOCUS UPON EMPLOYEES

7.1 PERSONNEL ISSUES

ORGANISATIONAL STRUCTURE

In compliance with the Institute's systemisation approved for 2022 pursuant to Act No 234/2014 Coll., on Civil Service, as of 01 January 2022, the number of systemised positions in the Institute was 583, of which 475 were civil service positions and 108 were employment positions.

As part of the organisational changes associated with the Institute's systemisation effective as of 01 January 2022, compared to 2021, the number of civil service and employment positions changed by ten requirements for extra positions and one position was created form a spared FTE. All of the newly created positions are covered by extra-budgetary funds. The reason for the creation of the new positions was the implementation of new agendas stipulated by legislation (such as the implementation of the new Medical Device Information System and new powers of SÚKL in the sphere of surveillance over advertising).

In the course of 2022, several other systemisation modifications were implemented with effect as of 01 April 2022, 01 July 2022, and 01 December 2022; these modifications concerned service position changes and amendments in the appointment of managerial staff permanent substitutes. On 01 July 2022, the number of civil service positions changed to 476 and the number of employment positions to 107.

The number of physical employees on the Institute's payroll as of 31 December 2022 was 532 persons, of which 415 were women (i.e., 78 %) and 117 were men (i.e., 22 %).

583

systemised civil service and employment positions

As part of the Personal and Working Life Harmonisation Policy support, as of 31 December 2022, the total of 67 employees of the Institute (of which 66 were women), i.e., 12.6 % of the total number of employees, worked part-time.

Tab. 50 Numbers of employees at local workplaces as of 31 December 2022

Brno	35
České Budějovice	3
Hradec Králové	7
Olomouc	4
Ostrava	4
Plzeň	2
Praha	477

AGE STRUCTURE OF EMPLOYEES

Average age: females 44.6 years; males 43.4 years. The overall average age of all employees is 44 years.

Tab. 51 Age structure of employees as of 31 December 2022

Year	% of employees under 35 years	% of employees aged 36-55 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
2022	22.4	57.6	20.0

QUALIFICATION STRUCTURE OF EMPLOYEES

Tab. 52 Kvalifikační struktura zaměstnanců dle dosažené úrovně vzdělání ke dni 31. prosince 2022

Highest achieved education	Primary	Secondary	Technical colleges	University – bachelor's degree	University – master's degree	Postgraduate
Number of employees	1	104	6	30	422	45
% of the total number of employees	0.16	17.08	0.99	5.09	69.29	7.39

** The data include employees taking their compensatory leave, maternity leave, and parental leave.*

STAFF TURNOVER

The overall staff turnover taking into account all entries and terminations of employment/civil service amounted to 10.1 %, which was a slight increase compared to 2021.

In total, 308 tenders for vacancies were opened in the course of 2022, on the basis of which the total of 82 job openings were filled (Tab. 53 refers).

Tab. 53 Overview of tenders completed pursuant to the Act on Civil Service (civil service positions) and pursuant to the Labour Code (employment positions) and associated entries into employment/civil service

	Civil service		Employment	
	No. of positions to be staffed through tenders	Staffed	No. of positions to be staffed through tenders	Staffed
Total	**168**	**39**	**140**	**43**

In 2022, the total of 54 employees terminated their employment or civil service.

Tab. 54 Overview of employment and civil service terminations in 2022 by reason of employment/civil service termination

	Employment	Civil service
Cancellation of employment/civil service in probationary period	1	9
Agreed time expiry	4	0
Termination by agreement (Section 49 of the Labour Code)	6	0
Notices given by employees/termination of civil service upon request of the civil servant	11	15
Notices given due to organisational reasons/by decision of the civil service authority	1	2
Termination of civil service performance in SÚKL due to transfer of the civil servant to another civil service authority	-	1
Retirement	1	3
Total	**24**	**30**

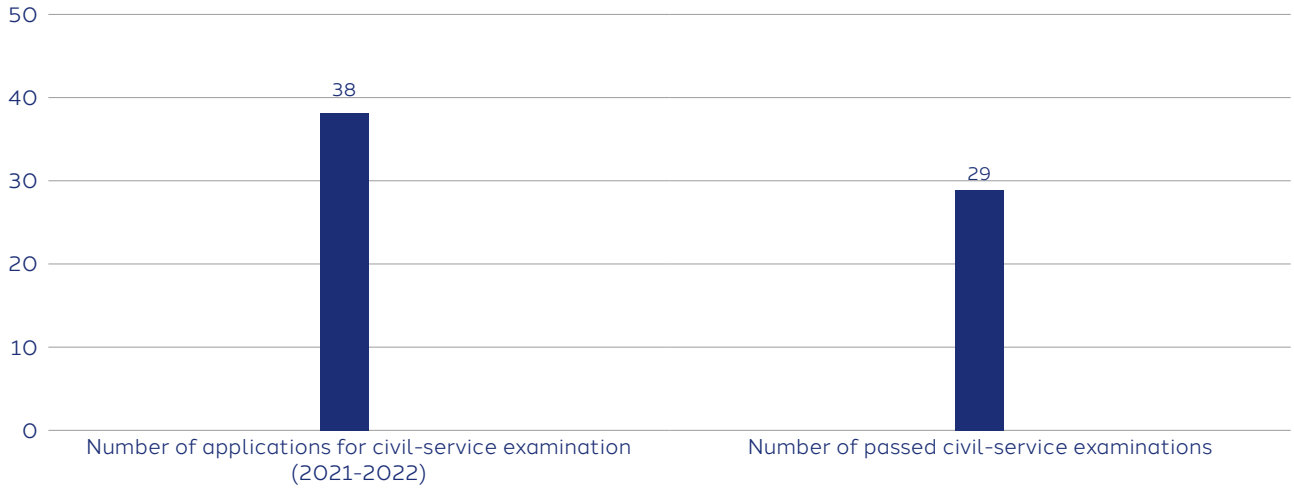
CIVIL-SERVICE EXAMINATION

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

Fifteen applications were brought forward from 2021 to the next calendar year and in the course of 2022, 23 applications submitted by the employees of the Institute were newly registered, which amounts to 38 applications in total. Of the total number, 29 employees successfully passed both parts of the civil-service examination in 2022. The remaining nine employees will take the examination in 2023 (within twelve months of their recruitment as civil servants, as stipulated by the Act on Civil Service).

All of the employees succeeded to pass the concerned civil-service examinations on the first attempt.

Fig. 34 Civil-service examinations in 2022



7.2 EMPLOYEE EDUCATION

In 2022, employee education was carried out in the form of personally attended courses, seminars, and trainings, as was the practice prior to the COVID-19 pandemic. Where a course or a seminar was offered also in the on-line form, the employees availed also of this form of education.

Within the scope of initial education, all new employees were trained in all topics stipulated by the currently 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 employee education focused particularly upon expert education, due to the high demands on staff expertise, implementation of legislative changes, and the need for continuous deepening and increasing of qualification and knowledge of our staff in individual fields. The employees again began to travel abroad for business trips during which they attended specialised educational events.

Management training was resumed and it focused particularly on the development of personal talents and management skills.

Due to the COVID-19 pandemic, language courses in the 2021/2022 academic year were organised in the on-line environment. Both individual and group courses took place in the form of distance learning. For this reason, in the first half of 2022, the courses continued in the aforementioned on-line mode. Courses in the 2022/2023 academic year started in September 2022 and they have resumed their regular face-to-face form.

Selected employees who actively participated in the Czech Presidency of the EU Council (CZ PRES), which took place in the second half of 2022, attended the education session called “Training in Communication, Negotiation, and Presentation Skills in the Sphere of Health Law”; the training assumed the form of group learning. The employees who completed this training were directly involved in legislative negotiations in the EU Council and they presented and prepared background materials for the organised events.

In 2022, 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 1,728,530 CZK.

Tab. 55 Overview of educational activities in 2022 – follow-up education

Type of event	Number of events	Number of hours	Number of attendees
Specialised courses & training; language courses	1,287	5,884	953
Mandatory training	65	130	1,037
Foreign specialised training	13	319	15

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 November 2022, the LL-C (Certification) Czech Republic, s.r.o., certification body conducted a review of some of the Institute's processes as part of the second surveillance audit and noted that the Institute's quality management system continued to meet the requirements of the aforementioned standard.

The Laboratory Control Department has developed a management system compliant with the ČSN EN ISO/IEC 17025:2018 standard. In 2022, a successful compliance check of the established system with the standard was conducted in the form of an international audit (MJA – Mutual Joint Audit) and the Laboratory Control Department received attestation/certification for the period of the next three years.

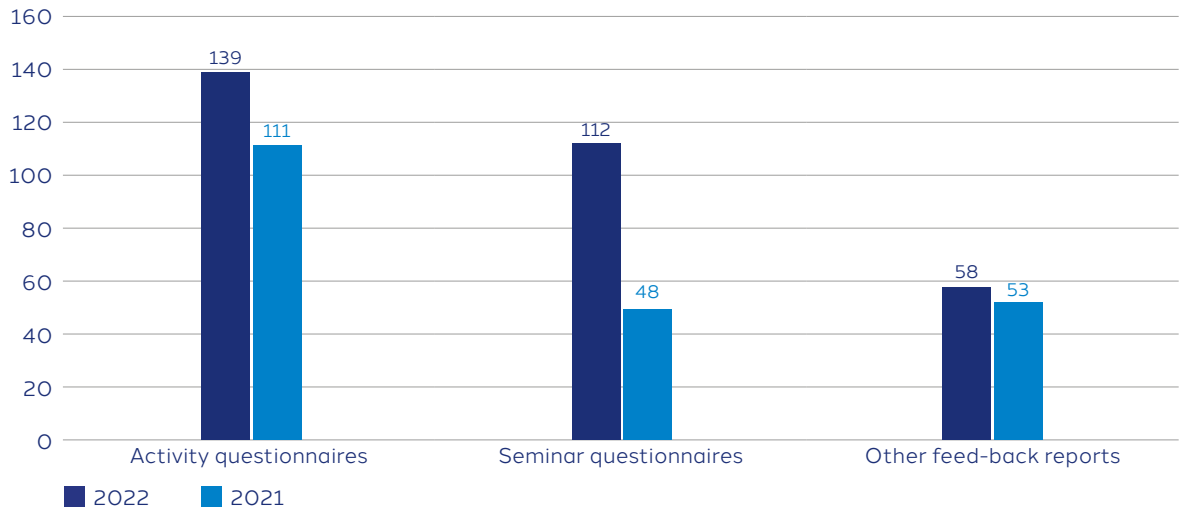
The functionality of the quality management system was verified on an ongoing basis also within the scope of internal audits. In 2022, eleven such internal audits took place. One of the scheduled internal audits of the quality management system was not conducted due to a change in the organisation structure and re-allocation of the process agenda to several units as of 01 January 2023; this internal audit was included in the internal audit schedule for 2023.

In order to fulfil its mission and achieve its vision, SÚKL has established a "Strategic Plan of the State Institute for Drug Control for 2021–2025", including its strategic goals, the fulfilment of which is being evaluated by SÚKL's management on an annual basis.

In the sphere of quality, SÚKL continuously strives to carry out activities at a high standard, predictably, using transparent documentation, at as short timelines as practicable, and in the required quality, keeping an open mind to stimuli, observing ethic rules, environmentally friendly behaviour, and safety at work. All of these efforts are aimed at increasing stakeholder satisfaction, at creating a positive image of SÚKL, and at achieving international recognition.

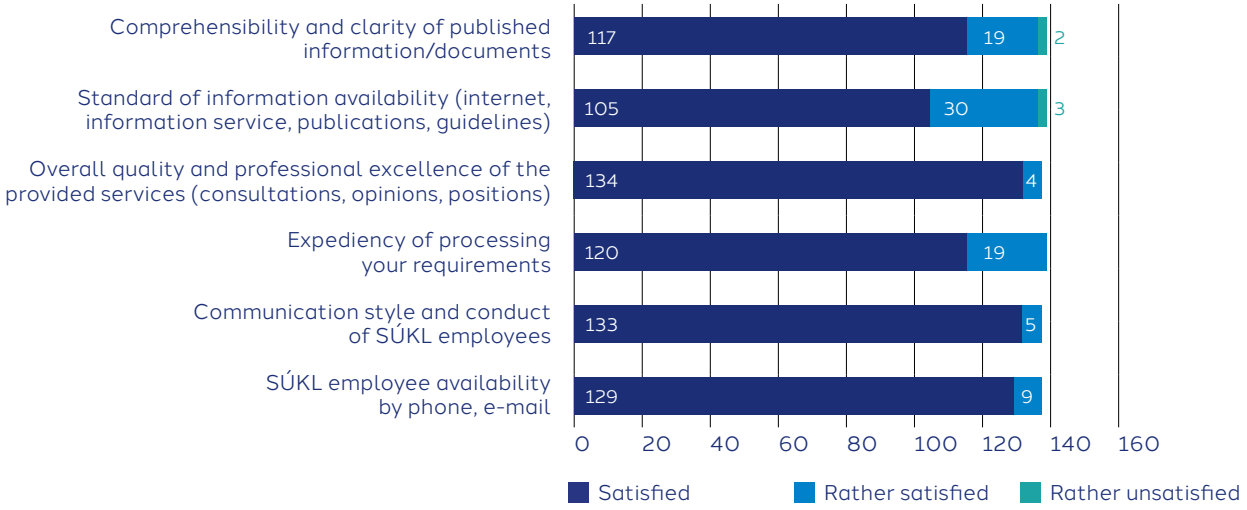
In 2022, we received 309 feed-back reports from stakeholders which were provided in the form of answers to questions in satisfaction surveys or as opinions submitted in other forms.

Fig. 35 Feedback reports for 2021–2022



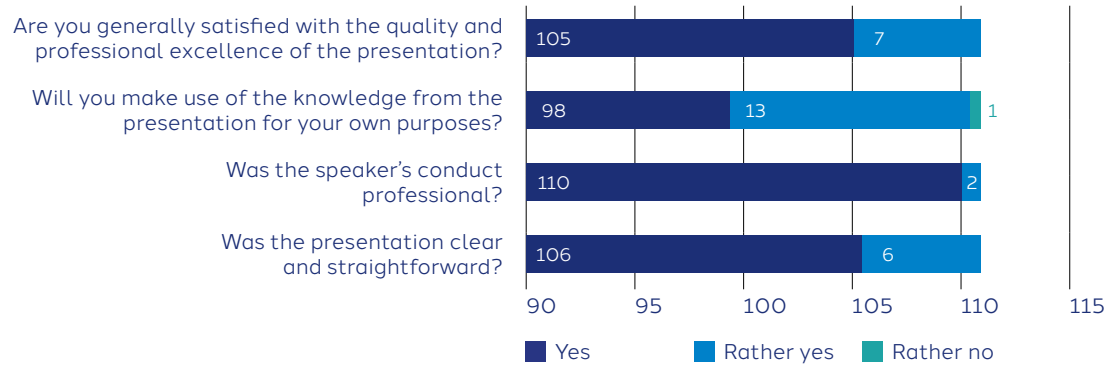
The answers to questions from questionnaires focusing upon SÚKL's activities suggest that the stakeholders were the least satisfied with the "standard of information availability", where three responders were rather unsatisfied and 30 respondents were rather satisfied.

Fig. 36 Outcomes of questionnaires focusing upon SÚKL's activities



The answers to questionnaires focusing upon SÚKL seminars or presentations suggest that the lowest satisfaction level was for the item "Will you make use of the knowledge from the presentation for your own purposes?", where one respondent answered "rather no" and 13 respondents answered "rather yes".

Fig. 37 Outcomes of questionnaires focused upon SÚKL's seminars or presentations



SÚKL much appreciates any stimuli and comments from the obtained feed-back, as these are a step towards ensuring a higher effectiveness and improvement of our activities. Of the stimuli for improvement received in 2022, for example, the request to publish major changes to published guidelines and updates of the list of distributors on SÚKL's website www.sukl.cz was implemented. Works resulting in modifications and better clarity of the website will continue and we will also strive for enhanced effectiveness of the telephone Infoline. Also in the coming year, our employees will organise seminars for external entities to provide education on good practice.

9. INFORMATION SECURITY MANAGEMENT POLICY AND CYBERSECURITY

Every year, the demands for ensuring cybersecurity are higher and higher and this trend did not stop in 2022, either.

In March 2022, a cybersecurity exercise took place in SÚKL in cooperation with the National Cyber and Information Security Agency (NÚKIB), the purpose of which was to check the knowledge of the necessary procedures, responses, and adoption of measures in a situation in which SÚKL would become the target of a cyber-attack.

In April 2022, the role of the Cybersecurity Manager was re-staffed.

In the sphere of cybersecurity, emphasis was placed upon the process of increasing the security awareness of all staff of the Institute, particularly those in positions that have a higher influence on securing the adequate level of cybersecurity.

The number of noted cybersecurity attacks aimed at SÚKL's information systems was high also in 2022; nevertheless, none of them was successful.

Furthermore, internal regulations were amended in the effort to better define the responsibilities for the security of the operated information systems.

In December 2022, the Institute successfully passed a surveillance audit of the information security management system (ISMS) pursuant to the ČSN ISO/IEC 27001:2014 standard, which means that it has been the holder of the relevant certificate for as long as 15 years.

10. OUTLOOK FOR 2023

In 2023, the Institute expects the launch of cross-border exchange of electronic prescription, which will provide access to ePrescriptions for pharmacists in other involved EU Member States than the one where the concerned ePrescription was issued. Czech patients will be able to collect their medicines in any other EU Member State taking part in the production operation of this cross-border electronic prescription exchange. And vice versa, patients from European countries operating in the production environment will be able to collect their medicines in Czech pharmacies. SÚKL has been involved in the Deployment of Cross Border Services in the Czech Republic - NIX-ZD.CZ II. (ePrescription/eDispensation) project, with the Vysočina Region acting as the main partner, since 2018. The launch of the cross-border exchange of electronic prescription will increase the safety and quality of provided health care as well as patient comfort. The reconstruction of the back-up data centre, scheduled for 2023, is also relevant for the ePrescription system.

It is encouraging to see that in recent years, the number of decentralised procedures with the Czech Republic acting as the Reference Member State has been significantly increasing on the European level (in 2022, SÚKL ranked 7th in the EU in terms of the number of completed procedures); furthermore, SÚKL's involvement in the assessment of centralised procedures has been equally growing. SÚKL has been newly involved in another renowned EMA working group – the Scientific Advice Working Party. We intend to build SÚKL's global position as that of a transparent, open-minded regulatory authority sought by regulated entities also in the coming years. We assume that SÚKL will be successfully increasing its involvement in centralised procedures both in the role of the CHMP rapporteur/co-rapporteur and the PRAC rapporteur also in the near future. We will continue to support and develop the provision of important safety information on medicinal products via the ePrescription and medication record functionalities. SÚKL will continue its active involvement in the sphere of submission of clinical trial applications via CTIS.

In 2023, the Medical Device Regulation Section will continue to enhance inspection activities in the sphere of new obligations of economic operators implied by the implemented amendments associated with the coming into effect of EU Regulations 2017/745 and 2017/746. SÚKL will keep improving the newly set-up processes implied by the powers stipulated by the aforementioned legislation, with special emphasis upon the newly established obligations in the area of regulation of advertising for medical devices. Works on the electronization of agendas of the Medical Device Regulation Section via a new medical device information system (ISZP) will continue also in 2023. Until the launch of the fully functional European medical device database (EUDAMED) system, it will be necessary to safeguard the full functional operation of the RZPRO system.

In the course of 2022, the amended Act No 48/1997 Coll., on Public Health Insurance, was successfully implemented in SÚKL's regulatory processes and procedures. The amendment brought particularly the establishment of a new process for orphan medicinal products, a change of processes pertaining to highly innovative medicinal products, and a change in the conduct of in-depth reimbursement revisions. Also in 2023, SÚKL will continue to participate in the NCAPR program and will continue to be involved in the newly established HTA Coordination Group. SÚKL continues its trend of shortening the timelines for the publication of assessment reports and decisions for new pharmaceuticals and new indications (by 50% compared to 2017). The aforementioned concerns approximately 50 innovations each year that have to pass a complete assessment of their added clinical value, economic aspects, and financial impacts. In respect of these significant innovations, SÚKL will continue their ongoing publication for the general public, focusing upon patients and healthcare professionals.

Also in 2023, SÚKL will continue to cooperate with marketing authorisation holders in addressing issues concerning safety features, which was one of the factors helping to reduce the total number of alerts, and this has been a continuing trend. In compliance with the new legislation, a list of websites offering medicinal products contrary to legal regulations has been compiled. SÚKL publishes this list on its website, and it will continue to pay much attention to this area, with special focus upon the protection of health and safeguarding patient safety, also in 2023. The new trend of failing to keep records of medicinal products in pharmacies in compliance with the Act on Pharmaceuticals and penalties imposed therefor will form one of the priority areas for SÚKL's inspection activities also in the next year.

In 2023, SÚKL will continue to pay much attention to the medicinal product availability agenda. The stabilised and coordinated approach to this issue will be supported and effective communications addressed to marketing authorisation holders, submitters of specific therapeutic programmes, distributors as well as physicians, experts, and the general public, will continue to be issued. Activities aimed at improving the functionality of the publicly accessible electronic database of Market Reports notifying of the placement of products on the market, their suspended, resumed or terminated supplies form an integral part of this approach.

SÚKL will be active also in agendas on the European level. The employees of the Institute have been involved in negotiations concerning new legislative drafts and non-legislative documents on the working level of the EU Council and they provide expert support for all levels of negotiations, including the meeting of the Employment, Social Policy, Health and Consumer Affairs Council (EPSCO) of ministers. SÚKL, as the lead manager, draws down the framework position, which is approved by the government and which defines the basic position of the Czech Republic and essential, insuperable limits, so called red lines. During the negotiations, SÚKL then prepares instructions and engages in negotiations with other Member States aimed at reaching so called general approach of the Council and in finding a common compromise also in the following phase of trialogues with the European Parliament and the European Commission.

As regards SÚKL's powers, we expect that in 2023, main attention will be paid to negotiating the revision of general pharmaceutical legislation, i.e. Regulation (EU) 726/2004 and Directive 2001/83/EC, which is to be submitted together with the Council Recommendation on antimicrobial resistance (AMR). The Regulation on fees payable to the European Medicines Agency is expected to be finalised. SÚKL will continue to be involved as the co-lead manager in negotiations concerning the revision of legislation governing blood, human tissues and cells as well as the new regulation on the European Health Data Space (EHDS).

11. LIST OF ABBREVIATIONS

AIFP	Association of Innovative Pharmaceutical Industry (Asociace inovativního farmaceutického průmyslu)
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
CMDh	Coordination Group for Mutual Recognition and Decentralised Procedures - Human
CMS	Concerned Member State
CNS	Central nervous system
CRO	Contract Research Organization
CRS	Chemical Reference Substance
CRLN	National chemical reference substances
CTAG	Clinical Trials Advisory Group
CTCG	Clinical Trials Coordination Group
CTEG	Clinical Trial Expert Group
CTFG	Clinical Trials Facilitation Group
CTIS	Clinical Trial Information System
CÚEO	Central Repository of Vaccination Records (Centrální úložiště záznamů o očkování)
CÚEP	Central Repository of Electronic Orders (Centrální úložiště elektronických poukazů)
CÚER	Central Repository of Electronic Prescriptions (Centrální úložiště elektronických receptů)
ČAFF	Czech Association of Pharmaceutical Companies (Česká asociace farmaceutických firem)
Cz.Ph.	Czech Pharmacopoeia
ČSN	Czech technical standard
ČSSZ	Czech Social Security Administration (Česká správa sociálního zabezpečení)
DCP	Decentralised Procedure for marketing authorisations
DDD	Daily defined dose
DG	Diagnosis
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
HVLP	Proprietary medicinal products
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 medical devices
KB	Blood bank
KH	Clinical trial
KHV	Clinical trials and Vigilance Unit
KLP	Cannabis for medical use
KIVS	Public administration communication infrastructures
KOP	Medical Device Control and Expert Opinion Unit
CIMD	Clinical investigation of medical devices
LMS	Lead Member State
MP	Medicinal Product
ATP	Advanced therapy products
HTC	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
MSS	Market Surveillance Study
MSSG	Executive Steering Group on Shortages and Safety of Medicinal Products
MoH	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
RAN	Registration and Notification Unit
RATC	Rapid Alert System for Human Tissues and Cells
RF	Radiopharmaceuticals
RLPO	Registry of Restricted Active Substances (Registr pro léčivé látky s omezením)
RMS	Reference Member State
ROB	Registry of Inhabitants (Registr obyvatel)
RZPRO	Registry of Medical Devices (Registr zdravotnických prostředků)
SAE	Serious Adverse Event
SAKL	State Agency for Medical Cannabis
SDP	Good Distribution Practice
SKP	Good Clinical Practice
SLP	Good Laboratory Practice
SpTP	Specific therapeutic programme
SPOC	Single point of contact
SPOC WP	Single point of contact Working party
SRLM	Strategic review and learning
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
SYS	Systems, Education, and European Affairs Unit
CAFIA	Czech Agriculture and Food Inspection Authority
ŠÚKL	Slovak State Institute for Drug Control
TIO	Press and Information Unit
TP	Transfusion products
TZ	Tissue centres
UHR	Reimbursement
UZP	Medical Device Reimbursement Unit
ÚZIS	Institute of Health Information and Statistics of the Czech Republic (Ústav zdravotnických informací a statistiky)
VHP	Voluntary Harmonization Procedure
VUC	Materially regulated price
WGEO	Working Group of Enforcement Officers
WHO	World Health Organisation
SAR	Serious adverse reaction
ZNU	Serious incident
ZoRR	Act on Advertising Regulation
ZoZP	Act on Medical Devices
ZP	Health insurance
ZP	Medical device
ZTS	Blood centre
ZP	Zdravotnický prostředek
ZTS	Zařízení transfuzní služby

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