

**Applied Health Research Support Program for 2020-  
2026**

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## **1. Title of the Program**

Applied Health Research Support Program for 2020-2026 (hereinafter referred to as the "Program").

## **2. Legal Framework of the Program**

The Program will be implemented according to:

- Act No. 130/2002 Coll., on the Support of Research and Development from Public Funds and on the Amendment to Some Related Acts (Act on the Support of Research and Development), as amended (hereinafter referred to as "Act No. 130/2002 Coll.");
- Commission Regulation (EU) No 651/2014 of 17 June 2014, as amended by Commission Regulation No 2017/1084 of 14 June 2017 that, in accordance with Articles 107 and 108 of the TFEU, declares certain categories of support compatible with the internal market, Official Journal of the EU L 187 of 26.6.2014, p. 1 (hereinafter referred to as the "Commission Regulation");
- the Framework for State Support for Research, Development and Innovation - Official Journal of the European Union of 27 June 2014 (2014/C198/01) (hereinafter referred to as the "Framework");
- and according to other related regulations.

The Program is exempted from the notification requirement under Article 108 (3) TFEU as it fulfills the conditions of the Commission Regulation.

Under this Program, the payment of support to an enterprise meeting the definition of an enterprise in difficulties set out in Article 2 (18) of the Commission Regulation is excluded. The payment of individual support is also excluded in favor of an enterprise against which an unpaid recovery order has been issued subsequent to a decision of the Commission under which the support received from a provider from the Czech Republic was declared illegal and incompatible with the internal market.

The program will be implemented in accordance with the National Priorities of Oriented Research, Experimental Development and Innovation (hereinafter referred to as "R&D&I Priorities"), which were approved by Government Resolution of the Czech Republic No. 552 on July 19 2012, and in accordance with the document entitled The Implementation of National Priorities of Oriented Research, Experimental Development and Innovation, approved by Government Resolution of the Czech Republic No. 569 on 31 July 2013. The Program is in line with the key areas of change of the National Research and Innovation Strategy for the Smart Specialization of the Czech Republic (National RIS3 Strategy), which was approved by Government Resolution of the Czech Republic No. 634 on 11 July 2016. The Provider reserves the right to announce thematically oriented public tenders focused on the priorities of the National RIS3 Strategy. Furthermore, the Program is in accordance with the "National Strategy for Rare Diseases for 2010-2020", approved by Resolution No. 466 of 14 July 2010 by the Government of the Czech Republic. The Program also takes into account Health 2020, the strategic document of the WHO, the Concept of Hygiene Service and Primary Prevention in Public Health Protection.

### **3. Provider**

The support is provided by the Ministry of Health, with its registered office on Palackého náměstí 4, Prague 2.

### **4. Program Identification Code**

For the purposes of registration in the research, experimental development and innovation information system, the Program has been assigned the code "NU".

### **5. Categorization of the Research Character**

In particular, the Program will support projects that have the nature of applied research under the Commission Regulation and Framework (including industrial research and experimental development or their combination). Applied research in healthcare aims to solve problems related to the diagnostics, treatment and prevention of human diseases. A part of the applied research can be basic research, which is necessary for obtaining the results of applied research. The terms and conditions will be described in detail in the dossier for public tenders in research, experimental development and innovation through which the Program will be implemented.

### **6. Analysis of the Issues Solved**

The Program builds on the running Applied Health Research Support Program for 2015-2022 with the code NV (hereinafter referred to as the "NV Program"), which was approved by Government Resolution No. 59 of 22 January 2014. So far, the NV Program has not been assessed, the first projects supported under the NV Program have been completed as of 31 December 2018, and only in 2019 will the first final outputs of these projects be known and assessed. In 2016, the completed Departmental Research and Development Program of the Ministry of Health III with the code NT was assessed (the R&D&I Council submitted the assessment to the government for information in May 2017). At the time of the evaluation of the NT program, it was found from available sources that more than 3,600 results were achieved thanks to the support of projects under this Program, of which the vast majority consisted of results of a publishing character (especially articles in professional periodicals).

Similarly to the NV Program, this follow-up Program will be based on the currently applicable Health Research Concept until 2022, which was approved by Government Resolution No. 58 of 22 January 2014, and will be updated as the concept expires. The program will continue to pursue the National Priorities for Research, Experimental Development and Innovation, namely Priority no. 5: A Healthy Population, where the most common diseases in the population are defined, as well as their causes, which represent major challenges for health research. The aim of the Program is not to solve all societal problems related to the health of the population, as it is a matter influenced by many different factors. The intention of the Program is to support health-related applied research in the form of suitably set up projects in order to achieve results that, to a greater or lesser extent, contribute to solving some of the problems defined in the R&D&I Priorities.

Data from the Czech Statistical Office for 2017 show that the most common cause of death was diseases of the circulatory system – they were responsible for 44.3% of deaths, followed by neoplasms with a 25.0% share of deaths. The third most common were diseases of the respiratory system with 7.2%. These three most common causes of death are the same for both men and women in the long term, but a slight decrease in the first two causes can be observed in the long term. In 2006 - 2016 the proportion of circulatory diseases decreased by 6% on average and the incidence of neoplasms by 1.2% on average. This is followed by external causes (prevailing in men – 6.7% of all deaths), diseases of endocrine nutrition and metabolism (prevailing in women – 4.5% of all deaths) and digestive diseases (3.7% of all deaths). However, an increase (by more than 4% on average) was recorded in other causes of death between 2006 and 2016, which included nervous system diseases, infectious and parasitic diseases, and mental illness and behavioral disorders, among these Alzheimer's disease and dementia. Infant mortality has been steadily decreasing in the long term and reached 2.7 per mille in 2017.

Furthermore, the data of the Czech Statistical Office for 2017 show that the population of the Czech Republic increased by 31.2 thous. during the year 2017 to 10.61 million. Both foreign migration (28.3 thousand) and natural variation (3 thousand) contributed to the total annual increase. Fertility and the number of live births continued to grow, rising for the fourth consecutive year, reaching 114.4 thousand in 2017. The total fertility rate increased from 1.63 to 1.69 per woman year on year, with specific fertility rates growing at almost any age. The mean age of a mother giving birth was 30 years for the third consecutive year. The number of seniors aged 65 and over and children under 15 increased again in 2017, while there was again a year on year decrease in persons of working age. Most of the population belonged to the age group 40-44 years. The population continued to age, resulting in a year on year increase in the average age of the population, the age index and the proportion of persons aged 65 and over. The index of economic dependence also increased. In recent years, the age group of seniors (persons aged 65 and over) has changed the most dynamically from all of the three main age groups. At the end of 2017, there were a total of 2,040,183 inhabitants of this age in the Czech Republic, thus the number of seniors exceeded 2 million for the first time in history. There were 527.3 thous. more than in 2007 and 51.3 thous. more than at the end of 2016.

It follows from the above statistical data that the setting of A Healthy Population priority is still current even after several years, and in the area of applied health research, it is necessary to focus inter alia on the most common causes of death and then on the issues of population aging and the quality of life of the elderly. However, it is not possible to rely solely on demographic data on mortality, it is also necessary to consider diseases and their causes, which are the greatest threat to the quality of life of the living population, and also focus on their prevention. In order to better target healthcare research, an epidemiological study will be carried out prior to the announcement of the 1<sup>st</sup> public tender under this Program and its findings will be reflected in the project orientation requirements in the dossiers of the individual public tenders.

In addition to the aging of the population, it is necessary to mention that researchers in the health sector are also aging and it is therefore desirable to target support on the younger generation, which is reflected in the sub-program of the Program.

## **7. Duration of the Program**

The duration of the Program is set between 2020 and 2026, i.e. 7 years.

The duration of a project will be at least 3 years and no longer than 5 years, with the duration in the individual public tenders in research, experimental development and innovation set in such a way that the available state budget expenditures are used optimally. Projects implemented under the Program must be completed by 31 December 2026 at the latest. Further specifications will be given in the tender dossier.

The timeframe according to the Commission Regulation has been set until 2026, given that no new projects will be launched between 2024 and 2026, but multi-annual projects launched by 2023 will be finalized.

## **8. Deadline for the announcement of Program public tenders**

A total of 4 single-stage public tenders are planned under the Program. The first tender will be announced in 2019 with the commencement of support in 2020. This first tender will replace the originally planned last tender under the previous NV Program, which cannot be implemented due to a lack of time. Subsequently, an annual announcement of public tenders is planned for the years 2020, 2021 and 2022, with the provision of support starting in 2021, 2022 and 2023. Only projects with a maximum duration of 4 years will be able to apply for the public tender in 2022, so that the projects are completed by 31 December 2026 at the latest. Public tenders will be implemented with regard to financial possibilities and needs related to the achievement of the Program's objectives.

## **9. Total Program Expenditure**

The total expenditure for the duration of the Program between 2020 and 2026 is expected to be CZK 6,050 million, of which CZK 5,500 million will come from state budget expenditure on research, development and innovation, while the Program will be financed according to the possibilities of the state budget.

As the originally planned public tender for 2020 will not be announced under the previous NV Program (with a planned budget of CZK 300 million for each year between 2020 and 2022), the resources from the NV Program will be used for the first public tender announced under this Program in 2019. The average intensity of the Program support is 90% due to the anticipated representation of research organizations and enterprises in the Program projects.

The total Program expenditure for the duration of the Program is allocated in accordance with the expected gradual announcement of tenders and in relation to the expected average duration of projects. The budget for the individual tenders was planned according to the current development and with regard to the growth of the Czech economy in recent years, during which both wages and the prices of goods and services increased, thus also increasing the costs of the projects.

**Tab. no. 1: Total Program Expenditures and State Budget Expenditures (in millions of CZK)**

year	2020 <sup>1</sup>	2021	2022	2023	2024	2025	2026	total
Total expenditures	330	825	1155	1430	1155	770	385	6050
State budget expenditures	300	750	1050	1300	1050	700	350	5500
Non-public sources	30	75	105	130	105	70	35	550

## 10. Form, Intensity and Amount of Support

Support will be provided in the form of a subsidy for eligible costs to legal or natural persons, as an increase in the expenditure of state organizational units or organizational units of ministries.

The intensity of support, set as a percentage of the project's eligible costs, will be calculated for each Program project and for each beneficiary and other participant separately under the Commission Regulation. The maximum allowable support intensity per project in accordance with Act No. 130/2002 Coll. and the Commission Regulation for projects involving only research organizations may be up to 100% of the total eligible costs, for non-economic activities of research organizations under point 19 and the following Framework. For projects involving enterprises, the maximum allowable intensity of support for applied research<sup>2</sup> and individual categories of beneficiaries and other participants will be specified in the dossier for each tender according to current European Union regulations.

The maximum amount of project support allowed (without a notification obligation or a more detailed assessment of the EC) set out in Article 4 (1)(a)(i) of the Commission Regulation shall not be exceeded. The amount of support will be assessed on a case-by-case basis for each project. The amount of support requested must be justified and proportionate to the objectives, the duration of the project and expected project results.

The following table shows the maximum allowable support intensities for basic and applied research by category of participants (according to Article 25, paragraphs 5 and 6 of the Commission Regulation).

**Tab. no. 2: Permitted intensity of support according to research and enterprise category**

	Small enterprise	Medium enterprise	Large enterprise
<b>Basic research</b>	100%	100%	100%
<b>Industrial research</b>	70%	60%	50%
<b>Industrial research in the case of:</b>	80%	75%	65%

<sup>1</sup> The difference between Program expenditures and planned state budget expenditures will be covered by claims from unused expenditures from previous years.

<sup>2</sup> In accordance with Article I, paragraph 1.3. (15)(e) of the Framework, applied research is defined as industrial research, experimental development or a combination of the two.

<ul style="list-style-type: none"> <li>effective cooperation between enterprises; for large enterprises: cross-border cooperation with at least one small or medium-sized enterprise</li> </ul>			
or			
<ul style="list-style-type: none"> <li>cooperation with a research organization</li> </ul>			
or			
<ul style="list-style-type: none"> <li>the public dissemination of results</li> </ul>			
<b>Experimental development</b>	45%	35%	25%
<b>Experimental development in the case of:</b>			
<ul style="list-style-type: none"> <li>effective cooperation between enterprises; for large enterprises: cross-border cooperation with at least one small or medium-sized enterprise</li> </ul>	60%	50%	40%
or			
<ul style="list-style-type: none"> <li>cooperation with a research organization</li> </ul>			
or			
<ul style="list-style-type: none"> <li>the public dissemination of results</li> </ul>			

## 11. Beneficiaries

The candidate for, i.e. beneficiary of support from the Program for a project under Act No. 130/2002 Coll., the Commission Regulation and the Framework, as well as other participants of the project, may be:

1. Organizations for research and the dissemination of knowledge (hereinafter referred to as "Research Organizations") – legal entities that meet the definition of a research organization under the Commission Regulation<sup>3</sup> and which address the project individually or in cooperation with other participants and demonstrate the ability to co-finance the project from non-public funds.
2. Enterprises – legal and natural persons who, according to Annex 1 of the Commission Regulation, carry out an economic activity and handle the project independently or in cooperation with other participants and demonstrate the ability to co-finance the project from non-public funds. The beneficiary of the support in accordance with Article 1 (4)(a) of the Commission Regulation cannot be an enterprise for which a recovery order has been issued.

The assessment of whether the candidate or other participant fulfills the definitions of a research organization pursuant to Act No. 130/2002 Coll., the Commission Regulation and the Framework will be performed by the provider individually for each candidate or other participant during the assessment of the project proposal and during the project itself. The fulfillment of the definition of a research organization will be verified by submitting the documents specified in the tender dossier.

<sup>3</sup> In accordance with Article 2 (83) of the Commission Regulation, "an organization for research and the dissemination of knowledge" is an entity (e.g. university or research institute, technology transfer agency, innovation intermediary, a physical or virtual cooperating research-oriented entity) irrespective of its legal status (established by public or private law) or the method of financing, whose main objective is to independently conduct basic research, industrial research or experimental development or to disseminate publicly the results of such activities through teaching, publishing or knowledge transfer.



Based on long-term experience, the provider assumes that the main beneficiaries will be universities (especially medical faculties), contributory organizations of the Ministry of Health (university hospitals and specialized institutes) and professional institutes of the Academy of Sciences of the Czech Republic. To a lesser extent, legal entities registered in the Commercial Register or healthcare facilities established by regions or other organizational units of the state will probably also be involved in the projects.

## **12. Eligibility of Candidates for Support**

Only those candidates who meet the eligibility conditions set out in Section 18 of Act No. 130/2002 Coll. may receive project support in this Program. If more than one candidate is jointly involved in a single project, the obligation to demonstrate eligibility applies to all such candidates. The candidate demonstrates eligibility through the submission of documents according to Act No. 130/2002 Coll. in a manner stipulated by the provider in the tender dossier.

Compliance with the eligibility condition will be evaluated by the committee for the acceptance of project proposals before the project proposals are assessed. Failure to comply with any of the eligibility conditions is a reason for not including the project proposal in the tender.

## **13. Cooperation between Enterprises and Research Organizations**

Effective cooperation on a project between an enterprise and a research organization is understood, in accordance with the Commission Regulation, as their share in the project design, their (joint) contribution to project implementation and (joint) risk and project result sharing. Contracted research and the provision of research services are not considered to be forms of cooperation. Compliance with the conditions set out in Article 25(6) of the Commission Regulation (i.e. the required minimum share of the research organization in the eligible costs and the right of the research organization to publish the results of the research project) allows the provider to provide the enterprise with a premium for effective collaboration with the research organization.

The basis for assessing whether the project proposal involves effective cooperation between an enterprise and research organization will be the draft cooperation agreement between the tenderer(s) and the proposed additional participants from which compliance with the above conditions of effective cooperation will be apparent.

This evaluation will be carried out during the assessment of the project proposals.

## **14. Eligible and Recognized Program Costs**

Support will be provided for recognized project costs defined in accordance with Act No. 130/2002 Coll. and the Commission Regulation (Article 25(3)). Recognized costs are those eligible costs that the provider approves, are justified, accountable, and their necessity for the project must be evident from the project proposal. Recognized costs must be reasonable (they

must be in line with the usual prices at the given time and place) and be spent in accordance with the principles of economy, efficiency and effectiveness.

Eligible costs of the Program project are:

- a) personnel costs: researchers, technicians and other support staff to the extent necessary for the purpose of the project
- b) the cost of tools and equipment to the extent and for the time they are used for the project. If these tools and equipment are not used in the project throughout their lifetime, only depreciation during the project calculated on the basis of generally accepted accounting principles is considered an eligible cost;
- c) the cost of buildings and land to the extent and for the time they are used for the project. In the case of buildings, only depreciation during the project calculated on the basis of generally accepted accounting principles is considered an eligible cost. In the case of land, eligible costs are considered transfer costs or the actual capital costs incurred,
- d) the costs of contract research, knowledge and patents purchased or acquired under license from outside sources under normal market conditions, as well as the cost of consulting and equivalent services used exclusively for the project,
- e) additional overheads and other operating costs, including material, supplies and similar costs incurred immediately as a result of the project.

## **15. Program Focus**

A decisive prerequisite for an economically, socially and humanly successful society is a healthy population. A fundamental aspect of "health" is the dynamics of change and processes, but their effects in society manifest with a certain delay. This creates many discrepancies, the most significant being between the development of medical science and the country's economic potential. Attention should also be paid to the external influences of the environment undergoing major changes. The mission of healthcare is to adapt to changes in environment, knowledge and society so that all citizens are given access to the support and protection of their health in order to increase motivation to a healthy lifestyle and that the rules for effective disease prevention are consistently applied.

In the medical field, we need to focus on the most common and most dangerous areas: chronic non-infectious diseases such as cardio- and cerebrovascular diseases, oncology, dementia and other mental illnesses or chronic musculoskeletal disorders, etc. A major challenge will be to combat chronic non-infectious civilization diseases, caused largely by the unhealthy behavior of broad levels of the population. It is important to promote the emergence and development of new therapeutic technologies (genetics, nanotechnology). Furthermore, new infectious diseases and the increasingly present resistance of new agents should be monitored. It is therefore necessary, among other things, to support the importance of virology.

## 16. Compliance of the Program with R&D&I Priorities

The focus of the Program, its main objective and its classification are fully in line with R&D&I Priorities, namely Priority no. 5: A Healthy Population. Priority no. 5: A Healthy Population is divided into three areas (1. The origin and development of diseases; 2. New diagnostic and therapeutic methods; 3. Epidemiology and prevention of the most serious diseases) which are further subdivided into 21 sub-areas and 43 sub-objectives, similarly to the Program classification.

The following table shows the breakdown of the Program (which is the same as the structure of Priority no. 5: A Healthy Population). The Program is also in line with the National Rare Disease Strategy for 2010-2020.

**Tab. no. 3: Compliance of the Program with R&D&I Priorities**

<p><b><u>Area 1 - The Emergence and Development of Diseases</u></b></p> <p><u>Sub-area 1.1 Metabolic and Endocrine Diseases</u></p> <ul style="list-style-type: none"><li>• Priority sub-objective 1.1.1 Etiology and Pathophysiology of Insulin Resistance</li><li>• Priority sub-objective 1.1.2 Etiology and Pathogenesis of Immune-Mediated Endocrine Diseases</li><li>• Priority sub-objective 1.1.3 Pathogenesis and treatment of diabetes complications</li></ul> <p><u>Sub-area 1.2. Circulatory diseases</u></p> <ul style="list-style-type: none"><li>• Priority sub-objective 1.2.1 Clarification of etiological factors and pathophysiological processes affecting the onset and course of cardiovascular and cerebrovascular diseases</li><li>• Priority sub-objective 1.2.2 Development of the early diagnosis of cardiovascular and cerebrovascular diseases and finding treatment modalities and procedures in the treatment of cardiovascular and cerebrovascular diseases with higher therapeutic efficacy and greater patient friendliness</li></ul> <p><u>Sub-area 1.3. Cancer</u></p> <ul style="list-style-type: none"><li>• Priority sub-objective 1.3.1 Tumor biology in relation to diagnostic and therapeutic targets</li><li>• Priority sub-objective 1.3.2 Host-tumor relationship analysis as a means of individualizing diagnosis and treatment</li></ul> <p><u>Sub-area 1.4. Nervous system and mental diseases</u></p> <ul style="list-style-type: none"><li>• Priority sub-objective 1.4.1 Mental and neurological diseases</li><li>• Priority sub-objective 1.4.2 Diagnosis of Nervous System Diseases</li><li>• Priority sub-objective 1.4.3 Increased effectiveness of treatments for nervous system diseases</li><li>• Priority sub-objective 1.4.4 Ensuring quality of life in patients with nervous system diseases</li></ul>
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Sub-area 1.5 Diseases of the musculoskeletal system and inflammatory and immunological diseases

- Priority sub-objective 1.5.1 Etiology and pathogenesis of degenerative and metabolic diseases of the musculoskeletal system
- Priority sub-objective 1.5.2 Defining risk factors for allergic diseases and identifying new objectives for the targeted treatment of these diseases

Sub-area 1.6 Infection

- Priority sub-objective 1.6.1. Etiology and treatment of major infectious diseases

Sub-area 1.7 Childhood diseases and rare diseases

- Priority sub-objective 1.7.1 Prenatal, perinatal and early childhood diseases
- Priority sub-objective 1.7.2 Rare diseases

**Area 2 - New diagnostic and therapeutic methods**

Sub-area 2.1 In vitro diagnostics

- Priority sub-objective 2.1.1 To deepen knowledge in the field of omic and high-capacity methods
- Priority sub-objective 2.1.2 New IVD technologies

Sub-area 2.2 Low molecular weight drugs

- Priority sub-objective 2.2.1 New low molecular compounds
- Priority sub-objective 2.2.2 Identification of new therapeutic targets, new methods and procedures for biological testing

Sub-area 2.3. Biological drugs including vaccines

- Priority sub-objective 2.3.1. New vaccines for the prevention and treatment of diseases and addictions

Sub-area 2.4. Drug delivery systems

- Priority sub-objective 2.4.1. Development of new carriers for the controlled release and delivery of drugs
- Priority sub-objective 2.4.2 Systems for overcoming biological barriers and chemo-resistant diseases

Sub-area 2.5 Gene, cell therapy and tissue replacements

- Priority sub-objective 2.5.1 Sources for cell and tissue therapy
- Priority sub-objective 2.5.2 Methods for the differentiation and gene modification of cells/tissues
- Priority sub-objective 2.5.3. Biomaterials

Sub-area 2.6 Development of new medical devices and equipment

- Priority sub-objective 2.6.1 Electrical and magnetic mapping and stimulation
- Priority sub-objective 2.6.2 Endovascular procedures
- Priority sub-objective 2.6.3 Navigation and robotic systems, neurostimulators.

refinement and control of invasive techniques

Sub-area 2.7. Innovative surgical procedures including transplantation

- Priority sub-objective 2.7.1 Surgical procedures and transplantation
- Priority sub-objective 2.7.2 Non-invasive treatment

**Area 3 - Epidemiology and prevention of the most serious diseases**

Sub-area 3.1 Metabolic and endocrine diseases

- Priority sub-objective 3.1.1. Evaluation of the impact of preventive measures on the occurrence of the most common metabolic disorders

Sub-area 3.2. Circulatory diseases

- Priority sub-objective 3.2.1 Population study: disease data
- Priority sub-objective 3.2.2 Population interventions, evaluation of the impact of preventive measures

Sub-area 3.3. Cancer

- Priority sub-objective 3.3.1 Tumor screening and prevention
- Priority sub-objective 3.3.2 Identification of risk factors and individuals in populations

Sub-area 3.4. Nervous system and mental illness

- Priority sub-objective 3.4.1 Population study: disease data
- Priority sub-objective 3.4.2 Population intervention, assessment of the impact of preventive measures

Sub-area 3.5 Diseases of the musculoskeletal system and inflammatory and immunological diseases

- Priority sub-objective 3.5.1 Epidemiology of degenerative and metabolic diseases of the musculoskeletal system

Sub-area 3.6 Addiction

- Priority sub-objective 3.6.1. Links
- Priority sub-objective 3.6.2 Social impact

Sub-area 3.7. Infection

- Priority sub-objective 3.7.1 Epidemiology of infectious diseases
- Priority sub-objective 3.7.2. Domestic and imported food as a source of infections

## 17. Objectives of the Program

The main objective of the Program is to contribute through the outputs and impacts of supported projects to improving the health of the Czech population in the medium and long term and to continue to meet current health needs in the Czech Republic. As part of the supported projects, new findings will be achieved which will contribute to the improvement of clinical procedures in the diagnosis, treatment and prevention of the most common, but

also rare or completely new diseases. The aim of the Program is also to contribute to making the level of medical research in the Czech Republic comparable to that of advanced European Union countries.

The Program has three main areas: The emergence and development of diseases, new diagnostic and therapeutic methods and epidemiology and prevention of the most serious diseases, which are further divided into 21 sub-areas and 43 sub-objectives. Specific objectives characterize each sub-area. The Program's thematic definition is fully consistent and based on the National Priorities of Research, Experimental Development and Innovation, namely on Priority no. 5: A Healthy Population, and on the National Rare Disease Strategy for 2010-2020.

Projects proposed in this Program must be assigned to one or more of the following sub-areas and ensure that one or more of the Program's sub-objectives are fulfilled. The provider reserves the right to also support projects that do not fall into these sub-areas. The provider shall specify the requirements for the professional focus of the project proposals, i.e. the characteristics of the individual objectives, in the tender dossiers published during the announcement of individual public tenders.

## **Area 1 - The Emergence and Development of Diseases**

### **Sub-area 1.1 Metabolic and endocrine diseases**

#### **Key objective 1.1:**

The etiology and pathogenesis of major metabolic and endocrine disorders in the current population will be elucidated, thereby preventing their progression, mitigating their course and, in particular, reducing their consequences, which affect almost all medical areas and contribute to the overall mortality.

This will not only increase the length, but also improve the quality of active life of a wide group of the population with an adequate social and economic impact.

#### **Sub-objective 1.1.1: Etiology and pathophysiology of insulin resistance and metabolic syndrome**

Clarification of the pathogenesis of interrelationships of congenital, developmental and environmental factors for the development of obesity, insulin resistance syndrome and disorders of intermediary metabolism leading to type 2 diabetes mellitus and related diseases.

#### **Sub-objective 1.1.2: Etiology and pathogenesis of immune-mediated endocrine diseases**

Identification of inducing factors and mechanisms of autoimmune-mediated endocrine disorders, particularly type 1 diabetes mellitus, thyroid disease, adrenal and pituitary gland disease, as well as diseases of other endocrine glands and polyglandular autoimmune syndromes. Identification of etiological and pathogenetic factors involved in the development of other endocrine diseases, their complications and associated diseases. There is also a need to support the study of the etiopathogenesis of inherited metabolic disorders and to develop new diagnostic and therapeutic approaches based on this knowledge.

#### **Sub-objective 1.1.3: Pathogenesis and treatment of diabetes complications**

Identification of mechanisms of the development of chronic diabetes complications such as diabetic nephropathy, retinopathy, polyneuropathy, diabetic foot syndrome and diabetic

macroangiopathy, and the introduction of new methods in their prevention and therapy. It is also necessary to support the creation of patient registries with all the diseases described above, which will allow the data thus obtained to be used for science and research.

### **Sub-area 1.2: Circulatory diseases**

#### **Key objective 1.2:**

Major progress in the prognosis, diagnosis, and therapy of coronary heart disease, its risk factors, and other CVDs would be unthinkable without the close cooperation of theoretical and clinical cardiologists, cardiac surgeons, angiologists, and vascular surgeons.

This cooperation has a long tradition in our country and is the driving force of scientific progress. The aim of the research will be to contribute to the elucidation of etiological factors and molecular and cellular pathogenetic mechanisms involved in the development of coronary heart disease and its risk factors, heart failure, heart rhythm disorders, structural and inflammatory heart disease, congenital heart defects and diseases of the arterial and venous system, with particular attention to improving their prevention, early diagnosis and highly individualized treatment. New etiological factors and new pathophysiological mechanisms will be identified, affecting the onset and progression of cardiovascular diseases, in particular: ischemic heart disease, heart failure, heart rhythm disorders, hypertension, structural heart disease, CIHD, aortic aneurysms, chronic venous insufficiency, inflammatory heart disease and other diseases of the arterial and venous system; with a clear impact on improving their prevention, early diagnosis and highly individualized treatment.

Etiopathogenetic mechanisms, which are the cause of strokes, and possibilities of their influence, especially from the area of "non-traditional" risk factors, will be examined. In addition, mechanisms that lead to neurological disability in patients with cerebral infarction, spontaneous cerebral hemorrhages, and spontaneous subarachnoid hemorrhages will be recognized and the potential for their influence will be elucidated. The reasons for the success and failure of therapeutic procedures in patients with strokes will be explained. Regeneration mechanisms, which are responses to nervous system disabilities, including mechanisms of cerebral plasticity and the regeneration of brain tissue within neurorehabilitation, will be understood.

#### **Sub-objective 1.2.1: Clarification of etiological factors and pathophysiological processes affecting the onset and course of cardiovascular and cerebrovascular diseases**

Multi-disciplinary biomedical research will be preferred, bringing qualitatively new insights into the causes and mechanisms affecting the development and course of cardiovascular and cerebrovascular disease, with clearly defined clinical benefits for improving their prevention, diagnosis or treatment.

#### **Sub-objective 1.2.2: Development of early diagnosis of cardiovascular and cerebrovascular diseases and finding treatment modalities and procedures in the treatment of cardiovascular and cerebrovascular diseases with higher therapeutic efficacy and greater patient friendliness**

Multi-disciplinary research is preferred, as well as the development of new technologies, methods, drugs, and diagnostic and treatment procedures with clearly defined clinical benefits for the early diagnosis or highly effective targeted treatment of both types of diseases, while

respecting each patient's uniqueness. This area also includes research to identify and validate regenerative, rehabilitation, re-socialization, and educational procedures for patients with cardiovascular and cerebrovascular diseases to shorten the recovery and incapacity of patients and improve their social welfare.

### **Sub-area 1.3: Cancer**

#### **Key objective 1.3**

Multi-disciplinary research is preferred, bringing qualitatively new knowledge of the causes and mechanisms affecting the development and progression of cancer with clearly defined clinical benefits for subsequent improvement in prevention, diagnosis and treatment.

New diagnostic procedures for the early detection of tumor diseases will be developed using newly identified tumor biomarkers useful for the rapid and inexpensive screening of the entire population and the individualization of treatment. Therapeutic approaches based on the description of individual tumor biology with minimizing side effects will be developed.

#### **Sub-objective 1.3.1: Tumor biology in relation to diagnostic and therapeutic targets**

The study of the biological mechanisms of tumor formation. The identification of new therapeutic targets and biomarkers to better diagnose and treat cancer. Special attention will be paid to linking diagnostics with targeted therapy and the introduction of new therapeutic approaches based on combined treatment, epigenetics, sophisticated drug-delivery systems and the treatment of resistant cancer.

#### **Sub-objective 1.3.2: Host-tumor relationship analysis as a means of individualizing diagnosis and treatment**

The study of the relationship between the tumor and its host will contribute to the development of diagnostic and therapeutic methods to monitor and therapeutically utilize the interaction between normal and tumor cells, to understand the importance of tumor stroma, and inflammatory and immune responses to tumor formation and development.

### **Sub-area 1.4. Nervous system and mental illnesses**

#### **Key objective 1.4:**

The main objective is basic and applied research to elucidate the etiology and pathogenesis of major nervous system diseases to the extent that correct diagnosis can be established as soon as possible and causal treatment initiated.

The final outcome is a cure or minimization of the difficulties and improvement of the functional capacity and quality of life of the patients. Part of the key objective is the early identification of risky individuals and preclinical conditions so that the most effective prediction and timely prevention of nervous system and mental illnesses are possible.

#### **Sub-objective 1.4.1: Mental and neurological diseases**

Clarifying genetic, epigenetic and environmental factors contributing to the emergence and development of mental and neurological diseases is a prerequisite for improving prevention, developing new therapies, and improving the complex care of patients with a wide range of diseases, including strokes, epilepsy, dementia, schizophrenia, depression, bipolar disorders, anxiety disorders, autism, hyperkinetic disorder, eating disorders, multiple sclerosis,



extrapyramidal and cerebellar diseases, neuromuscular and neuropathic disorders, and other nervous system disorders manifested through psychological or neurological diseases.

**Sub-objective 1.4.2: Diagnosis of nervous system diseases**

Expansion and innovation of existing diagnostics, including molecular genetics (e.g. whole exome sequencing), electrophysiological techniques of all modalities, structural and functional neuroimaging methods and technologies to elucidate physiological, developmental, and specific diagnosis of cerebral connectivity changes in patients with autism, epilepsy, schizophrenia, and other disorders connecting key areas of the brain. Diagnostics includes searching for biological markers of individual diseases and new experimental and clinical neuropsychological tests.

**Sub-objective 1.4.3: Increased effectiveness of treatments for nervous system diseases**

Finding new therapeutic modalities and refining and upgrading existing treatments based on genotype or endophenotype, including pharmacogenetic analyses to minimize adverse effects. The criterion of effectiveness will not only be the curing or alleviation of clinical problems, but also the maximum possible quality of life, including a dignified psychosocial level of the patient and his family.

**Sub-objective 1.4.4: Ensuring quality of life in patients with nervous system diseases**

In the context of the previous objective, the main priority of neuroscientific research must be to ensure the highest possible quality of life for individuals suffering from nervous system diseases, not only through early diagnosis and therapy, but also through continuous neurorehabilitation, psychotherapeutic and psychosocial care, psychoeducation and modern community social care, including stationary and respite services.

The aim is not only to increase the functional capacity and quality of life with a limitation of reversion (frequency and length of hospitalization) and to increase the resilience resistance of the patient, but also economically significant savings associated with shortening the sick leave and recovery of patients.

**Sub-area 1.5: Diseases of the musculoskeletal system and inflammatory and immunological diseases**

**Key objective 1.5:**

The etiopathogenesis and appropriate treatment of inflammatory, in particular major systemic, rheumatic, degenerative, metabolic and immune diseases will be identified.

The etiology and pathogenesis of musculoskeletal diseases will be clarified, which will significantly contribute to increasing the quality of life of the older population.

**Sub-objective 1.5.1: Etiology and pathogenesis of degenerative and metabolic diseases of the musculoskeletal system**

The study of the molecular biology of bone, cartilage and muscle cells. The study of genetic polymorphisms and epigenetic factors in autoimmune diseases. The monitoring of environmental factors in the development of these diseases. Further development of imaging techniques for bone microstructure to better assess bone quality. The development of imaging methods to assess the progression of osteoarthritis. Understanding other factors that allow fracture healing. The development of tissue engineering methodologies to prepare artificial

cartilage and bones. The study of chondrocyte and extracellular matrix metabolism, especially understanding the disbalance of degradation and repair processes that enable the synthesis of targeted preparations.

**Sub-objective 1.5.2: Defining risk factors for allergic diseases and identifying new objectives for the targeted treatment of these diseases**

Gene polymorphisms and the epigenetic regulation of molecules involved in allergic reactions will be studied, as well as external factors for the development of these diseases. Attention will be paid to interactions of the immune system with microorganisms and environmental factors, as well as regulatory mechanisms of allergic inflammation.

**Sub-area 1.6: Infection**

**Key objective 1.6:**

Clarify the etiology, epidemiology, and pathogenesis of diseases in relation to new, re-emerging, opportunistic and overlooked infections, enabling the individualization of treatment and improving the quality of life of patients and the population as a whole.

The development of new diagnostic methods for the early detection of infections and new treatments for important infectious diseases. Characteristics of molecular mechanisms of antimicrobial resistance, including the analysis of molecular-epidemiological markers of resistance. The development of new antimicrobial agents and the determination of alternative targets for rational chemotherapy.

**Sub-objective 1.6.1: Etiology and treatment of major infectious diseases**

Clarification of molecular-genetic mechanisms responsible for changes in the virulence and resistance of infectious agents. Determination of the pathogenic potential of microorganisms in the formation and development of infectious, metabolic (including endocrine), tumor, cardiovascular and neurodegenerative diseases and mechanisms/factors responsible for the activation of latent or opportunistic infections. The definition of basic molecular epidemiological markers of the spread of multi-resistant bacteria, yeasts, fungi and viruses in the human population, with the aim of slowing their formation and spreading and maintaining the effectiveness of anti-infectives. The development of new diagnostic methods for the early detection of infectious diseases and searching for new markers of infectious diseases as potential diagnostic and therapeutic targets. The development of new antimicrobial agents and their basic characteristics.

**Sub-area 1.7: Childhood diseases and rare diseases**

**Key objective 1.7:**

The main objective of basic research in this area is to deepen the knowledge of the etiopathogenesis of serious rare diseases (especially of those with monogenic heredity) and developmental diseases of the prenatal age, perinatal complications and chronic childhood diseases using comprehensive approaches.

The acquired knowledge of basic research will be translated into clinical practice, applied research will be focused on the development of new diagnostic methods and algorithms and

on the development of new therapeutic and preventive procedures, including prenatal and preimplantation diagnostics.

#### **Sub-objective 1.7.1: Prenatal, perinatal and early childhood diseases**

The study of the impact of genetically determined factors and negative environmental effects on the etiopathogenesis and pathophysiology of serious childhood diseases. The development of non-invasive diagnostic methods of chronic childhood diseases. Preparation of preventive procedures and treatment methods for the care of a sick child in order to improve the quality of life of chronically ill children.

#### **Sub-objective 1.7.2: Rare diseases**

The number of known rare diseases is not definitive and new genetic conditioning units have been described with the gradual development of modern new generation sequencing technologies. However, discovering mutations and genes in a new disease does not mean the work is over; a number of other techniques from the field of genomics, metabolomics, proteomics, molecular and cell biology need to be used to elucidate pathogenetic mechanisms and, in many cases, animal models must also be utilized. The development of preimplantation and prenatal diagnosis is significant for as yet untreatable genetic rare diseases, as it ensures the effective primary and/or secondary prevention of these diseases in affected families. The main priorities of this area are research aimed at elucidating the etiology of diseases with unknown causes and the study of molecular, biochemical and cellular mechanisms in etiologically defined rare diseases (as a prerequisite for follow-up research on new diagnostic and therapeutic approaches). Another priority is to support research on their nosological classification (i.e. phenotypic ontology), epidemiology, development of methods for the early prevention of these diseases and research on the cost-effectiveness of diagnostic and therapeutic procedures for rare diseases.

## **Area 2 - New Diagnostic and Therapeutic Methods**

### **Sub-area 2.1: In vitro diagnostics**

#### **Key objective 2.1:**

The pathogenetic mechanisms of selected genetic variants found in genome-wide sequencing and their association with various human diseases will be elucidated, new in vitro diagnostic methods will be developed to address these outcomes, as well as emerging threats or newly discovered biomarkers, and in silico and systemic biology approaches will be developed to exploit the large amount of data generated by massively parallel methods.

Diagnostics will be integrated with the treatment itself through systemic and translational medicine approaches.

#### **Sub-objective 2.1.1: To deepen knowledge in the field of omic and high-capacity methods**

High throughput screening (HTS) methods produce a huge amount of data and information that will need to be understood and the clinical applicability of which will need to be systematically verified. One of the objectives will be to elucidate the molecular and cellular pathogenetic mechanisms of selected genetic variants found in whole-genome sequencing and to verify their association with various human diseases. To effectively analyze data from HTS

technologies, in silico approaches and approaches of system biology will be developed to exploit the large volume of data generated by HTS methods. The identification of new diagnostics, prognostic and predictive biomarkers through "omics" technologies. The integration of acquired data with their link to clinical characteristics in health and disease.

#### **Sub-objective 2.1.2: New IVD technologies**

New technologies or their components will be developed to enable rapid, sensitive, specific, mini-invasive or non-invasive diagnosis and monitoring of the disease course. These new technologies will work with either patient material derived from blood or other body fluids, tissues (tissue sections, e.g. tumors) or with the patient as a whole in the form of whole body functional imaging (MRI, PET-CT); research in this area focuses on the preparation of new imaging enhancers and specific radiopharmaceuticals, which will allow pathological events (e.g. angiogenesis, specific localized metabolic processes, receptor imaging) to be displayed over time in a particular patient. Some of these substances will also have a therapeutic character (e.g. antibodies with a PET-radiopharmaceutical).

### **Sub-area 2.2: Low molecular weight drugs**

#### **Key objective 2.2:**

New biologically active low molecular weight substances with therapeutic potential demonstrated in proof-of-concept studies will be prepared.

More effective procedures in monitoring the biological activity of drugs using a comprehensive approach to assessing the desirable, undesirable and toxic effects of new low molecular compounds (the improvement of biological tests, introduction of new testing methods, biological activity prediction, toxicity and side effects in silico) will lead to the timely elimination of non-active or toxic molecules. Through the identification of new leading structures and their modification or the modification of clinically proven drugs, their pharmacotherapeutic utility will be enhanced.

#### **Sub-objective 2.2.1: New low molecular compounds**

The preparation of new low molecular weight compounds and structural motifs with relevant pharmacological effects. New molecules can be synthesized and found by studying the relationship between structure and activity, combinatorial chemistry, high throughput screening, or isolation from natural, especially plant, sources. In many areas (e.g. in the area of high throughput screening (HTS)), there is a global level of infrastructure in the Czech Republic.

#### **Sub-objective 2.2.2: Identification of new therapeutic targets, new methods and procedures for biological testing**

New therapeutic targets will be generated based on the results of basic research, and new procedures and methods will be found in the evaluation of efficacy and toxicity in vitro to increase the likelihood of the clinical utility of small molecules. The selected candidate compounds, new methods and procedures will subsequently be validated at the preclinical in vivo level.

### **Sub-area 2.3: Biological drugs including vaccines**

#### **Key objective 2.3:**

There will be a wider utilization of biological therapy and immunotherapy, in particular thanks to knowledge on the exact mechanism of action and the specific target, a reduction in production costs, and new knowledge associated with in vivo monitoring of the biological response to treatment.

New biological drugs will be introduced with, for example, improved stability, the possibility of non-invasive administration, as well as new vaccines with an improved efficacy and safety profile.

#### **Sub-objective 2.3.1: New vaccines for the prevention and treatment of diseases and addictions**

New vaccines (e.g. for the treatment and prevention of major societal threats) or new vaccination approaches will be developed (DNA vaccines, reverse vaccinology – the development of vaccines by sequencing the entire genome of the infectious agents, anti-tumor, desensitization, etc.).

### **Sub-area 2.4: Drug delivery systems**

#### **Key objective 2.4:**

New drug delivery systems and combinations of genes will be developed and used, as well as genes allowing the treatment of target tissues or cells, the controlled release of drugs and drug penetration at therapeutically relevant concentrations into difficult to reach organs (skin, CNS), tissue, cellular or subcellular structures.

#### **Sub-objective 2.4.1: Development of new carriers for the controlled release and delivery of drugs**

New drug carriers on the principle of macromolecular structures or nanoparticles will allow for the controlled release of drugs throughout the body, or the targeted transport and controlled release of biologically active molecules (drugs, genes) in specific tissue, cellular or subcellular structures. Research will lead to the development of more effective, safer (less toxic) drugs with more advantageous pharmacokinetic and pharmacodynamic properties and, where appropriate, personalized therapy.

#### **Sub-objective 2.4.2: Systems for overcoming biological barriers and chemo-resistant diseases**

The study of the nature of biological, chemical and physical barriers in the body leading to the development of new ways of overcoming them and the development of new types of drugs, formulations and drug-delivery systems that overcome biological barriers such as the cutaneous, blood-brain, testicular, or ocular barriers, and of overcoming drug-resistant phenotypes, etc. The outcomes of this sub-objective will be directly utilized, for example, in the treatment of patients with neurological, inflammatory, infectious, oncological, reproductive, or ocular diseases and, last but not least, in the treatment of diseases resistant to existing therapy.

## **Sub-area 2.5: Gene, cell therapy and tissue replacements**

### **Key objective 2.5:**

The introduction of new safe procedures based on the use of autologous or modified autologous, allogeneic or xenogeneic cells and biomaterials, and gene therapy methodology for the treatment of diseases in which treatment has failed or is too costly.

### **Sub-objective 2.5.1: Sources for cell and tissue therapy**

The preparation and characterization of cells and cell lines capable of differentiation into desired phenotypes. These can be allogeneic or xenogeneic sources, the development of lines with defined properties including not only the required differentiation but also a high degree of safety. (e.g. autologous adipose stem cells, continuous and bone marrow, immortal cell lines from fetal and embryonic tissue, iPSC, tissue grafts, transgenic animals, etc.). For the needs of cancer immunotherapy, lines from genetically modified tumor cells and activated immune cells.

### **Sub-objective 2.5.2: Methods for the differentiation and gene modification of cells/tissues**

Methods for the differentiation of target cells or tissues, possibly related gene modifications. The differentiation may involve both the use of low molecular weight or high molecular weight substances, as well as genetic modification. The induction of stem or precursor cells into cells with the desired phenotype and degree of safety.

The utilization of activated dendritic cells for the immunotherapy of tumors. The genetic modification of tumor cells and cells of the immune system *in vivo* and *ex vivo*. The isolation and characterization of lines suitable for tumor immunotherapy. New gene therapy procedures for human diseases, including the verification of new, safer and more effective gene transfer vectors

### **Sub-objective 2.5.3: Biomaterials**

Defined structures with a specific function, e.g. as part of tissue replacement (scaffolds, biohybrid devices, etc.) The development of these materials includes polymeric carriers, hydrogels, nanofibrous structures, nanoparticles, allogeneic materials, and a decellularized extracellular matrix from allogeneic and xenogeneic sources.

## **Sub-area 2.6: Development of new medical devices and equipment**

### **Key objective 2.6:**

New hardware and software technologies and methods will be developed for the early diagnosis, effective and standardized treatment of cardiovascular, neurological, oncological and other diseases. Imaging methods based on the use of nanotechnologies will also contribute to the early diagnosis of these diseases. Nanotechnology is likely to find therapeutic applications.

### **Sub-objective 2.6.1: Electrical and magnetic mapping and stimulation**

Multi-disciplinary research and the development of new hardware and software technologies for the electrical or magnetic mapping of and/or stimulation of the activities of individual cells, tissues and organs is clearly preferred, with a clearly defined clinical objective in the

field of disease diagnosis and/or treatment. The research projects must include at least the development of fully functional prototypes.

**Sub-objective 2.6.2: Endovascular procedures**

Multi-disciplinary research and development of new technologies to create new endovascular diagnostic and treatment procedures with a clearly defined clinical objective in the field of disease diagnosis and/or treatment is preferred. Research projects include at least the development of fully functional prototypes or biological models, as well as the introduction of new proven techniques and technologies in the endovascular area.

**Sub-objective 2.6.3: Navigation and robotic systems, neurostimulators. refinement and control of invasive techniques**

Multidisciplinary research leading to the standardization of intervention and mini-invasive surgical procedures to increase their safety and efficacy is preferred. Neuromodulation is another emerging direction of treatment for various diseases (arterial hypertension, heart failure, obesity, pain, neurodegenerative disease, epilepsy, psychiatric disease). It is the development of technological units using intervention or mini-invasive methods controlled by mapping and navigation systems, imaging techniques and various sensors (tissue contact measurement, etc.). Neuromodulation consists of the use of neurostimulators, or in the targeted destruction of parts of the nervous system. In cardiovascular surgery, it is mainly about extending and standardizing robot-assisted cardiac interventions (the heart muscle, valves, coronary arteries), as well as interventions on arteries, especially the aorta (aneurysms, obliterating disability, addressing some complications in endovascular procedures). Research must include development to the stage of technological units or functionally fully usable prototypes.

**Sub-area 2.7: Innovative surgical procedures including transplantation**

**Key objective 2.7:**

The aim is to develop and use new surgical procedures with lower invasiveness and therefore less stress on the patient's body. New methods will be more effective, will enable better healing, reduce potential complications, and will bring a good long-term prognosis for the patient. This will, on the other hand, allow for more extensive interventions for as yet untreatable findings.

In the field of transplantation, tissue culture, artificial organ formation and the facilitation of transplant acceptance by the patient's body will occur. Increasing treatment options will allow for the transition to the minimization of necessary hospitalization or offer the possibility of outpatient treatment, with a reduction in overall treatment time.

**Sub-objective 2.7.1: Surgical procedures and transplantation**

New, gentler operating procedures will be developed with sophisticated navigated techniques. The goal is to research and develop new surgical techniques and procedures. The result will be a shift to one-day surgery or a significant reduction in hospitalization while maintaining safety and efficiency. Biological replacements of tissues and organs, immunomodulatory and protective procedures will be developed to enhance the efficacy, safety and tolerance of surgical and transplantation treatments. The aim of multidisciplinary research will be tissue

and organ transplants both from donors and grown in vitro that will be well received by the body and the function of which will replace organs (tissue).

**Sub-objective 2.7.2: Non-invasive treatment**

Focused radiation therapy, non-invasive local and locoregional treatment (e.g. radiosurgery, lithotripsy, ultrasound therapy including sonothrombolysis). Multidisciplinary and multimodal research is aimed at non-invasive but surgical techniques without penetration of the skin cover. The precise diagnosis and development of new therapeutic methodologies will increase their use in outpatient treatment. New modalities will be developed into a clinically useful prototype.

**Area 3. Epidemiology and prevention of the most serious diseases**

**Sub-area 3.1: Metabolic and endocrine diseases**

**Key objective 3.1:** Validated epidemiological data will be available on (1) the incidence, trends, health and economic consequences of the most commonly occurring metabolic disorders and (2) their social, socio-economic, behavioral and biological determinants.

The effectiveness of individual interventional preventive and therapeutic procedures will be analyzed and simulated so that it is possible, based on these results, to promote and strengthen a complex, most effective society-wide program also outside of the health sector, the acceptance of which would contribute to stopping the increase or even decreasing their incidence and to a positive impact on the overall health of the population.

**Sub-objective 3.1.1: Evaluation of the impact of preventive measures on the occurrence of the most common metabolic disorders**

The clinical and community evaluation of new pharmacological and non-pharmacological procedures aimed at the prevention of obesity, disorders of glucose metabolism, hyperlipoproteinaemia and hypertension, thyroid disorders, endocrine-related reproductive disorders and other autoimmune endocrine diseases.

**Sub-area 3.2: Circulatory diseases**

**Key objective 3.2:** The monitoring of both classical and new (unconventional) risk factors of cardiovascular and cerebrovascular diseases in the Czech population will help reduce the incidence of these diseases in the Czech Republic. It will contribute to the innovation and streamlining of prevention programs by incorporating current knowledge and the needs of society when implementing health policies at individual levels.

**Sub-objective 3.2.1: Population study: disease data**

Data collection and processing on the incidence and prevalence of cardiovascular and cerebrovascular diseases and their risk factors.

**Sub-objective 3.2.2: Population intervention, assessment of preventive action impact**

Verification of intervention procedures leading to a) a reduction in the incidence, social and economic impact of cardiovascular and cerebrovascular diseases and their risk factors, b) educating the population with the aim of early recognition of symptoms by the patient, allowing for early diagnosis and treatment.



### **Sub-area 3.3. Cancer**

**Key objective 3.3:** The epidemiology of cancer, risk factors in individual populations, specific and non-specific methods of their prevention, and accurate and specific screening will be identified, ultimately leading to the identification of at-risk individuals, the early detection of tumors, their recurrence and side effects of treatment, with an impact of reduced mortality, morbidity and anticancer treatment costs with respect to the subjective assessment of the patient's quality of life.

The need for specialized palliative care in patients with depleted specific anticancer treatment possibilities will be recognized. The number of quality clinical trials in the above areas will increase, as will the availability of their outcomes.

#### **Sub-objective 3.3.1: Tumor screening and prevention**

Special attention will be paid to the possibilities of tumor chemoprevention, the strengthening and refinement of existing and the introduction of new, highly sensitive, specific, non-invasive or minimally invasive screening programs that will be useful for the early detection of cancer in the general population or in higher-risk groups of individuals.

#### **Sub-objective 3.3.2: Identification of risk factors and individuals in populations**

The research will focus on identifying factors involved in the onset and development of cancer, risk factors in the population (especially genetic, environmental, physical, addictive, nutritional, locomotive and infectious) and will propose specific preventive measures and further investigate biological mechanisms.

### **Sub-area 3.4: Nervous system and mental illnesses**

**Key objective 3.4:** The main demographic and epidemiological characteristics of the diseases of the nervous system will be mapped, their linkages found (e.g. age, gender, geographical and environmental, developmental, genetic and co-morbidities) and prevention measures and programs implemented to decrease the incidence and prevalence of diseases of the nervous system, including mental disorders, to limit reversion (the frequency and length of hospitalization) and to reduce the socio-economic burden that nervous system diseases present.

At the same time, research into the effectiveness and efficiency of interventions and services will be carried out to optimize the supply and coordination of these interventions.

#### **Sub-objective 3.4.1: Population study: disease data**

The creation of registries (mental and nervous system diseases, suicides, somatic comorbidities, early and late morbidity in at-risk newborns, etc.) and support for longitudinal studies will be the basis for databases on which preventive interventions will be based.

#### **Sub-objective 3.4.2: Population intervention, assessment of the impact of preventive measures**

Above all, primary preventative population-wide interventions will focus on the destigmatization of individuals suffering from brain disease: stigmatization represents a stressor potentially worsening the course of the disease and results in delaying the search for therapeutic assistance, while the delay may adversely affect the patient's outcome.

The primary prevention programs will further focus on at-risk populations, such as perinatally at-risk children or individuals with an increased risk of developing a psychotic disorder, stroke or dementia. The most up-to-date methods will be used, including, for example, telemedicine. At the same time, research into the effectiveness and efficiency of interventions and services will be carried out to optimize the supply and coordination of these interventions.

### **Sub-area 3.5: Diseases of the musculoskeletal system and inflammatory and immunological diseases**

**Key objective 3.5:** Not only will the prevalence and incidence factors become known, other significant environmental factors involved in the etiopathogenesis of these diseases will also. The most important ones are the relationship of infection to the development of autoimmune diseases, endocrine factors, the effects of aging, environmental pollution factors, and the effects of smoking and other addictive substances.

#### **Sub-objective 3.5.1: Epidemiology of degenerative and metabolic diseases of the musculoskeletal system and autoimmune-mediated diseases of the gastrointestinal tract**

To describe the epidemiological context of external causes for the development of degenerative joint and spine diseases, such as joint dysplasia, obesity, trauma, inflammation, lifestyle factors and exercise. To map the epidemiologically important connections leading to the formation of various types of metabolic osteopathies, such as nutritional factors, calcium and vitamin intake, the effects of physical activities, the effects of smoking and addictive substances, the influence of various drugs (e.g. glucocorticoids) and the development of idiopathic intestinal inflammation and celiac disease.

### **Sub-area 3.6: Addiction**

**Key objective 3.6:** The Program aims to reduce the prevalence and incidence of addictions including alcoholism, smoking and gambling, and to reduce their health and socio-economic impacts. A prerequisite for achieving these goals is to map out the epidemiology, risk of development, social burden and predictors of addiction treatment, and to prepare documents for preventive measures and programs, and for political, legislative and economic decisions.

#### **Sub-objective 3.6.1: Links**

Finding the genetic, epigenetic, environmental, public-health, behavioral, and social links of addiction, including their link to other related diseases.

#### **Sub-objective 3.6.2: Social impact**

Reducing the social and economic impact of addictions.

### **Sub-area 3.7: Infection**

**Key objective 3.7:** Reducing the incidence and spread of infectious agents, including nosocomial and emerging etiological agents with zoonotic potential, and improving their laboratory diagnosis.

#### **Sub-objective 3.7.1: Epidemiology of infectious diseases**

Monitoring morbidity and mortality due to infectious diseases and studying factors affecting their occurrence. Identification of new sources and ways of spreading infectious diseases and the development of effective anti-epidemic measures. Developing new diagnostic methods to identify agents and test their properties. Developing infectious disease surveillance programs in accordance with European Union requirements. Optimization of information systems and registries. Monitoring the effectiveness of vaccination programs and suggesting their updating according to the epidemiological situation and the availability of newly developed vaccines. Educating the population.

**Sub-objective 3.7.2: Domestic and imported food as a source of infections**

The identification of risk factors for food imports from different places of origin, the identification of sources of contamination and the elaboration of procedures leading to the protection of the population of the Czech Republic. Fast laboratory diagnostics of foodborne infectious agents and the testing of their properties. The optimization of information systems. Educating the population.

**18. Subprograms**

The Program is divided into two subprograms, where the criterion for division is the age of the solvers. The practice and experience of the provider show that the age of the project solvers is continually increasing, therefore Subprogram 2 is focused on favoring projects whose researchers will be young researchers under the age of 35. In terms of professional focus, both subprograms will fulfill the objectives of this Program as described in the previous chapter.

**18.1 Subprogram 1**

The main objective of Subprogram 1 is to further develop the existing platform of applied medical research in the Czech Republic, focusing more on improving the conditions for the development of international cooperation.

Subprogram 1 will support projects whose solver may only be a natural person engaged in research, with a Ph.D. or its equivalent at the time of submitting the project proposal for the public tender. Further conditions will be described in the dossier for public tenders. Approximately 90% of the targeted support funds allocated to this Program will be allocated to Subprogram 1.

**Tab. no. 4: Subprogram 1 Expenditure (in millions of CZK)**

year	2020	2021	2022	2023	2024	2025	2026	total
Total expenditure	297	743	1039	1287	1039	693	347	5445
State budget expenditure	270	675	945	1170	945	630	315	4950
Non-public sources	27	68	94	117	94	63	32	495

### Objectives of Subprogram 1:

- 1) to support the development of new preventive measures or practices in the health sector (focusing on all types of prevention, i.e. primary, secondary and tertiary),
- 2) to support the development of new diagnostic and therapeutic methods,
- 3) to support the development of international cooperation in applied medical research,
- 4) to support multidisciplinary cooperation in applied medical research
- (5) to promote excellence in applied medical research;
- 6) to ensure that the results of applied medical research are used as inputs for the development and updating of clinical guidelines in the Czech Republic.

The fulfillment of the set objectives of Subprogram 1 will be evaluated on an ongoing and final basis by means of partial and final reports on project solutions, in which primarily the indicators listed in Table no. 5 will be monitored.

**Table no. 5: Indicators of Subprogram 1 Objectives**

Objective	Indicator
1) to support the development of new preventive measures or practices in the health sector (focusing on all types of prevention, i.e. primary, secondary and tertiary)	number of Program results
2) to support the development of new diagnostic and therapeutic methods	number of N and P type results
3) to support the development of international cooperation in applied medical research,	number of synergic international projects addressed by beneficiaries
4) to support multidisciplinary cooperation in applied medical research	number of projects solved by workplaces from various fields of medical research
5) to promote excellence in applied medical research	the number of Jimp type publications
6) to ensure that the results of applied medical research are used as inputs for the development and updating of clinical guidelines in the Czech Republic.	the number of results applied in clinical guidelines in the Czech Republic

## 18.2 Subprogram 2

The main objective of Subprogram 2 is to support the development of young researchers in their research activities and the associated rejuvenation of the healthcare research community in order to maintain the continuity of applied medical research for future generations.

Subprogram 2 will support projects whose solver can only be a natural person engaged in research who, at the time of submitting the project proposal, has reached a maximum age of 35 and has a Ph.D. or its equivalent, or shall obtain it at the latest prior to the conclusion of the contract/issuing of the decision on the project solution. Further conditions will be described in the dossier for public tenders.

Approximately 10% of the funds allocated for this Program will be allocated to projects of young scientists.

**Tab. no. 6: Subprogram 2 Expenditure (in millions of CZK)**

year	2020	2021	2022	2023	2024	2025	2026	total
Total expenditure	33	82	116	143	116	77	38	605
State budget expenditure	30	75	105	130	105	70	35	550
Non-public sources	3	7	11	13	11	7	3	55

**Objectives of Subprogram 2:**

- 1) support the development of new diagnostic and therapeutic methods
- 2) to encourage young researchers to be more interested in research, development and innovation activities in the health sector,
- 3) by supporting the integration of young professionals into domestic and international research and thus also practical medicine, to contribute to the slowing of their outflow from the Czech Republic;
- 4) to increase the number of jobs for young researchers,
- 5) to rejuvenate the scientific community in healthcare and support young researchers in their continuing vocational training,
- 6) to extend the personnel base of research organizations dealing with applied medical research.

The fulfillment of the set objectives of Subprogram 2 will be evaluated on an ongoing and final basis by means of partial and final reports on project solutions, in which primarily the indicators listed in Table 7 will be monitored.

**Tab. no. 7: Indicators of Subprogram 2 Objectives**

Objective	Indicator
1) to support the development of new preventive, diagnostic and therapeutic methods	number of Program results
2) to encourage young researchers to be more interested in research, development and innovation activities in the health sector	number of projects led by young researchers
3) to contribute to the slowing of their outflow from the Czech Republic by supporting the integration of young professionals into domestic and international research and thus also practical medicine	number of young researchers involved in project solutions
4) to increase the number of jobs for young researchers	number of young researchers involved in project solutions

5) to rejuvenate the scientific community in healthcare and support young researchers in their continuing vocational training	number of young researchers involved in project solutions
6) to extend the personnel base of research organizations dealing with applied medical research	number of newly registered authors of project results

## 19. A Comparison of the Current Situation in the Czech Republic and Abroad

A detailed analysis of the recent state of research and development in healthcare in the Czech Republic is given in Annex no. 3 (Analysis of Research and Development in Health Care in the Czech Republic) “Health Research Concept until 2022”. As for the current situation, it can be briefly stated that the largest share of specific legal forms among participants dealing with health research projects consisted of state contributory organizations of the Ministry of Health and regions - hospitals, etc. (in the last three years their share represents approximately 46%); public universities (in the last three years their share has risen to more than 40%) and then public research institutions, especially the Academy of Sciences of the Czech Republic (in the last three years their share ranges from 5 to 8%). The share of other legal forms is negligible. This condition has remained unchanged for a long time. Project participants are not changing much, only their share is changing. A significant change can be seen in the growth of public universities in the share of projects by about 10-15% at the expense of contributory organizations of the Ministry of Health and regions.

The running NV program has not been assessed yet, the first projects were completed as of 31 December 2018, thus the provider does not yet have the results of these projects available to evaluate the benefits and efficiency of the money spent. Only ongoing data on evaluated tenders, the amount of support provided, the number of solved projects and data on the structure of solved health issues are available.

The total expenditure of targeted support for projects supported in the NV Program amounted to approximately CZK 281 million in 2015, approximately CZK 701 million in 2016, approximately CZK 981 million in 2017 and approximately CZK 1,186 million in 2018. So far, the projects have been supported in 4 public tenders, for which the Ministry of Health approved and provided a total targeted support of CZK 4.88 billion. In 2018, a total of 467 projects were dealt with under the NV Program.

There were 2,171 project proposals delivered to these 4 tenders, the average financial allocation per 1 tender, that is, the success of the project, is 21.5%, which suggests that only the highest quality project proposals are selected for support. The average cost of one project over the last 4 years is CZK 10.4 million. As they are usually four-year projects, the average cost of one year of project solution is CZK 2.6 million. In terms of content, the highest number of the project proposals is focused on solving the issues of cancer, which represents 21% of all supported projects, and this trend has remained unchanged for a long time. This is followed by projects focusing on biomedical technologies, which represent 15% of the supported projects. Other projects include those on neuroscience and mental health (13%),

immune disorders and infectious diseases (11%), followed by preventive medicine and nursing (10%), metabolic and endocrine diseases (9%) and circulatory diseases (7%).

Regarding the results of medical research, based on the conclusion of the bibliometric report in 2018, it can be stated that in terms of bibliometric parameters, the Czech Republic has excellent centers in clinical medicine; the share of excellent publications is even higher than the international base, and the proportion of outputs in the 1<sup>st</sup> quartile is very good, better than expected. In contrast, the Czech Republic also has a higher representation in the lowest, 4<sup>th</sup> quartile, while the 2<sup>nd</sup> and 3<sup>rd</sup> quartiles including average publications is less represented in the Czech Republic, rather less than expected. As regards the representation of individual specializations, cardiology and oncology are the leading fields in our country.

Regarding the comparison of the programs of other providers in the Czech Republic, the Ministry of Health is the exclusive provider of targeted support for projects addressing the most common diseases in the population, thus maximally contributing to the fulfillment of the objectives of National Priorities, A Healthy Population.

Projects dealing with the issues of applied medical research can be marginally traced in the national programs of the Ministry of Industry and Trade (the TRIO program – it focuses on key technologies in various fields, health is only one of many areas) and the Technology Agency of the Czech Republic (e.g. the programs DELTA, EPSILON – the number of projects is in the order of units)

The newly prepared program of the Ministry of the Environment entitled Environment for Life will address the impact on human health, especially as regards the monitoring of all relevant environmental components and minimizing the negative impacts of pollution on human health, which is synergistic and complementary to this Program. Furthermore, several projects of applied medical research can be found within the EU operational programs provided by the Ministry of Education, Youth and Sports (in particular the Operational Program Research, Development and Education - OP RDE). The aim of the OP RDE is to contribute to the shift of the Czech Republic towards an economy based on an educated, motivated and creative workforce, to produce quality research results and to use them to increase the competitiveness of the Czech Republic.

OP RDE focuses on improving the quality of education, ensuring conditions for quality research, linking education and research with the labor market, and strengthening the principle of equal access to education. The key principle of the OP RDE is the development of human resources for a knowledge-based economy in a socially cohesive society, followed by the theme of promoting quality research, for which a skilled workforce is a key input factor. Synergies in the focus of the Program can be traced back to the 8<sup>th</sup> framework program for research and innovation, Horizon 2020, whose societal challenge titled "Health, Demographic Change and Wellbeing" should contribute to improvements in health and living conditions for all EU citizens. At the same time, Horizon 2020 declares that the EU should become a very strong partner in a rapidly developing global health and wellbeing market. One of the prerequisites is excellent research, understanding of the basic determinants of health and disease, the aging process, and many others.

The way to achieve this is through long-term and coordinated support for international, cross-sectoral and cross-field cooperation.

As a civilized country with developed and high-quality healthcare, the Czech Republic should continue to provide adequate support for health research to capitalize on the years of building high-quality teams and workplaces, whether clinical or primarily research. The share of R&D&I state budget expenditures in healthcare (including both targeted and institutional support) in the total public R&D expenditures from national sources was around 5% in 2014-2018.

A detailed analysis of medical research abroad is provided in the Annex (Analysis of Health and Medical Research in Selected Countries and in the EU) "Health Research Concept until 2022". Two small countries, one medium-sized one, two large ones (Switzerland, Austria, the Netherlands, the United Kingdom, the USA) and the European Union as a whole have been selected for the analysis, objectively presenting the current state of health and medical research in OECD countries.

Several common status characteristics can be derived from the information obtained:

- Health research is supported in all countries by a combination of institutional funding and targeted funding. Considering the existence of a single Joint Research Center (JRC), which also deals with medical research, this is also true for the EU.
- Health research is still closer to basic research. This results in the absence of large specific national health research programs, with the exception of Austria. If programs exist, they are usually programs of selected providers or institutions, and they are of a more general character. Bottom-up approaches prevail in the development of public support research projects, where researchers and research organizations themselves choose topics and procedures.
- Research institutions and organizations in all of the countries surveyed are sufficiently aware of the need for the rapid and effective use of research results. This is evidenced by the great attention and support devoted to translational research, i.e. the linking of basic research and clinical research. In addition, this is evidenced by the fact that in many medical research institutes, legal protection units for results and units for transferring results are being set up. And even in the case of those involved in basic research.
- There are no significant health research priorities. Medical research is extremely broad in all of the countries under review and in the EU. With some caution, the following could be considered 'mild' priorities: neurological research, especially brain research; molecular medicine; genomics, cancer research; health problems associated with an aging population. With such a large thematic breadth of medical research and a very diverse structure of research institutes (universities, public research organizations, state research institutes), there are considerable potential opportunities for duplicates and even several identical research papers.
- In some countries, health research coordination institutions are established (e.g. the Netherlands, Switzerland, United Kingdom). Detailed information systems on health research are being set up or further developed in most countries.
- Transdisciplinary efforts can be observed in all of the countries under review. Life sciences and technical sciences are also gradually being incorporated into medical research, which has long been a standard part of life sciences. Health research is being



conducted at a number of universities that do not have medical faculties, as well as at traditional technical universities. It is gratifying that this trend is also reflected in the Czech Republic.

- In all of the countries under review, there is considerable care for the preparation and training of new staff for medical research.

## **20. Expected Results**

Following the objectives set, only those projects that justify the achievement of at least one major<sup>4</sup> and one secondary R&D result will be supported. It is also acceptable to achieve at least two main results or one result published in a prestigious international journal, ranked in the 1<sup>st</sup> quartile according to the Methodology of Evaluation of Research Organizations and Programs of Targeted Support for Research, Development and Innovation. A higher number of results will be required for projects requiring special-purpose support over CZK 12 million for the entire period of resolution (detailed conditions will be described in the dossier of public tenders).

Individual types of results are defined in the separate Annex no. 4 – Methodology of Evaluation of Research Organizations and Programs of Targeted Support for Research, Development and Innovation, approved by Government Resolution No. 107 on 8 February 2017, entitled “Definition of the Types of Results” (approved by Government Resolution No. 837 on November 29 2017).

A main result is one of the following types of results:

- J<sub>imp</sub> – peer-reviewed scientific article - an original article in a peer-reviewed scientific journal that is included in the Web of Science database with the attribute "Article"<sup>5</sup>
- F - utility model, industrial design
- G - prototype, functional sample
- N - methodology, treatment procedure, specialized map with specialized content
- P - patent
- R - software
- Z - pilot operation, proven technology

A secondary result is one of the following types of results:

- J<sub>imp</sub> – peer-reviewed scientific article - an article in a peer-reviewed scientific journal that is included in the Web of Science database with the attribute "Review" or "Letter"
- J<sub>sc</sub> – peer-reviewed scientific article - an original/review article in a peer-reviewed scientific journal which is included in the SCOPUS database with the attribute "Article", "Review" or "Letter"

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<sup>4</sup> Classification as main results (only reported in the Program) and secondary results (also reported in other activities or programs) is proposed for the future evaluation of the Program – in the absence of main (separate) results, the project will be evaluated as unsuccessful.

<sup>5</sup> During assessment, an emphasis will be placed on the applicability of this type of result in practice.

- B - professional book
- C - A chapter in a professional book

Other results are one of the following types of results:

- J<sub>ost</sub> – peer-reviewed scientific article - an original/review article in a peer-reviewed scientific journal that does not belong to the J<sub>imp</sub> or J<sub>sc</sub> category of results. (The list of peer-reviewed non-impacted periodicals is not used. The decisive factor is whether the peer-reviewed scientific article meets the general requirements for this kind of result and has undergone a proper review process.)
- D - essay in a symposium
- H - results reflected in legislation and standards, results reflected in directives and regulations of a non-legislative nature binding within the competence of the relevant provider, results reflected in approved strategic and conceptual documents of the government or public authorities
- S - specialized public database
- V - research report, summary research report
- A - audiovisual production
- E - organization of an exhibition, organization of an exhibition with a critical catalog
- M - organization of a conference
- W - organization of a workshop
- O - other results

For the purposes of this Program, a main, secondary and other result of R&D&I is defined as a new result obtained through a project supported by this Program and in the information registry on results in the R&D&I Information System, it is regarded as a result of this project. At least one main or secondary result of each completed project must be registered in the R&D&I Information System information registry on results solely as a result of this project (except for a result published in a journal ranked in the 1<sup>st</sup> quartile according to the Methodology of Evaluation of Research Organizations and Programs of Targeted Support for Research, Development and Innovation).

The users of the results will be predominantly healthcare providers, in particular general or specialized hospitals, specialized institutes and laboratories, outpatient doctors, social and nursing facilities, specialized private healthcare facilities, and/or other important institutions in the health sector, e.g. health insurance companies.

## **21. Expected Benefits**

Meeting the Program objectives should provide, in particular, the following expected benefits:

- 1) continuing the development of clinical research in the Czech Republic as a basic source of new clinical procedures in diagnosis, treatment and prevention in healthcare,
- 2) achieving higher quality prevention, early diagnosis and treatment of human diseases,
- 3) reducing long-term healthcare costs in connection with the promotion of new preventive procedures,

- 4) ensuring the development of new preventive, diagnostic and therapeutic methods,
- 5) a favorable influence on the mortality and chronic morbidity of serious diseases,
- 6) providing treatment for currently untreatable diseases,
- 7) helping to reduce the side effects of current therapies,
- 8) expanding collaboration with leading foreign workplaces and teams,
- 9) ensuring the continuity of medical research in the Czech Republic with the development of world science,
- 10) creating conditions that support a wider involvement of young researchers.

The benefits and impacts of the Program will only be evaluated several years after its completion. Indicators for the verification of the long-term impacts of the achieved results are also described in the Health Research Concept until 2022 in Chapter 11 - Review and Evaluation of the Concept. This information will then be used to comprehensively evaluate the benefits of public support. The following table describes examples of specific indicators for monitoring some Program benefits/impacts.

**Tab. no. 8: Method of Monitoring Program Benefits/Impacts**

<b>Benefits of the Program</b>	<b>Indicator</b>
improving the health of the Czech population	<ul style="list-style-type: none"> <li>- an increase in the number of early diagnosed metabolic, cardiovascular, tumor, neurological and other serious diseases</li> <li>- a reduction in cardiovascular disease mortality</li> <li>- a reduction of cancer mortality</li> <li>- stopping the growth of the number of patients with diabetes,</li> <li>- shortening the length of hospitalization or reducing the number of rehospitalizations of people with mental illness,</li> <li>- decreasing the incidence of infectious diseases, etc.</li> </ul>
the benefits of newly applied methods and procedures	- quantitative and qualitative assessment of streamlining clinical procedures
the quality of medical research	<ul style="list-style-type: none"> <li>- quality of publications (citation response)</li> <li>- international awards</li> <li>- membership in international bodies,</li> </ul>
increasing the international prestige of medical research	<ul style="list-style-type: none"> <li>- the amount and volume of international cooperation,</li> <li>- the number and quality of co-publications with international workplaces,</li> <li>- membership in international bodies</li> </ul>
strengthening the personnel base of medical research	- the number and quality of research results carried out by young researchers
strengthening interdisciplinary cooperation in health research	- the intensity of interdisciplinary research activities

long-term development of research activities	- the number of projects directly linked to projects implemented in the program
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## 22. Incentive Effect

The program will contribute to increasing, streamlining and improving the quality of applied research in healthcare. In order to meet the objectives of the Program and the conditions of the Commission Regulation, the provider will assess the presence of the incentive effect of the support under Article 6 of the Commission Regulation for all tenderers for the whole project as part of the project proposal evaluation process. The evaluation of the incentive effect will be part of the assessment report prepared by the provider's expert advisory body. According to the Commission Regulation, the incentive effect of the support is demonstrated automatically by an SME if it commences work on the project after the contract on support comes into effect and fulfills the conditions set out in the tender dossier. According to Article 2 (23) of the Commission Regulation, commencement is defined either as the start of construction work under the investment or the first legally enforceable obligation to order equipment, or another obligation that results in the investment becoming irreversible, whichever occurs first. The purchase of land and preparatory work such as obtaining permits and feasibility studies are not considered to be the commencement of work.

In the case of a takeover, the "start of work" is defined as the moment when the property directly related to the purchased establishment is acquired.

If the beneficiary or other participant is a large enterprise, in order to meet the incentive effect in accordance with the Commission Regulation in the project proposal it must comply with the requirements of Article 6 (3) of the Commission Regulation, particularly demonstrating that the support will contribute to a significant increase in the scope of the project or activities as a result of the support, or significantly increase the total amount spent by the beneficiary on the project or activity as a result of the support, or a significant acceleration of the completion of the project or activity.

## 23. General Assessment Criteria for Project Proposals

In accordance with the rules stipulated by Act No. 130/2002 Coll., the provider designates a project proposal acceptance committee. The proposals received are reviewed by the committee for the acceptance of project proposals for the fulfillment of all the requirements set out in the tender dossier for project proposals.

The provider decides whether to accept the project proposal into the public tender or eliminate it in accordance with Section 21 paragraph 3 of Act No. 130/2002 Coll. on the basis of a protocol prepared by the committee for the acceptance of project proposals, that is, the expert advisory body. Project proposals excluded from the tender are not further evaluated.

## 24. Project Proposal Evaluation Process

The evaluation will take place within a three-tier system based on the Project Evaluation System:

- The deciding authority is the provider.
- The Scientific Council is an expert advisory body pursuant to Section 21 (4) of Act No. 130/2002 Coll.
- Expert evaluation panels are expert bodies of the Scientific Council under the Project Evaluation System.

The project proposal assessment system is designed to reduce the space for interest influence and avoid conflicts of interest at all levels of assessment.

### **Assessment criteria for project proposals**

The evaluation and selection of project proposals is carried out by the provider's advisory bodies on the basis of the following criteria:

1. The applicant's eligibility, in particular the applicant's technical and institutional background.
2. The solver's abilities and groundwork. In particular, the solver's professional abilities and results achieved so far are assessed.
3. Economic intensity of the project – project proposals exceeding the requirement for targeted support over CZK 12 million for the entire duration of the project will have to declare achieving a higher number of results, while emphasizing their higher quality. The specific conditions will be described in the tender dossier, where stricter criteria will be set for evaluating both project proposals and final reports on these projects.
4. Quality of the proposed project:
  - a. project objectives - whether clear project objectives, their novelty, difficulty, significance and feasibility were defined;
  - b. proposal for solution - how the solver intends to achieve the set objectives and results (clarified concept, preparation and adequacy of the proposed methodology);
  - c. outputs - relevance of the overview of expected results; this will form the basis for solving known or anticipated, current or future problems or options;
  - d. foreign cooperation - the involvement of foreign workplaces in the solution is evaluated; the mutual use of devices of cooperating workplaces; using complementary approaches and methodologies;
  - e. compliance with R&D&I Priorities - it is assessed whether the proposal contributes to their fulfillment in the section of oriented research, or whether the National Strategy for Rare Diseases for 2010-2020 is complied with.

The specific procedure for evaluating proposals will be set out in the tender dossier for each of the Program's public tenders.

## **25. Interim Evaluation of Solved Projects**

The provider evaluates the progress of the project every year based on an assessment by expert advisory bodies (expert evaluation panel and Scientific Council), on the basis of submitted partial reports and results of the provider's inspection activities.

The provider evaluates the project resolution procedure using the following main criteria:

- the progress of work and its compliance with the set objectives;
- the provision of professional and personnel solutions;
- the use of technical and instrumental equipment acquired from the project;
- personnel, organizational and technical procedures for building a new team;
- achieving the objectives of the solution compared to the plan set out in the project proposal, the prerequisites for the overall time and material performance of the task;
- evaluation of the current management of allocated funds, possibly the proposed budget for the following period (checking the drawing of allocated funds, the effectiveness of their spending and the maintenance of their composition, proper justification of possible transfers or changes);
- assessment of results according to categories defined in Section 18 of the Program.

The expert advisory bodies shall draw up a written report on the outcome of the evaluation and submit it to the provider.

If the conditions for continuing project support are met and the provider decides to continue with the project support, it will provide the beneficiary with funding for the following year of the project.

If the preconditions for continuing with the project support are not met, the provider is entitled to withdraw from the contract on support or issue a decision to terminate the support.

The interim evaluation will also assess the fulfillment of obligations on the submission of information to the research, experimental development and innovation information system (pursuant to Section 31 of Act No. 130/2002 Coll.).

## **26. Result Evaluation of Projects (ex post):**

The evaluation of the completed project is carried out on the basis of an assessment by the expert assessment panel, the Scientific Council, based on the final report and the result of the audit activity on the management of funds.

The provider evaluates the final report and the procedure for solving the project according to the following main criteria:

- the fulfillment of the main objective of the Program;
- the progress of work and its compliance with the set objectives;
- the provision of professional and personnel solutions;
- the use of technical and instrumental equipment acquired from the project;
- an evaluation of the current management of the allocated funds (checking the drawing of allocated funds, the effectiveness of their spending and the maintenance of their composition);
- an assessment of the results according to the categories defined in Section 18 of the Program. When evaluating project results, an emphasis will be placed not only on the publication of results in reputable magazines, but also on their use in practice. Stricter evaluation criteria will be set for projects more costly than CZK 12 million.

The Scientific Council and the expert assessment panel also take into account compliance with the conditions for managing the allocated funds in the overall evaluation of the completed project.

The expert advisory bodies will draw up a protocol on the outcome of the evaluation of the completed project and submit it to the provider, who will discuss and decide on the assessment proposal.

The project solution is evaluated as follows:

- **fulfilled** - the declared objectives of the project have been achieved, the applied results from the project and publications, or other results, are excellent or very good in terms of their number and potential response or possibilities of use in solving issues stated by the project, and will significantly affect development in the field, especially in the international context.
- **not fulfilled** - the published or otherwise applied results from the project (publications or other results) are not excellent or very good in terms of their number and potential response or possibilities of use in solving the issues stated by the project, and they will probably not significantly affect development in the field.

Outstanding results of a project evaluated as excellent can be nominated by the Scientific Council for a special award, the so-called Health Minister's Award for Health Research and Development.

## **27. Presumed Program Parameters**

In relation to the Program focus and experience from the previous program supporting applied research from public funds, the average amount of support per project is expected to be CZK 11 million, i.e. the average project expenditure is CZK 12.1 million. Given the total budget of the Program, a min. of 500 supported projects are presumed, while a min. of 25 projects (i.e. about 5%) are expected to be solved as cooperation between research organizations and enterprises. The program envisages the involvement of about 900 entities in the solution of supported projects.

## **28. Criteria for Meeting the Program Objectives**

Achievement of the main and sub-objectives of the Program will be evaluated in accordance with the Methodology for the Evaluation of Research Organizations and the evaluation of programs for the targeted support of research, development and innovation applicable at the time of the evaluation of the Program, or other conditions specified by the provider, as well as according to definitions for the submission of results to the R&D&I Information System valid at the time of the Program evaluation.

Achieving the Program objectives will be evaluated on the basis of a set of indicators designed to monitor the progress of the Program and assess its overall performance and success.

The indicators are classified into four categories according to their nature, namely Program Implementation Indicators, Program Result Indicators, Indicators of Scientist Motivation and Indicators for Meeting Program Objectives.

**Tab. no. 9: Program Indicators**

Indicator	Number
<b>Program Implementation Indicators</b>	
Minimum number of project proposals received in tenders	2000
Minimum number of selected (supported) projects <sup>6</sup>	500
Minimum number of completed projects in total	375
Minimum number of projects cooperated on between companies and research organizations	25
<b>At least 75% of projects will be successfully completed</b>	
<b>Program Result Indicators</b>	
Minimum number of main Program results	500
Minimum number of secondary Program results	500
Minimum number of other Program results	1000
<b>Minimum number of all Program results</b>	<b>2 000</b>
<b>Indicators of Main Program Results</b>	
J <sub>imp</sub> – an original article in a peer-reviewed scientific journal that is included in the Web of Science database with the attribute "Article"	460
N – methodology, therapeutic procedure	20
P – patent	10
R – software	10
<b>Indicators of Secondary Program Results</b>	
J <sub>imp</sub> – an article in a peer-reviewed scientific journal that is included in the Web of Science database with the attribute "Review" or "Letter"	300
J <sub>sc</sub> – an original/review article in a peer-reviewed scientific journal that is included in the SCOPUS database with the attribute "Article", "Review" or "Letter"	150
B – a professional book	25
C – a chapter in a professional book	25

<sup>6</sup> The minimum number of selected projects is dependent on the funds available for the implementation of the Program projects from the state budget.



Indicator	Number
<b>Indicators of Scientist Motivation</b>	
Number of projects for young researchers	50
Minimum number of awards awarded for outstanding results	15
<b>Indicators for Meeting Program Objectives</b>	
<b>We assume that 65% of the Program's sub-objectives will be addressed in the projects</b>	

## 29. Risks Associated with the Implementation of the Program

Based on its many years of experience, the provider has identified the most probable risks that could jeopardize the proper implementation of the Program and meeting the set objectives and indicators:

- 1) not allocating sufficient funds from the state budget;
- 2) little interest in public tenders from research institutes;
- 3) a low number of project proposals received in tenders meeting the quality requirements of the provider;
- 4) an insufficient number of enterprises involved in cooperation with research organizations;
- 5) lack of interest or unwillingness of young researchers under 35 to engage in project solutions;
- 6) objective reasons preventing researchers from providing a statistically significant research and control population in population studies;
- 7) staffing and technical issues of the provider with ensuring the proper announcement and management of tenders (in particular a functional online application for tender management);
- 8) legislative changes.

### Measures to eliminate selected risks:

Risks 1 and 8 are hard to influence by the provider. Risks 2 to 5 can be eliminated by providing greater publicity for health research. An increase in the budget of targeted support in the health sector could also be of great help, as the success of supported projects from the total number of submitted project proposals for tenders has been around 20% in the long term.

Risk 6 can be avoided by the quality evaluation of project proposals during the assessment period of the public tender or during the ongoing evaluation of the projects solved in the form of partial reports. Risk 7 can also hardly be influenced by the provider because, for example, an internet application for tendering is usually managed by external contractors whose selection is very much bound by both the law and the provider's internal regulations, which is not always a guarantee of their quality. In this case, it is necessary to provide sufficient personnel capacity on the part of the provider and to rely on the personal qualities of its individual employees.

### 30. Methods of Monitoring and Evaluating the Program

The program will be continuously monitored through the collection of information on projects, their implementation and results. The fulfillment of all set objectives will be evaluated on an ongoing and final basis by means of partial and final project solution reports. In the year following its completion, the Program will be evaluated, including an assessment of the results achieved, and an evaluation report will be drawn up, comparing the actual results of each project with the assumptions in the Program, and its benefits will be evaluated. As part of the assessment of the Program, the following indicators will be evaluated and the benefits of the Program at the level of individual projects will be monitored and evaluated. Approximately four years after the completion of projects, the actual utilization of the results achieved in practice and their impact on healthcare or impact on the health of the population, etc., will be continuously evaluated.

Indicators to verify the long-term impact of the results are also described in the Health Research Concept until 2022 in Chapter 11. Review and Evaluation of the Concept. This information will be used to comprehensively evaluate the benefits of public support. The provider assumes that it will be necessary to prepare a rather extensive study for these purposes.

**Tab. no. 10: Program Assessment Schedule**

<b>Year</b>	<b>Subject of assessment</b>	<b>Objective of assessment</b>
2019	Ongoing assessment of the NV program	Evaluation of Program implementation processes, project orientation in relation to program objectives and existing outputs and results in relation to Program objectives. The assessment will form the basis for the second public tender.
2020	Assessment of the results of the 1 <sup>st</sup> tender	Evaluation of the processes of the 1 <sup>st</sup> public tender and the focus of the projects in relation to the objectives of the Program. It will form the basis for the 2 <sup>nd</sup> public tender.
2021	Assessment of the results of the 2 <sup>nd</sup> tender	Evaluation of processes of the 2 <sup>nd</sup> public tender and the focus of the projects in relation to the objectives of the Program. It will form the basis for the 3 <sup>rd</sup> public tender
	Continuous assessment of the NU Program	Evaluation of Program implementation processes, project orientation in relation to program objectives and existing outputs and results in relation to Program objectives. It will form the basis for the third public tender.
2022	Assessment of the results of the 3 <sup>rd</sup> tender	Evaluation of processes of the 3 <sup>rd</sup> public tender and the focus of the projects in relation to the Program objectives. It will form the basis for the 4 <sup>th</sup> public tender and for the preparation of a new program.
2023	Assessment of the results of the 4 <sup>th</sup> tender	Evaluation of processes of the 4 <sup>th</sup> public tender and the focus of the projects in relation to the objectives of the Program.
2027	Assessment of the NU Program Results	Final assessment of the results of the Program and implementation processes. It will form the basis for the

		preparation of a concept and related programs.
2030	Program Benefit/Impact Assessment	Assessment of the benefits and impacts of the Program. It will form the basis for the preparation of a concept and follow-up programs.