

REPORT ON THE FULFILLMENT OF TASKS FROM THE
1ST NATIONAL ACTION PLAN FOR RARE DISEASES (2012-2014)
AND THE 2ND NATIONAL ACTION PLAN FOR RARE DISEASES (2015-2017).
(Czech Government Resolution n. 76 from February 4, 2015)

INTRODUCTION

Rare diseases (or RD) are clinically heterogeneous group of approximately 6000-8000 various clinical entities whose joint characteristic is their very low prevalence in the general population (i.e. for each of the individual diseases less than 1:2000 inhabitants). In the event of erroneous and late diagnoses of RD, there can often be irreversible damage to the patient's health, or even premature death. RD comprise all groups of diseases and are responsible for up to 5% of morbidity and mortality in early childhood.

On 14 June 2010, the government of the Czech Republic (CZ), via Government Resolution No. 466, passed the "*National Strategy for Rare Diseases for 2010-2020*" (NAS) which summarizes the issue of RD from the standpoint of the EU and application of EU Council recommendations within CZ health care system. The National Strategy established the frame for action in the field of RD in CZ and proposes the main goals and measures for improving the situation in this area in the country. The primary goals of the National Strategy comprise timely diagnosis and accessibility of adequate treatment of RD, improvement in education and RD awareness for medical professionals and public at large, cooperation at the national- and international levels and also the improved identification of RD within the International Classification of Diseases (ICD) system, as well as further development of European cooperation. The subsequent first "*National Action Plan for Rare Diseases for 2012-2014*" (NAP1) specifies priority tasks and activities in such a way that the goals and measures of the NAP1 are to be gradually fulfilled within the respective time frame. Component tasks, tools, responsibility, deadlines, possible financial resources and indicators for the fulfillment of individual tasks of the NAP1 had been set in such a way as to be feasible and to have a minimal financial impact on the state budget and/or the public health insurance system.

From 2012-2014, main tasks and activities stipulated in NAP1 were:

- Improving awareness of RD among the medical professional and public at large;
- Education in the area of RD, especially inclusion of specific RD issues into pre-graduate and post-graduate education of health care professionals;

- RD prevention with a focus on the development of preconception- and prenatal diagnostics;
- Expansion of the number of RD diagnoses in the framework of the nationwide laboratory neonatal screening scheme;
- Improved accessibility and quality of care for patients with RD, making diagnostics, treatment and ensuring equal access for all patients with RD to the indicated and high quality of health care, in accordance with relevant European standards;
- Improving the quality of life and social inclusion of persons with RD;
- Support for science and research in the area of RD, development of basic and applied research in this field;
- Unification and development of the collection of data (via registries) and biological samples in the framework of RD at the national- and regional levels;
- Support and strengthening the role of RD patient organizations;
- Inter-ministerial, inter-departmental and international cooperation in the area of RD.

The second "National Action Plan for Rare Diseases for 2015-2017" (NAP2) specifies priority tasks and activities in such a way that the goals and measures of the NAS continue to be fulfilled in the upcoming period. Tasks and activities continually relate to priority tasks fulfilled within NAP1, and have been set in such a way as to be feasible in the given period and to have a minimal financial impact on the state budget and/or public health care system.

Report on the fulfillment of tasks stemming from the National Action Plan for Rare Diseases for 2012-2014

1. Improving awareness of RD

1.1. Operation and updating of an RD-related web portals

In order to improve awareness in the area of RD, websites and portals have been created and are in operation. Web pages for individual specialized centers for RD treatment were created, and the overarching web portal www.vzacnemoci.cz for RD was launched; it has the goal of increasing general awareness of RD not only among the public at large, but also among medical professionals providing health care to patients with these diseases.

The portal www.novorozeneckyscreening.cz, intended for the general and professional publics, provides detailed information on available CZ newborn screening programs, which are targeted at serious RD among newborns. The portal is divided into two parts - for the general public, especially for families who are immediately impacted by the nationwide newborn screening programme and a section for the medical professionals.

The portals www.ebcentrum.cz (on epidermolysis bullosa) and www.debra-cr.cz serve the field of dermatology and are also intended for a general- and professional publics. There, basic information on the EB Centrum (Brno) and contacts on individual specialists can be found. In this regard the CZ EB Center is a specialized workplace which was established already in 2001 at the Department of Pediatric Dermatology at the Brno University Hospital in the Černá Pole district. The EB Centrum is associated with the web pages of DEBRA ČR, which are intended for patients, their families and for the general public.

The Czech Republic has participated in the European Orphanet project (www.orpha.net) and expanded Orphanet's Czech version at www.orphanet.cz. The Orphanet pages for the Czech Republic provide news, documents and information on events of national importance in RD, current status related to orphan medicinal products (OMP) and an overview of diagnostic- and clinical services provided in the country.

The national register for RD biochemical testing has been developed and is posted at www.registr-raritnich-vysetreni.cz, including diagnosis and monitoring of a sub-group of rare congenital defects at the www.vrozene-vady.cz portal, associated to the Eurocat EU

consortium. The portal www.vzacna-onemocneni.cz was launched, where the pages of the overarching Czech Rare Diseases Association (or "ČAVO") can be found; it brings together RD patient organizations as well as individual patients from all over CZ. The portal is strengthening awareness on specific RD issues among experts in health care, policy makers and international institutions, and the public. ČAVO also became member of Eurordis.org.

A project to create the National Information and Education Portal on Pediatric Oncological Diseases, was undertaken in cooperation between the Brno University Hospital and the Bioinformatics Institute at Masaryk University in Brno with the goal of objective information to the general public on pediatric tumors, their treatment and prognosis (www.registry.cz).

1.2. Raising awareness of RD among the medical professionals and the general public

In the 2012-2014 there has been a marked improvement in terms of RD awareness in the media (e.g. radio, television, social media and print). Promotional video documents on RD, the "*Rare Diseases*" documentary film were made available and were broadly distributed, lecture series and seminars for the expert and general public, and experts' appearances on Czech Television and Czech Radio, all took place. In daily newspapers and health care-related media, articles were published on RD, the quality of life and social inclusion of patients with these diseases. It is envisioned that these activities would continue within the period of NAP2. This is particularly important since a recent poll proved that RDs are generally unknown to the general public and that these are often confused with bizarre or unusual diseases (www.aifp.cz/cs/aktuality/informace-pro-media/vzacna-onemocneni-jsou-pro-vetsinu-z-nas-velkou-neznamou/).

In cooperation with patient organizations and with the European patient organization for rare diseases, Eurordis.org, the World and European Rare Disease Days were promoted in the media. ČAVO published Zpravodaj ČAVO [ČAVO News] and held regular member meetings. Multiple information seminars were held in the Chamber of Deputies of the Parliament and in the Senate in order to inform policy makers on the situation of RD in CZ.

2. Education in the area of RD

The issue of RD became part of pre- and post-graduate education for doctors and other health care workers, whereby individual specialized centers offer educational courses and seminars. But this education has not been systematic so far, and in the next period it will be

necessary to expand the specific issues of RD, especially in the areas of educational programs for general practical medicine and internal medicine at all CZ medical faculties. As part of the fulfillment of the NAS, seminars and workshops were organized for the expert public, and expert blocks relating to RD were included in individual CZ medical congresses. A number of research and overview articles were published in the Czech and foreign press on the topic of RD. For education in the area of RD, expert organizations, accredited facilities, medical faculties and the Institute of Postgraduate Education in Health Care (www.ipvz.cz) took part. Two monographic publications were produced on the topic of RD, "*Rare Diseases in a Nutshell* (MF Publishing 2014)," and a special issue of "Postgraduate Medicine (January 2015 issue)", which were broadly distributed to all medical specialties.

ČAVO implemented a project, "Early diagnosis of rare diseases," intended for practicing physicians for children and adolescents and general practitioners. The great majority of Czech practicing pediatricians were addressed, and lectures on the topic of RD took place in cooperation with the Expert Society of Practicing Pediatricians. A poster, "Early Diagnosis," was distributed to their practices to make them aware of early signs of RD.

The EB Center and DEBRA ČR produced seminars for practicing pediatricians and general practitioners in 2013 and 2014. The Czech Society of Dermatology of the Czech Medical Association of J. E. Purkyně held a conference on pediatric dermatology that was focused on RD in the field of dermatology.

A help mail service was started at help@vzacna-onemocneni.cz. In the event of specific information needs in the area of RD, it is possible to turn to this consultation e-mail address, which is intended for doctors and the general public. Operation of the informational e-mail on the expert side is provided by the National Coordinating Center for Rare Diseases at University Hospital Motol (NKCVO) in cooperation with other *de facto* and *de iure* (see below) RD centers and relevant experts from across the country.

3. RD primary and secondary prevention programs: preconception, preimplantation and prenatal screening

In terms of preconception screening, the necessary activities were not carried within NAP1 due to the unresolved ethics problems connected with it. In the area of prenatal screening, a unification of recommendations for its implementation has been promoted by the CZ medical genetics professional association - "Society of Medical Genetics of the Czech Medical Association of J.E. Purkyně" (www.slg.cz). This professional body has published a number of

recommendations in the field of genetic testing of RD which are in line with relevant European guidelines, e.g. put forward by ESHG.org, ASHG.org or ACMG.net. In addition, an up to date database of RD DNA diagnostics and its links to international initiatives in this domain has been developed (www.slg.cz). Prenatal diagnosis, and centralised treatment of congenital heart defects has been established as part of routine care in all pregnant women. The EB Center has implemented prenatal and preimplantation genetic diagnosis in cooperation with gynecology clinics and assisted reproduction centers in the entire country. As part of a comprehensive genetic counselling programme, the EB Center is implementing genetic examinations in relatives of patients with EB. Within the 2012-2014 period, a network of echocardiological laboratories was founded; they cooperate on early diagnosis for pulmonary hypertension syndrome.

4. Improving screening and RD diagnosis

4.1 Expansion of cross-the-board neonatal screening to include early RD diagnosis

A pilot study by the Institute of Hereditary Metabolic Disorders (www.udmp.cz) in Prague was completed in 2014. It dealt with the "Optimization of Newborn Screening for Hereditary Metabolic Disorders (2011-2014)." The study was produced as part of a research grant project funded by the Internal Grant Agency (IGA) of the CZ Ministry of Health (MH), and was focused on the possibility of expanding the current nationwide neonatal screening program to include additional hereditary metabolic disorders, and for the development of new laboratory technology aimed at decreasing the false positive rate. The planned expansion of the nationwide screening program from 1 January 1, 2015, which should include a total of 15 hereditary metabolic disorders, was approved by the Inter-ministerial and Inter-disciplinary Taskforce for Rare Diseases (Taskforce) of the MH. In addition, two new health insurance reimbursement codes were published within the annual amendment of Regulation No. 134/1998, which publishes a list of health care reimbursement codes with arbitrary point values for health insurance reimbursement. Expanding the number of screened disorders will be presented in the "Methodological Guide for the Provision of Newborn Laboratory Screening and Follow-up Care," which will be published in the Bulletin of MH in early 2015. A recommendation has been made to expand the current newborn laboratory screening to include the following diseases: Type I citrullinemia, the pyridoxine non-responsive form of cystathionine β -synthase deficiency (CBS deficiency), methylene tetrahydrofolate reductase deficiency, and biotinidase deficiency.

Informing the public is an important part of the screening program. In 2014, a questionnaire study was conducted on newborn mothers' awareness about newborn laboratory screening (NLS), which pointed out certain deficiencies in families' awareness and understanding of NLS. A multiyear prospective study of families' stress as a result of NLS false positivity was also begun in 2014.

For the implementation of NLS on inborn newborn hearing disorders, the "Methodological guidelines for the implementation of screening of hearing disorders in newborns" was created and was published in the Bulletin of MH- 7/2012 edition. Selective genetic testing (i.e. investigation of patients or persons at risk of genetic diseases) took place as part of standard medical-preventive care at all relevant genetics departments in the Czech Republic as catalogued at www.s/g.cz. In 2014, the EB Center began diagnostics for all types of EB and an additional 13 genetic dermatoses by next-generation sequencing (NGS). All genetic tests are fully reimbursed by the public health insurance.

4.2 Amendment to Act. 98/2012 Coll. on medical documentation related to RD

The amendment to Act No. 98/2012 on medical documentation has resulted in confusion in terms of the storage period for blood spot cards (Guthrie cards) utilized in NLS at individual health care institutions involved. The storage periods varied, lasting up to 43 or more years from the last examination of a patient. Such inconsistent interpretation of these storage periods has caused problems for health care providers. In this regard health care providers have had problems with establishing the proper period for retaining of blood spot cards in accordance with of Annex 3 of Act No. 98/2012 Coll. on medical documentation. Fulfillment of Annexes 1 and 3 to Act No. 98/2012 Coll. on medical documentation on Guthrie cards for the implementation of NLS administratively unified the periods of their "official retention" within respective "health care documentation" in all CZ medical institutions. The MH proposed amendment will be presented for discussion to the Government of the Czech Republic in early 2015.

4.3 Quality and accessibility of diagnostic laboratories for RD

From the standpoint of quality of genetic diagnostic laboratories, further development in their laboratory accreditation according to ISO 15189 took place in accordance with the provisions of Law No. 373/2011 Coll. (§ 28-29), on specific health care services and in cooperation with the National Accreditation Body – the Czech Institute for Accreditation (www.cai.cz). Work has begun on an amendment to the law on specific health care services, because practical

findings and the rapid development of genomic technologies resulted in the need to update of its certain provisions, mainly due to rapid introduction of NGS. In this regard “*Recommendations on indications for genetic testing*” were established by SLG. In addition, updated “*Minimal laboratory standards (personnel and equipment)*” for laboratories carrying out genetic testing in CZ were published by SLG in 2014. Cooperation took place between the SLG and NKCVO at the University Hospital in Motol together with main health insurance companies such as the General Health Insurance Company (www.vzp.cz) and the Association of Health Insurers of the Czech Republic (www.szpcr.cz) from the standpoint of genetic diagnostics in RD and cross-border diagnostic care. An expert recommendation was issued by SLG relating to “*Informed consent prior to genetic testing*” taking into account NGS and array-based molecular cytogenetic DNA diagnostics in RD. In addition, a recommendation was updated for “*Good laboratory practice*” for a selected group of “more common” RD was issued by SLG. Finally, SLG and NKCVO were involved in the update of Decree No. 134/1998, which publishes a list of medical procedures with arbitrary health insurance reimbursement point values related to the provision of DNA diagnostics, mainly reflect rapid implementation of NGS and array-based techniques (so called “cultivation” of the current “Rate Book” of MH). From the point of view of accessibility, the network of state and private genetic diagnostic facilities is adequate, and regional differences are minimal as catalogued at www.slg.cz.

5. Improving access and quality of care in RD

5.1. Centralization, coordination and integration of care in RD

Within the NAP1 period (2012-2014) and in accordance with Act No. 372/2011 Coll. (§ 112) on medical services and the terms of their provision, and following EUCERD.eu recommendations, a pilot group of five RD *Centers of expertise* (RDCE) were established and published in the official MH Bulletin 4/2012 for a four year period (2012-2015; www.mzcr.cz/Legislativa/dokumenty/vestnik-c4/2012_6288_2510_11.html). At the end of this period these will undergo a professional audit organized by MH. These centers comprise the a) National Coordinating Center for Patients with Rare Diseases in UH Motol (NKCVO; www.fnmotol.cz), b) centers for patients with cystic fibrosis (www.cfregistry.cz), c) center for hereditary metabolic disorders (www.udmp.cz) and d) center for epidermolysis bullosa congenita (EB; see above). The aforementioned RDCE thus operate *de iure*, while additional RDCE on e.g. pulmonary hypertension, rare hereditary and congenital heart defects function *de facto* based on their long-term expertise and professional reputation. In cooperation with health insurers and representatives of expert organizations, a review was carried out of the

existing networks of *de facto* centers for patients with RD by the MH Taskforce. In cooperation with representatives of expert organizations, tenders organized by MH were prepared for establishing RDCE within other fields of medicine within NAP2 (e.g. RDCE for children and adult patients in neurology, epilepsy, dermatology, orofacial surgery, autoimmunity, endocrinology, hematology, rare cancers, nephrology).

In mid-2014, and in accordance with provisions of §112 of Act No. 372/2011 Coll., on medical services published, MH published a tender for RDCE for patients (adults and/or children) with rare hereditary and acquired disorders of hematopoiesis, and (adults and/or children) with hemophilia and other hemostasis disorders in its Bulletin 3/2014. The status of RDCE for patients with aforementioned disease groups would be granted for a five year period. These RDCE will provide patients with these hematological disorders comprehensive diagnostic and medical care, including management of surgical operations and treatment with coagulation factor inhibitors falling into the category of OMP.

The centralization of care for RD patients and the granting of the statute of RDCE will continue in the next period of NAP2. The Council recommendation from 2009 determines that these centers should have international research links (for example the to the European *E-rare2* or *Horizon2020* research programs) and should be connected to international research initiatives or European research projects in the given areas. EUCERD.eu recommendations should also be respected in this regard.

5.2. Recommended procedures for the diagnosis and treatment of selected RD

Implementation of the up to date knowledge for diagnosis and treatment of RD into clinical practice in CZ has been supported in the form of a IGA MH research grants, as well as in the expansion of the spectrum of existing patient RD registers and the implementation of new ones (www.registry.cz), MH appropriations for the improvement of RD screening and diagnosis, and professional societies driven efforts to implement standards of care for individual RDs falling into their remit. An overview of subsidies and research projects for the 2012-2014 period are listed in the attachment (*Note: not provided in the ENG version*).

5.3. Effective and timely RD pharmacotherapy with orphan medicinal products in accordance with internationally-accepted standards and recommendations

Between 2012 and 2014, a large number of OMP for the treatment of RD entered into the CZ health care reimbursement system, regardless of whether OMP were in the regime of highly

innovative products (according to current CZ legislation which includes not only OMPs) or in the regime of so called “permanent reimbursement”, which is usually linked to their provision at RDCE. The reimbursement of OMP is usually connected to specialized centers (i.e. health care providers who have centers with a “special contract” issued by health insurance companies). This approach renders not only efficiency and effectiveness of OMP prescription, but also their appropriate utilization associated with the highest levels of RD expertise. At the same time, the pharmacotherapy of RD is influenced by the establishment of CZ market prices and the reimbursement of OMP by national health insurance companies. Price and reimbursement regulation of OMP takes place within the confines of the Law on Public Health Insurance (Act 48/1997 Coll). Valid legislation does not directly mention the term 'rare diseases' or even 'treatment for rare diseases', which is a clear deficit to be addressed. For this reason, the evaluation of OMP treatment schemes in RD takes place *de facto* according to the same criteria as the evaluation of other treatments in common diseases.

OMP are made accessible to RD patients via the same mechanisms as other medicines. On average, their local approval (registration, establishment of their local prices and health insurance reimbursement) lasts approximately two years from the time of their approval by the European Medicines Agency. Decision on the reimbursement for OMP used in ambulatory care is within the competency of the State Institute for Drug Control (SÚKL; www.sukl.cz), while SÚKL does not have the legal mandate to decide on reimbursement for OMP used within hospitalization of patients with RD. There are additional possibilities for reimbursement of OMP aside from the setting of reimbursement by SÚKL. Thus, OMP may become available for treatment based on professional recommendations by individual medical societies of the Czech Medical Association of J. E. Purkyně (www.cls.cz), most commonly in accordance with provisions related to their European registration. Issues related to OMP reimbursement are based on the individual agreement between health care providers and manufacturers / distributors of specific OMPs. Another possibility is individual access based on the provisions of § 16 of the Law on Public Health Insurance (Act 48/1997 Coll.), which could be applied to OMP if these represent the only option for treatment in specific RDs. Nonetheless, the application of § 16 of this law falls within the competence of health insurance companies and has to be renewed every approx. 3 months based on their degree of impact in these specific individual instances.

6. Improving the quality of life and social inclusion of persons with RD

In the 2012-2014 period, Czech RD patient organizations have fulfilled an important psychological and social support function. Many patient organizations and their activities have reached beyond exchange experience, and have gradually become real partners for patients and their family members, which mediate the advice of doctors, lawyers, psychologists and social workers. Patient organizations have also significantly assisted doctors, nurses, professional organizations and the health care system by raising awareness of RD prevention and of the possibilities of their preconception and prenatal / postnatal screening, and thus contributed to the timely detection of certain diseases. The overarching role of ČAVO is very important in this regard.

6.1. Implementation of the International Classification of Functioning, Disability and Health in RD

On the basis of international recommendations, input from the CZ medical community, professional societies, implementation and use of the International Classification of Functioning, Disability and Health (ICF) was launched. The reintroduction of statutory duties for using ICF in selected areas of expertise are being discussed and fall within the competence of the Czech Ministry of Labor and Social Affairs (www.mpsv.cz; MPSV).

6.2. Education of professionals on the ICF system for RD

Medical professionals serving at the MPSV are prepared for the implementation of ICF with the majority of them having undergone appropriate training that enabled them to receive international ICF-related certification.

6.3. Health and social services in RD

It should be noted that due to the complexity of the issue in the area of health and social services there is a necessity for cooperation of CZ several ministries, health insurers and patient organizations, so that tasks in this domain could be gradually satisfactorily resolved. For the streamlining of cooperation between the MH and the MPSV, an inter-ministerial working group has been formed to resolve the issue of cross-cutting social and health care services with the goal of continuing the work on further resolution of the issues of long-term health and social services, and to create conditions for bringing to bear the principle of equality in the area of health and social services.

An important activity in support of sick children has been the organization of summer camps for children and their family, such as the Czech Association of Hemophiliacs, for the purpose of training on the intravenous application of coagulating factors in home treatment. An important contribution to the quality of life has been the prophylactic treatment with coagulation factors in this group of patients. Similar activities have taken place for other RD in cooperation with patient organizations, such as cystic fibrosis or muscular dystrophy patient associations.

DEBRA ČR regularly organizes weekly health visits with educational programs for patients and family members and contributes to patients' seaside visits. The DEBRA ČR conference brings patients and their families updates not only in the area of care for those with epidermolysis bullosa and up-to-date information on the activities of DEBRA ČR, but also information and assistance in the social and legal areas, as well as psychological support.

7. Support for basic and applied research in RD

7.1. Targeted support for science and research in the area of RD at the national and international levels

In the 2012-2014 period, *de facto* and *de iure* RD centres have been involved in joint research projects, such as the cardiovascular research program "Invasive Approaches for Salvage or Regeneration of the Myocardium" as part of the PRVOUK program of Charles University Prague. As part of the IGA CZ MH research programs in the past period the Institute for Hereditary Metabolic Disorders carried project "Optimization of Neonatal Screening for Hereditary Metabolic Disorders (2011-2013)." In addition, many other projects in the field of RD have been carried within the IGA research funding scheme

The activities of the Center for Hereditary Ataxia were also supported by an IGA grant. For instance, the University Hospital Brno is carrying out a project with the IGA support "Comprehensive Diagnosis of Selected Genodermatoses." It is a joint project with the Center for Molecular Biology and Gene Therapy at Hematooncologic clinic (IHOK), the Children's Dermatology Department of the Pediatric Clinic, the University Hospital Brno's Clinical Genetics Department and the 1st Pathological Anatomical Institute at the St. Anne's Faculty Hospital demonstrating the need for a multidisciplinary approach in RD.

Unfortunately, CZ participation in the European ERA-net programme "E-rare" could not be assured in the past period. The E-rare project is linking research funding organizations that

carry out joint funding initiatives in the domain of RD, whereby national teams are financed from national sources within international research consortia. The topic of RD was included in the Advisory Commission of the newly-formed medical research funding Agency for Healthcare Research (www.azvcr.cz). However, calls specifically related to RD have not yet been published. In cooperation with the Department for Science and Research at MH, RD have been placed into the Agency to be included within one of its research priorities for upcoming calls.

The role of EU framework funding was reflected in international collaborative RD-related research activities such as participation of Czech research teams in the projects such as lately e.g. Eurogentest.org, Orpha.net, Techgene.eu, Treat-NMD.eu, Care-NMD.eu, RD-connect.eu, RD-neuromics.eu and Eurenomics.eu. With the support of the European Agency for Health and Consumers (CHAFAEA), an international registry of RD patients (E-IMD, EHOD and INPDR) was created with the active participation of the Institute for Hereditary Metabolic Disorders at the General University Hospital in Prague and the 1st Medical Faculty of Charles University Prague.

Implementation of the project "National Coordination Center for Rare Diseases at the University Hospital in Motol" has begun in 2014 and this project is supported by EEA Norway Grants (PDP3 project) with partners in Bergen and at Frambu.no. The project's objectives are aimed at increased awareness of RD among the professionals, general public, and to implement of new methods of molecular cytogenetic and genetic diagnosis for prenatal- and postnatal diagnostics of RD, to improve pharmaco-economic modeling of diagnostic and treatment costs in selected RD, to improve comprehensive care for patients with RD utilizing the experience from Norwegian health care services and Frambu.no, and to develop pre-graduate and post-graduate training in RD. The project will be completed in mid-2016 and is conducted in collaboration with ČAVO and UH Brno.

8. Unification and development of data and biological samples collection in RD

8.1 National data collection in the area of RD, improving collection methodology and supporting participation in international projects

The collection of data relating to RD has been limited primarily by the lack of codification of the majority of RD in the commonly-used International Classification of Diseases (ICD-10) including the absence of a minimal data set for the collection of data in RD. Both problems are being intensively sorted out by the Institute of Health Information and Statistics of the

Czech Republic (ÚZIS ČR; www.uzis.cz) through the introduction of a detailed coding and classification system (OMIM, Orphacodes, SSIEM) into the collection of data of the National Register of Reproduction Health and into the MH “Data Standard”. A part of the plan has been the partial translation, support and documentation of these tools and to intensify international cooperation related to their use. A representative of ÚZIS has taken part in seminars abroad on this topic organized by the Orphanet consortium.

Use of the Orphacodes codification system, which will be included as a whole into ICD-11, should help in the automated transition into the ICD-11 classification. By using international coding schemes and methodology, ÚZIS also created a minimal data set for the collection of RD data (hence the RD “minimal data set”; MDS). The MDS should become a model for the creation of any new RD registries (and/or the adaptation of existing ones), databases and data models of electronic health records for further use, from the point of view of identifying RD cases in the Czech health care system.

As part of individual medical specializations, RD registries were installed in the 2012-2014 under the auspices of individual professional societies (such as the cardiologic registry KARDIO-ICD, KATAB, REPACE, REPLY, TAVI, the red blood cell disorder registry and the Center for Hereditary Ataxia's registry; www.registry.cz). A joint Czech and Slovak registry was created for pulmonary hypertension and long-term data collection took place in the cystic fibrosis patient registry (www.cfregistr.cz).

9. Support and strengthening the role of organizations for patients with RD

9.1. Support for activities- and development of cooperation with European patient organizations.

ČAVO, the Czech RD Association, is the umbrella organization for CZ RD patient organizations (www.vzacna-onemocneni.cz). ČAVO has 30 member patient organizations and an additional 18 individual members with ultra-rare diagnoses with regards to the overall population of the country. In the 2012-2014 period, the involvement of individual members in ČAVO's activities took place, as did the organization of educational meetings for ČAVO members in an effort to further involve individual patient organizations into the realization of the NAS and NAP1. In addition, education of patient organization representatives took place in the Academy of Patient Organizations.

DEBRA ČR is a member of DEBRA International, which organizes an annual congress for patients and experts. The organizations communicate amongst themselves throughout the year as well, and share experience.

10. Inter-ministerial and inter-departmental cooperation in the field of RD

In 2010, the MH established the Inter-ministerial and Inter-departmental RD Taskforce (Taskforce), composed of representatives of the MH, MPSV, the General Health Insurance Company, the Association of Health Insurers of the Czech Republic, selected experts of the Czech Medical Association of J.E. Purkyně (www.c/s.cz), the CZ WHO office, ÚZIS and patient organizations (such as ČAVO). In the 2012-2014 period, this Taskforce was acting for the fulfillment of tasks and activities stemming from NAS and NAP1.

Interdepartmental cooperation was implemented as part of expert centers of individual medical expertise, where specialized care of patients with RD is provided. The centralization of health care in RD creates conditions not only for interdepartmental cooperation, but also for the gaining and maintaining of management's erudition and efficacy. However, decrease of resources and austerity from 2012 negatively impacted upon on diagnostics, treatment and further monitoring of RD patients. This represents a substantial challenge for NAP2.

11. International cooperation in the area of RD

11.1. Cooperation at the international level

In the area of cardiology, cooperation took place in the 2012-14 period between individual centers with similar working groups abroad, between existing patient organizations with similar organizations in European countries and with umbrella European organizations. Czech experts' participation took place on the creation of a recommended European approach for diagnosis and treatment of RD in cardiology and in the area of hereditary metabolic disorders.

The EB Centrum at the University Hospital Brno is a member of the international "EB Clinet" team of clinical experts and takes part in the preparation of internationally-recommended approaches for the diagnosis and treatment of EB. The pediatric dermatology department of the Pediatric Clinic at the University Hospital Brno is a member of the international network of clinical experts for rare skin diseases - the Genodermatoses Network - which regularly

meets, organizes meetings for young dermatologists, and prepares guidelines focusing on RD in dermatology.

The NKCVO in University Hospital Motol organized an international workshop in 2013 on "Rare Genetic Diseases: Diagnosis and Discovery Workshop" in cooperation with the International Rare Disease Research Consortium (www.irdirc.org) and cooperated in 2014 with the EU Department at MH in the preparation of a conference presenting the results of the 2nd EU Action Program of Public Health together with the European agency CHAFAEA (formerly EAHC DG Sanco, Luxembourg; www.chafea-rare-diseases.eu). Cooperation took place with the IRDIRC, in which the Czech Republic has a representative on the Diagnostic Committee.

ČAVO cooperated with the European organization for rare diseases - Eurordis.org - and established cooperation with the Norwegian patient organization Frambu.no. The patient organization DEBRA ČR took part in the DEBRA International conference.

11.2. RD classification in cooperation with the Orphanet consortium

At the present time, ICD-10 does not enable the adequate, precise and effective coding of RD. Thus, ÚZIS intends to use the Orphacodes-based system developed by the Orphanet consortium. Orphanet cooperates with the WHO and the Orphacodes system would likely be included in ICD-11.

In the 2012-2014 period, ÚZIS took part in international workshops focusing on RD registers and primarily on the coding of RD in such registers and health care information systems. ÚZIS is currently working on the analysis of RD classification schemes and the use of the Orphacodes system together with the Online Mendelian Inheritance in Man (OMIM) database coding and the classifications of the Society for the Study of Inborn Errors of Metabolism (SSIEM.org) in a unified data model for RD, and, on a pilot basis, also in a national register of birth defects. The implementation (in the future including the translation of expert terminology into Czech, and with it their codification into the Czech version of the system) of the Orphacodes system in the CZ health care system and building it into the MDS RD model will enable the classification of RD according to international standards. At the same time, the coding of these diseases in the country will be prepared in the transition to the planned ICD-11.

National Action Plan for Rare Diseases for 2015-2017

In the National Action Plan for RD for the period 2015-2017 (NAP2) emphasis is especially placed on the support of early RD identification and diagnosis, on the further centralization of care for RD patients, the unification and development of data collection and the creation of standards of care for patients with RD, as well as on the improvement of awareness and education in RD, on continuity with the already established foreign cooperation and on establishing new contacts, and on the connecting of Czech RD centers with common European databases and registers aggregating clinical and laboratory data. At the same time, it will be important to join international RD research projects (such as E-rare2 and/or Horizon2020 funding schemes), domestic research projects as part of the Agency for Healthcare Research and the development of cross-border diagnostic and medical care in accordance with the provisions of the Directive on Patients' Rights in Cross-Border Care, which was transposed into Czech legislation in 2014.

The establishment of centers for home care, social subsidized hospital beds, respite centers and rehabilitation facilities, and the expansion of long-term care beds with trained personnel and special equipment will be important for the improvement of quality of life and social inclusion of RD patients. Attention must be placed toward effective and timely pharmacotherapy of RD following internationally-accepted standards and recommended approaches, and increasing the education and awareness on RD issues among the medical professionals and the public at large. The goals, tasks, deadlines, outputs, administrators, cooperating entities and assumptions of fulfilling the second NAP are presented in Annex 1.