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RD-ACTION

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Introduction

RD-ACTION works towards an integrated, European approach to the challenges faced by the rare disease (RD) community.

The missions of the RD-ACTION are:
1) Promote, catalyse and trigger multistakeholder debates around RD;
2) Work on priority issues for People Living with a RD (PLWRD) by implementing the actions identified in the EU Council Recommendation on an action on RD and ensure sustainability of these actions;
3) Contribute to solutions to ensure codification of RD in Health Information Systems across Europe;
4) Support the development and sustainability of Orphanet.

By supporting the development of European and national policies, RD-ACTION brings together efforts to improve knowledge on rare diseases and orphan drugs, and support the rare disease community European projects. RD-ACTION contains 6 work packages. A work package[1]" (WP) can be thought of as a sub-project, which, when combined with other work packages, form the completed project. The activities carried out within each WP are described below.

Workpackage 1 – Coordination

Within WP1 (lead by INSERM, France) the governance of RD-ACTION is organised into three levels (fig.1), in order to gather specific expertise and build shared strategies to address the specific issues of RD:

- A General Assembly, composed of one member per designated authority, which is the decision-making body of the consortium in charge of reviewing and steering the project;
- An Executive Committee composed by the 7 WP leaders in charge of the supervision, communication and cross-talk promotion;
- WP teams in charge of executing and monitoring the tasks and establishing cross-talks with the other work packages;
- In addition to these three levels, Workgroups are established 'à la carte' according to the need identified.

[1] http://ec.europa.eu/chafea/management/Fact_sheet_2010_03.html

The Executive Committee of RD-ACTION has met every two months to discuss the advancements of the project and the actions to be taken.

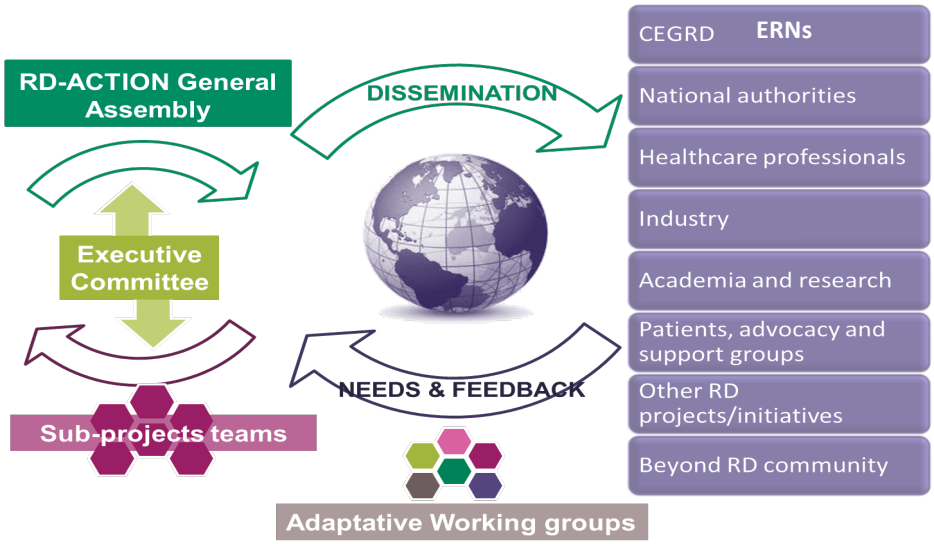

Figure 1 RD-ACTION governance and stakeholders interactions

All partners of the action are kept informed on all progresses, issues and identified risks through the internal newsletter, RD-ACTIONews which is sent every two months and through the internal website. The General public can also keep-up with the project progresses through the public website, www.rd-action.eu, where news are regularly posted as well as all material produced by the different WPs and also through Orphanews, the RD-ACTION public newsletter which is issued every two weeks. An informative RD-ACTION leaflet for all audiences is also available on www.rd-action.eu. Orphanet Report Series covering topics relevant to RD are also regularly published and available here.

Workpackage 2 – Dissemination

Beside the actions done by WP2 (co-lead by EURORDIS and Istituto Superiore de Sanità) to disseminate RD-Action achievements, through its website (www.rd-action.eu), a leaflet and a newsletter (Orphanews International), two major tasks were undertaken directed to the National level: the support to EUROPLAN conferences in EU member states, and the development of Policy Briefs for sustainable health systems for RD.

1. EUROPLAN CONFERENCES

EUROPLAN national conferences/ workshops are intended to promote the implementation of national plans or strategies for rare diseases in European countries based on the Recommendation of the EU Council on *an action in the field of rare diseases*, 8 June 2009, as well as to facilitate the integration of EU rare disease policies and recommendations into the national health system (for example on European Reference Networks (ERNs), access to orphan drugs, utilisation of ORPHAcodes, patient registries, research…).

EUROPLAN national conferences/ workshops are jointly organised in each country by a National Alliance of rare disease patients' organisations (hereafter National Alliance) and EURORDIS–Rare Diseases Europe.

Within the EU co-funded project EUROPLAN (2008-2011), led by Dr Domenica Taruscio from the Istituto Superiore di Sanità and partner of RD-ACTION, 15 EUROPLAN conferences took place in 15 countries. A second round of 25 EUROPLAN conferences took place within the EU Joint Action of the European Union Committee of Experts on Rare Diseases – EUCERD – (2012- 2015), led by Prof Kate Bushby from the University of Newcastle, also partner of RD-ACTION. Within RD-ACTION, 19 conferences or round tables were organised in 18 countries (Belgium organised two round tables).

Altogether, between 2008 and 2018, **59** EUROPLAN national conferences (or workshops/round tables) were organised in 25 EU Member States and 5 other European countries (Georgia, Macedonia, Russia Serbia, Ukraine). Some National Alliances organised several EUROPLAN conferences in their country.

These EUROPLAN conferences have been assessed **instrumental and one of the best forums to discuss national plan or strategy for rare diseases.** The outcomes of the conferences have undoubtedly contributed to the adoption of national plans or strategies in the EU over the past ten years:

In 2009, only 5 EU Member States had a national plan for rare diseases: Bulgaria, France, Greece, Portugal, Spain.

As of July 2018, 20 EU Member States have an **ongoing** national plan or strategy for rare diseases; Bulgaria, Cyprus, Germany, Greece and Latvia are **discussing their second national plan**; Malta, Poland and Sweden have not yet adopted a strategy/plan.

The **strength** of a EUROPLAN national conference lies in its shared philosophy and format:

- **Patient-led**: National Alliances are in the best position to address patients' needs;
- **Multi-stakeholder**: National Alliances ensure to invite all stakeholders involved for a broad debate and serve as catalysers;
- **Integrating both the national and European approach to rare disease policy**;
- Being part of an overarching **European Joint Action** that provides the legitimacy and the framework for the organisation of EUROPLAN national conferences/workshops;
- Helping national authorities **adhere to the obligations stemming from the EU Council Recommendations.**

With over 6000 rare diseases, no one country can tackle the issue of rare diseases alone, and therefore rare diseases have a strong European added value in terms of collaboration.

The EUROPLAN conferences /workshops **are unique** since they offer the opportunity to raise awareness of European policies and recommendations on a specific topic relevant for rare disease and discussing the integration of these European policies/recommendations into the national healthcare system, while taking into account the specificities of each country.

For instance, the issue of mapping the existing medical expertise on rare diseases at the national level were often discussed within EUROPLAN conferences. The recommendations of the EUCERD on the quality criteria of Centres of Expertise for rare diseases were regularly presented, and many EU countries have based their policy for designating national centres of expertise on these recommendations.

Within the EUROPLAN project and the EUCERD Joint Action, the National Alliances had to address all the pillars of the Council Recommendation in each EUROPLAN conference:

- Governance of a national plan;
- Adequate definition, codification and inventorying of rare diseases (including registries, databases as well information and training);
- Research on rare diseases;
- Centres of Expertise and European Reference Networks (ERNs) for Rare Diseases (including access to treatments, orphan drugs);
- Gathering the expertise on rare diseases at European level;
- Empowerment of patient organisations;
- Sustainability.

Within RD-ACTION, in order to adapt to each country's specific needs, the National Alliances identified **key national priorities** to be discussed with all the stakeholders and national authorities. Most of them tackled the issue of:

- Centres of Expertise on rare diseases and ERNs;
- Integrating rare diseases into mainstream social policies;
- Access to treatments;
- Research / Registries/ Data collection.

Out of the 15 EU Member States where a RD-ACTION - EUROPLAN conference took place, only Luxemburg and Poland did not have a plan for rare disease. The national plan / strategy for rare diseases of the other 13 EU Member States do contain measures for the designation of Centres of Expertise, integration of these Centres into ERNs; facilitating the access to orphan drugs, innovative treatments. However, these measures need to be adequately implemented and efforts in this direction must be sustained.

Besides, some national plans do not address the issue of access to social care for people living with rare diseases though these people do need specialised social services adapted to their particular needs. The EU co-funded project INNOVCare analyses this situation and proposes several

recommendations for improving a holistic approach to care. A pilot project has been conducted. The ongoing work of INNOVCare was presented in several RD-ACTION-EUROPLAN conferences.

The National Alliances of Luxemburg, Poland, Macedonia, Serbia and Ukraine addressed specific issues in their RD-ACTION – EUROPLAN conferences, while also concentrating their efforts on the necessity to adopt a national plan or strategy for rare diseases, based on existing draft plan and work done by their respective public health authorities.

NB: It is worth noting that Luxemburg adopted its national plan for rare diseases in May 2018.

Each National Alliance issued a brief conference's report first describing the national situation for each topic addressed and making a set of proposals or recommendations for improving the implementation of national measures in the field of access to medical and social care for people living with rare diseases.

The national public authorities and the rare disease community (patients, patients' representatives, healthcare professionals, academia, industry) shall be able to capitalise on the proposals and recommendations made in each of the EUROPLAN conferences.

EUROPLAN conferences' reports can be found on the RD-ACTION website here.

List of RD-ACTION/ EUROPLAN conferences:

Austria / Pro Rare
Belgium / RaDiOrg
Croatia / Rare Diseases Croatia
Cyprus / C.A.R.D
Czech Republic / CAVO
Denmark / Rare Diseases Denmark
Hungary / Huferdis
Italy / Uniamo
Lithuania / Lithuanian National Alliance
Luxemburg / ALAN
Macedonia / Macedonian National Alliance
Poland / Polish National Forum for RD Therapy
Romania / RONARD
Serbia / NORBS
Slovakia / SAZCH
Slovenia / Slovenian National Alliance
Spain / FEDER
Ukraine / NGO Rare Diseases of Ukraine

2. Resilient and sustainable health systems for RD

In order to capitalize the experience and in line with the Communication from the European Commission, an important task of RD-ACTION is intended to support national authorities to quantify the burden of RDs and identify available resources for sustainable and resilient health systems, taking into account the principles of equity, quality and efficiency, and involving stakeholders, policy makers and civil servants in charge of national strategies on RDs.

A literature review on Health System Resilience for RD, now published in a peer-reviewed journal (here), allowed to identify priority areas that were defined during the first workshop. Altogether, six working groups were established (list available here) to conduct an analysis on these priority areas. Their work was discussed in two additional workshops and led to the production of six Policy Briefs:

1. Resilience
2. Actions on Educational Programmes and Training for Professionals
3. Primary Prevention as an essential factor ensuring sustainability of health systems: The example of congenital anomalies
4. Health Systems for Rare Diseases: Financial Sustainability
5. Integrated Care
6. Patient Empowerment

A relevant synergy was made with the project "Transfer of Organizational Innovations for Resilient, Effective, Equitable, Accessible, Sustainable and Comprehensive Health Services and Systems" (TO REACH); and in order to establish an European network aiming to reduce health inequalities in rare diseases.

The policy briefs will be disseminated through standard channels (mailing, newsletters). However, de visu discussions are essential for their dissemination: hopefully future EUROPLAN meetings will be a dissemination vector but ad hoc events should also be organised.

Workpackage 3 – Evaluation

Overall, the Joint action's evaluation is based on indicators measuring the process, output, outcomes and impact. Further to this global evaluation, the evaluation of Orphanet, the European database for RD, was undertaken as well with the final aim to establish a sustainability plan. The following actions have been taken within WP3 (lead by Vienna University, Austria):

1. Internal strategic committees were set up every 6 months in order to review the current organisational structure (SWOT analysis) and establish and revise a strategic plan, validated by the Orphanet Management Board. In particular, an external audit on the IT infrastructure was performed in November-December 2014 before RD-ACTION starts and its conclusions were integrated to the strategic discussions on Orphanet's future. A massive transformation is ongoing in order to go from the old relational database to the new era knowledge base.

2. All Orphanet services are evaluated on an annual basis via an online survey, where a pop-up window opens to Orphanet users on the first page they access. This survey is translated into all seven Orphanet languages (Dutch, English, French, German, Italian, Portuguese, Spanish,). (for more details, please refer to the Orphanet Reports Series page)

3. An evaluation phase of the stakeholder awareness, use and needs regarding Orphanet's services was undertaken prior to the elaboration of a sustainability plan. It was proactively sent to representatives of all stakeholders in the field of RD in all Member States (MS) in order to guarantee participation of all stakeholder groups in at least one survey instrument. The survey aimed to provide a clearer vision on the services that deserve long-term sustainability as well as some clues of what some stakeholders are ready to support in the future. Indeed, as Orphanet has become increasingly important as an information and data source for official authorities and institutions at a European level and within Member States, it was necessary to analyze its use with a specific focus on this particular audience. This includes also potential users who may not yet be familiar with Orphanet and its services, but might find it useful for their own professional use or for their institutions in the future. Survey report with its detailed methodology is available here.

   • All stakeholders strongly encourage the objective to sustain Orphanet and to provide a framework allowing its continuation.

   • Regarding the future financing of Orphanet, a clear majority of stakeholders recommends a joint funding mechanism with contributions from the European Commission, as well as from the Member States.

4. A Sustainability Plan was prepared as a result of the evaluation process, and steps towards Orphanet's sustainability are ongoing according to this plan. It is available on the RD- Action website at http://www.rd-action.eu/leaflet-and-documents.

Workpackage 4 - Orphanet, the European database for RD

Orphanet is a unique resource, gathering and producing knowledge on rare diseases so as to contribute to improving the diagnosis, care and treatment of patients with rare diseases. Orphanet aims to provide high-quality information on rare diseases, and ensure equal access to knowledge for all stakeholders. Orphanet also maintains the Orphanet rare disease nomenclature (ORPHA number), essential in improving the visibility of rare diseases in health and research information systems.
Over the past 20 years, Orphanet has become the reference source of information on rare diseases. As such, Orphanet is committed to meeting new challenges arising from a rapidly evolving political, scientific, and informatics landscape. In particular, it is crucial to help all audiences access quality information amongst the plethora of information available online, to provide the means to identify rare disease patients, to guide patients and doctors towards relevant services for an efficient patient care pathway, and to contribute to generating knowledge by producing massive, computable, re-usable scientific data useful for research as well as for policy decision-making.

Orphanet works towards meeting three main goals:

- **Improve the visibility of rare diseases in the fields of healthcare and research by maintaining the Orphanet rare disease nomenclature (ORPHAcodes): providing a common language to understand each other across the rare disease field.**
- **Provide high-quality information on rare diseases and expertise, ensuring equal access to knowledge for all stakeholders: orientating users and actors in the field in the mass of information online.**
- **Contribute to generating knowledge on rare diseases: piecing together the parts of the puzzle to better understand rare diseases.**

Orphanet database has been funded by EC since early 2000, mainly through Joint Actions, to generate data and knowledge on RD devoted to all the stakeholders, and necessary for policy decision making in a European collaborative manner. Over the years Orphanet confirmed its position as the Reference database for RD with wide geographical coverage and multitude of topics addressed and as the producer of the RD nomenclature, including rare cancers (**ORPHAcodes**), aiming to improve the visibility of RD in health and research information systems, and to act as an interoperability vector between healthcare and research. Orphanet, and its nomenclature are now an internationally recognised standard.

Within RD-Action, WP4-Orphanet (lead by INSERM, France) improved the nomenclature of rare diseases by a better characterization of terms (which includes categories, groups of disorders, disorders and subtypes, in a hierarchical structure), and by producing a definition for each rare disorder, most of them already published. Partnerships around the nomenclature have been developed, in order to ensure interoperability between medical terminologies: GARD (NCATS), SNOMED CT, ICD 11. The Orphanet nomenclature exists currently in 9 languages, Polish and Czech having been added, which helps promoting interoperability between member states. Finally, new IT languages have been made available in order to facilitate the integration of the nomenclature in information systems.

Scientific annotations have been produced for each rare disease, following the development of knowledge and based on peer-reviewed publications: around 3900 genes are associated to rare diseases, virtually all rare diseases are annotated with epidemiological and natural history data, and half of them are described with their phenotypes using Human Phenotype Ontology (HPO).

Expert resources in each country have been collected and updated: specialised expert centres and centres of expertise, medical laboratories, research projects, clinical trials, patient registries and mutation databases, networks, technological platforms and patient organisations. In particular, the information on diagnostic tests has been improved, so as to reflect the rapid evolution of practices in this field. A cartographic representation of European Reference Networks (ERNs) is also provided to facilitate their identification as a one-stop shop.

During RD-Action, Orphanet website was given a new look and feel, and the new site has been designed to improve navigation. The design is responsive, making it easier to consult on a range of different devices, and the lay out makes data easier to read. Notably, the new site allows for new languages to be added, and Polish Orphanet website was therefore launched during RD-Action.

Furthermore, Orphanet launched a YouTube channel to host video tutorials aimed at helping users understand the Orphanet nomenclature of rare diseases, and search for a disease/gene on the website. Videos are available in English and French, with other languages (subtitles) added progressively.
A substantial effort was undertaken to increase transparency of Orphanet procedures and traceability of databasing decisions. Orphanet methodological procedures are available on the online portal. With a view to ensure both transparency and traceability of the available data a curation platform (curation.orphanet.org) has been released: it allows rare disease experts to contribute to the update of Orphanet data (nomenclature and texts).

The Orphanet network has grown during RD-Action with the welcoming of Argentina in 2015 and of Japan in 2017. Behind the scenes, the Orphanet network has undergone a in-depth transformation both at the governance level and at the organizational level, in order to ensure a more collaborative decision-making process, allowing procedures to be adapted to national/regional situations, and to reach the same level of corporate culture. An open and distributed organizational model was put in place to decentralise core activities historically carried-out by the France-based coordinating team to National teams in the network. Finally, and importantly, a Network Agreement has been signed between participants to regulate the functioning of the network towards a sustainable model.

With the same aim, an in-depth transformation of the Orphanet Information system has started during RD-Action. It will allow Orphanet being a more open system and connected resource to better serve the users, and to enable future developments done in partnership with other relevant endeavours. An effective Partnerships strategy has indeed been developed during RD-ACTION in order to avoid duplication of work and potentiate synergies with other relevant projects (including ERNs).

A Quality Management System has been put in place in Orphanet during RD-Action. It ensures a controlled continuous improvement cycle, the production and transmission of formalised standard operating procedures across the network, the continuous training of staff, and the detection and mitigation of errors.

Finally, concrete steps have been taken to ensure the sustainability of Orphanet over the last three years: the database will be co-financed by a grant from the EU Health Programme for the next three years and discussions are underway at INSERM and at the "Steering Group for Health Promotion and Disease Prevention", created by the European Commission, in which Member States are represented.

The legacy of Orphanet following RD-Action for the field of rare diseases is threefold:

- a standard common language for health and research (Orphanet nomenclature) ;
- a complete and reliable database for decision-making (for both Member States and ERNs) ;
- a website providing information for professionals and patients.

Workpackage 5 - Steering, maintaining and promoting the adoption of ORPHAcodes

Based on the Commission Expert Group on Rare Diseases' (CEGRD) "Recommendation on Ways to Improve Codification for Rare Diseases in Health Information Systems" the Work package 5 team (WP5, lead by DIMDI, Germany) aimed to develop a toolset to assist European countries in implementing a specific coding system for RD, the ORPHAcodes, in a standardized and interoperable way. This should improve the codification of RD and hence their traceability in healthcare systems.

A major ambition of WP5 was the definition of common guidelines addressing the quality of codification and the coherence of exploitation at European level. To support these goals, the WP5 included 4 tasks. Each task had its own focus but they were created to build on each other. Deliverables and milestones were set to ensure the achievement of the objectives.

With the first task, a survey about the State of the Art of the implementation of RD coding was conducted to update the knowledge about medical coding systems in all participating countries and to create a European roadmap for RD coding based on this knowledge. The necessary strategy and tools were defined and set to implement the ORPHAcodes in the European countries in line with already existing approaches of implementations.

In the second task, the WP5 produced a document describing the standard procedure and guide for the coding with ORPHAcodes. This document also includes coding rules propositions for RD coding at European level. A first Master file for statistical reporting with ORPHAcodes (MF) was created for this purpose. Even though ORPHAcodes can be implemented at any granularity level in health systems, the WP5 recommends aligning/aggregating them to the MF level to produce national statistics, so they can be comparable between countries. After feedback from testers of Member States, it was adapted and a new version was published including a specification and implementation Manual of the MF.

The third task consisted of testing the MF, together with the guidelines, against already existing systems. In a first phase a retrospective analysis of data from the French RD registry (BNDMR) and from Veneto region RD registry (Italy) was performed showing that use of ORPHAcodes to describe RD entities and RD patients was highly comparable, although baseline differences in terms of organisation of the RD care network and sources of information used to record patients existed in the two settings.
Based on that, in the second phase, which was designed according to a prospective approach, a fine-tuning and the adapting of the MF and the "Standard procedure and guide for coding with ORPHAcodes" led to the development of a coding helping tool and a users' guide.

During the final task, the next steps to address long-term maintenance and sustainability of the resources and guidelines were determined. The outcome of this task was a recommendation for routine maintenance produced by WP5 and its collaborators and partners.
The document includes 10 recommendations for the distribution and the correct use of codification resources for RD, and open issues to be followed up upon after the end of RD-ACTION.
Products and documents created by the WP 5 team (click on links for further reading):

- Review document of existing technical implementations for RD coding
- Standard procedure and guide for coding with ORPHAcodes
- Specifications and implementation manual for master file for statistical reporting with ORPHAcodes
- Master file for statistical reporting with ORPHAcodes
- Specifications for an integrated coding application with ORPHAcodes
- Coding helping tool incl. users' manual
- Recommendation for routine maintenance of codification resources for rare diseases

Workpackage 6 - Policy development for RD and integration

Of the three main goals of RD-ACTION, WP6 (led by Newcastle University, UK) focused primarily on supporting the implementation of EC recommendations relating to rare diseases at Member State level. After supporting the final meetings of the Commission Expert Group on Rare Diseases, the WP team relied increasingly on its dedicated Consultative Group to steer and implement policies in the field of rare diseases. This Group was composed of representatives of almost 30 RD-ACTION partner institutions, largely Ministries of Health/Departments of Health, and the decision was made to focus much of the WP policy activities on continued support for the development of European Reference Networks (ERNs), in view of the central importance of these Networks for the European RD community. Thus there are three main areas of achievement in this WP:

1. **Supporting the RD field in conceptualising, implementing and evolving the ERNs**
2. **Generating the new resource on the *State of the Art of Rare Disease Activities in Europe*.**
3. **Integration and Collaboration with complementary fields and initiatives**

1) Support for the European Reference Networks (ERNs)

The RD-ACTION mission to support the implementation and evolution of ERNs comprised three main aspects:

a. **Early in the project, the Team assumed a practical, hands-on role in preparing the broad RD field for the upcoming ERN applications:**

- ✓ a large workshop was organised in summer 2015, to build capacity amongst field leaders and identify possible Coordinators based around the Disease-Grouping defined by this Joint Action team and based on the Addendum to the EUCERD Recommendations on ERNs for RDs.
- ✓ a 'Matchmaker tool' was created, to allow cross-talk between centres interested in joining or leading an ERN: the Matchmaker tool received 801 responses in total, and helped to ensure 24 collaborative and (crucially) non-competitive proposals.

b. **Ensuring meaningful patient involvement in ERNs**

- ✓ In early 2016, in parallel to the launch of the EC Call for expression of interest for ERNs, EURORDIS established European Patient Advocacy Groups **(ePAGs),** bringing together patient organisations by groups of diseases, as defined in the Addendum to the EUCERD Recommendations on ERNs. EURORDIS organised elections amongst the rare disease patient community to elect ePAGs' representatives.
- ✓ The ePAGs' representatives were involved in the development of ERNs' applications and are currently members of the ERNs Boards, Steering Committees and task forces.
- ✓ The WP6 team ensured that the ePAGs' representatives were always involved in its activities supporting the development of ERNs, notably by providing fellowships to ePAGs' representatives to participate in thematic workshops as described below, based on their respective knowledge of the topic addressed.

c. **ERNs represent unprecedented opportunities to optimise healthcare for people with rare and complex diseases, to reduce inequalities, and to stimulate much-needed research - the RD-ACTION team recognised the major added value in embedding good practices in the embryonic ERNs, practices which could hopefully then be disseminated into broader healthcare systems.**

- ✓ RD-ACTION's vision was that, as ERNs were established and evolved, dedicated guidance would be important to support but also to ensure a baseline compatibility and interoperability (at many levels) between the ERNs.
- ✓ WP6 organised 6 major workshops (many co-organised by DG Sante) involving over 360 multi-stakeholder experts, each addressing a particular policy area or topic in which the ERNs could add value and capitalise on past investments and lessons learned:

  - **Exchanging Data for Virtual Care in the ERN framework** – September 2016 , Brussels
  - **Using standards and embedding good practices to promote interoperable data sharing in ERNs** – April 2017, Brussels
  - **Indicators and Outcomes for ERNs** - June 2017, Newcastle

- **How can ERNs generate, appraise and utilise clinical practice guidelines, to enhance the impact of consensus guidelines in national health systems?** December 2017, Rome
- **Creating a Sustainable Environment for Holistic & Innovative Care for Rare Diseases & Complex Conditions** - April 2018, Frambu, Norway
- **How ERNs can add value to clinical research in rare diseases and highly specialised domains** - May 2018, London

Many reports, concept papers, and Recommendations were created following the organisation and delivery of these workshops – these can all be accessed here, along with links to the individual workshop pages. The support for ERN activities encompassed a very wide range of topics, and was an opportunity for RD-ACTION partners to fulfill its mission to actually implement many key Recommendations (issued by the EUCERD and CEGRD) in the field and ensure the impact of past Policy Guidance.

2) The Resource on the 'State of the Art of Rare Disease Activities in Europe'

The well-established Report on the 'State of the Art of Rare Disease Activities in Europe' (SoA) was adapted somewhat under RD-ACTION, when production moved to Newcastle University. The revised Resource is now entirely web-based and consists of three 'components':

a. An Overview Report

- ✓ The Overview Report provides a broad outline of the history and status quo of rare disease activities across Europe, with an emphasis on topics such as the RD legislative and policy framework, European Commission investment, achievements of the most relevant funded initiatives (e.g. Joint Actions), and research activity. There is also a summary of global RD policy frameworks and national achievements outside of Europe.
- ✓ Two versions of the Overview Report, each totaling ca. 60 pages, were produced.

b. Country-level information

- ✓ In the current climate, with no Expert Group to unite Member State representatives and other key stakeholder groups to discuss the status quo and strategic direction for rare disease issues, it is more important than ever to have comprehensive, reliable data on the actual situation facing rare disease patients in each country.
- ✓ Significant changes were made to the national elements of the SoA Resource: to enable a more diverse, multi-stakeholder perspective, a 'Data Contributing Committee' (DCC) was created for each MS, to collaboratively complete a comprehensive online survey concerning that country's rare disease activities. The DCC is made up, for each country, by the public health official in charge of RDs at national level, the National Alliance of patients living with RDs, the national Orphanet team.
- ✓ The questions were carefully constructed to yield comparable information to explore practices between countries: they include the data which EU countries pledged to collect in the 2013 *Recommendations on Core Indicators for National Plans/Strategies for Rare Diseases* – again, enhancing the real-world impact of these Recommendations documents.

- ✓ All the countries which provided data have a dedicated web-page, bearing a short summary of activities alongside a more detailed report on the status quo.
- ✓ This data collection process, now established, will continue under the Newcastle University rare disease team.

c. Topic Summaries

- ✓ Following the next submission and analysis of country-level data, transversal summaries will be generated on topics including the Status Quo of national plans and strategies, Registration, and Newborn screening, to help identify successful, innovative approaches being deployed by EU countries to address the challenges posed by rare diseases.

It is essential that this information continues to be collected, analysed, and presented -especially at a time when many National Plans and Strategies are approaching their expiration dates- to demonstrate the continued commitment of European countries to supporting people living with rare diseases, and also enable a pan-European assessment of trends and developments around key topics

3) Integration and Collaboration with Complementary Initiatives

The WP6 team ensured an open and proactive approach to forging new alliances with communities traditionally outside of the rare disease field, where collaboration could add value. To this end, cross-disciplinary alliances were consolidated with, for instance:

- ✓ the eHealth field (most prominently via a dedicated Task-Force established between the Rare Disease and eHealth communities, which will be sustained post RD-ACTION)
- ✓ The 'big' data management and data interoperability field, most notably the FAIR data and ontologies community
- ✓ Health technology assessment experts
- ✓ Precision public health communities
- ✓ … and many more.

A particular goal of RD-ACTION's Integration activities was to forge collaborations between these communities and the new ERNs, to ensure the Networks have the opportunity to benefit from the fruits of past and future investment in these related communities.

RD-Action Partners

DESIGNATED PARTNERS

- Medical University of Vienna (MUV)
- Federal Public Service Health (FPS Health) Scientific Institute for Public Health (WIV-ISP)
- Bulgarian Association for Promotion of Education and Science/Rare Diseases Institute
- Croatian Alliance for Rare Diseases
- Coordination Center for Rare Diseases in University Hospital in Motol (NKCVO)
- University of Tartu (UT)
- Rinnekoti Foundation Norio Centre (Rinnekoti)
- Institut National de la Santé et de la Recherche Médicale (INSERM)
  Direction Générale de la Santé, Ministère des Affaires Sociales, de la Santé et des Droits des Femmes (DGS)
  Assistance Publique - Hopitaux de Paris (APHP)
- Medizinische Hochschule Hannover (MHH)
  Deutsches Institut für Medizinische Dokumentation und Information (DIMDI)
- Orszagos Tisztifoorvosi Hivatal Semmelweis Egyetem (SE)
- Health Service Executive (HSE)
- Ospedale Pediatrico Bambino Gesù (OPBG)
  Istituto Superiore di Sanita (ISS-CNMR)
  Regione del Veneto
- Center For Disease Prevention and control of Latvia
- Vilnius University Hospital Santariskiu Klinikos (VULSK)
- Leids Universitair Medisch Centrum (LUMC)
- The Norwegian Directorate of health (HDIR)
  Norwegian National Advisory Unit For Rare Diseases (NKSD)
- Instytut Pomnik - Centrum Zdrowia Dziecka (IPCZD)
- Directorate-General of Health (DGS)
- University of Medicine and Pharmacy"G.R.T.Popa" Iasi Orphanet Center
- Faculty of Medicine in Bratislava (UniBA FoB)
- University Medical Centre Ljubljana (UKC Ljubljana)
- Centro de Investigación Biomédica en red (CIBER)
- Karolinska University Hospital (Karolinska)
- University of Newcastle (UNEW)
  UK Department of Health (UK PHE)
- European Organisation for Rare Diseases (EURORDIS)

DESIGNATED COLLABORATING PARTNERS

- Austrian Health Institute (GÖG)
- Ministry of Health
  Medical University Sofia
- Croatian Institute of Public Health (HZJZ)
- Ministry of Health (MoH CY)
- Robert Koch Institut (RKI)
  Universitatsklinikum Frankfurt (UKF)
- Fehlbildungsmonitoring Sachsen-Anhalt an der Medizinischen Fakultät der Otto-von Guericke-Universität Magdeburg
- Institute for Research of Regulatory policies (INERP)
- Pécsi Tudományegyetem (PTE)
- Landspitali University Hospital Ragnar
- Directorate of Health (Ministry of Health)
- Ministry for Energy and Health (MEH)
- Poznan University of Medical Sciences
- Instituto de Salud Carlos III
  Fundación para la Investigación Sanitaria y Biomédica de la Comunidad Valenciana

COLLABORATING PARTNERS

- Ministry of Health
- Center of medical genetics and primary health
- Office Population Health Genomics, Department of Health Government of WA
  Garvan Institute of Medical Research
- Institute of Health Information and Statistics of the Czech Republic
- University Hospital of Aarhus
- Foundation for Genetic and Rare Diseases (GeRaD)
- Institute for Rare Diseases, Institute of Medical Genetics
  The Chaim Sheba Medical center
- Institut National d'Hygiène, Department of Medical Genetics
- Mc Gill University
- Belgrade University
- CMU Institute of Medical Genetic
- Service de Cytogénétique et de Biologie de la Reproduction, CHU Farhat HACHED, Sousse
- University of Istanbul

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