RD-ACTION

Report on Resources to Support European Reference Networks

July 2018

RD-ACTION WP6 Output

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Document History

This document was prepared by the UNEW team leading WP6 on Policy and Integration, namely Victoria Hedley and Hannah Murray. It was drafted in July 2018 and finalised in August 2018, for submission to the RD-ACTION Coordinator as Deliverable 6.5. The work outlined and the reports included as appendices are in many cases collaborative outputs, generated with partners of WP6 (in particular partner EURORDIS)

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ERN Policy Support

It was agreed in late 2015, early in the project, that an important focus of RD-ACTION (WP6, especially, on Policy and Integration) would be to continue the valuable work of the EUCERD Joint Action in supporting the implementation and evolution of ERNs.[1] This decision was made jointly with the members of the WP6 Consultative Group (largely representatives of Competent National Authorities such as Ministries of Health) following one-to-one interviews on possible policy directions, and was supported by the Commission Expert Group on Rare Diseases (CEGRD). This was primarily in recognition of the anticipated added value the ERNs would bring to the rare disease field.

Therefore, the WP leaders revisited the long list of policy priorities proposed in the RD-ACTION grant preparation stage and agreed to focus these around ERNs. Thus, instead of delivering a piece of work on 'clinical practice guidelines' per se, the WP would explore how ERNs could generate/use clinical practice guidelines. Rather than seeking to generally advance the cause of rare disease registration and data standardisation, the WP would focus on the opportunities and challenges facing ERNs in collecting and utilising data, and in establishing/linking registries. In the first year of the project, the CEGRD was updated on all plans and given the opportunity to influence and direct this work. However, after the expiration of the CEGRD mandate at the end of 2016, the activities were planned by key WP partners and discussed with the Consultative Group.

A short, comprehensive summary of RD-ACTION support for the conceptualisation and implementation of the ERNs is available here: http://www.rd-action.eu/wp-content/uploads/2018/05/Summary-of-RD-ACTION-Support-for-ERNs-2015-18.pdf **(APPENDIX 1)**

Practical Support to the Implementation of ERNs during the proposal phase

In the overlap period between the end of the EUCERD JA and the beginning of the RD-ACTION activities, the team organised a major workshop to support the identification of possible field leaders to steer ERN applications according to the Thematic Groupings espoused in the *Addendum* to the *EUCERD Recommendations on Rare Disease ERNs*. This workshop was delivered in the Summer

[1] For a summary of the role played by the EUCERD Joint Action in supporting the conceptualisation and implementation of ERNs, see for instance Lynn, Hedley et. al (2017) 'How the EUCERD Joint Action supported initiatives in rare diseases', Eur J Med Gen https://www.ncbi.nlm.nih.gov/pubmed/28087401and http://www.eucerd.eu/wp-content/uploads//2016/03/EJADeliverable10.pdf

of 2015, in Brussels. To continue to raise awareness amongst the rare disease community –and especially, stakeholders involved in so-called 'pilot' networks- the RD-ACTION team sought to dispel myths and impart reliable information on the ERN application process (this was much needed, as at this time there were no formal DG SANTE support webpages available).

Addressing key questions around ERN creation and operations

The workshop in Brussels demonstrated that in the summer of 2015, stakeholders in the rare disease community had many unanswered questions and harboured many mispconceptions about ERNs. For instance, people were unsure at what level to establish a Network i.e. whether to aim for a small group of diseases (e.g. Lysosomal Storage Disorders) or go broader (e.g. all rare metabolic diseases). To add clarity, and to highlight the remaining 'unknowns', the WP6 produced an *Informal FAQs and Discussions on RD ERNs* document, which was based primarily upon the discussion sessions which took place in the Brussels workshop in July 2015. This document was disseminated widely, to help engage would-be ERN coordinators and members, and was uploaded to a dedicated ERN page on the RD-ACTION website in January 2016.

OUTPUT and Impact

- ✓ Main Output: 'Informal FAQs and Discussions on ERNs' (**APPENDIX 2**)
- ✓ What is it? **A 29 page document summarising the key features of ERNs as emerged from discussions during the Joint Action workshop** on 1st-2nd July 2015 in Brussels. **Most importantly, it included a number of key questions, relating to ERN added-value, application procedure, eligibility, funding etc. based upon those workshop discussions, to help would-be coordinators and HCP representatives understand the ERN concept and begin to prepare for the application process**

- ✓ Impact: **This document was used by DG SANTE to form the basis of its own official FAQ section** on the EC website (https://ec.europa.eu/health/ern/implementation/faq_en)

What formalised structure will ERNs assume?	Health care provider applicants will be approved member of a European Reference Network which will have an institutional value. Networks' Members should be licensed to use the 'European Reference Network' logo. The logo, owned by the European Union, should constitute the visual identity of the Networks and their Members
Some the existing networks (formally or informally) involve many experts from outside of the EEA: how might these countries participate?	In addition to the EU 28, the three EEA countries are eligible and indeed already participate in the Board of MS for ERNs. The policy and legal documents state that members of ERNs are expected to collaborate with others centres and networks; however, it is not possible to include them as formal members as they cannot be included in any formal EU assessment of the centres and networks. Therefore, external participation and contributions are encouraged, but cannot formalised.
Participants highlighted the concern that MS have adopted radically different approaches to designating centres of expertise (CEs) for RD. Many MS do not yet have formal designation processes to acknowledge RD expertise. In some countries, many CEs are self-nominated and the formal designation process as such is still embryonic; therefore, how can they participate in ERNs?	Although a key pillar of the RD policy agenda has been to encourage MS to officially designate national providers as 'CEs for RD', in accordance with Council Recommendation (2009) C 151/02, this is in fact a separate issue to the national endorsement process for ERN participation. MS have full capacity and responsibility in the endorsement process for national centres to join ERNs: in some cases, countries will endorse officially designated/recognised CEs for RD, but in others this will not be the case.

ERN 'Matchmaker'

This Matchmaker resource was conceived and implemented by RD-ACTION WP6 following a clear need identified during the 2nd Official ERN Conference in Lisbon, in the Autumn of 2015: there was no mechanism for the European Commission to know or reveal which HCPs might be interested in *leading* ERN proposals around each Thematic Grouping, which created the risk of competing proposals. Similarly, there was no way for interested HCPs to know which centres might be preparing proposals for an ERN in their field, and thus no way for them to join these proposals. To meet this urgent need, RD-ACTION created a web-based tool based upon the Thematic Groupings defined in the Addendum to the EUCERD Recommendations on RD ERNs. The process was straightforward: anyone interested in joining an RD ERN/establishing cross-talk with others in the same Thematic Grouping could visit a web-page and click on one of the 21 areas (e.g. Rare Liver)

1. The user was directed to a Form which requested several core details
2. Upon submission of the form, the data was transmitted to the RD-Action team at Newcastle University, UK
3. At intervals of approximately 2-3 weeks a spreadsheet of the responses received for each Thematic Grouping was emailed to all those who have submitted their data under that same Thematic Grouping
4. The onus was then on the specialists to use this information to make contact with one another, to continue to shape applications in each field, with the aim of encouraging collaboration and avoiding duplication

The tool was launched on 15th December and closed on 1st May 2016. It received 801 responses and was widely praised by the rare disease community and the CEGRD, as a means of shaping collaborative proposals in large disease areas which could conceivably have prepared competitive proposals. The results of the Matchmaker resource were as follows:

Country	No. of HCPs registering interest via Matchmaker
Europe –wide (EUROCAT)	**14**
Austria	**9**
Belgium	**51**
Bulgaria	**3**
Croatia	**2**
Cyprus	**1**
Czech Republic	**11**
Denmark	**5**
Finland	**9**
France	**80**
Germany	**53**
Greece	**6**
Hungary	**29**
Ireland	**3**
Israel	**1**

Italy	**204**
Latvia	**1**
Lithuania	**20**
Luxembourg	**2**
Malta	**2**
Netherlands	**114**
Norway	**3**
Poland	**8**
Portugal	**4**
Romania	**3**
Serbia	**1**
Slovenia	**3**
Spain	**66**
Sweden	**15**
Switzerland	**8**
Turkey	**7**
UK	**61**
Totals	**801**

Thematic Grouping	Total MM Responses in this TG	No. of HCPs who initially selected (a) 'wish to coordinate'	No. of ERN Proposals likely under each TG* (as of end April '15)
Rare Bone	19	2	1
Rare Cancer/Tumours	41	3	1 adult, 1 paediatric
Rare Cardiac	47	7	1
Rare Connective Tissue &	44	4	1
Rare Craniofacial & ENT	30	8	1 or 2
Rare Endocrine	56	6	1
Rare Eye	24	4	1
Rare Gastrointestinal	32	4	1
Rare Gynaecological and Obstetric	3	0	1
Rare Haematological	34	1	1
Rare Hepatic	15	1	1
Rare Hereditary Metabolic	68	12	1
Rare Immunological & Auto-Immune	46	6	1
Rare Congenital Malformations &	47	6	1
Rare Multisystemic Vascular	36	7	1
Rare Neurological	48	13	2
Rare Neuromuscular	45	6	1

Rare Pulmonary	41	8	2
Rare Renal	20	4	1
Rare Skin	95	15	1 or 2
Rare Urogenital	10	2	1
Total	**801**	**119**	

OUTPUTS and IMPACT

From this Matchmaker tool, a number of outputs were generated:

- ✓ A summary report, updated in May 2016, which detailed the Concept of the Matchmaker, a summary of the responses to date, key outputs and next steps and a summary of the likely applications across the thematic groups. (**APPENDIX 3**)
- ✓ A table comparing where Matchmaker respondents place their disease expertise (in relation to the Addendum Groupings) alongside patient perspectives as established by EURORDIS. (**APPENDIX 4**)
- ✓ As proposals became more mature, a more exhaustive list of diseases was compiled (as an active GoogleDocs spreadsheet) **to help the potential coordinators identifying particular conditions/areas with a strong likelihood of overlap between Networks**.
- ✓ WP6 also wanted to provide a list of the approved Healthcare Providers (HCPs) coordinating the ERN in each thematic grouping. **To complement the official summaries provided by DG Sante, information was collected by EURORDIS partners and synthesised into summaries** of ca. 5 pages each – these were compiled into a table, and users could click on the Network name (e.g. BOND) and find an overview of the structure and goals of each of the ERNs (the link to this table is here: http://www.rd-action.eu/european-reference-networks-erns/coordination-of-rare-disease-erns/

Network Name	Thematic Grouping	Coordinating HCP	Name of Coordinator	Website
BOND	Rare Bone Disorders	Istituto Ortopedico Rizzoli, ITALY	Luca Sangiorgi	ERN-BOND
CRANIO	Rare Craniofacial anomalies and ENT disorder	Erasmus Medical Centre, Rotterdam – THE NETHERLANDS	Irene Mathijssen	ERN-CRANIO
ENDO-ERN	Rare Endocrine Diseases	Leiden University Medical Centre – THE NETHERLANDS	Alberto Pereira	ENDO-ERN
EpiCARE	Rare and Complex Epilepsies	UCL Institute of Child Health – UNITED KINGDOM	Helen Cross	EpiCARE
ERKNET	European Rare Kidney Diseases Reference Network	Heidelberg University Hospital – GERMANY	Franz Schaefer	ERKnet

IMPACT:

- ✓ These resources **helped the RD field in Europe to organise itself around a limited number of consensus Coordinators, and to submit robust, comprehensive proposals**. Where necessary, and where requested, the RD-ACTION team stepped in to mediate between would-be rivals to help communities rally around a single Coordinator (and thus avoid competition and disharmony within the disease fields).
- ✓ The disease list **helped to limit overlap in terms of the disease coverage for each ERN**, or at least to identify those areas of overlap in advance, to encourage collaboration.
- ✓ By providing details of the 24 proposals before the ERNs were actually approved, the RD-ACTION team again filled an important knowledge gap and **helped the broader RD field to understand the scope and objectives of each Network**

Canvasing ERN perspectives and representing ERN interests

From the Spring of 2016, the identity of the would-be coordinators for each ERN was reasonably clear. However, the Networks were not approved until the very end of 2016, which made it difficult for DG SANTE and broader stakeholders in the rare disease field to engage these potential coordinators formally, in events which may be of great relevance to them. In this critical period, therefore, **RD-ACTION WP6 played an important (and often unnoticed) role in canvassing the perspectives of the potential ERN coordinators and presenting on behalf of the Networks at key meetings and workshops, to enable the 'voice' of the ERNs to be heard**. Where possible, WP6 provided budget to enable potential coordinators to attend relevant meetings in-person.

Identifying the IT needs of the ERNs, to support the provision of an appropriate IT platform

In the Spring of 2016, whilst field leaders were elaborating their ERN proposals, there was a significant amount of concern regarding one fundamental issue: what sort of platform which would be provided for the ERNs to conduct their virtual consultations, and when would it be available? No details were available as to the specifications or capabilities of such a platform, and some would-be coordinators consequently began to discuss the possibility of purchasing their own bespoke IT solutions, to ensure they would be able to quickly and efficiently commence virtual consultations for complex patients. This would have been disastrous for the Networks, as it would have resulted in numerous systems unable to interoperate with one another, limiting the potential for cross-ERN involvement in case reviews and for data to be pooled for secondary purposes.

RD-ACTION WP6 thus conducted a review of IT needs of the potential Coordinators, to identify what would be their mandatory specifications. Partner EURORDIS disseminated a template in April 2016 to collect ERN viewpoints, and UNEW compiled the replies **into a Document entitled 'What do Coordinators require from an ERN ICT platform?' which was prepared that summer**. The document highlighted key questions resulting from the Coordinators' responses, as these two screenshots demonstrate:

Public-facing Website

The ANCs requested an easy-to-manage public website: The publically-accessible area should include information on the network (scope, thematic areas of expertise, diseases or groups of diseases covered, overall structure and characteristics, as well as information on the steering committees (progress report, contact information). Respondents emphasised the need for this to be available as soon as possible, ideally in Month 1 of each ERN's operations. The site should be continuously updated. The Network Coordinator should be responsible for the content management and the regular activity on this website. The network members should gather and deliver content for the feeds, updates, and articles.

Question: Is the EC planning to provide websites for each ERN, or will it provide a public page for all websites, with the expectation that each ERN hosts and updates its own site? Several would-be ERNs have created their own websites already...

- The information discussed in virtual consultations will always be sensitive; therefore, ethical and legal requirements must be clarified before the launch of the Networks and henceforth respected. Some stipulated that the encryption and the secure exchange of data is essential for their ERN due to the anatomical nature of the images that need to be shared.

Questions:

It is assumed by most that the consultations organised by the ERN to discuss specific patient cases will be considered an extension of the usual national 'care team' one encounters when seeking healthcare at home:

- *Presuming the patient signs an informed consent form to agree to data being shared within the ERN for care (with another 'box'/form relating to research, presumably) - is it then the case that no anonymization of patient information would be necessary for these consultations (i.e. photographs could be shown, names used)?*
- *Or, will patients always need to be de-identified and distinguished using a string of numbers or letters opposed to using names?*

The elaboration of this document was an important step towards elucidating the real ICT needs and requirements of ERNs – these needs were then conveyed to the appropriate authorities, to try to optimise the Platform eventually delivered to the Networks by the European Commission (EC). WP6 had previously established a dedicated 'Task Force on Interoperable data-sharing between ERNs and the eHealth field' to ensure synergies between the eHealth field and the rare disease community (see below). The specifications of the system which would be provided to the ERNs was of utmost importance for these discussions, and between December 2015 and September 2016, **this Task-Force advocated for the provision of the most appropriate and efficient system possible, to meet the needs and specificities of the rare disease field.**

A meeting with the DG SANTE teams working on ERNs and eHealth was arranged for 18th February 2016, to illuminate the realistic needs around the sorts of rare disease data the ERNs would be collecting and exchanging. Crucially, this meeting discussed a number of different use cases likely to be encountered by the ERNs, which helped to explain the needs of the ERN community to the IT teams in charge of drafting and eventually launching a Tender for the ERNs' Clinical Patient Management System.

- The RD-ACTION colleagues liaised with the potential ERN coordinators and presented these activities, to try to dissuade Networks from purchasing individual solutions.
- **Once the Tender for the IT Platform had been published, the WP6 Team mapped the published specifications *against* the declared requirements of the ERN coordinators**, to assess and then illustrate -by means of a comparison table- the degree of concordance and areas of convergence (i.e. areas for further attention). This comparison table was added to the original '**What do Coordinators require from an ERN ICT platform?'** document.

OUTPUTS and IMPACT:

- ✓ 'What do Coordinators require from an ERN ICT platform?' **(APPENDIX 5)**
  - This illustrates the reported ICT requirements of the (potential) ERN coordinators, relating to components such as public websites and communications, but mainly focusing on the 'wish list' for a virtual consultation system, and also for registries
- ✓ 'Report from the meeting of the 'Task Force on Interoperable data-sharing within the framework of the operations of ERNs' 15.2.16' **(APPENDIX 6)**
  - This report illustrates the sorts of use cases ERNs might encounter, highlighting the specific needs relating to rare disease data collection and reuse
- ✓ 'Report: Activities of the Task-Force on Interoperable Data-sharing in the framework of the operations of ERNs – 1st year summary and workplan 2017-2018' **(APPENDIX 7)**
  - This report summarises the actions prioritised by the RD-ACTION Task-Force over its first year, including advocacy for the prompt launch of a Tender with appropriate specifications

	The cases reviewed by the ERN in collaborative virtual consultations should afterwards be retained in a case record repository within or accessible via the IT Platform	**(xiv) encrypts and stores the data;** **(xv) pseudonymises patient data for sharing, use in clinical decision making tools, protocols, guidelines, case library or research;** **(xvi) hosts the data storage within EU borders and ensures that the hosting is single-tenant with stable, fast and easy data storage and retrieval, back-up and recovery;** **(xvii) ensures that hosting is redundant at both the database and application server level;**
Training & Education	*Training and education programmes should be delivered via an eLearning programme" made available as part of the Platform of IT-related tools.*	? No apparent reference to training, education and eLearning. This came across as a really important component of an ideal ERN ICT platform, in view of the potential for disseminating good practices and reducing inequalities in access to high quality care.
Patient Portals	*Many respondents attested the value of the ERNs' IT platform being able to support direct patient input via patient portal*	No specific mention of patient *portals* etc, however it seems there is a goal to enable multi-user usage of the platform and patients are listed as users **(xx) uses solutions proven in telemedicine, teledermatology, teleradiology, telepathology etc. to suit the needs of specific Networks** **(xi) enforces privacy with role-based user security (patient, health professional, researcher), authentication, identification and authorisation mechanisms to share and store data and information;** **(xii) provides a moderated user-management console with different rights to create and or share and or view data within a single Network or between Networks (e.g. for patients with multiple conditions);**

IMPACT:

- ✓ Gathering information on the ICT requirements of ERNs enabled important discussions on this key topic to advance, and (hopefully) helped to influence the final Tender specifications in a positive way
- ✓ Meetings and workshops enhanced and then sustained pressure, to ensure the prompt provision of an adequate ICT solution for the ERNs to use
- ✓ Mapping the professed ICT requirements (around a broad range of data-related issues, including registries) against the contents of the Tender helped to identify remaining key questions and issues requiring further attention (e.g. potential for data patient-reported data and data portability)

Exploring research priorities of the ERNs

Under the auspices of the Maltese presidency, EURORDIS organised a dedicated policy event, entitled "Integrating research and healthcare for rare diseases: a structured cooperation with high community added value". RD-ACTION supported the 'Parallel session to the Informal Meeting of EU Health Ministers', which took place on March 20th 2017 in Valetta. **To enable the perspectives of the 24 ERNs to be shared at this key event, RD-ACTION WP6 asked the Coordinators to provide responses to the following questions:**

- What are the main research priorities –ideally translational research in particular- of your ERN, at present? Are there any goals from your proposal or 5 year grant plans you would like to highlight?
- What would support you in achieving your research goals?
- Does your ERN consortium engage with particular multinational/European research infrastructures/tools/resources at present? If not, do you have any plans to do so (for instance, are there any Research Infrastructures that you would particularly like to work with, if supported to do so?)

The responses received were collated to a single PwP presentation on the topic of ERN research priorities. This was presented at the Valetta meeting, to which RD-ACTION directly funded the participation of several ERNs.

OUTPUT and IMPACT

- ✓ RD-ACTION Presentation: Results of canvassing on ERNs and Research priorities **(APPENDIX 8)**
- ✓ What is the Output? This is a PwP presentation, synthesising some of the research priorities identified by the ERNs in early 2017, relating to basic research, clinical research, socio-economic research, etc.

Added Value:

- ✓ By thus capturing and sharing the perspectives of the ERNs regarding their respective research priorities, and by presenting some of the *specific* plans proposed by the Networks, RD-ACTION was able to convey a cross-section of views to a broader audience.
- ✓ **This presentation stimulated concrete discussion on the added-value ERNs might bring to rare disease research, and raised awareness of the Networks' plans at a critical time (when Member States were debating the creation of a European Joint Programme Co-Fund for Rare Diseases).**
- ✓ The presentations and discussion at this Valetta meeting helped to demonstrate the necessity for an EJP for Rare Diseases, and also to illustrate the added value and unique role ERNs could play.

Eliciting ERN Plans and Priorities relating to Rare Disease Registries

WP6 participated to the JRC workshop on Interoperability in November 2016. Only a limited number of ERN coordinators (potential Coordinators, as they were then) were invited to attend in-person. Therefore, to enable the perspectives of the 24 ERNs to be presented in aggregate form, the team elicited some key information from each Network on the registry status quo in their field. Each ERN was asked to supply the following information:

1. Could you describe/summarise the 'registry landscape' in your Thematic Grouping?
2. Do you have any thoughts on how you ideally plan to organise rare disease registries under your ERN?
3. What kind of support do you believe the EU Platform for RD Registration could/should ideally provide to ERNs?

The resulting data was presented at the JRC workshop by the UNEW RD-ACTION team. This workshop illustrated the depth of confusion amongst some stakeholders in the rare disease field, regarding the difference between 'registries', on the one hand, and on the other the Clinical Patient Management System (CPMS) which would soon be provided to the ERNs to enable virtual consultations and case review. Important issues and questions were raised, including how one actually defines a registry; what different sorts of registries exist in the rare disease field?; what questions each type of registry can answer; what sort of data would be captured in the future CPMS during a healthcare consultation; etc.

To attempt to dispel certain misunderstandings and points of confusion, the RD-ACTION UNEW team created an document entitled '*Post JRC Workshop – RD-ACTION WP6 analysis of issues concerning the ERN Platform for clinical patient management and the EU Platform for RD Registration*'. The purpose of this document was to provide some clarity on a crucial topic, by distilling the various issues under discussion and attempting to clarify the role of the CPMS compared to traditional registries.

OUTPUT and IMPACT

- ✓ 'RD-ACTION WP6 analysis of issues concerning the ERN Platform for clinical patient management and the EU Platform for RD Registration' **(APPENDIX 9)**
- ✓ **What is it?** This document summarises some of the key discussions and points of confusions illuminated in the aftermath of the JRC workshop on Interoperability and Registries in October 2016. Issues discussed include:
  - The difference between the EU Platform for Rare Disease Registration, and the CPMS
  - How far can we harmonise the data elements entered into the CPMS in the course of a referral? Could the same data elements be collected, regardless of the disease areas?
  - How might the data collected via the CPMS during a virtual referral be re-used? What purposes could it serve?
  - How -if at all- could CPMS interact with a registry, in the true sense?
  - What different types of registries exist in the RD field, and what 'questions' can they answer?
  - Should the RD field still seek to agree a Common Dataset for all RD registries?

- ✓ **What was the added value?** This output helped to clarify the different sorts of data the ERNs might collect/come into contact with, and restored focus at a crucial point on the definition of a registry. It distilled the core issues that needed to be addressed, to progress with both the CPMS and the EU Platform on RD Registration

Generating policies and guidance *for* ERNs, *with* ERNs - a new era

With the first call for ERNs closing in June and July of 2016, the RD-ACTION focus changed somewhat, evolving from guidance to support the *creation* of ERNs, and the hands-on role the JA played in bringing together the applicants, to working with the new ERNs (or 'ERNs-in-waiting') and all key stakeholders, **to help the ERNs generate shared solutions to common challenges, bringing in the expertise of the wider rare disease field.**

A particular goal was to work with the new ERNs to generate future policies and guidance *with* the Networks, *for* the Networks. These policies would cover some of the topics the WP set out to analyse at the onset of the project, such as registries, data-sharing, clinical practice guidelines, research, etc.

Thus it was agreed with RD-ACTION partners (largely Member State representatives and rare disease experts), the EC, and the Commission Expert Group on Rare Diseases, **that there was an important role to be played in bringing the broader experiences of the rare disease field to the ERN sphere, and vice versa, and that a Joint Action approach was a logical vehicle for this sort of integration activity**.

Meeting between the Board of Member States and the ERN Coordinators

On the morning of Wednesday 28th September 2016, RD-ACTION invited a representative from each of the proposed ERNs to join members of the Board of MS in a 'pre-workshop' meeting. This was the first occasion for these two essential stakeholder groups to come together in this way and discuss their most pressing issues relating to the implementation and evolution of the Networks. The meeting was attended by 14 representatives from 12 MS and 19 Applicant Networks Coordinators (ANCs). The meeting focused discussions around two main topics:

1. Geographical membership coverage of the ERNs and means of 'affiliation' to the Networks. The discussions clarified the rules for future membership of the Networks, and the participants agreed the importance of gaining greater clarity of the timelines and process by which MS will designate centres as 'affiliated' partners to participate in an ERN, thus ensuring that countries (especially the smaller countries) which do not have -and are perhaps unlikely to have in the future- a member in a given ERN nonetheless have a 'hub'/'gateway' to access and contribute to the expertise of that particular ERN.
2. Integration of ERNs with national health systems. The participants emphasised the potential for ERNs to, in time, bring about major innovation in health systems, functioning as true game changers in terms of equity of access across Europe to high quality care for patients whose conditions require a particular concentration of expertise. The challenges and opportunities on the sides of the ANCs and the Board members were shared in lively debate.

OUTPUT and IMPACT

- ✓ Report of Meeting between Applicant Network Coordinators and the ERN Board of Member States 28.9.16 **(APPENDIX 10)**
- ✓ Added-Value: this meeting enabled the ERN Coordinators and the BoMS members to meet for the first time face-to-face. The discussions which ensued demonstrated the political support for ERNs from DG SANTE and Commissioner Andriukaitis. The Report of this meeting captured the opportunities and challenges participants perceived, concerning ERN implementation, and highlighted next steps to address these

Workshops Dedicated to ERN Policy Support

The ERNs represent a great opportunity to embed good practices and disseminate these into broader healthcare systems. RD-ACTION's vision was that, as ERNs were established & evolved, dedicated guidance would be important to support but also to ensure a baseline compatibility and interoperability (at many levels) between the ERNs. RD-ACTION partners thus developed a workplan for the years 2016-2018, designed to capitalise on the lessons learned in the broader RD field and 'pilot' Networks and bring these to the ERN stakeholder community, to agree together how to address shared challenges.

- ✓ This workplan was communicated to the ERN coordinators and to DG SANTE, and was discussed in-depth with each group of stakeholders (with the former, for instance, via a dedicated meeting ahead of the Vilnius ERN Conference).
- ✓ The precise focus of the workshops, and the objectives and agendas for each event, were open for debate and feedback at every stage.
- ✓ Most workshops were co-organised with DG SANTE.
- ✓ In the case of the later workshops, dedicated Workshop Organising Committees were established to ensure meaningful input and collaboration from the ERNs themselves
- ✓ Particular efforts were made to involve patients, through ePAG (European Patient Advocacy Group) advocates

By the end of the project, 6 major workshops with an emphasis on ERN activities had been delivered, each addressing a particular policy area in which consensus-building was deemed important. By the end of May 2018, ca. 360 experts had participated to the six main workshops.

Workshop: Exchanging data for virtual care in the ERN framework

27-28 September 2016, Brussels

The first workshop organised with known-Coordinators took place in Brussels in September 2016. This topic was selected because at the heart of the ERN concept is the opportunity to provide healthcare through virtual means, enabling expertise to travel as opposed to patients or physicians,

where possible and appropriate. The workshop was well attended, with over 55 participants across the two days: 21 Applicant Networks; 10 European Commission DG SANTE experts leading various aspects of the ERN work; 10 ePAG advocates; experts from RD-ACTION and several other projects with experience and expertise in the standardisation of data in the RD field; and a legal expert with many years of experience in addressing the legal challenges facing the field of eHealth, Petra Wilson.

The workshop focused on several aspects relating to the organisation and execution of 'virtual consultations' for complex patient presentations requiring access to the pooled expertise of the ERN:

- The form such encounters might take were explored (for example a real-time gathering of experts through virtual systems, the ability to review uploaded case information in the professional's own time through a secure platform, etc.)
- The legal issues around data protection -especially in view of the new General Data Protection Regulation- and the legal, ethical and social issues relating to consent for the sharing of data in the ERN framework
- Practical advice on the organisation and execution of efficient and effective virtual consultations, from colleagues engaged in this work at present
- Perspectives on how patients will enter/ be 'referred' to the expertise of the ERN for virtual care
- Proposals on standardising RD data in terms of disease coding and ontologies for phenotypic (clinical) information, to explore the good practices which should be embedded in the ERNs

OUTPUTS and IMPACT

Agenda

Key Outputs and Impact:

- ✓ Workshop Report (**APPENDIX 11**)
- ✓ Highlights and Conclusions (**APPENDIX 12**)

Added-Value: The report summarises the presentations and discussions for the workshop, arranged around the 4 main sessions of the agenda:

- ✓ legal and ethical issues around data protection and consent (demystifying some of the issues around sharing data in the ERN framework, emphasising the need for the EC to address some of the legal concerns raised, and introducing a legal expert to the debates, who would go on to deliver a future Tender on ERN consent forms
- ✓ the issue of patient pathways and referrals into ERNs (identifying different scenarios to attempt to crystalize how patient cases will enter the ERNs);
- ✓ sharing concrete examples and proven good practices in organising and conducting virtual consultations, both real-time and otherwise, to support other Networks in avoiding common pitfalls;
- ✓ proposing methods of standardising data to enable optimal use of that data for the purpose at hand, but also to render it reusable, for secondary purposes.

The key conclusions and proposed next steps/future actions were summarised in the shorter Highlights and Conclusions documents.

This was a broad workshop, touching upon many crucial issues: in some of these cases, the workshop pointed the way ahead; for others (e.g. patient pathways), the points raised remain highly relevant 2 years later

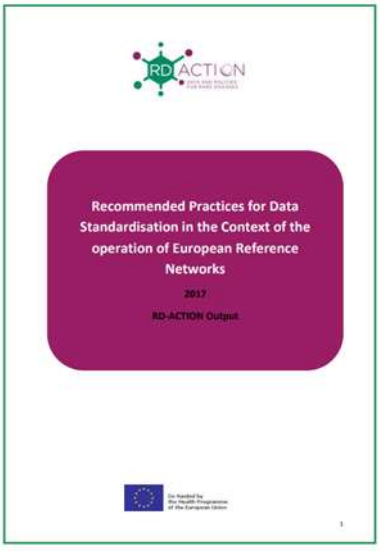
Workshop: Using standards & embedding good practices to promote interoperable data sharing in ERNs

26-27th April 2017, Brussels

The main impetus for this workshop was the final session of the previous workshop on exchanging data for virtual care in the ERN framework (APPENDICES 11 and 12) which explored how to make the most of data collected in the ERNs for care purposes. After identifying the value of using the ontologies deemed most sensitive and appropriate for rare diseases, participants had expressed a desire to learn more about how to use these sorts of tools practically, to optimise the use and re-use of data collection in the ERN context.

68 participants joined this workshop, a mixture of ERN Coordinators, EURORDIS, and Orphanet partners, eHealth specialists, Coding experts, Phenotype ontology experts, data linkage experts, and DG Sante representatives. The event was co-organised with and hosted by DG SANTE, at the offices in Brussels.

After clarifying the sorts of benefits stakeholders perceived from the data collected via the CPMS for clinical consultations, the workshop explored four key resources or approaches presented as particularly relevant for optimising the interoperability and re-usability of rare disease data: the OrphaCode; the Human Phenotype Ontology; the concept of a Privacy-Preserving Record Linkage system; and 'FAIR' data. Participants were able to understand how each could be used, and the benefits these tools could bring for ERN-collected data. In so doing, the workshop ensured that all ERNs were familiar with the state of the art in data management and data interoperability concepts, as established over many years of EC-funded initiatives.



OUTPUT and IMPACT

Agenda and workshop outline

Main Outputs:

- ✓ Recommended Practices for Data Standardisation in the Context of the operation of European Reference Networks (2017) (**APPENDIX 13**)
- ✓ This is a set of 'Recommendations' in the style of EUCERD and CEGRD Recommendations, capturing the main conclusions of the workshop in Brussels. **It is an important output, as it explains the various ways in which ERN data (mainly focusing on data entering the CPMS) could be used for multiple purposes, and could be in some ways interoperable with external data sources, for instance in the research field.** The Coordinators were all involved in finalising the document, thus it can legitimately be viewed as a consensus document on ways to standardise data in the ERN framework. The logical consequence is that the EC IT team should take these recommendations into consideration when refining the CPMS, seeking ways to incorporate the OrphcaCode and the childhood cancer codes (ICCC3), the HPO, a PPRL (such as the rest of the RD field is embracing), and finally, ensure the data in the CPMS is FAIR.
- ✓ 'Tool-kits' of resources (all accessible via http://www.rd-action.eu/european-reference-networks-erns/rd-action-workshop2/)
    - for Orphanet Nomenclature
    - for HPO
    - for FAIR Data)
    - for PPRL (Privacy-Preserving Record Linkage)

Added-value:

This workshop created significant added value and impact. For instance;

- ✓ The Tool-Kits are composed of **practical resources and 'how-to' guides for stakeholders**
- ✓ **The workshop illuminated the 'state of the art' in RD data standardisation and interoperability to a much wider audience,** ensuring all ERN coordinators (and not just those who worked closely on research-oriented projects like RD-Connect) and their member HCPs were aware of the fruits of past EC investments, which will hopefully prevent Networks 'reinventing wheels'
- ✓ **The Recommended Practices document has been very important for advocacy purposes**, to prompt the teams in charge of delivering and adapting the CPMS to consider how this Platform can be optimised and made more interoperable with the broader sphere of RD data. This has resulted in early benefits:
    - The OrphaCode and the ICCC codes are now included in the CPMS data fields
    - Discussions are ongoing to replace the current pseudonymisation tool (which is unable to link patient data with data from external RD resources) with a PPRL system, specifically the EUPID. The RD-ACTION team continues to seek the implementation of these Recommendation points
    - Several ERNs have already made significant efforts to implement the Recommendations, e.g. by organising a workshop to optimise the HPO for their disease area (ERN-EYE). Other networks (including ERN BOND, ERN-EYE, ERK-Net and EPICARE) are prioritising the improvement of the OrphaCode for their domain, and are in discussions to curate the nomenclature via the new Orphanet platform demonstrated at this workshop.
    - The EU profile of a PPRL (and particularly of the EUPID) was significantly increased – later in 2017 the EU Platform for RD Registration embraced the EUPID as the pseudonymisation solution for RD registries in Europe, which is a major step forwards
    - Several ERNs developed contacts with the creators of the FAIR data concept, and these collaborations are now taking shape

Workshop: Indicators and Outcome Measures to demonstrate the impact and added value of ERNs

1-2 June 2017, Newcastle

This workshop, organised in collaboration with DG SANTE, united 40 participants to work closely on issues related to the impact and monitoring of ERNs.

ERNs have a broad and ambitious mandate – they need to be able to demonstrate their impact across a wide range of fields and activities, which requires carefully-selected indicators. At the same time, monitoring systems including Key Performance Indicators should be set up to follow up the activity and caseloads of the ERNs. Alongside the efforts of the ERNs themselves to address these issues, there is growing recognition in DG SANTE and in the ERN BoMS of the need for continuous monitoring and assessment at various levels.

This workshop explored two main types of Indicators:

- ERN Common Indicators i.e. indicators which should be shared by all 24 ERNs and which are based upon the common activities and objectives of the Networks
- ERN-Specific Indicators i.e. based upon disease area or specialised procedures/techniques

<u>Key Questions for discussion included the following:</u>

- How will ERNs demonstrate their added value? What sort of impact will be demonstrable quickly, and what will only be feasible in the long-term?
- How will the operation of the ERNs be monitored. Which activities/ actions and events other that the clinical performance and outcomes should be collected?
- What can realistically be measured across each Network? How can this information be collected, and by whom, and how often?
- What Indicators have ERNs already proposed to monitor in their Grants? What could be common to all?
- What kind of clinical outcome measures have the ERNs identified, to demonstrate their effectiveness?
- How can ERNs embed a culture of knowledge generation, through the implementation of clinical outcome measures that are centred upon learning through complex case studies?
- How can ERNs optimise use of patient-reported outcomes and promote good practices in this area?

- How might health systems compare outcomes for patients who receive care via the ERN vs. those who do not?

OUTPUTS and IMPACT

Agenda and workshop Outline

- ✓ **Main Output: 'Annotated second version of the proposal on continuous monitoring of ERNs' (APPENDIX 14)**
  - This was a significantly expanded version of the original EC-generated draft, capturing the comments and perspectives of the workshop groups concerning the initial proposal for common Indicators applicable to all ERNs.

Added-Value

This workshop advanced ERN stakeholder knowledge of several key issues: specifically, it helped the participants to:

- ✓ **better understand terminology around indicators and become acquainted with the different types of indicators (structure, process, outcome) and their use in health systems**
- ✓ In terms of Common Indicators, participants were able:
  - To debate and critique a proposed set of indicators, designed to be common to all ERNs
  - To discuss key issues and challenges on data collection and reporting
- ✓ In terms of disease/process –specific *clinical* outcomes, participants were able:
  - To appreciate the challenges in selecting clinically-oriented indicators
  - To gain an overview of which indicators are currently being used in some disease areas and explore how such decisions might be made in the ERN context
  - To clarify the options for collecting patient-reported outcomes
- ✓ **The main output, which was the detailed annotated table of proposed common Indicators (APPENDIX 14), served as a centrepiece for the newly-established Working Group (WG) on Monitoring and Assessment under the ERN Coordinators' Group.**
- ✓ RD-ACTION colleagues joined this WG, to take forwards the achievements of the workshop and illustrate the challenges and complexities in attempting to agree on common indicators. Using their insights from the workshop, the team was able to offer solutions as to how best to phrase and define each Indicator, to ensure they made sense and were in fact feasible to collect.
- ✓ RD-ACTION provided comprehensive support and input to future versions of this document, supporting the creation of the final consensus table of Common Indicators. Simultaneously, the RD-ACTION partners (EURORDIS in particular) called for a renewed future focus on some of the more complex (but nonetheless crucial) areas, such as patient experience and satisfaction.
- ✓ The final report of the workshop, including the presentation summaries, is expected to galvanise discussions on how ERNs might approach the selection of disease-relevant clinical outcomes, to enable a longer-term assessment of the impact of the Networks

Workshop: How can ERNs generate, appraise and utilise clinical practice guidelines, to enhance the impact of consensus guidelines in national health systems?

6-7th December 2017, Rome

Clinical practice guidelines (CPGs) serve as a great equaliser in the RD field: they can mean the difference between no care/substandard care and patients living longer, healthier lives with few complications. Guidelines, whether designed to support diagnosis or care, can serve as a blueprint of excellence, to advise doctors closer to the patients on how to treat them in a way that reflects the best possible knowledge and will generate the best possible outcomes.

The workshop united 63 participants, the majority of whom were nominated by the ERNs themselves (23 of the 24 ERNs were represented). In addition, several projects/initiatives have received EC funding to address this issue and it was felt that the fruits of such investment and expertise should be considered in the light of the ERN mission, to help the Networks understand and gauge the applicability of existing cross-cutting (disease-agnostic) tools; therefore, presentations were organised to illustrate the resources resulting from Rare-BestPractices and Orphanet. The approach of the rare cancer community (i.e. the JARC) was also considered. However, **the plans and priorities of the ERNs themselves were at the heart of the workshop:** a survey had been conducted, to gather preliminary information on these plans, and five quite different Networks presented detailed cases studies on their activities. Through a combination of expert presentations and lengthy discussion sessions, the group therefore sought to identify good practices, which could be shaped into 'recommendations' addressing several aspects of this vast and complex topic, including:

- methodological approaches to the generation and appraisal of CPGs;
- strategies for engaging with key stakeholder groups, such as patients and learned societies to partner in all CPG activities
- highlighting financial issues and time-commitments of guideline activity, proposing strategies to address the need for ethical engagement with stakeholders such as Industry
- options to engage national authorities, to ensure that CPGs emerging from ERNs can actually be used 'on the ground' in countries
- outlining concrete future activities needed to support the ERNs in their CPG-related tasks

OUTPUTS and IMPACT

Agenda and Workshop Outline

- There will ultimately be several outputs from this workshop: the final form of these remains to be defined, as the imminent publication of a Tender on ERNs and CPGs may affect what is finally produced as 'workshop follow-up', and by whom. However, it is expected that there will be:
    - A workshop Report (FORTHCOMING)
    - A publication summarising ERN activities and plans relating to CPGs (FORTHCOMING)
    - A 'Tool-Kit' of existing resources applicable to all rare diseases and rare cancers (FORTHCOMING)
    - A Thesaurus of Terminology relating to CPGs (FORTHCOMING)
- The main output, however, is a set of Recommendations /Key conclusions on ERNs and CPGs (**APPENDIX 15**)

Added-Value

- ✓ **The workshop initiated discussions on many aspects of the broad CPG topic, and thus the participants were able to propose good practices and identify necessary 'next steps' across a range of important areas: the resulting 'Recommendations/Key Conclusions' document therefore addresses many relevant sub-topics:**
    - Terminology and methodology for ERN-led Guidance
        - In particular, the issues surrounding a possible 'ERN methodology' for generating Guidance were elucidated, and several potential approaches were presented, for consideration under the future Tender
    - Appraising CPGs
    - Exploitation of disease-agnostic resources for rare diseases
    - Engaging patients in generating CPGs
    - Engagement with Professional/Scientific Societies
    - Translating and disseminating Guidelines
    - Addressing legal and national barriers to implementation of ERN-led Guidance at national level
- ✓ This was the first RD-ACTION workshop conducted in the era of Working Groups (WGs) under the ERN Coordinators' Group: by collaborating with the Chair of the most relevant WG, **RD-ACTION was able to ensure meaningful involvement of the ERNs at every stage of planning and delivery**. This was achieved through the constitution of a dedicated Workshop Organising Committee (WOC).
- ✓ The drafting and finalisation of outputs is being overseen by this same multistakeholder WOC, which involves key representatives of RD-ACTION partners (UNEW, INSERM, EURORDIS and ISS), select ERN Coordinators, DG SANTE, and the Board of MS of ERNs.
- ✓ The future activities of this Group will depend somewhat upon the outcomes of the Tender regarding CPGs, to be launched in the autumn of 2018. However, it is important to note that **the conclusions and main discussion points of this workshop - and especially the concrete action points identified for a future project to address- were understood to have been taken into account when preparing the Tender specifications**.

Workshop: Creating a Sustainable Environment for Holistic & Innovative Care for Rare Diseases & Complex Conditions

12-13 April 2018, Frambu (Norway)

In April 2018, the RD-ACTION WP6 team united with the INNOVCare project, to deliver a large workshop intended to share the state of the art in terms of integrated, holistic care for people with rare diseases, and to explore the possible added value which ERNs might bring to this important area.

The workshop was hosted at Frambu Resource Centre and brought together 67 participants from 22 countries, to share the latest developments and outputs of the INNOVCare initiative, and also explore how and where the ERNs might add value to provision of integrated, holistic care for people with rare and complex diseases. The roles which ERNs –and very often, the centres of which they are composed- could play in advancing this mission, were explored. For instance, ERNs could:

- Spread *understanding* of the benefits of joined-up, holistic care pathways for patients (encompassing the less-strictly-medical professionals, such as physiotherapists, psychological therapists, and social support appropriate to the specific needs of people with rare diseases and their families);
- Support and propel the drive to identify how best to provide holistic care for patients with rare and complex conditions and define this in patient care pathway (or at least identify the core components of the sorts of support which *should* be available to patients in the paramedical and social spheres, whilst acknowledging that national procedures and specificities will often vary.)
- Embed good practices to support integrated care for patients in their constituent HCPs (and eventually 'affiliated' partners), and in time help to diffuse good practices to broader health systems;
- Contribute to the collection and integration of data, to improve knowledge and understanding of rare diseases and the impact of patients and wider society.

The workshop concluded with five parallel breakout sessions, in which participants discussed together how to make progress in optimising concepts such as care coordination and case management, knowledge generation, and patient engagement in the provision of integrated and

holistic care. The themes of the discussions arose from Member State interviews and work conducted within the INNOVCare project as well as from the work of the RD-ACTION and of the previous joint action identifying key issues to support people living with a RD overcoming their daily life challenges and to support the provision of holistic and integrated care for RD.

OUTPUTS and IMPACT

Agenda

Workshop Outline Document **(APPENDIX 16)**

- ✓ Recap of the Breakout Sessions (**APPENDIX 17**)
- ✓ OrphaNews Editorial 'European Initiatives unite to address Integrated and Holistic care needs for rare and complex conditions' (**APPENDIX 18)**
- ✓ Workshop Report (FORTHCOMING)
- ✓ Concept Paper on 'ERNs and Integrated, Holistic Care for rare and complex diseases' (FORTHCOMING)

Added Value

This workshop has already had a significant and far-reaching impact:

- ✓ **The group discussions –as summarised in APPENDIX 17- raised many key points, and highlighted some concrete roles for ERNs and their member HCPs, respectively**. For instance;
  - Stakeholders hailed the unprecedented opportunity ERNs offer, in terms of their potential to become a 'voice' to ascertain the true extent of the needs and burden facing people with rare and complex diseases, but also to 'set the standard' in terms of *defining* the sorts of paramedical specialists, social actors, services and support which should be available to patients in their local environments: often, this will entail encouraging Centres of Expertise/HCPs to fulfil *their* crucial roles in establishing links and forming collaborations with institutions and professionals in the wider health and social care environment, to enable their patients to receive a more integrated and holistic experience.
  - The need for balance and collaboration was also emphasised, however – mechanisms need to be found for experts and stakeholders *not* formally involved in ERNs to nonetheless collaborate with the Networks for mutual benefit.
- ✓ The workshop **helped raise awareness in the ERN community of the range and severity of difficulties facing people living with rare diseases** (and their families/carers), at every level: from attempting to traverse often-fragmented health and social care systems, to struggling to function in normal society in terms of accessing education, social care, employment, etc. By sharing these realities and raising awareness of the achievements and outputs of the INNOVCare initiative, ERN participants were able to identify new collaborations and consider how they might make a positive difference.
- ✓ There was a distinct feeling that this topic, although 'new' in a sense for the ERNs, is an area where the Networks and their HCPs can potentially have a huge impact, in ways which really matter to patients. The generation of a concept paper specifically focusing on the applicability of this topic to ERNs should help to illuminate these issues for the wider group of ERN Coordinators.
- ✓ **Collaboration has already been initiated with the BoMS Working Group on Integration of ERNs to health systems, to determine points of mutual relevance.** The RD-ACTION and INNOVCare partners will also seek to advance these discussions with the ERN Coordinators.

Workshop: How ERNs can add value to clinical research in rare diseases and highly specialised domains

29-30th May 2018, London

The final RD-ACTION workshop geared towards supporting the ERNs was organised jointly with the European Medicines Agency (EMA) and DG Sante. The workshop united 65 participants from many different stakeholder groups, to explore one fundamental question: How ERNs can provide added value in the area of clinical research. 22 of the 24 ERNs were represented directly, through a combination of Coordinators, Research Leads, and (ten) ePAG representatives. EMA colleagues from many teams and units participated, along with DG SANTE and DG Research. A range of experts from RD-ACTION and research-related initiatives also participated.

The workshop had four main goals:

1. **To share the state of the art of tools and resources which exist in 2018 to streamline and optimise each 'point' in the clinical research pipeline**

2. **To better understand the priorities and needs of the ERN community specific to clinical research, and explore case studies (both of pre-ERN successes on the part of research networks, and early ERN-era achievements/goals) in particular detail**

3. **To elucidate the services and opportunities offered by the European Medicines Agency which are of relevance to clinical research in rare and highly specialised domains**

4. **To identify concretely *how* and *where* ERNs could make a positive difference to each 'timepoint' in the clinical trial pathway, including points of engagement specifically with the EMA, to agree a 'roadmap' to a more strategic and streamlined collaboration in future.**

The first day was dedicated to establishing the status quo, in term of ERN plans and potential relating to clinical research, patient involvement in research, and EMA services and resources to support clinical research in rare and specialised domains. An important centrepiece was the pre-workshop survey distributed to ERNs, which resulted in an overview presentation of cross-cutting research priorities and perceived challenges, supplemented by a number of in-depth case studies.

The second day was entirely dedicated to debate, across several key topics:

- What sorts of activities under the heading of 'clinical research' will ERNs engage in, and what are the advantages of the ERN structure?
- What opportunities exist under current EMA structures and resources presented on Day 1, and how might ERNs engage with these?
- Identifying concrete roles and recommended practices to involve patients in the various types of ERN-related Clinical Research
- How can ERNs generate/link/exchange data to support the planning and execution of clinical trials and studies?

To optimise engagement and support dissemination of key messages, the first day of the workshop was broadcast live via the EMA website.

OUTPUTS and IMPACT

Workshop Documents:

Agenda

Outline of the Workshop

- ✓ The main output is a 'Summary of the Workshop Conclusions and Next Steps' **(APPENDIX 19)**
  - This captures the main points of discussion on the second day of the workshop, and identifies numerous Action Points concerning each of the 4 main discussion topics. The document was agreed by the dedicated Workshop Organising Committee
- ✓ A more traditional workshop report is being elaborated, to consist of a Report of the Presentations on Day 1 (a series of brief summaries, essentially), followed by the 'Summary of the Workshop Conclusions and Next Steps' document. (FORTHCOMING)

Added Value:

- ✓ This workshop, like the CPG workshop, was planned with the aid of a dedicated Workshop Organising Committee (WOC), to ensure active input from a range of important stakeholder groups. The WOC was composed of the UNEW RD-ACTION team and representatives of EURORDIS, key ERNs (namely Luca Sangiorgi and the current and future Chairs of the ECG), the EMA, and DG SANTE. This WOC will continue to oversee certain workshop-related outputs in the future
- ✓ **The workshop was a first opportunity to really analyse what individual ERNs are planning to do in the clinical research sphere** e.g. to explore whether ERNs plan to focus on particular types of trials or studies, to clarify the difference between an 'ERN trial' and any other trial in the rare disease field, to ascertain the sort of resources available within and outside of the rare disease field at present which could be exploited by the ERNs, etc.
- ✓ The workshop increased EMA understanding of the ERN status quo and elucidated the many ways in which ERNs could add-value to clinical research. Preliminary steps were taken during this workshop, to formalise engagement between the Networks and the EMA. For instance, a dedicated EMA contact was provided for the ERNs, and the ERNs were invited to enrol their respective experts to the EMA expert databases, etc. **The collaboration between the Agency and the ERNs will foreseeably strengthen and evolve further, based upon these initial discussions.**
- ✓ The survey gathered very useful insights as to how ERNs perceive their research responsibilities, and on the kinds of practical support that would facilitate their activities; for instance, several respondents requested an ERN-specific help-desk of sorts, and there was strong support for the notion of ERNs becoming legal entities. The results of this survey will be utilised further in the near-future, either as the centrepiece of a publication on ERNs and research, or to advance the development of a research strategy for the ERNs.
- ✓ **The workshop proposed many key action points.** For instance, an important discussion took place concerning the lack of understanding around rare disease registration and the exact scope of initiatives such as the EU Platform for RD Registration and the EMA Patient Registries' Initiative. The group unanimously called for urgent and comprehensive cross-talk between all initiatives involved in RD registration and requested a clearer communication of the tools, resources and recommendations each can offer to would-be registry creators/users: this sort of information is crucial, to help ERNs understand how best to proceed in the registry domain

Alliance with eHealth initiatives, for the benefit of ERNs

Very early in RD-ACTION, it was recognised that for ERNs to become functional, they needed a means to exchange sensitive health-related data across borders. The most obvious means of exchanging such data was the promised platform for the organisation of virtual consultations or virtual reviews, for the most complex patient cases. In 2015, however, there was limited understanding as to the process by which such a platform would be procured, what its features might be, and when it would become available.

The RD-ACTION WP6 team had already sought to expedite and support this crucial activity, by canvassing the IT needs of the ERNs coordinators (see above, section 'Identifying the IT needs of the ERNs, to support the provision of an appropriate IT platform'). However, to complement this goal, and to explore wider opportunities for collaboration between the eHealth domain and the rare disease field inside and outside of ERNs, RD-ACTION WP6 created a *Task Force on Interoperable data-sharing within the framework of the operations of ERNs* (later rebranded as the *Task-Force on Interoperable data-sharing between the rare disease and eHealth communities,* to reflect the fact that its focus exceeded ERNs alone).

Initially however, the main purpose of that Task-Force was to assess the potential for eHealth tools and assets developed through years of EC funding (most specifically the eHealth Digital Service Infrastructures) to support the exchange of data across borders in the ERN framework.

- This Task-Force convened a large workshop on December 12th 2015 in Lisbon, to which potential ERN coordinators were invited and several participated (funded by RD-ACTION) to advance discussions on areas of collaboration.

- A meeting (on 18th Feb 2016) with the DG SANTE teams working on ERNs and eHealth was also arranged, to help the EC colleagues understand the realistic needs around rare disease data such as the ERNs would be collecting and exchanging. This meeting crucially discussed a number of different use cases likely to be encountered in the ERNs, which helped to illuminate the needs of the ERN community for the IT teams in charge of drafting and launching a Tender for the ERNs' IT platform.
- Once the Tender for the Clinical Patient Management System (CPMS) was launched (in June of 2016) the TF arranged another workshop, again involving ERN coordinators, to discuss the content and specifications of this Tender, what it meant for the ERNs, and also how future collaboration between the eHealth DSIs and the CPMS might be enabled.
- All activities and proposed future use cases were summarised in a single comprehensive report, late in 2017: http://www.rd-action.eu/wp-content/uploads/2016/05/1st-year-summary-and-next-steps-for-2017.pdf
- Meanwhile, RD-ACTION WP6 continued to represent the ERN community at eHealth meetings throughout 2016 and 2017, including workshops of the VALUeHEALTH and the eSENS initiatives. By delivering presentations, the team illustrated the needs of the rare disease community, regarding eHealth and cross-border activities in particular, and ensured that the eHealth field was able to follow the development and implementation of ERNs. From the other side, the RD-ACTION team raised awareness (by publicising the aforementioned Task-Force reports, and via presentations at ERN-related meetings) of the key eHealth projects and their activities, to support cross-talk between the new ERN coordinators and the 'epSOS-legacy' and CEF-funded initiatives. Once the Networks were clearly established, RD-ACTION proposed individual Coordinators be directly invited to eHealth meetings and workshops, based upon their role in Chairing WGs or Chairing the ERN Coordinators' group: as an example, the Chair of the ECG was engaged in the final workshop of the Joint Action to support the eHealth Network (JASeHN), which should open up further opportunities for collaboration between eHealth projects (such as the new Joint Action for eHealth) and the Networks themselves.

OUTPUTS and IMPACT

- ✓ The dedicated web-page for the Task-Force on Interoperable data-Sharing in Rare Diseases and eHealth communities is available here: http://www.rd-action.eu/ehealth-and-european-reference-networks/
- ✓ Key Outputs include:
  - Activities of the Task-Force on Interoperable Data-sharing in the framework of the operations of ERNs – 1st year summary and workplan 2017-2018 **(APPENDIX 20)**
  - Report from the meeting of the 'Task Force on Interoperable data-sharing within the framework of the operations of ERNs' 18.2.16 **(APPENDIX 21)**
  - Report from the workshop of the 'Task-Force on Interoperable data-sharing in the framework of the operations of ERNs' 30.6.16 **(APPENDIX 22)**
- ✓ As above, **this work ensured mutual awareness and created understanding between the eHealth and rare disease communities, particular around the nature and development of ERNs. This Task-Force, established to fill an identified gap, initiated cross-talk and proposed future use-cases for ERNs and eHealth, and will continue to operate post-RD-ACTION, with a broad goal to build synergies between eHealth and the wider rare disease fields**

APPENDIX LIST: Key ERN-Related Outputs of RD-ACTION WP on Policy & Integration

APPENDIX 1	How has RD-ACTION supported the conceptualisation and implementation of ERNs (2015-2018)?	http://www.rd-action.eu/wp-content/uploads/2018/05/Summary-of-RD-ACTION-Support-for-ERNs-2015-18.pdf
APPENDIX 2	Informal FAQs and Discussions on RD ERNs (2015)	http://www.rd-action.eu/wp-content/uploads/2015/12/Informal-FAQs-and-Discussions-on-RD-ERNs-Jan-2016.pdf
APPENDIX 3	Summary of the RD-ACTION 'Matchmaker' for Rare Disease ERN (2016)	http://www.rd-action.eu/wp-content/uploads/2015/12/RD-ACTION-ERN-Matchmaker-Summary-Final.pdf
APPENDIX 4	Summary of disease expertise per ERN (2016)	http://www.rd-action.eu/wp-content/uploads/2015/12/RD-Action-Matchmaker-Summary-of-disease-expertise-recorded-under-each-Thematic-Grouping.pdf
APPENDIX 5	What do Coordinators require from an ERN ICT platform?	http://www.rd-action.eu/wp-content/uploads/2015/12/What-do-Coordinators-require-from-an-ERN-ICT-platform.pdf
APPENDIX 6	Report from the meeting of the 'Task Force on Interoperable data-sharing within the framework of the operations of ERNs' 18.2.16	http://www.rd-action.eu/wp-content/uploads/2016/05/Meeting-Report-Task-Force-on-Interoperable-Data-Sharing-in-the-framework-of-ERNs.pdf
APPENDIX 7	Report: Activities of the Task-Force on Interoperable Data-sharing in the framework of the operations of ERNs – 1st year summary and workplan 2017-2018	http://www.rd-action.eu/wp-content/uploads/2016/05/1st-year-summary-and-next-steps-for-2017.pdf
APPENDIX 8	Presentation: Results of canvassing on ERNs and Research priorities	http://www.rd-action.eu/wp-content/uploads/2015/12/RD-ACTION-presentation-results-of-canvassing-on-ERNs-and-Research-Malta-March-2017.pptx
APPENDIX 9	RD-ACTION WP6 analysis of issues concerning the ERN Platform for clinical patient management and the EU Platform for RD Registration	http://www.rd-action.eu/wp-content/uploads/2015/12/RD-ACTION-analysis-of-the-key-issues-regarding-ERNs-and-Registries-Dec-2016.pdf
APPENDIX 10	Report of Meeting between Applicant	http://www.rd-action.eu/wp-

	Network Coordinators and the ERN Board of Member States 28.9.16	content/uploads/2016/11/Report-of-Meeting-between-Applicant-Network-Coordinators-and-Board-of-Member-States-of-ERNs-28.9.16-Final.pdf
APPENDIX 11	Report: 'Exchanging data for virtual care within the ERN Framework'	http://www.rd-action.eu/wp-content/uploads/2016/12/Report-of-RD-ACTION-Workshop-Exchanging-Data-for-Virtual-Care-within-the-ERN-Framework-1.pdf
APPENDIX 12	Exchanging Data for Virtual Care in ERNs – Highlights and Conclusions	http://www.rd-action.eu/wp-content/uploads/2016/12/Highlights-and-Conclusions.pdf
APPENDIX 13	Recommended Practices for Data Standardisation in the context of the operation of ERNs	http://www.rd-action.eu/wp-content/uploads/2017/05/Recommended-Practices-for-Data-Standardisation-in-the-Context-of-the-operation-of-ERNs-final-2017.pdf
APPENDIX 14	Annotated second version of the proposal on continuous monitoring of ERNs (a record of workshop discussions)	http://www.rd-action.eu/wp-content/uploads/2017/06/Draft-proposal-on-continuous-monitoring-of-ERNs-version-2-20.8.17.pdf
APPENDIX 15	Key conclusions and Recommendations on ERNs and Clinical Practice Guidelines	http://www.rd-action.eu/european-reference-networks-erns/workshop4/
APPENDIX 16	Outline and context for RD-ACTION and INNOVCare workshop on integrated and holistic care for rare diseases	http://www.rd-action.eu/wp-content/uploads/2018/08/Outline-for-Workshop-April-2018-.pdf
APPENDIX 17	Recap of Breakout Session from workshop 'Creating a Sustainable Environment for Holistic & Innovative Care for Rare Diseases & Complex Conditions'	http://www.rd-action.eu/wp-content/uploads/2018/04/Breakout-Sessions-Recap_ALL_INNOVCare-RD-Action_Workshop-Holistic-Care-RD_Norway_12-13-April.pdf
APPENDIX 18	OrphaNews Editorial for Workshop on integrated and holistic care for rare diseases	http://international.orphanews.org/newsletter-en/editorial/nl/id-20-april-2018.html#or_id-20-april-2018

APPENDIX 19	Workshop on ERNs and Clinical Research: Summary of the Workshop Conclusions and Next Steps	http://www.rd-action.eu/european-reference-networks-erns/rd-action-workshop-co-organised-with-ema-and-dg-sante/
APPENDIX 20	Activities of the Task-Force on Interoperable Data-sharing in the framework of the operations of ERNs – 1st year summary and workplan 2017-2018	http://www.rd-action.eu/wp-content/uploads/2016/05/1st-year-summary-and-next-steps-for-2017.pdf
APPENDIX 21	Report from the meeting of the 'Task Force on Interoperable data-sharing within the framework of the operations of ERNs' 18.2.16	http://www.rd-action.eu/wp-content/uploads/2016/05/Meeting-Report-Task-Force-on-Interoperable-Data-Sharing-in-the-framework-of-ERNs.pdf
APPENDIX 22	Report from the workshop of the 'Task-Force on Interoperable data-sharing in the framework of the operations of ERNs' 30.6.16	http://www.rd-action.eu/wp-content/uploads/2016/05/Meeting-Report-30.6.16-Task-Force-on-interoperable-data-sharing-in-the-framework-of-ERNs.pdf