

# **EJP RD**

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### **Del 2.9**

## **Second Scoping Paper**

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## 1. Introduction and Objectives:

Deliverable 2.9 “Second scoping paper” is a public document foreseen by the GRANT of the European Joint programme on rare diseases (EJP RD). It is intended as an additional document and tool regarding the mapping of research and innovation (R&I) needs of the EJP RD. Such R&I needs have been detailed (after a thorough search and inputs from different sources and bodies) in the Deliverable 2.3, “Summary document on mapped Research and Innovation needs”, produced in 2019, and Deliverable 2.4 “Second Summary document on mapped research and innovation needs produced in 2020. Therefore, in the planning of the EJP RD it was anticipated that this Scoping Paper should have a double use

- **Internal use** of this Scoping Paper in the EJP RD: to reformulate the outcomes of the mapping and prioritization actions to be transmitted to the leaders of Task 2.3, 2.4 and 2.5 for complementary actions. That is the main utility of this document internally, within the activities of the EJP RD.
- **External use:** It is intended as a document to be promoted (and implemented) by the national mirror groups and within the current and forthcoming EC Framework Programme.

This public report has been prepared by ISS in close collaboration with Task 2.2 leaders (ISCIII, ISS) and with the Coordination, as part of the WP2 “Integrative research and Innovation Strategy”. A specific aim of Task 2.2 of the EJP RD is to identify and regularly update the research and innovation needs that feed the EJP RD Annual Plans and contribute to the development of the long-term strategy of the EJP RD.

The summary documents and Deliverables on which the formulation of the present Scoping Paper is based on are:

- D2.1 (“Final list of prioritization criteria”) (Public Report),
- D2.2 (“Prioritization Scheme for EJP RD actions, including decision-making process-Guidelines for prioritization”) (Public Report),
- D2.4 (“Second Summary document on Mapped Research and Innovation Needs”) (Confidential Report).

The comprehensive summary included in the present document will be transmitted to the Task Leaders of the WP2 for complementary actions in their respective tasks, specifically:

- “Scientific programming of joint transnational calls” (Task 2.3),

- “Management of the medium, longer-term research strategy questions and dedicated linkage with Task Forces of IRDiRC” (Task 2.4)
- “Translation/impact of prioritization on national and EU strategies” (Task 2.5).

All these activities are part of Pillar 0 (“Coordination and transversal activities”), the central coordination Pillar that assists the actions of the four major Pillars of the EJP RD.

Pillar 0 which includes WP2: “Integrative research and innovation strategy”. The general objectives of WP2 are:

- To map the needs for RD research and innovation;
- To define the prioritization model for the EJP RD actions as part of the annual planning and in connection to WP3 (Sustainability) and WP4 (Ethical, Legal and IPR framework);
- To prioritize topics for the joint transnational calls (JTCs) to be implemented within Pillar 1;
- To feed the medium and long-term RD research and innovation strategy in collaboration with IRDiRC;
- To prepare a Scoping Paper to be promoted (and implemented) by the national mirror groups and within the current and forthcoming EC Framework Programme.

Therefore, the Objective of the Scoping Paper is to transmit (internally in the EJP RD and externally, from the EJP RD), a summary of the mapped R&I needs identified, for more focused actions. Del 2.9 helps to assess progress and contributes to long-term strategy of the EJP RD

## 2. Methodology

As it has been explained in the Introduction, given the premises set by the general objectives of WP2, deliverables D2.1, D2.2 and D2.4 are taken as reference in the project to reformulate the outcomes of the mapping and prioritization activity which are regularly monitored and updated, according to the needs in a continuously changing scenario. This flexibility is indeed needed to keep the project aligned with the real current needs in the field of rare diseases research.

### 3. Summary Results

EJP RD pursues the fast translation of research results into clinical applications and uptake in healthcare with a remarkable potential for research and innovation (R&I), supporting key policy recommendations for addressing rare diseases (RD).

Identifying and regularly updating the research and innovation needs leads to a regular and controlled mapping exercise, that is a crucial operation for the accurate construction and information of the Annual Work Plans (AWPs). It should be pointed out that as all the major activities were already accurately detailed in the proposal of the EJP RD that was approved by the European Commission, there should only be a need (if any) to apply the prioritization strategy to those major activities in exceptional circumstances for major reasons. This year 2020, for instance, COVID-19 pandemic caused by SARS-CoV-2, has impacted almost all the activities worldwide. However, the contingency plan in the EJP RD for each task, work package and Pillar has prevented any significant deviation from the proposed activities, and some mitigation measures have been implemented. On the other hand, as the project itself included also a part of flexibility of the Annual Work Plans, it can be useful for task and subtask leaders to adopt the prioritization strategy to establish the most convenient order of the activities of each Annual Work Plan.

The summary document on mapped R&I needs is generated yearly and sent to the Policy Board and ExCom as a basis for the prioritization activity of the research and innovation needs of the EJP RD. It contains, through different sources, the inputs from different types of stakeholders, going even beyond the EJP RD beneficiaries and their Linked Third Parties and expanding to the domains of “Diagnosis & Healthcare”, “Regulatory & ethics (including the open data & science issues)” and “EU competitiveness and innovation”.

The contributions and inputs collected for the mapping exercise comprise:

- Internal inputs from the EJP RD Operating Group
- National and EU needs represented by the EJP RD Policy Board and in connection to National Mirror Groups (to date still under construction in many countries)
- Yearly analysis of the state of play of funded research and drug development, overlaps and trends at international level (based on data collected in Pillar 2, WP 11, task 11.2)

- International research strategy developed by the International Rare Diseases Research Consortium (IRDiRC) and represented by its Scientific and Constitutive Committees.

Besides these fundamental sources, other relevant elements for the mapping of 2020 were:

- Information obtained from reports and publicly available documents produced by EURORDIS ;
- information coming from ERNs
- data regarding Joint Transnational Calls
- Information coming from IRDiRC's documents and products
- data from the European Commission (Horizon Programme)
- data from existing infrastructures, extracted from ESFRI, the European Strategy Forum on Research Infrastructures
- other sources of information, like articles, reports, scientific literature, or formal documents of previous EU projects, among others.

### Summary of the prioritization criteria from D2.1 and D2.2

The main points of the prioritization aims, criteria and process reported in D2.1 and D2.2 are summarized below in order to provide these tools together with the mapping of the R&I needs, so they can be prioritized for further actions.

#### D2.1, "Final list of prioritization criteria".

It states that the aims of the prioritization activity are:

- to support and assess the decision-making process to prioritize mapped needs and actions that contribute to the EJP RD objectives
- to facilitate the planning of future actions within the Annual Work Plan
- to prioritize choices and actions in case of onset or need of deviation from planned activities
- to further ameliorate the criteria, indicators and methodology used for the process of prioritizing, after assessing the impact of the decisions taken.

A set of four wide scope prioritization criteria, also defined in the D2.1 document and applicable (accordingly particularized) to each Pillar of the EJP RD, is composed of:

- i. scientific evidence aspects
- ii. demands of the RD community
- iii. regulatory concerns
- iv. financial and technical feasibility.

Different aspects for each criterion may be used depending on the Pillar and specific activity to which they need to be applied.

For a detailed description of the single criteria and a list of possible aspects for each Pillar see D2.1 and its Annex.

The list of prioritization criteria is meant to be updated and reviewed before the definition of each Annual Work Plan if needed, to better approach the real needs of the EJP RD.

D2.1 is in close relation with D2.2 (“Prioritization scheme for EJP RD actions, including decision-making process”) and should be read and implemented in conjunction with the content of D2.2. Such D2.2 focuses on giving details on how to apply the criteria to the prioritization process and guidelines on the prioritization and decision-making process, respecting the principles of transparency and non-arbitrariness, to achieve the goals of the EJP RD for the benefits of patients. Four main categories for prioritization have been identified for the the different elements that are subject to prioritization: (i) must be done (ii) should be done (iii) could be done (iv) will not be done.

D2.2, “Prioritization Scheme for EJP RD actions, including decision-making process-Guidelines for prioritization”.

It provides different practical methods that have proven to be effective in the reviewed literature and that will ensure homogeneity in the EJP RD activities, as well as flexibility to adapt to the emerging specific needs of the project.

For the 9 steps of preparation of D2.2 adopted by WP2 components and the premises (16 items) regarding the elaboration of the prioritization and decision-making process see the public deliverable D2.2.

The main methods of the prioritization process summarized in D2.2 derive from the review of the scientific literature, describing several different methods rather than a single best practice, in line with the prioritization strategy adopted by the WHO.

From that analysis general solutions, encompassing qualitative and quantitative methods and going from the simplest to the more complicated, are presented and discussed:

- Simple qualitative assessment of the different activities, and further voting/agreement
- Qualitative assessment of the different activities through a SWOT analysis and further voting/agreement
- Quantitative assessment of the different activities, based on just one criterion
- Quantitative assessment of the different activities, based on 2 or more criteria, with all the criteria equally considered
- Quantitative assessment of the different activities, based on 2 or more criteria, with different weighing of the criteria.

For the detailed description of the above mentioned solutions see the public deliverable D2.2.

Moreover, the main steps identified in D2.2 for the prioritization process of the EJP RD, starting from the recognition and deepening of a situation that needs prioritization and decision-making and ending with the final agreement/consensus are analyzed and discussed.

The decision-making process is described as the process of making choices by identifying a decision, usually after gathering information and assessing alternative resolutions.

The levels and governance structures of the EJP RD who might face a decision-making process are listed in D2.2 in their bottom-up order, as well as the Satellite Boards, which complement the decision-making process of the project.

Moreover, D2.2 illustrates a 9-step decision-making process to help taking more deliberate, thoughtful decisions by organizing the most convenient alternative possible for the purpose of the EJP RD and the RD Community in general. Some procedures and methods that can be applied transversely to any element of the EJP RD as tools to facilitate the planning of future actions are therefore provided.

#### D2.4 "Second Summary document on Research and Innovation (R&I) Needs"

It constitutes the second output, of the series to be produced annually up to 2023, on the collection and mapping of the EJP RD R&I needs,



D2.4 focus on the outcomes corresponding to year 2020 and updating the results of the First Summary Document on R&I Needs (D2.3).

It also has to be mentioned that, apart from the sources below specified, the production of D2.4 integrates the focus on a new Horizon Programme (2021-2027), as well as the exceptional health and social situation given by the COVID-19 pandemic.

Section 3 of D2.4 discusses extensively the results of the Summary Results on R&I needs.

### **Some of the main sources consulted to identify the R&I needs**

1. Data on the R&I needs coming from Patients, with the active engagement of public and Patients in research. A continuing and consistent patients engagement/involvement is expected to build-up a major source for identifying and prioritizing the needs

2. Data on R&I needs coming from the European Reference Networks (ERNs) and researcher's surveys. In 2019, the survey provided as an outcome of Subtask 10.2.2 of the EJP RD, addressed ERNs' needs. The results were presented at the Pillar 2's First Annual Retreat meeting (22-24 May 2019, ISS, Rome), whereas the survey launched in April 2020 by Task 10.2.2 addressed researchers. Preliminary results of this second survey were presented at the Pillar 2's Second Annual Retreat meeting (4-6 May 2020, ISS, Rome) a meeting that was adapted as online due to the COVID19 situation. ERNs purposes turned out to be more concentrated on improving diagnostics and innovative care, while researchers responding to the survey seemed more focused on developing disease models and on understanding the mechanisms of the diseases.

3. Data from JTCs, decided after deliberations with several Scientific External Advisory Bodies (including the IRDiRC Scientific Chairs), on the needs of the RD community and the possibilities and interests of the funding agencies. Topics are built annually by WP2, Task 2.3, Pillar 1 leaders, WP6 representatives and the Coordination, before validation by the Executive Committee and the Board of Funders.

The EJP RD-JTC 2019 topic was research to accelerate diagnosis, whereas the EJP RD-JTC 2020 topic regards "pre-clinical research to develop effective therapies for rare diseases", with subsequent research areas that are based on the perceived needs and interest for the RD community at large.

Currently, the 2021 Call is under the process of identification of topics, refinement and launching.

4. IRDiRC's contributions to the delineation of R&I needs. IRDiRC's overall vision, that reflects the need of people living with a RD to be timely diagnosed and to have an integrated care pathway, is itemized in three goals for the period 2017-2027, that regarding R&I needs cover diagnosis, treatment and the assessment of their impact.

The most recent TF launched by IRDiRC that could feed the mapping of R&I needs are:

- Chrysalis Project
- Integrating New Technologies for the Diagnosis of Rare Diseases
- Shared Molecular Etiologies
- Rare Disease Treatment Access Working Group
- Clinical Research Networks for Rare Diseases
- Indigenous Population
- Identification of barriers to patient participation in RD research and recommendations to remove them

EJP-RD is lined up with IRDiRC Goals. IRDiRC goals responds to three groups of R&I needs, around diagnosis, treatment and impact. The work carried out by IRDiRC Task Forces (TF) on specific topics for RD, are also relevant for understanding the needs on R&I, since they work through the identification of barriers, gaps and needs that should be covered in RD research, targeting projects and ascertaining actions that can obtain results and represent a solution to RD research obstacles.

5. Data regarding existing infrastructures ESFRI (the European Strategy Forum on Research Infrastructures). The 2021 ESFRI roadmaps, focused on clustering of Research Infrastructures, their horizontal linkages and the projection of the Open Science concept, including social and global challenges, will cover topics that may be easily applicable to RD research needs.

The ESFRI landmarks that include RD research in their goals, established in the last roadmap are:

- ESFRI Landmark EATRIS ERIC (European Advanced Translational Research Infrastructures in Medicine)

- ESFRI Landmark ECRIN ERIC
- EPCTRI (European Paediatric Clinical Trial Research Infrastructures)
- Biobanking and BioMolecular Resources Research Infrastructure (BBMRI-research infrastructure for health research in Europe by providing a gateway for access to biobanks and biomolecular resources coordinated by the National Nodes)
- European Research Infrastructure for the generation, phenotyping, archiving and distribution of mouse disease models (INFRAFRONTIER-provides access to animal models and research tools with associated data to the biomedical research community, enhancing medical research in multiple conditions, including the group of rare diseases)

6. Data from the European Commission, with the next Horizon Europe (2021-2027) still under construction. The results of the EU Research and Innovation Days' dedicated session to RD will guide the future needs of R&I.

7. Data from the Directorate-General for Research and Innovation of the European Commission, recognizing the essential need of collaboration at European and international level for the progress in the RD field.

## **4. Conclusions and next actions**

EJP-RD is consistent with IRDiRC goals, which pivot around the R&I needs for diagnosis, treatment and impact. IRDiRC activities, in particular its TFs, provide significant inputs on barriers, gaps and needs; even though IRDiRC TFs may work on specific RD issues, their conclusions can be exploited at a broader level, to face challenges and overcome obstacles for RD research.

The engagement of patients and the rest of stakeholders allows a broad cooperation at a large scale, with research and clinical global networks, especially relevant for undiagnosed diseases. Advancement in complementary approaches to improve research with phenotypic data and genomic information is enhancing the translation into diagnostics. In the same framework, improving therapies and drug development on a global scale with innovative approaches (e.g. small clinical trials, data benefits, natural history studies), and research on methodologies for new and more efficient approaches and processes, with research on measurement of health outcomes and impact assessment, including utilities and costs, is still a need for R&I.

R&I needs recognized by patients highlight the improvement of healthcare pathways through patients' empowerment and collaborative processes, including the relevance of data strategies, especially for ERNs (European Reference Networks).

Maintaining the synergies with ERNs is relevant for the research community and policy makers, as well the collaboration with other stakeholders, to impulse innovation.

To date, two surveys on research needs have been launched in EJP RD, one addressed to ERNs and another to researchers-community. The results are depicted in Deliverable 2.4, with specific attention to differences and challenges they face when conducting research. ERNs' purposes are higher for improving diagnostics and innovative care, while researchers responding to the second survey are more focused to develop disease models and understanding the mechanisms of the disease. ERNs use mostly patient information, natural history, biological samples, electronic medical health records, phenotypes and medical images as data types, whilst researchers use more biological samples, phenotype and genotype data. Researchers face difficulties to access to health data and would favour collaborations with clinicians to facilitate the access to patient samples and the clinical aspects of the diseases. Both for ERNs and researchers' community share interest in: collaboration, data-sharing, and education/dissemination of information, facilities to find patient registries, biobanks and software are important for research, favouring fairness of data (time, money, workflow and workforce saving), large interest in clinical/translational research guides and templates. Barriers such as complex procedures and legal issues and use of data still represent an obstacle for both ERNs and researchers. Lack of knowledge on existing resources adds up to this, and lack of general understanding on standards and data FAIRification concepts.

Ethical, legal and social implications (ELSI) remain an area of special interest regarding needs on R&I. Related issues as research on the assessment of equality and equity, at any level, and research on ELSI itself have demonstrated to be essential in innovation in this area.

Overall, the Scoping Paper represents a perspective synthesis of the deliverable 2.4 on Research and Innovation; it also points out issues to be addressed by further actions as well as the standpoints of the different actors.

The outcomes and conclusions will be extended and updated yearly through the next Scoping Papers, based on the inputs from the Consortium.

The EJP RD-JTC 2021 will be launched at the end of year 2020 and opportunities to enhance RD research are envisioned with the new programmes under

preparation, as the new ESFRI (European Strategy Forum on Research Infrastructures) roadmap for 2021, the upcoming European Commission (EC) Framework Program Horizon Europe 2021-2027, and the continuous support of the Directorate General for Research and Innovation of the EC.

The creation of a framework for National Mirror Groups, still in development, will also aid to bring closer results of the EJP RD to the community and, on the other hand, to obtain the feedback necessary to the EJP RD project to acknowledge needs on research and innovation.

The R&I needs of the EJP RD are under continuous monitoring and updating, and the results of the mapping exercise on R&I are formulated in a series of summary documents,

The list of prioritization criteria is regularly updated before the preparation of each Annual Work Plan if necessary, to better approach the real needs of the EJP RD. The prioritization scheme and decision-making process can be considered as a useful transversal tool that can be adopted in each Pillar of the EJP PD to facilitate the planning of future actions

The present Scoping Paper will be transmitted to leaders of task 2.3, 2.4 and 2.5 of WP 2 for complementary actions for the achievements of the EJP RD objectives.