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Del 2.17
List of research and innovation needs requiring medium- or long-term approach and related Task Forces

Organisation name of lead beneficiary for this deliverable:
Partner 1 – INSERM

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Table of Contents

1. Background

The management of the medium and long-term research strategy questions and their dedicated linkage with Task Forces of the International Rare Diseases Research Consortium (IRDiRC) is part of the WP2 – Strategy, Task 2.4 in EJP RD.

As a reminder, IRDiRC unites national and international governmental and non-profit funding bodies, companies (including pharmaceutical and biotech enterprises), umbrella patient advocacy organizations from all over the world to drive and promote international collaboration and advance rare diseases research strategy worldwide. It's overarching vision for 2027 is to "**Enable all people living with a rare disease to receive an accurate diagnosis, care, and available therapy within one year of coming to medical attention".** Many of the EJP RD countries and the European Commission are also members of IRDiRC and participate actively in different committees. Furthermore, the Chair and Vice-Chair of IRDiRC are members of EJP RD Policy Board. Finally, the Scientific Secretariat (SciSec) of IRDiRC is ensured by the coordination team of the EJP RD. Such strong connection is a mutual advantage and prevents duplication of efforts.

It is important to underline that EJP RD agreed that close collaboration and follow up of the IRDiRC goals and strategic recommendation is central to all EJP RD actions and thus no specific Scientific Board have been established within EJP RD. However, the EJP RD consortium has the possibility to analyse the RD landscape and propose relevant complementary actions that are of benefit for all RD community. This is being done in collaboration with EJP RD Policy and Governing Boards. **The content of this deliverable describes the list of pre-identified research and innovation needs that are either complementary or subsequent to IRDiRC Task Forces.** It is also possible that some of the topics are relevant only to the European or national needs expressed by the members of the EJP RD Policy Board.

It was agreed that any research strategic question or need identified by the EJP RD Policy Board as requiring medium or longer-term approach will be studied in relation to the ongoing or future Task Forces planned within IRDiRC activities.

At present, each of the IRDiRC Scientific (Diagnostics, Interdisciplinary, Therapies) or Constituent (Funders, Patients Advocacy, Companies) Committees has the possibility to seize upon specific RD research need or bottleneck and propose a Task Force aiming at issuing recommendations or concrete actions to overcome the identified obstacle. These proposal are evaluated, prioritized and submitted to the final validation vote of IRDiRC Consortium Assembly.

Whenever an issue recognized by Policy Board is either of national or EU-specific nature, a dedicated, IRDiRC-independent Task Force(s) or actions may be proposed. Any other issue with identified synergy to IRDiRC TF will be proposed and treated jointly. Finally, needs/questions of international relevance, not yet treated by IRDiRC could be proposed as subjects for new collective Task Forces to IRDiRC CA and included in its annual Roadmap after prioritisation and validation process by IRDiRC bodies.

The setting up of a Task Force (TF) follows a well-established scheme proposed by IRDiRC, composed of the following steps:

i. Analysis and preparation of background document;
ii. Call for experts to constitute TF working group;
iii. Establishment of TF work plan;
iv. Up to 12 months of work including regular conference calls;
v. Production of final recommendations and/or roadmap to be followed by the engaged stakeholders (enquirers);
vi. Dissemination.

Usually, the EJP RD Coordination office (including IRDiRC SciSec) is be responsible for the management of the Task Forces. However, in case of additional actions proposed and considered of high importance the involvement of additional partners on both EJP RD and IRDiRC side would be expected.

2. Pre-identified research and innovation needs and challenges

2.1. Methodology

The focus of this deliverable is different and complementary to the Del. 2.3 (First) and 2.4 (Second) "Summary document on Research & Innovation Needs" that were also used for this analysis and that focus on the overarching study of research and innovation needs of rare diseases community. **The goal of the Del.2.17 is to provide**

guidance only for research and innovation needs that require medium (2021-2023) and long-term (next phase of the EJP RD – beyond 2023) actions and that could be transformed into future Task Forces.

The following elements were analysed, and their content/conclusions captured into few thematic groups of converging interest:

- The recommendations provided by the Policy Board during the First EJP RD Policy Board Meeting[1]
- The expected outcomes of currently running IRDiRC Task Forces and Working Groups and their potential impact on the medium- and long-term strategic approaches
- The IRDiRC long term plan (emerged from a mapping exercise conducted by Funders Constituent Committee back in 2017 in response to newly launched IRDiRC goals 2017-2027) that identified 14 priority actions calling upon short-, medium- and long-term implementation to reach the IRDiRC's objectives.
- Deliverables 2.3 and 2.4 (first and second summary documents on mapped research and innovation needs)
- The contribution of EURORDIS to the public consultation on Horizon Europe
- The Rare 2030 Foresight in Rare Diseases Policy scenarios[2]
- The Chan Zuckerberg Initiative "Rare As One Project"[3]
- The newly initiated work of EJP RD done in collaboration with C-PATH RDCA-DAP[4].

2.2. Research and innovation needs

All themes identified below were categorised based on the Rare 2030 favored scenario "***Investments for Social Justice"***. Each theme is preceded by a short description of the need and includes a list of pre-identified challenges to address from ongoing, foreseen or initially proposed (but not implemented) IRDiRC Task Forces as well as other recommendations pinpointed in the analysed documents. Some options for possible types of support (also going beyond Task Force implementation) are indicated.

2.2.1. Theme "Data"

- **The need:**

"Growing evidence-base (is) achieved through comprehensive health data collection that goes beyond consumer and profit driven companies. Data is shared smoothly across borders through systems that are interoperable and infrastructures that are connected. Health data governance frameworks that are legally, ethically sound, do not compromise patients' safety and respond to their needs."

[1] EJP RD_Policy Board_2019-07-04_minutes slides_VF
[2] https://www.rare2030.eu/trends/
[3] https://chanzuckerberg.com/science/programs-resources/rare-as-one/
[4] https://c-path.org/programs/rdca-dap/

- **Pre-identified challenges:**

Challenge 1: Sustain the common ERN and RD community (virtual) data platform and its customisation ability to address arising research and care needs *(source: EURORDIS "No time to lose: Building a data strategy for the ERNs")*

and

Challenge 2: Enable Healthcare (including genomics) Data access for research purposes *(source: EURORDIS "No time to lose: Building a data strategy for the ERNs" and 1+ Million Genomes initiative and EJP RD Policy Board recommendation)*

Possible type of support:

- FUNDING: funding instruments convergence; non-competitive stable block funding mechanism; multi-stakeholder contractual in-kind contribution including patient organisations and industry;
- POLICY: support wider policy agenda on the digital transformation of health and care – could be supported by a dedicated TF?
- OPERATIONAL: Development and integration of the ERN comprehensive data strategy in EJP RD developments (including the "federated" Virtual Platform) [e.g. starting with the identification, contribution and the implementation of the ERN prioritised use-cases/scenarios into EJP RD development process]

Challenge 3: Establish a process for standards and ontologies integration or use across multiple datasets, databases, warehouses and data lakes *(source: EJP RD C-PATH RDCA-DAP working group, IRDiRC priority action, EJP RD Policy Board recommendation)*

Possible type of support:

- POLICY: could be supported by a dedicated Task Force
- OPERATIONAL: use case/proof-of-concept study (the International Charter for data sharing (including biological samples and genomic data) developped by RD-Connect and that received the label by IRDiRC as a recognised resource should be taken into account)

Challenge 4: Establish a process for transatlantic (personal pseudonymised) data processing for secondary research addressing GDPR *(source: EJP RD C-PATH RDCA-DAP working group)*

Possible type of support:

- POLICY: could be supported by a dedicated Task Force
- OPERATIONAL: use case/proof-of-concept study (leverage on previous IRDiRC TF including the PPRL one)

Challenge 5: Develop processes and Implement recommendations for the regulatory acceptability of RD data (e.g. CDISC implementation, HMA-EMA Joint Big Data Taskforce recommendations implementation, EMA Cross-Committee Taskforce on Registries) *(source: EJP RD C-PATH RDCA-DAP working group)*

Possible type of support:

- POLICY: could be supported by a dedicated Task Force
- OPERATIONAL: use case/proof-of-concept study

2.2.2. Theme "Innovation in diagnostics and therapies"

The need:

"Needs-led innovations continues and are evaluated with greater transparency, accountability, cost-effectiveness. Preventative, rehabilitative and palliative needs of people living with rare diseases are better understood."
people living with rare diseases, their families and all citizens are mobilized to be actively involved in policy decisions in a highly competitive innovation market.

Pre-identified challenges:

Challenge 6: Development of clinical trial methodology Framework exploiting Model-Informed Drug Development Tools (for design and analysis optimisation) *(source: EJP RD C-PATH RDCA-DAP working group)*

Possible type of support:

- OPERATIONAL: use case/proof of concept study complementary to the actions implemented in EJP RD (WP20)
- POLICY: possible Task Force targeting regulators

Challenge 7: Alternative business models for rare disease drug development *(source: IRDiRC priority action, Eurordis recommendations to HE)*

Rationale for IRDiRC action: IRDiRC's main goal is to promote rare diseases research globally. In recent years, new business models (e.g. patient-led R&D efforts) – alternative to the predominant pharmaceutical and academic R&D models – have emerged to address remaining patient unmet need, specifically in under-researched and/or low prevalence rare conditions. We recommend launching an IRDiRC Task Force to investigate the reality, strategy and operations, and overall value of these new business models. The main aim of the project is to identify key take-aways and potential recommendations to IRDiRC stakeholders regarding the suitability and key recurring elements on alternative business models for development and commercialization of orphan drugs. The non-commercial routes to clinic for cases with no positive return scenarios should also be considered.

Possible type of support:

- POLICY: joint Task Force

Challenge 8: Repurposing *(source: IRDiRC priority action; Eurordis Round Table of Companies workshop on repurposing; Eurordis recommendations to HE; action of interest for EC)*

Rationale for IRDiRC action: Although the field of rare diseases could benefit largely from the datamining and repurposing opportunities, their potential is not fully realized, and the current incentives and programmes do not seem to suffice to foster the interest of developers for these types of approaches. In

addition, from the patient's perspectives point of view, the identification of off-label use of therapies, which might be good candidates for being repositioned and licensed in these rare indications, is to be put in balance with the fact that some previous attempts have led to an increase of the price of products. In this latter case, instead of improving the access of patients to therapies, it has had the reverse effect. This Taskforce will explore both the Building Blocks (incentives, regulatory tools, initiatives, development tools) that exist or are missing for public and private developers, as well as the type of business model which would close the gap between attractiveness for developers and access to therapies for patients.

Possible type of support:

- POLICY: joint Task Force (EJP RD, IRDiRC, EC, ERTC?)
- OPERATIONAL: series of workshops and trainings

2.2.3. Theme: Patient needs driven rare diseases research

The need:

Multistakeholder initiatives prioritize investments in rare disease research that responds to patient needs thus focusing on as many diseases as possible and not just focusing on low hanging fruit.

Pre-identified challenges:

Challenge 9: "Disregarded rare diseases" *(source: IRDiRC priority action, Eurordis recommendation to HE, Rare 2030)*

Rationale for IRDiRC action: To identify which are and what characteristics share those rare diseases that are currently not attended by academic research and industrial development alike, in order to understand what are the roadblocks shrinking the chances of seeing effective treatments developed for these diseases in the near future. To increase the interest in rare diseases, it is expected that some specific (minimum) conditions must be fulfilled to facilitate the uptake by industry and/or to maximize the potential of already existing research. Identification of key criteria that would make industry research and development in rare diseases attractive (in terms of investments of time and resources) is therefore critical to ensure an ongoing pipeline of progress. Funders (both public and private) have scientific programmatic interests in various diseases but the work that they fund can improve the barriers to entry for therapeutic research investments (e.g., via natural history studies, patient registries, epidemiology studies) or to "de-risk" critical aspects at pivotal stages of development. Based on the results of this analysis, potential recommendations to funders and developers to overcome existing limitations and roadblocks for research and development for these "disregarded" diseases should be provided.

Possible type of support:

- POLICY: is partially supported by IRDiRC Task Force but will require additional support for full development
- OPERATIONAL: series of workshops and trainings
- FUNDING: follow up funding and strategy on investment
- FUNDING: support for new patient-led RD projects (depending on the level of the research – roadmaps, basic research, therapy development, engagement with different stakeholders etc.)

Challenge 10: Relevant RD biomarkers and modifier discovery and validation *(source: IRDiRC priority action; EJP RD C-PATH RDCA-DAP working group)*

Possible type of support:

- POLICY: joint Task Force
- OPERATIONAL: use case/proof of concept study
- FUNDING: follow up funding and strategy on investment

Challenge 11: Foster Patient Centricity in research design and conduct – how to move from research projects "accompanied by patients" to research projects "driven by patients". *(source: Rare 2030, Chan Zuckerberg project, EJP RD PENREP work)*

Rationale: Support to urgencies identified by patients - No one knows a disease better than those who live it every day. Patients' active involvement is critical for accelerating the development of treatments. Science happens at its own pace, often with slow movements toward new treatments. Rare disease patients and advocates have a different level of urgency that can drive the field to move at an accelerated pace.

Possible type of support:

- OPERATIONAL: series of workshops and trainings
- FUNDING: support for new patient-led RD projects (depending on the level of the research – roadmaps, basic research, therapy development, engagement with different stakeholders etc.)

Challenge 12: Patient registries *(source: Eurordis recommendations to HE, EURORDIS "No time to lose: Building a data strategy for the ERNs)*

Rationale: support to community ownership of the registry and data in order to ensure that the assets are enduring, longitudinal resources for the patient population that are not subject to disruptions in funding, resources, and business priorities or impacted by proprietary or legacy ownership restrictions). Patient registries must be built with a modular framework, with the agility and ability to expand as studies progress, incorporating new data elements and measurement tools as scientific discovery continues to evolve and in-depth disease-specific knowledge emerges.

Possible type of support:

- OPERATIONAL: support for FAIRification of existing patient registries
- FUNDING: support to patient-led registries

2.2.4. Theme "Health(care) Policy"

The need:

societal responsibility, equity and the regulatory frameworks. European Union's increased legislative power in areas of health and social welfare healthcare systems are led by these holistic patient needs.

Pre-identified challenges:

Challenge 13: Healthcare model for rare diseases as a model for other health services and health threats *(source: Rare 2030, EJP RD Policy Board recommendation)*

Possible type of support:

- POLICY: joint Task Force
- OPERATIONAL: use case/proof of concept

Challenge 14: Accelerate identification and recruitment of RD patients in studies *(source: IRDiRC recommendation)*

Challenge 15: Create globally inclusive methodology for counting RD diagnostics and therapies and Qualify the number of RD patients who receive diagnosis and treatment to ensure that research reaches and benefits patients *(source: IRDiRC recommendation)*

Challenge 16: Strengthen collaboration with EU13 and Nordic countries *(source: EJP RD Policy Board recommendation)*

Possible type of support:

- POLICY: specific EU-level Task Force
- FUNDING: engagement of Nordic countries in funding activities
- OPERATIONAL: partially covered by EJP RD targeted actions (widening, dedicated trainings, dedicated strategic approaches)

Annex:

Rare2030 scenario: SCENARIO - ***Investments for Social Justice***

If we prioritize **societal responsibility, equity and the regulatory frameworks** to achieve them, we will end up in the ***Investments for Social Justice*** world where **major investments have been made by governments and are equally shared across Europe to ensure the health and well-being of all European citizens** – including those living with a rare disease. The **European Union's increased legislative power in areas of health and social welfare** reduces the risk that patients in some European countries are left behind.

Not only the curative, but **also the preventative, rehabilitative and palliative needs of people living with rare diseases are better understood**. As such, **healthcare systems are led by these holistic patient needs** and are driven by better outcomes based on a **growing evidence-base achieved through comprehensive health data collection that goes beyond consumer and profit driven companies**. **Data is shared smoothly**

across boarders through systems that are interoperable and infrastructures that are connected.

Multistakeholder initiatives prioritize investments in rare disease research that responds to patient needs thus focusing on as many diseases as possible and not just focusing on low hanging fruit. The **resulting innovations are evaluated at the European level and with greater transparency, accountability, cost-effectiveness** and considering the patient experience. Given the limitation in government funding and regulations required of increased collaboration, cutting edge innovations may develop much more slowly but despite a lowered competition, **needs-led innovation continues** in the long run. **Existing medicines, non-pharmaceutical treatments and assistive technologies are affordable and equally available** no matter where you live in Europe. The **healthcare model for rare diseases has become a model for other health services and health threats** where the system is resilient enough to tackle both acute and long-term patient needs. **Centres of expertise dedicated to care for rare disease are well-identified, well connected to local primary care as well as to networks within and outside the country**. To ensure sufficient funds for these networks, **health care decisions are not only driven by cost savings and governments are able to increase the proportion spent on healthcare**.

To achieve this scenario **people living with rare diseases, their families and all citizens are mobilized to be actively involved in policy decisions in a highly competitive innovation market.** The field of rare diseases has played a pioneering role in promoting such a deep change in European health and social policy.