Report

IRDiRC Consortium Assembly Meeting

16-17 October 2024
Milan, Italy

IRDiRC
INTERNATIONAL
RARE DISEASES RESEARCH
CONSORTIUM

MEETING REPORT CONTENTS

THE REPORT

The International Rare Diseases Research Consortium (IRDiRC) organized a meeting of the Consortium Assembly (CA) on October 16-17, 2024, in Milan, Italy, in partnership with **Fondazione Telethon**. A total of 32 participants attended the meeting in-person in Milan and 2 project managers representing the Scientific Secretariat.

1. New IRDiRC Members

IRDiRC is pleased to announce the addition of new members and representatives to the Consortium. We extend a warm welcome to all.

- New Members of the FCC
  - **Hope for Rare Foundation**, China. Represented by Boya Yu, Project Manager.
  - **National Rare Diseases Registry System**, China. Represented by Zhang Shuyang, President.
  - **China Alliance for Rare Diseases (CHARD)**, China. Represented by Linkang Li, President.

- New Members of the PACC
  - **Wilhelm Foundation**, Sweden. Represented by Helen Cederroth, Founder.

- Change of representation
  - **INSERM**, France, represented by Emmanuelle Genin (Director of INSERM Thematic Institute Genetics, Genomics & Bioinformatics).
    - *Alternate representative*: Daria Julkowska (Assistant Director, Thematic Institute of Genetics, Genomics & Bioinformatics, INSERM, and ERDERA Coordinator).
  - **Ultragenyx**, Switzerland, represented by Marta Valente (Vice President Head of Medical Affairs Europe).

2. Parallel Sessions

- *Funders Constituent Committee*

  - Participants discussed how can IRDiRC funders better support patient engagement in research projects as patient groups can raise money for research but then need scientific, administrative and funding support to get involved into the multiple steps of the projects. The following practices have been described by FCC members to support patient engagement:
    - Patient involvement in the identification of research priorities
    - Inclusion of patients in all the steps of the call process i.e., launching the call, proposal review, project monitoring
    - Funding of patient partnerships within the projects
    - Supporting fund management

- Development of training courses and guidelines on patient engagement in research activities
- Multi-stakeholder events to connect patients with researchers, clinicians, industry representatives

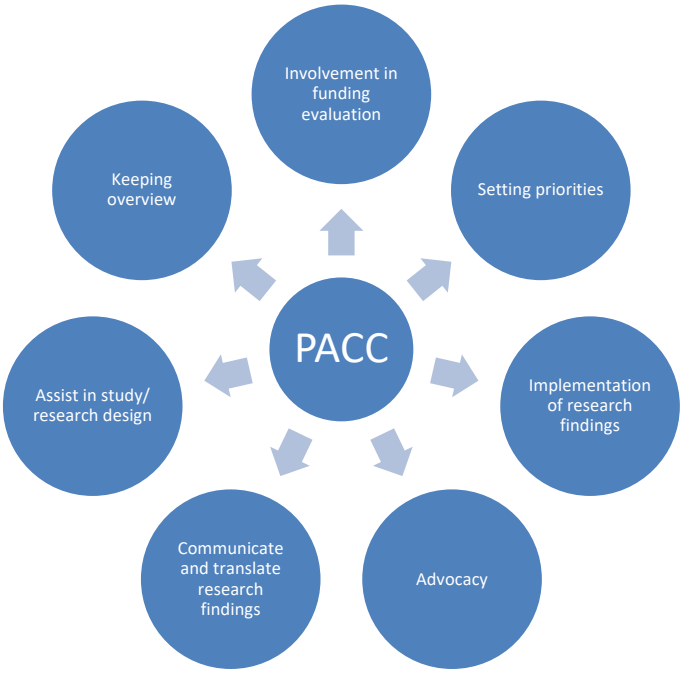
- FCC members agreed to put their best practices in a report so funding agencies can have an overview of what is being made, what is of value, and what they are missing.

➢ *Companies Constituent Committee*

- The session started with a short presentation of the consortium structure and activities to the new members, followed by a proposal to have a topic endorsed by the Companies Constituent Committee for the next Roadmap 2026, that will better reflect the committee's vision and priorities.
- One of suggested topics – **Clustering of diseases** – could be impactful in the funding calls. Ideally the group should engage with other groups/committees. The medical devices could constitute an interesting topic, as there are many small-medium enterprises (SMEs) that are developing such devices for bigger companies, however taking ownership for certain tools might be difficult as it needs to be in pre-competitive space.
- The group discussed also on the identification of synergies between the companies' part of the consortium and how it will be possible to leverage the type of work based on route of administration, and device-combination products.
- Advancing on shortening time to diagnosis within one year of coming to medical attention could also be a potential topic for development; or patient identification for treatment which raises a lot of difficulties currently in terms of recruitment for clinical trials. Having a state-of-the-art on how well is the healthcare system prepared to find patients when the companies provide treatment options, what are the discrepancies between diagnostic gaps and therapeutic availability, how the focus can be switched from "*diagnosis per se*" to patient identification, as several issues are around recruitment still persist (e.g. Duchenne project in UK, a model which cannot be applied in other countries). In addition, what is the diversity in clinical trials? As the focus is more on the public health, stigma represents an issue that touches the patients participating in clinical trials.
- Collaboration between public institutions and private sector for early diagnosis – What infrastructure could be used? How the laboratory capabilities and limitations will be handled? Having complex databases could pose difficulties in terms of data collection and quality. Moreover, the patient perspective is sometimes missing from the whole research process.
- Priorities for the next period:
  - **Novel endpoints for drug development** – how to come to an agreement between companies involved in the same therapeutic area and how to perform the alignment between EU and FDA and other local regulatory agencies.
  - **Biomarkers or surrogate endpoints to accelerate approvals**.

➢ *Patient Advocates Constituent Committee*

- During the PACC parallel session, the PACC committee members aimed to clarify the role of the PACC, as to further focus the involvement of PACC members in IRDiRC. They first discussed the different roles PACC members can play in research within the IRDiRC context. These different roles are highlighted in the figure below.



- After this discussion on the potential roles, the PACC then entered a discussion on how these different roles could concretely be brought to practice within the IRDiRC context. Specifically, the PACC discussed:
  - The potential to participate in and shape different Task Forces, ensuring patient centeredness, priorities and translation of findings
  - To bring together and present global, overall priorities that should be addressed, setting out recommendations for the IRDiRC funders, ensuring setting priorities
  - Translate needs from patients around to world to research needs, assisting in research design
  - Review different activities as PACC, to ensure patient centricity
  - The development of a patient-led research project was brought into discussion, whereby the PACC group could channel ideas (and it could be an open/publicly available hub) where patient groups can submit research ideas from their patient constituencies to meet a need, i.e. since they live 24/7 with the condition, know the gaps etc. This is a similar approach to the UK portal (https://plrh.org/) which is a project in collaboration with Cambridge Rare. It started out for all health issues but now focuses solely on rare diseases, since the majority of suggestions were about rare diseases. They essentially screen the suggestions and check there is nothing existing/in the pipeline and then work with the patient groups to develop a proposal for funding

- The PACC members indicated the need to have a dedicated time slot at least once a year at the face-to-face IRDiRC meeting, to work on setting out the priorities gathered throughout the year.
- These different propositions would help provide a purpose and focus for the group and could potentially increase the PACC membership if there are perceived benefits.

3. Cross-Committee Exchange

➢ *Patient Advocates Constituent Committee*

- The following questions were raised to clarify the role of the PACC. What are other committees looking for in terms of patient engagement? How can PACC be critical in the functioning of IRDiRC? How does PACC participate in that process? What are opportunities but also what are the challenges?
- Participants mentioned that there is a need to clarify the mechanism for better interaction with the patients i.e., what is currently done, what is working, where are the challenges and the gaps.
- Several PACC members emphasised the need for a more structured mechanism for exchanges between the different Constituent Committees and was suggested the inclusion of PAC members in the initial discussion stages of the ideas for new Task Forces.

➢ *Companies Constituent Committee*

- The session discussed the clustering of rare diseases based on their shared molecular etiology and pathophysiology. The objective of the session was to have a discussion on what needs to happen for this strategy to have an impact at scale on discovery, development and access to therapy, including for ultra-rare diseases.
- Basket trials can overcome the problem of small population and eventually reduce the cost of drug development.
- It was mentioned that companies are disengaging from RD drug development and that therapeutic platforms, basket trials, and regulatory harmonization could contribute to reverse the trend.

➢ *Funders Constituent Committee*

- The session discussed the need for international convergence in regulatory approvals of RD therapies with a focus on Advanced Therapy Molecular Products (ATMPs)
- The FCC, the CCC and the RSC submitted a Task Force proposal to address this topic. The proposal is presented in the point 6 of this report: IRDiRC 2025 Roadmap
- It was mentioned during the discussion that harmonisation in the assessment of gene therapy could not only reduce the cost, but possibly stimulate reciprocity in access (timely and across jurisdictions).

- The European Rare Diseases Research Alliance (ERDERA) is developing a technology hub focusing on ATMPs, gene therapies, to make the available tech regulatory compliant and standardized.

4. IRDiRC Strategies

➢ *Upcoming meetings*

- Consortium Assembly meetings
  - Online CA Meeting December 9-10 (2 hours on each day)
  - In-person CA-SC meeting, March 3-4 2025, Brussels, Belgium
- RE(ACT) Congress and IRDiRC Conference in 2025
  - Back-to-back with CA-SC meeting
  - March 5-7, Brussels, Belgium
  - Venue: Pullman hotel Brussels Centre Midi
  - https://www.react-congress.org/
- Discussing partnership with China Alliance for Rare Diseases for the International Rare Disease Conference of China (IRDCC) on 24 May, 2025 at Haikou, Hainan Province, China.

➢ *Communication activities*

- Website
  - Completion of IRDiRC website transfer from OVH to new provider (o2switch) in August
  - Evaluation of website functionalities completed (September)
  - New website implementation to start soon, the communication manager is evaluating other providers for comparison prices (per new EC rule)
- Newsletter
  - New edition published for September-October
  - The participants agreed that the newsletter can be published very 3 months and prior to major events

- New publications

(1) **The complexity of funding rare disease research: an IRDiRC assessment of the landscape**
Authors: Lucia Monaco, Mary Catherine V. Letinturier, Naohiko Aketa, Dimitrios Athanassiou, Jida el Hajjar, Simon Frost, Alicia Granados, Anthony R. Haight, Anneliene H. Jonker, Susan R. Kahn, Sukhun Kang, Persefoni Kritikou, Christina Kyriakopoulou, Christopher McMaster, Samantha Parker, Daniel Scherman, Nivedita Valentine, Samuel Wiafe, Adam L. Hartman.
Task Force: Funding Models to support the spectrum of rare disease research and development

Journal: Rare Disease and Orphan Drugs Journal
Link: https://www.oaepublish.com/articles/rdodj.2024.18

(2) Leaving No Patient Behind! Expert Recommendation in the use of Innovative Technologies for Diagnosing Rare Diseases
Authors: Clara D. Van Karnebeek, Anne O'Donnell-Luria, Gareth Baynam, Anais Baudot, Tudor Groza, Judith Jans, Timo Lassman, Mary Catherine V. Letinturier, Stephen B. Montgomery, Peter N. Robinson, Stefaan Sansen, Ruty Shai, Charles Steward, Kenjiro Kosaki, Patricia Durao, Bekim Sadikovic.
Task Force: *Integrating New Technologies for the diagnosis of rare diseases*
Journal: *Orphanet Journal of Rare Diseases*
Link: https://pubmed.ncbi.nlm.nih.gov/39334316/

(3) Patient organizations: advocating for timely newborn screening and improved quality of life
Authors: Helen Malherbe, Ritu Jain, Victoria Antoniadou, Marie-Christine Ouillade, Diego Fernando Gil Cardozo, Gulcin Gumus, Nokuthula Sikhethiwe Kitikiti, Lucy McKay, Chiuhui Mary Wang
Other IRDiRC activities: Newborn Screening Initiative
Journal: Rare Disease and Orphan Drugs Journal
Link: https://www.oaepublish.com/articles/rdodj.2024.11

(4) Access in the rare disease landscape
Authors: Anneliene H Jonker, Maria Cavaller-Bellaubi, Yukiko Nishimura, David A. Pearce
Cross-commitee work (TSC + PACC)
Journal: The Lancet Global Health
Link: https://www.thelancet.com/pdfs/journals/langlo/PIIS2214-109X(24)00341-3.pdf

(5) Addressing diagnostic gaps and priorities of the global rare disease community: Recommendation from the IRDiRC diagnostics scientific commitee
Authors: David Adams, Clara van Karnebeek, Sergi Beltran Agullo, Victor Faudes, Saumya Shekhar Jamuar, Sally Ann Lynch, Guillem Pintos-Morell, Ratna Dua Puri, Ruty Shai, Charles Steward, Birute Tumiene, Alain Verloes
DSC work
Journal: European Journal of Medical Genetics
Link: https://www.sciencedirect.com/science/article/pii/S1769721224000430

(6) The state-of-art of N-of-1 therapies and the IRDiRC N-of-1 development roadmap
Authors: Anneliene H. Jonker, Elena-Alexandra Tataru, Holm Graessner, David Dimmock, Adam Jaffe, Gareth Baynam, James Davies, Shruti Mitkus, Oxana Iliach, Rich Horgan, Erika F. Augustine, Alison Bateman-House, Anna Maria Gerdina Pasmooij, Timothy Yu, Matthis Synofzik, Julie Douville, Larissa Lapteva, Daniel O'Connor, Annemieke Aartsma-Rus
Task Force: Preparing for N-of-1 treatments of patients with ultra-rare mutations

Journal: Nature Reviews Drug Discovery
Link: https://www.nature.com/articles/s41573-024-01059-3

(7) A landscape map of the Key Global Rare Disease Organisations (editorial)
Authors: Daniel O'Connor, Anneliene Jonker
TSC work
Journal: Rare Disease and Orphan Drugs Journal
Link: https://www.oaepublish.com/specials/rdodj.1523

(8) **Lessons learned from the RE(ACT) Conference on Medical Devices for Rare Diseases**
Authors: Anneliene Jonker, Tim Buckinx, Lucia Pannese, Paulien Klap, José-Alain Sahel, Marc Dooms
Post congress paper
Journal: European Journal of Medical Genetics
Link: https://www.sciencedirect.com/science/article/pii/S1769721224000685

(9) Drug device combination products in rare diseases: significance, examples and opportunities
Authors: Alexandra Tataru, Anneliene Jonker, Marc Dooms, Claudia Gonzaga-Jauregui, Marjon Pasmooij, Daniel O'Connor
TSC + ISC work
Journal: submitted to Drug Discovery Today

(10) Telehealth for Rare Disease Care, Research, and Education Across the Globe: A Review of the Literature by the IRDiRC Telehealth Task Force
Authors: Faye Chen, Melissa Parisi, Adam Hartman
Task Force: Enabling and Enhancing Telehealth for Rare Diseases Across the Globe
Journal: European Journal of Medical Genetics
Link: https://www.sciencedirect.com/science/article/pii/S1769721224000697

- *Scientific Secretariat composition*

  - Starting September 2024 and for a period of 7 years, the Scientific Secretariat is supported by the European Commission through the **European Rare Diseases Research Alliance (ERDERA)** programme.
  - The SciSec will be hosted by the Foundation for Rare Diseases, Paris, France.
  - It will be coordinated by Daniel Scherman.
  - Two project managers: Alexandra Tataru (CCC, DSC, ISC) and Galliano Zanello (FCC, PACC, TSC, RSC)
  - Communication manager (part-time): Pascale Milani

- *Scientific Secretariat budget*

- The SciSec is funded through Horizon Europe program *(exact budget distribution remains confidential to the Consortium Assembly members)*
- Following the new Horizon Europe rules, the SciSec has to prove "best value for money":
  - 3 quotes for each purchase (travel, accommodation, venue, etc)
  - Unless some justified rationale, the SciSec will have to select the least expensive option
  - With a reduced budget for the organization of internal events and no budget for publication costs, additional funds through alternative sources (e.g., Voluntary Monetary Fund) are needed in the future.

➢ *Membership definition*

- The current requirements to become a member of IRDiRC are the following:
  - National and international governmental and non-profit funding bodies, as well as pharmaceutical and biotech companies – each investing a minimum of 10 million USD over 5 years in research projects/programs in rare diseases, to engage and participate in collaborative actions thus contribute towards IRDiRC objectives;
  - Umbrella patient organizations should represent broad patients' interests for all rare diseases in at least one country or larger area, and contribute to research that shares and will advance the IRDiRC Vision and Goals (e.g., developing and providing tools to accelerate research, diagnostic and therapeutic development, evaluation of processes).
- The chair introduced the discussion about the reflections on the membership requirements and if those should be revisited to stimulate representation in some geographies, such as in Low-Middle Income Countries (LMICs).
- No elaborated discussion took place and the chair proposed to re-discuss the topic in the forthcoming IRDiRC CAs. IRDiRC Membership also foresees, Groups of Funders. There was also the suggestion to consider creating alliance or bringing on board, umbrella policy organisations, such as, the World Health Organisation (WHO).

➢ *Election of the Consortium Assembly Chair and Vice Chair*

- The mandate of David Pearce (CA Chair) and Samantha Parker (CA Vice Chair) is ending on the 31st of December 2024
- David Pearce and Samantha Parker are candidates for running a second 3-year mandate
- The Scientific Secretariat will organize an electronic vote

➢ *IRDiRC as member of the C-Path Rare Disease Clinical Outcome Assessment (COA) Consortium*

- The mission of the C-Path COA Consortium is to enable precompetitive, multi-stakeholder collaboration aimed at identifying scientifically sound tools and methodologies for collecting clinically meaningful outcomes data in treatment trials for rare diseases;
- IRDiRC, represented by Samantha Parker, has ben invited to become a member of the C-Path COA Consortium
- No objections were raised against IRDiRC joining the C-Path COA Consortium;
- The Operating Committee will now consider if the C-Path COA Consortium should also be invited to join IRDiRC.

5. Keynote presentations

- Clara van Karnebeek (DSC) - Accelerating drug repurposing for rare neurological, neurometabolic and neuromuscular disorders by exploiting SIMilarities in clinical and molecular PATHology (SIMPATHIC)
  - https://simpathic.eu/

- Vinciane Pirard (CCC) - Public-Private Partnerships: The Rare Disease Moonshot Perspective
  - https://www.rarediseasemoonshot.eu/

6. IRDiRC 2025 Roadmap

- *Methodology*

  - Six proposals were submitted to the SciSec:

    - Task Force on Regulatory Convergence (FCC, CCC, RSC)
    - Task Force on Bridging Diagnostics to Therapy and Care (DSC, TSC, ISC)
    - Task Force on Stigma (ISC, PACC)
    - Task Force on Preventive Medicines in RD (TSC)
    - Working Group on Young Patient Engagement in therapy development (TSC)
    - Models of care (ISC)

  - The proposals were assessed by the Operating Committee. The following questions were asked in the evaluation form.
    - Is the proposed activity relevant to IRDiRC Goals?
    - Are the activity-expected outcomes impactful on the rare disease community?
    - Is the proposed activity responding to urgent needs and gaps to advance towards IRDiRC goals?
    - Is the proposed activity feasible?
    - Is the proposal clearly exposed and complete in all parts?

- The top 5-ranked proposals were recommended by the Operating Committee *(from highest score to lowest score)*

  - Preventive medicines
  - Young patient engagement in therapy development
  - Regulatory convergence
  - Stigma
  - Bridging diagnostics to therapies and care

The proposal on "Models of care" was scored the lowest and didn't qualify for Roadmap 2025.

Facilitating the development of Preventive Medicines at scale for RDs

- Proposer: TSC

- Background
  - Amongst patients, industry, and policymakers there is a growing interest in disease prevention in order to improve population health, and many initiatives in non-communicable diseases have led the way in developing prevention strategies.
  - Despite this, a review of orphan designations at the European Commission shows that the vast majority of designations are for 'treatment' of a condition – currently only 80 designations are listed for prevention out of a total of 2029 EC designations (less than 4%), and the majority of these are clustered around just a few conditions.
  - This clearly demonstrates that more must be done to develop a proactive approach to developing preventative medicines at scale, rebalancing the delivery of healthcare away from acute care into prevention.

- Objectives
  - From a medicine's development perspective in small populations, what are the specific challenges that need to be resolved when successfully developing medicines in the preventative space?
  - How can the regulatory and access system evolve to support and optimise the field and mitigate the uncertainties?
  - Are there activities, incentives or policies that could help, noting the low uptake of prevention orphan designation?
  - How do we balance evidence generation from formal clinical trials versus real world data collection?
  - How do we ensure that preventive intervention opportunities from an early diagnosis are not missed, what healthcare infrastructure is needed to link the diagnosed patient to a potential therapeutic intervention?
  - How do we encourage global leadership in preventative medicines for rare disease patients?

- Foreseen impacts

- This Task Force will help provide thought leadership and practical solutions on what an optimised framework for preventative medicines will need to include, with the aim of developing a set of proposals and case studies that highlights the innovative potential and public health gains/goals in rare diseases, providing additional tools for small population research and creating future strategy and policy implications.
- This is crucial when considering the avalanche of future patients that might be presenting through newborn screening and other improvements in diagnostic capabilities, and the current lack of activity as seen in orphan designations and approved therapies to date (vast majority of which are for treatment).

Engagement of young people living with Rare Diseases in Therapy Development

- Proposer: TSC

- Background
  - Patient engagement (PE) is the effective and active collaboration of patients, patient advocates, patient representatives and/or carers during the entire medicines' lifecycle in corporation with the other relevant stakeholders.
  - From a research perspective, PE has been shown to improve inclusion/retention rates and research outcomes, preventing clinical trials failure and reducing trial-related costs but most importantly ensuring that health treatments and technology are being developed with the end user in mind.
  - However, PE is mostly focused on the adult study population, whereas the added value of the perspectives of the population of young people living with a rare disease have been largely underestimated, and therefore under investigated. There are considerable practical challenges and a lack of appropriate tools for meaningful engagement of young people.

- Objectives
  - Understand and map out the different patient engagement activities in therapy development by age groups (e.g., early childhood (2-5 yo), middle childhood (6-11 yo), adolescents (12-17 yo) and young people (18-25 yo that have transitioned to adult care since conditions), also looking into differences if young people lived with the condition their entire life, or if they were diagnosed it later on.
  - Understand and identify existing methodologies, tools, processes for PE of young people living with a rare disease and consider what is missing.
  - Understand new opportunities for engaging young people in the whole therapy development process by for example creating a decision tree in each development milestone with mapped activities & methodologies, available tools and processes to be used for patient engagement of young people in rare diseases taking into account their age and developmental stages.

- Foreseen impacts

- Engaging young people in therapy development have the potential to impact all along the development milestones and within all stakeholders involved:
  - Young people - therapies that bring improvements to their condition with a therapy/technology that is developed with them in mind.
  - Researchers - setting priorities and designing research with the input of parents/carers and young people.
  - Healthcare professionals (including nurses) - therapies for their patients.
  - Health systems and payers - reimbursement of therapies where patients were involved within the development and targeting relevant outcomes for them.
  - Funders, regulators and policy makers - public accountability and transparency.
  - Companies - involving patients during all the development to bring therapies targeting their needs.

Toward clarifications, improvement and international convergence in regulatory approvals of RD therapies with a focus on Advanced Therapy Medicinal Products

- Proposers: FCC, CCC, and RSC

- Background
  - The current regulatory and manufacturing environment for RD therapies is extremely complex. The current scheme struggles with adapting to the peculiarity of ultra rare diseases, more and more often treated with gene or cell therapies, and this lengthens their route to patients and increases costs of therapies.
  - The need to navigate different regulatory procedures in different jurisdictions further complicates the picture. Small biotechnology companies tend to privilege Food and Drug Administration (FDA) as the US market has the highest commercial interest while academic and not for profit developers limit their action to their own country/region as enlarging to others is too complex and expensive.

- Objectives
  - The overall objective of the task force is to identify barriers towards mutual recognition of the approval of therapies by different jurisdictions and propose concrete solutions. This general objective requires actions on two parallel tracks:
    - Policy: Propose solutions/changes in regulation and guidelines to remove the legal and administrative barriers to regulatory convergence
    - Investments: Engage with regulatory agencies to provide research funders with specific recommendations in areas where investments are used that require regulatory agency dialogue/approval

- Foreseen impacts
  - This activity will have a short-term impact on the RD community as it will highlight the need for policy change and trigger investments in research projects on “regulatory science”. This

will deliver to patients advocates and to policy makers a list of changes to the system that needs to be implemented and to research funders a list of topics where specific investments are needed to enable the international regulatory alignment.

- In the medium to long term, the impact for drug developers could be relevant as the alignment in requirements and procedures between different jurisdictions may allow to reduce the costs, time and burden of approval of new products.
- The essential impact however will be on patients as the joint assessment/mutual recognition will reduce the disparities in terms of medicines available in the different geographies. This will not automatically lead to improved access as the regulatory approval per se is not sufficient to ensure patients access to a therapy, but it is an essential step in that direction.

Stigma and Rare Diseases

- Proposers: ISC and PACC

- Background
  - Stigma is defined as a discrediting attribute that distinguishes an individual from others by reducing them 'from a whole and usual person to a tainted, discounted one'. Stigma is an overtly expressed challenge by approximately 1 in 3 Persons Living with a Rare Diseases (PLWRD);
  - Stigma generates inequality, marginalisation, discrimination and exclusion which impairs access to, and benefit from health, social and community participation and services. Stigma can and frequently does prevent the start or the progress through the rare disease diagnostic, therapeutic and care odysseys. Stigma's physical, mental and social consequences are likely a key contributor to the lower quality of life reported by PLWRD compared to those with more common diseases.
  - Until such time as addressing RD stigma worldwide is prioritised, comprehensively reviewed with an international lens, and the pathways for implementing culturally safe and responsive mechanisms are identified and acted upon, the global goals for diagnosis, care and social inclusion cannot be met.

- Objectives
  - Identify the state-of-play and unlock new knowledge to address stigma to accelerate diagnosis and enhance equitable care and support.
  - The Task Force will deliver a survey and whitepaper to identify technology and human factor solutions.
  - The overall achievement will be to guide and accelerate co-designed patient-driven research that also harnesses the power of technology for inclusivity and scale.

- Foreseen impacts
  - Patients – better healthcare access and engagement
  - Clinicians – improved compliance

- Scientists – a framework for research to address Stigma associated with rare diseases
- Health systems – reduced did not attends and discharge against medical advice
- Payers – improved physical and mental health, reducing healthcare expenditure
- Policy makers – a framework to generate policy to better address stigma and rare diseases

Bridging diagnostics to therapies and care

- Proposers: DSC, TSC, and ISC

- Background
  - Most rare diseases do not have specific therapies
  - Persons with rare disease experience barriers to obtaining treatment
    - Access (geographical, resource limitations)
    - Awareness (resources, specialized knowledge)
    - Research (initiation and funding)
    - Regulation
  - Development of therapies for many rare diseases require research infrastructure
  - Taken all together the need exists to link diagnosis to targeted therapy and individualized care and establish a better understanding of this trajectory

- Objectives
  - Create a list of critical elements required for the transition from diagnosis to therapy, including barriers, opportunities and recommendations for implementation.
  - Exhaust opportunities to connect newly diagnosed individuals to existing therapies, both approved and on a research basis. For example:
    - Towards SoC procedures/ disease management guidelines
    - Towards an approved, experimental, compassionate use, or off-label therapy
    - Towards self-management
    - Towards psychological support
    - Towards educational, disability, social and work support
  - Prioritization of case-specific tasks needed to instate available therapies.
  - Prioritize work needed to bridge existing gaps between newly diagnoses and effective therapy or research

- Foreseen impacts
  - Development of resources for further work
  - Framing of current issues
  - Research and practical recommendations
  - Implementation in clinical practice recommendations
  - Clarification of stakeholder perspectives to help in ongoing conversation
  - Funders: multiple funders take up the recommendations for research

7. IRDiRC Key Performance Indicators (KPIs)

- To better address the progression of IRDiRC towards its goals, the Consortium uses currently three metrics
  - The cumulative number of new rare diseases since 2010
  - The cumulative numbers of genes associated with a new rare disease
  - The cumulative number of new orphan drugs (FDA, European Medicines Agency [EMA]) since 2010

- However, it is hard to understand how these metrics are impacted by the work of IRDiRC and therefore, it was decided to develop an additional set of KPIs to reflect more on IRDiRC contribution to the rare disease community

- The below KPIs have been proposed:
  - Reach and engagement
    - Number of LinkedIn followers
    - Members and applications to scientific committees/TFs and geographical coverage
    - Invitations to events and geographical coverage (as IRDiRC speaker)
  - Relevant funding opportunities
    - Number of projects loaded into the funder database
  - Innovation and impacts
    - Number of peer reviewed publications & impact factor
    - Number of peer reviewed tools and guidelines

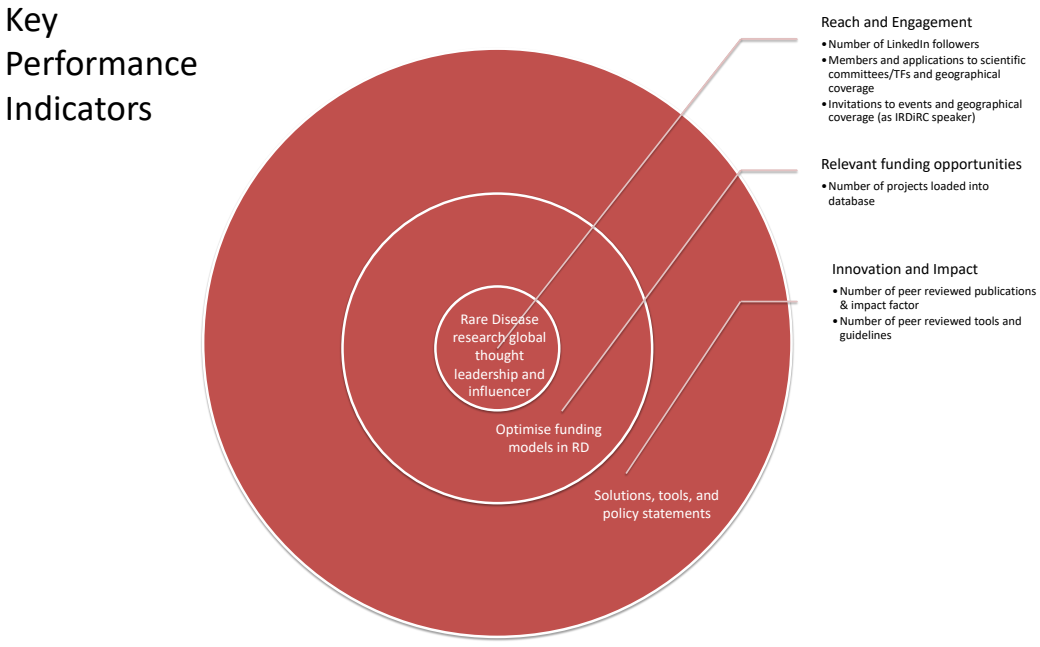


Fig. 1 - Photo from the CA meeting presentation highlighting identified KPIs.

- The participants identified the following metrics and actions to highlight IRDiRC contribution
  - How many initiatives spin off from IRDiRC collaboration
  - Development of use cases of IRDiRC work and how it impacted the community (e.g., Task Force on shared molecular etiologies, Working Group on ethical legal and social issues, SaME, Matchmaker Exchange, Orphan Drug Guidebook)
  - World Health Assembly (WHA) resolution on RD: IRDiRC members to respond to the public consultation
  - Investigate the impact of IRDiRC work on patients and health care provider education

Abbreviations

ATMPs - Advanced therapy medicinal products

CA – Consortium Assembly

CCC – Companies Constituent Committee

CHARD - The China Alliance for Rare Disease

COA – Clinical Outcome Assessment Consortium

DSC – Diagnostics Scientific Committee

EC – European Commission

EMA – European Medicines Agency

ERDERA – European Rare Diseases Research Alliance

FCC – Funders Constituent Committee

FDA – Food and Drug Administration

KPIs – Key Performance Indicators

IRDiRC – International Rare Diseases Research Consortium

ISC – Interdisciplinary Scientific Committee

INSERM – French National Institute for Health and Medical Research

IRDCC – International Rare Disease Conference of China

LMIC – Low-Medium Income Country

PACC – Patient Advocacy Constituent Committee

PE – Patient Engagement

PLWRD – Persons Living With a Rare Disease

RD – Rare Disease

RSC – Regulatory Scientific Committee

SaME – Shared Molecular Etiologies

SC – Scientific Committee

SIMPATHIC - Accelerating drug repurposing for rare neurological, neurometabolic and neuromuscular disorders by exploiting SIMilarities in clinical and molecular PATHology

SME – Small medium enterprise

SoC – Standard of Care

TSC – Therapies Scientific Committee

VMF – Voluntary Monetary Fund

WHA – World Health Assembly

WHO – World Health Organization

Acknowledgements

This report was written by IRDiRC project managers Galliano Zanello and Alexandra Tataru (Fondation Maladies Rares, Paris, France).