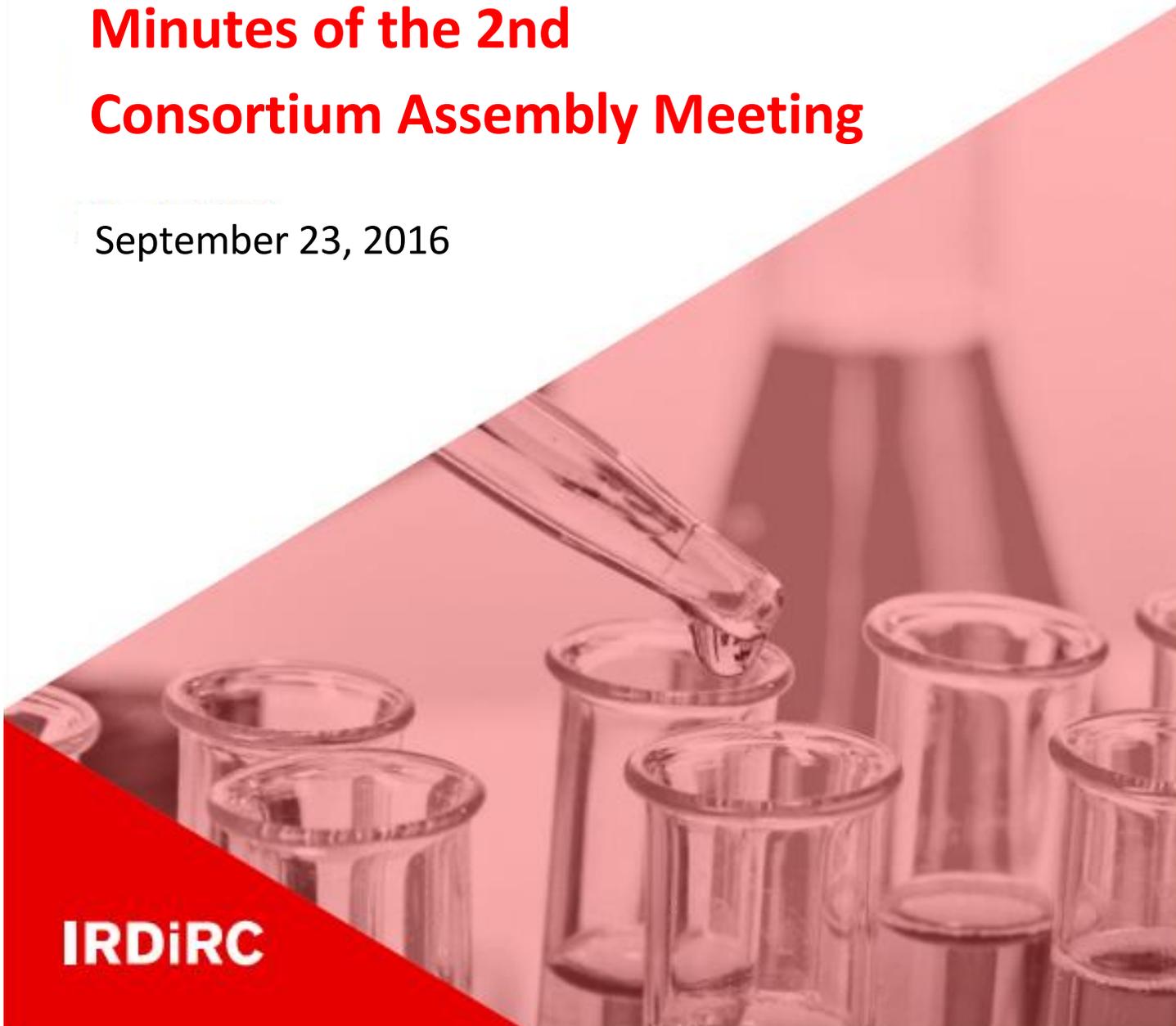




**INTERNATIONAL
RARE DISEASES RESEARCH
CONSORTIUM**

**Minutes of the 2nd
Consortium Assembly Meeting**

September 23, 2016



IRDIRC

EXECUTIVE SUMMARY

- ▶ The Consortium Assembly (CA) of the International Rare Diseases Research Consortium (IRDiRC) met on 23 September 2016 in Catania, Italy. It was attended by 27 participants in person and 4 via teleconference, representing 21 member organizations, the Scientific Committees (SCs) and the Scientific Secretariat (Sci Sec).
- ▶ Members have been actively participating in funding calls on topics including repurposing, new drug development, and undiagnosed diseases programmes. A strategy is needed to better capture these information to inform of future calls; Funders members were urged to collaborate on upcoming calls and share information to the extent they can for relatively real-time coordination.
- ▶ Five new members were nominated to the SCs, two were renewed, and four members would be thanked for their contribution as their mandates ended. The Chair of TSC informed the CA that he would step down, and an election of the new TSC Chair would be carried out.
- ▶ CA and SC Chairs and Co-Chairs have been involved in a number of article writing, some together with the Sci Sec. An article on “IRDiRC Recognized Resources” was accepted for publication, and several other articles are being drafted. Sci Sec members are also working with Task Force members on article writing.
- ▶ SC Chairs reported back on Task Force activities and advances made, and a new Task Force on Patient Engagement was approved. Other potential ideas were also pitched to the CA, of which the SC Chairs will go back to the SCs to elaborate the proposals.
- ▶ Constituent Committees (CCs) were given charge of a number of immediate actions, including election of Chair for each CCs and identify potential constituency members in the immediate future, think of goals to incorporate into IRDiRC goals in the short term, and identify roadblocks common to each constituent in the long term.
- ▶ The next IRDiRC face-to-face meetings will take place on 6-7 February 2017, followed by the 3rd IRDiRC Conference on 8-9 February 2017, in Paris, France.
- ▶ The Chair and Vice Chair of CA will take on the task of writing down strategic vision and compiling goals based on discussions to date, and together with the Conference Planning Committee (CPC) work on finalising the conference programme. Further speaker nominations may be sought, although current focus was on non-US/EU young and/or female investigators.

REPORT

1. Chair's Update

1.1 Publications:

- ▶ Paper on “IRDiRC Recognized Resources” have been accepted by the EJHG
→ [Paper available at <https://www.ncbi.nlm.nih.gov/pubmed/27782107>]
- ▶ Paper on “IRDiRC Policy and Guidelines” in preparation; already published on IRDiRC website but needs to be searchable in indexed publications

1.2 Presentations:

- ▶ Reminder that slides on IRDiRC background and activities available
- ▶ May request specific slides from the Sci Sec too

1.3 Voluntary membership fees:

- ▶ Will use current fund to pay expenses of IRDiRC 2017 conference
- ▶ Will continue to investigate route to operate the fund in the long term

1.4 Changes of representations in the CA:

- ▶ ANR: Catherine Dargemont replacing Bertrand Schwartz
- ▶ French Foundation for RD: Nadège Penhaleux, interim replacement of Marc Tardieu
- ▶ NIH/NINDS: Adam Hartman replacing Danilo Tagle

1.5 Representations from the NIH:

- ▶ 27 institutes and centers (i.e. ICs), some more RD-centric than others
- ▶ 8-9 ICs wish to be active members of IRDiRC, others through NIH-centric RD group

2. Roundtable with State-of-Play of funding initiatives, new member presentation

Representative of each member organization was asked to present 2-3 key things which happened in the past six months that this group could benefit from knowing and relevant to IRDiRC goals. New member, Roche, was presented to the CA in terms of its aims and general rare disease research activities.

3. Scientific Committees

3.1 Joint SC activities

- ▶ Continuous assessment of “IRDiRC Recognized Resources” applications
- ▶ Assessment of collaboration with Human Variome Project in recognition of resources
- ▶ Publications:
 - As updated by CA Chair on “IRDiRC Recognized Resources” and IRDiRC P&G

- Also, rewriting of TSC Recommendations as commentary

3.2 Diagnostics SC (DSC)

- ▶ Chair – Kym Boycott; Co-Chair – Gareth Baynam
- ▶ DSC membership changes approved:
 - Replacement: Yiming Wang, for Jun Wang
 - Nomination: Kenjiro Kosaki
 - End of mandate: Johan Den Dunnen, Woong-Yang Park, Pak-Chung Sham
- ▶ Task Force update:
 - Matchmaker Exchange (MME): number of connected nodes increased from 3 to 7, significant progress, ongoing effort (via GA4GH) to connect more databases with phenotype/ genotype data for gene discovery
- ▶ Upcoming Task Forces – to launch in Fall 2016:
 - Solving the unsolved: look at classic recognizable syndromes which numerous groups have applied exome/genome sequencing but failed to identify underlying causes
 - Clinical data sharing for gene discovery: to prepare for transition into clinical sequencing and facilitate access to data for secondary use, i.e. discovery of disease mechanism
- ▶ Publications:
 - DSC/ISC commentary: in preparation, shows complete data until 2015 on pace of discovery, steady increase and peaked in 2012-2013 but levelling off, unsure if reflect hitting ability to use WGS/WES for discoveries
 - Special AMJG issue on “Solving the remaining unsolved genetic syndrome”; will have introduction paper by IRDiRC and its TF, 10 manuscripts of classical unsolved syndromes (e.g. due to clinical heterogeneity, mosaicism, etc); publication in Spring 2018

3.3 Interdisciplinary SC (ISC)

- ▶ Chair – Hanns Lochmüller; Co-Chair – Petra Kaufmann
- ▶ ISC membership changes approved:
 - Nominations: Ken Ishii, Edmund Jessop
 - Renewal: Petra Kaufmann
- ▶ Task Force updates:
 - Two current TFs, both in collaboration with GA4GH
 - Automatable Discovery and Access (ADA): product ADA-matrix opened for public comment; enable standardized, computer-readable representation of consent
 - Participants Unique Identifiers (PUID): workshop to take place in Paris on 8-9 Dec 2016; 6 uses cases to be analysed based on both ethical/legal and technical considerations

- ▶ Additional topics to address in coming months:
 - Development of guidelines for post-marketing industry-independent surveillance registry; emphasis on modular, easy-to-use, web-based, patient-centred registry
 - Enabling patients' access to therapy through consideration of health economic from research point of view

4.4 Therapies SC (TSC)

- ▶ Chair – Yann Le Cam; Co-Chair – Diego Ardigò
 - Yann will step down as Chair at the end of October but staying on as member
 - TSC election of a new Chair in November
- ▶ TSC membership changes approved:
 - Nomination: Michela Gabaldo
 - Renewal: Yann Le Cam
 - End of mandate: Asla Pitkänen
- ▶ Revised method to count therapies
 - Current method: new medicinal products with orphan designation approved in EU/US
 - Revised method: new medicinal products for therapeutic indication in the scope of RD, approved in EU/US, with or without orphan designation (OD) → agreed by CA
 - Prepare new count table: shows count with or without OD
 - Prepare clear communication re: motivation in change of count methodology (i.e. not just to amplify the number)
 - Update website count page – transparency in methodology used
 - Contact FDA to work on therapy count without OD
 - Confer with EMA/FDA on prevalence and orphan condition if borderline cases
 - Additional information that may be useful
 - Add column for number of diseases for which there are therapies
 - Add column for number of therapies due to repurposing → DMR TF to help
 - Consider new liaison beyond EU/US, e.g. PMDA
 - Develop report format for Japanese representative and PMDA to provide therapy count that can be easily incorporated with current EU/US counts
- ▶ Task Force updates:
 - Overall method of work focused on coordinating research policy and guiding funders
 - Major hurdle and time intensive: writing and submission of articles for publication
 - Patient-Centered Outcome Measures (PCOM): publication in drafting process by Thomas Morel together with Sci Sec
 - Small Population Clinical Trials (SPCT): publication in drafting process by Simon Day together with Sci Sec; to further disseminate work in PMI space too
 - Data Mining and Repurposing (DMR): workshop in Barcelona in November 2016, first recommendations expected in January 2017, finalise/publish in summer 2017

- ▶ **New Task Force on Patient Engagement:**
 - Final draft of Patient Engagement TF proposal → approved by CA
 - Sci Sec to start bibliography in Q4 2016 – background analysis of past and ongoing patient engagement initiatives, composed the TF and its Steering Comm, define writers for publication, workshop June 2017 or September 2017.
 - PCORnet have many tools and technology – PCORI a good starting point

- ▶ **Additional items to scope of TF on Patient Engagement recommended by CA**
 - Financing patient organisations: highly contentious, process can be difficult
 - Generating metrics: may limit to identification and highlight the needs
 - Liaising with similar external groups (e.g. CITY effort)
 - Identify time-points in R&D where patient engagement needed, i.e. research agenda to determine when, where and how patients are most useful
 - Recommendations to enhance the science of benefit-risk and best practices

- ▶ **Potential next Task Force proposal: Clinical Research Network for RD (CRNfRD)**
 - Potential partnership: NIH's RDCRN, EC Joint Action on RD – WP6 on Policy, Eurordis
 - Timing important as NIH are preparing evaluation of RDCRN and planning its next phase, and several EC initiatives that support clinical networks are coming together
 - Aim to develop integral items that each geographical area needs to utilize for consistency, interoperability and to enable coordination/harmonization
 - Lead into a global coordinated effort for clinical networks
 - Build on experience gained and ongoing initiatives in US, EU and other countries willing to take active part in identifying policy and funding recommendations in support of development and adoption of new diagnostic tools and therapies for RD
 - Proposal to start with US/EU: experience at the NIH on RDCRN (22 consortia, covering over 200 diseases), and EU starting the European Reference Network (ERN, 25 of them with potentially 900 centres, 4-5K experts networked) in 2017
 - Useful if know overlaps and gaps between diseases in both number and types
 - Compare diseases studied in RDCRN and ERN
 - Will later expand into global coordinated effort for clinical networks
 - Add partners from PCORnet, Care4Rare, Research Networks from Germany
 - Close consultation with DG SANTÉ
 - Coordinate with UDNI to connect parallel efforts
 - Potential new TF on linking effort to UDNI
 - Caution: diseases in ERNs will be decided and collaborated with EU Member States, be careful not to interfere with process and discussions
 - Note: all RDCRN has non-US components – clinical version of Matchmaker Exchange

- ▶ **Additional Task Force ideas**
 - Acceleration of identification and recruitment of patients in RD studies
 - Reducing uncertainties through better post-marketing data collection
 - Liaise with ISC idea on industry-independent post-marketing research

- Natural history studies and identification of end points as well as clinical trial evaluation
- Gene and cell therapy: risk management and acceptance, delivery model, long term data collection, post-marketing data

4. IRDiRC Constituent Committees

4.1 Charges for Constituent Committees (CCs)

- Elect Chair of each CC → will also serve on OC
- Identify people of constituency who should join the CC (e.g. enrich Company CC with diversity of representation different from the CA)
- Identify critical common issues in constituency space that limit achieving goals
- Identify potential TFs to address common issues
- Identify representatives from countries not currently represented

4.2 Funders CC (FCC)

- ▶ Communicate among funders at earlier stages re: focus of upcoming calls
 - Communicate via pre-publication notice
 - Share relative real-time info on focus of calls using shared space
- ▶ Analysis of current portfolio and funding already spent (also see point no 10)
- ▶ Globalise the process that E-Rare outlined during joint session
- ▶ Make use of IRDiRC State-of-Play document if it's more prospective rather than retrospective
- ▶ Discuss regulatory impact in global world

5.3 Company CC (CCC)

- ▶ What prevents R&D process from getting through quickly and efficiently?
 - E.g. regulatory-relevant endpoint, changing requirements
- ▶ Inform funders re: how public programs should best translate discoveries
- ▶ Liaise with international industry group organisations (e.g. IFPMA, EFPIA)
 - Potentially invite them to join the CCC

5.4 Patient Advocates CC (PACC)

- ▶ Some common roadblocks
 - How to get educate to be member of a research team? Eurordis runs summer schools and training programmes but faces funding issues to run activities
 - Condition of engagement: patients not a project totem, needs early integration into project and make it truly collaborative
 - How to fund patient groups as members of research teams: metrics to measure how patient groups positively affect research becoming critical to leverage support need
- ▶ In term of expanding PACC membership, RDI may be called upon to nominate 3-4 person with diverse geographical representation

5. Next IRDiRC face-to-face meetings

- ▶ Logistics:
 - Dates: 6-7 February 2017 (before the IRDiRC 2017 Conference)
 - Venue: UPMC, Paris
- ▶ All committees – CA, CCs, SCs – will meet
 - ➔ Any member who wish to bring up topic for discussion, please contact the Chair of your committee and the Sci Sec

6. IRDiRC 2017 conference

6.1 Basic information

- ▶ Logistics:
 - Dates: 8-9 February 2017 (after the IRDiRC face-to-face meetings)
 - Venue: UPMC, Paris
- ▶ General updates:
 - Website: www.irdirc-conference.org
 - Tiered fee structure applicable
 - Abstract submissions open to all participants for talk and poster presentations
 - ➔ Encourage young, international and innovative investigators

6.2 Draft conference program

- ▶ [Updated conference program on <http://irdirc-conference.org/conference-program/>]
- ▶ Day 1: 8 February 2017
 - Plenary 1: Opening session – IRDiRC history and achievement
 - Plenary 2: Rare Disease Research in 2017 – an overview across the globe, State-of-Play
 - Parallel 1: IRDiRC outcomes from SCs/TFs
 - Parallel 2: Talks by established speakers
 - Flash poster presentations – lead into the poster session
 - Poster session and cocktail reception
- ▶ Day 2: 9 February 2017
 - Parallel 3 & 4: Talks by young investigators and selected abstracts
 - Plenary 3: Forward look and IRDiRC goals
 - Panel discussion: Forward look and IRDiRC goals
- ▶ Conference programme suggestions
 - Parallel 1 as plenary given interest in TF outcomes – prospective (vs Parallel 2 given by established speakers that are retrospective and research-focused)
 - Flip Parallel 1 and 2: bigger picture by established speakers, followed by TF outcomes, leads into poster session

- Parallel session formats: single themed (e.g. all diagnostics, all interdisciplinary, all therapies) or mixed, per past IRDiRC conferences
 - ➔ Selected option: mixed, per past IRDiRC conferences
- Present the 200 therapies counted (available on IRDiRC website) as poster panels
- Programme to include inspirational patient speakers: 1 for diagnostics, 1 for therapies?
- Need more young investigators, non-EU/US speakers, female speakers
- ▶ Suggestions to make conference a success
 - Speakers be given guidance on message of the conference
 - ➔ Teleconference in advance extremely helpful to tailor talks and direction
 - Mixed audience to energize discussions: include young investigators and patients
 - ➔ Targeted invitations to attend conference, present poster, etc

6.3 IRDiRC goals and vision

- ▶ Goals should be SMART (specific, measureable achievable, realistic, and timely)
 - Need to be sure of the story to tell, the intention: impetus to accomplish new goals and accelerate research – finding bigger challenges
 - ➔ All members to create a conceptual map/vision of where IRDiRC is going
 - ➔ CPC to start a document on strategic vision based on discussions to date
 - Conference as potential research activity
 - ➔ Survey attendees what goals and objectives should be, what they need from IRDiRC and from funders
- ▶ IRDiRC strategy
 - Go through all TFs and activities, see the transversality
 - Identify what to do to make this a reality: develop 1-page strategy document

6.4 Conference travel support

- ▶ Voluntary fee fund best suited for large invoices instead of reimbursements
- ▶ Members' support: AMED, EC and E-Rare will support the travel of some speakers
- ▶ Companies have grant portal for educational events: tight timeline, one 2016 cycle left
- ▶ Tiered registration fees to help cover travel costs too

7. Scientific Secretariat update

7.1 Sci Sec team

- ▶ Consists of a project coordinator and 4 team members
- ▶ Members reminded to copy scientificsupport@irdirc.org or scisec.admin@irdirc.org to get timely scientific or administrative support from the small team

7.2 Activities Mar-Sep 2016

- ▶ Teleconferences – organisations, management, report writing:
 - Averaging one teleconference per week
 - Bi-weekly contact with CA Chair to update and discuss activities

- ▶ Meetings – preparations and (travel) organisation:
 - IRDiRC conference in Paris (February 2017)
 - CA meetings in Catania (September 2016) and Paris (February 2017)
 - SC meetings in Paris (February 2017)
 - TF workshops in Barcelona (November 2016) and Paris (December 2016)
- ▶ State-of-Play report – 2-part report in progress:
 - Literature analysis: retrospective report
 - Data analysis: to provide landscape of rare diseases research in IRDiRC (e.g. by medical domain, disease type, what’s funded) – note: without rare cancer
- ▶ Publications – planning, drafting, editing, copy-proofing:
 - Working in close collaboration with OC, SC Chairs and members, TF Chairs and members
 - Goal to publish all TF works: background documents and workshop reports on website, recommendations for peer-review publication (e.g. as commentary, white paper)

7.3 Work plan Oct 2016-Feb 2017

- ▶ Continue supporting teleconferences and meetings
- ▶ Continue coordinating conference-related activities, oversight of conference budget
- ▶ New TFs to begin work on: writing background documents, composition of TFs (with SC Chairs)
- ▶ Maintain momentum on publications and make known IRDiRC activities to the community
- ▶ Continue management of “IRDiRC Recognized Resources” process, together with SC members

7.4 Communication plan Oct 2016-Feb 2017

- ▶ Conference promotion
 - Via newsletter, OrphaNews, social media (Twitter @irdirc), members’ network
 - ➔ Members to add a slide about the conference to publicize it when giving talks
- ▶ Wider communications on goals to be carried out after conference, when new goals set up
- ▶ Re-working IRDiRC website to better promote recent activities and publications
- ▶ Identification of conference where IRDiRC sessions may be held for 2017/2018

7.5 SUPPORT-IRDiRC contract-related items

- ▶ Preparation of 3rd reporting to the European Commission
- ▶ Performance review survey
 - Questionnaire will be sent to all CA/SC members, possibly TF members too
 - Results will be written up as report, made available to CA members
- ▶ Contract amendment
 - 4 years through, 2 years remaining
 - Amendment in preparation: will account for changes taking place in IRDiRC including governance structure and will finalise after live decision cycle cleared
- ▶ SUPPORT-IRDiRC beyond 2018
 - EC developing criteria for new contract within Horizon 2020 context
 - Meeting with EU member states to discuss the future of RD research funding and exploring possibility to strengthen collaborations

- Potential use of new funding instrument, e.g. EJP co-fund, to bring together activities by national funders and organisations involved in RD activities under one umbrella, integrating activities of member states → one element is to support IRDiRC Secretariat

8. IRDiRC MOU

- ▶ IRDiRC is not a legal entity, no treaty was signed to limit its existence beyond 2020
 - 2020 is the deadline chosen to deliver IRDiRC goals (so only goals expire in 2020)
 - Collaboration between funders active in RD research could continue
 - Next set of goals could be set for 2017-2022 or 2027
- ▶ If scope of consortium change, should consider renewing the letter of intents to reflect change

9. Matrix of funding (point from Joint IRDiRC – E-Rare meeting)

- ▶ Funding portfolio analysis
 - NIH produced “World Report” – relatively small database on neglected diseases
 - AMED started an analysis for practical research and development projects last year for Japan
 - Need one large database for international calls and scopes → i.e. matrix of what’s funded, where’s the gap; could be in part addressed by State-of-Play report but that’s limited to IRDiRC members who have provided information to the Sci Sec

Acknowledgements to the host

The CA and the IRDiRC Secretariat wish to thank E-Rare partners for their generosity and hospitality in hosting the meeting.

Annex - List of participants

<u>Members</u>	<u>Representative</u>
National Center for Advancing Translational Sciences, NIH/NCATS, USA	Christopher Austin, Christine Cutillo
Western Australian Department of Health, Australia	Hugh Dawkins
Canadian Institutes of Health Research, Canada	Paul Lasko
E-RARE-2 Consortium, EU	Daria Julkowska
European Commission, DG Research and Innovation, EU	Iiro Eerola
Academy of Finland, Finland	Heikki Vilen
AFM - French Association against Myopathies, France	Marie-Christine Ouillade
Agence National de la Recherche, ANR, France	Daria Julkowska
Federal Ministry of Education and Research, Germany	Ralph Schuster
Chiesi Farmaceutici S.p.A, Italy	Andrea Chiesi
Istituto Superiore de Sanita, Italy	Domenica Taruscio
Telethon Foundation, Italy	Leopoldo Laricchia Robbio
Japan Agency for Medical Research and Development (AMED), Japan	Takeya Adachi, Ken Ishii, Senkei Umehara
National Institutes of Biomedical Innovation, Health and Nutrition (NIBIOHN), Japan	Yoshihiro Yoneda, Akifumi Matsuyama, Mistuo Nagata, Hanayuki Okura
National Institute of Health Carlos III, Spain	Pedro Cortegoso Fernández
Roche, Switzerland (by TC)	Sangeeta Jethwa
Food and Drug Administration, USA (by TC)	Katherine Needleman
National Human Genome Research Institute (NHGRI), NIH, USA	Jeffery Schloss, Lu Wang
Pfizer, USA	Katherine Beaverson

<u>Invited Patient Advocacy Groups</u>	
EURORDIS, Europe	Yann Le Cam
Genetic Alliance, USA	Sharon Terry

<u>Scientific Committees</u>	
Diagnostics (by TC)	Kym Boycott, Gareth Baynam
Therapies	Yann Le Cam

<u>IRDIRC Scientific Secretariat</u>	
SUPPORT-IRDIRC Project	Lilian Lau, Ana Rath

Apologies

<u>Members</u>	<u>Representative</u>
Genome Canada	Cindy Bell
BGI, China	Ning Li
WuXi AppTec Co. Ltd., China	James Wu
Chinese Rare Diseases Research Consortium, China	Qing Wang
European Commission, DG SANTÉ, EU	Jaroslav Waligora
European Organisation for Treatment & Research on Cancer, EORTC	Denis Lacombe
Fondation Maladies Rares, France	Nadège Penhaleux
Lysogene, France	Karen Aiach
Children’s New Hospitals Management Group, Georgia	Oleg Kvlividize
Shire Pharmaceuticals, Ireland	Omar Francone
Saudi Human Genome Project, Kingdom of Saudi Arabia	Sultan Turki Al Sedairy
The Netherlands Organisation for Health Research and Development	Sonja van Weely
Prosensa, The Netherlands	Scott Clarke
Korea National Institute of Health, South Korea	Hyun-Young Park
National Institute for Health Research, UK	Willem Ouwehand
Genzyme, USA	Carlo Incerti
Ionis Pharmaceuticals, USA	Brett Monia
National Cancer Institute, NIH/NCI, USA	Edward Trimble
National Eye Institute, NIH/NEI, USA	Santa Tumminia
National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH/NIAMS, USA	Stephen Katz
National Institute of Child Health and Human Development, NIH/NICHHD, USA	Melissa Parisi
National Institute of Neurological Disorders and Stroke, NIH/NINDS, USA	Adam Hartman
NKT Therapeutics, USA	Robert Mashal
Office of Rare Diseases Research, NIH/ORDR, USA	
PTC Therapeutics, USA	Ellen Welch
Sanford Research, USA	David Pearce

<u>Invited Patient Advocacy Group</u>	
National Organization for Rare Diseases, NORD, USA	Peter Saltonstall

<u>Scientific Committee</u>	
Interdisciplinary	Hanns Lochmüller



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