

Meeting report series

Report of the 22nd Interdisciplinary Scientific Committee Meeting

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Agenda

1. Welcome and introduction/roundtable of participants.....	3
2. Current activities	4
2.1 <i>Privacy-Preserving Record Linkage (PPRL) TF</i>	<i>4</i>
2.1.1 Presentation of the Task Force and status update	4
2.1.2 Current follow up activity: Development of a pilot	5
2.1.3 Discussion around the extension of the RD-Connect pilot.....	6
2.1.4 Remaining challenges to a more global use of the EUPID system	8
2.1.3 Next steps.....	9
2.2 <i>Model Consent Clauses (MCC) TF.....</i>	<i>9</i>
2.2.1 Task Force: status update	10
2.2.2 Next steps.....	11
3. Roadmap 2018 activity	11
3.1 <i>Clinical Research Networks for Rare Diseases (CRNRD) TF (Activity G).....</i>	<i>11</i>
3.1.1 Presentation	12
3.1.2 Update of the proposal: discussion	12
3.1.3 Next steps.....	14
3.2 <i>Natural history and registry (NH/R) platform for use in real world evidence (RWE) data collection (Activity D)</i>	<i>15</i>
4. Potential 2019 activities	17
4.1 <i>Reflection around metrics to evaluate IRDiRC Goal 3.....</i>	<i>17</i>

REPORT

1. Welcome and introduction/roundtable of participants

The ISC Vice Chair welcomed all participants and opened the meeting with a roundtable.

Domenica Taruscio is the Director of the National Center for Rare Diseases, Istituto Superiore di Sanità (ISS). She leads the work package “Databases and Registries” in RD-Connect, and is actively involved in linking rare disease patient registries and development of the Registry & Biobank Finder. She was also involved in IRDiRC since the start of the Consortium and is the Vice Chair of the ISC.

Stephen Groft is a senior advisor, National Center for Advancing Translational Sciences (NCATS), NIH. He is the former Director Office of Rare Diseases, NCATS, NIH and has been working on rare diseases for over 40 years. He is involved in IRDiRC in different roles since its start.

Daria Julkowska works at the French National Research Agency (ANR) and represents E-Rare Consortium. She is also the Chair of the IRDiRC Funders Constituent Committee. She is present as an observer.

Dixie Baker is a senior Partner with Martin, Blanck & Associates. She is involved in health information technology, electronic health records, privacy and security technology, and the sharing and protection of genomic data. She co-chairs of the Security Working Group of the Global Alliance for Genomics and Health. She participated to the IRDiRC PPRL Task Force.

Elizabeth McNeil is a pediatric neurologist by training. She worked previously with IRDiRC as a TSC member. She left National Institute of Neurological Disorders and Stroke (NINDS) to work at Biogen on spinal muscular atrophy. She now works at Bluebird bio working on adrenoleukodystrophy.

David van Enckevort works at the Genomic Coordination Centre, led by Dr. Morris Swertz, as Technical Project Lead at the University Medical Centre Groningen. Within the genetic department, he is part of a technical group working on data management, data exploration and developing softwares. He is project manager for most the European projects, such as RD-Connect, Solve-RD and the future European Joint Program for Rare Diseases. He participated to the IRDiRC PPRL Task Force.

Edmund Jessop works, in England, at the National Health Service (NHS) which is a comprehensive healthcare system of 55 million people. The team he works for looks at people with ultra-rare diseases. He can bring a payer perspective.

Ana Rath is medical doctor by training. She is the director of Orphanet and coordinator of the IRDiRC Scientific Secretariat. She is present as an observer.

Christine Cutillo works for Christopher Austin at the National Center for Advancing Translational Sciences (NCATS), NIH. Since his election as IRDiRC Chair, she works closely with the Scientific Secretariat.

Marlène Jagut is the Communication Manager of the IRDiRC Scientific Secretariat (Sci Sec).

2. Current activities

2.1 Privacy-Preserving Record Linkage (PPRL) TF

2.1.1 Presentation of the Task Force and status update

- ▶ Two documents were sent to the committee before the meeting
 - Technology Primer: Overview of Technological Solutions to Support Privacy-Preserving Record Linkage ([download](#))
 - Privacy-Preserving Record Linkage: Ethico-Legal Considerations ([download](#))
- ▶ Task Force
 - Overall objectives of the task force: develop a guiding policy for the generation of participant-specific identifiers (pseudonyms) that enable data from the same individual to be connected across multiple projects without directly revealing the participant's identity.
 - Work, thus far -- developed two primers
 - One is focused on the ethical-legal issues, led by Bartha Knoppers
 - One provides a technology overview, led by Dixie Baker
 - Describes current state-of-the-art in the PPRL space
 - Describes existing projects with PPRL approaches
 - Provides recommendations on the PPRL approach used by RD-Connect
 - The European patient-identity management solution (EUPID) system
 - Both primers (technical and ethical-legal)
 - Can be downloaded from the IRDiRC website
 - Were publicized in the IRDiRC newsletter
 - A peer reviewed publication has been accepted for publication in the *EEE/ACM Transactions on Computational Biology and Bioinformatics (TCBB) Journal* and will be published soon
- ▶ Description of the recommended system: The European patient-identity management solution (EUPID) system
 - Identified as the current state of the art solution
 - Central server that manages the linkage between identities and data
 - Not limited to rare diseases

- A key feature is context-specific pseudonymization
 - Maintains identity linkages locally
 - Enables re-identification of a linked data set through a three-party collaboration involving the local context, the linkage agent, and a trusted third party
- EUPID system was originally developed by the European Network for Cancer Research in Children and Adolescents (ENCCA)
 - Was successfully implemented in that project
 - Currently being used
 - They already solved the issue of the implementation of the application programming interface (API) that enables query of the EUPID metadata for linkages (progress since the end of the PPRL TF)
- The EUPID system is mainly EU centered but could be exported to the rest of the world
 - In US, all medical data are governed by the Health Insurance Portability and Accountability Act of 1996 (HIPAA) that has specific instructions on creating:
 - Limited dataset
 - Data Use Agreement associated with this limited dataset
 - Not clear if someone will reach beyond this existing legal frame
 - ERNs are supposed to be embedded in health care and research
 - If this work for ERNs and Europe at large, it will probably give a good leverage to reach out to other communities

2.1.2 Current follow up activity: Development of a pilot

- ▶ Develop a small pilot for implementation of the EUPID system
 - The pilot will be developed within the RD-Connect project
 - RD-Connect has close relation with the team developing the EUPID. They will be the first to implement the system
 - RD-Connect allocated a budget to work with the developers of the EUPID system
 - RD-Connect amended its contract to allow the collaboration with the developers of EUPID
 - Collaboration has to happen before the end of the year as the funding period of RD-Connect itself only lasts until then (end 2018)
 - The idea for this pilot is to work with various existing structures/types of data:
 - Across 4-5 biobanks
 - Work with sequencing, genomic, and phenotypic data
 - **Complete technical proof of concept**
- ▶ Collaboration within the current pilot:
 - Different types of resources will be connected with this project
 - Genomics, phenotypes, biobanks and registries

- The Biobanking and Biomolecular Research Infrastructure Large Prospective Cohorts (BBMRI-LPC) was chosen as a data source because it includes each data type
 - BBMRI-LPC is one of the largest biobanking networks in Europe, aiming to facilitate scientists' access to large prospective study sets on human health and disease
- People developing the pilot have also developed strong connections with the European Commission's Joint Research Centre (JRC)
 - Project will soon be presented at the JRC
 - The JRC will also provide tools to support the development of the pilot

2.1.3 Discussion around the extension of the RD-Connect pilot

- ▶ Easy collaboration with the team who developed the EUPID system
 - EUPID has been contracted
 - Independent of RD-Connect
 - ERNs or other organizations can also contract via EIT for EUPID later on
 - If an organization wants to use the EUPID solution, they only need to give their agreement to spend their money specifically on this project via EIT
 - No need to combine funding from different sources
- ▶ Discussion of a potential extension of the pilot via a collaboration with the ERNs
 - EUPID and the PPRL work was presented at the RD-Action meeting last February
 - Positive feedback from people involved in patient management system of the ERNs
 - Some people reached out to the development group of RD-Action
 - People developing the RD-Connect pilot will have a meeting with the ERNs in June 2018
 - Discussion of a possible collaboration
 - ERNs could provide more samples/data
 - Seems easy to include them in the pilot in a second phase
Extension of the pilot
 - The ISC Vice Chair suggested the possibility to extend the RD-Connect pilot by a collaboration with the project EuRRECa (<https://eurreca.net/>)
 - EuRRECa is a 3 years (2018-2020) project funded by the European Commission
 - One work package of EuRRECa (WP3) is dedicated to "Quality assurance & Evaluation", which implies discussion on the "Core Data Set", including the ID patient
 - Co-directed by Luca Persani and Domenica Taruscio
 - Potential collaboration with the EUPID pilot?
 - The ISC Vice Chair proposed to discuss this possibility with the project coordinator
 - In the case of a collaboration:

- Include and discuss the EUPID in EuRECa WP3
 - Another possibility could be to use in the pilot the already existing registries from the European Reference Network on Rare Endocrine Conditions (ENDO ERN)
 - Interesting idea to explore further
 - Could be a two steps process
 - First the RD-Connect pilot
 - Addition of more examples with EuRECa
- ▶ Proof(s) of concept
 - RD-Connect pilot is the first proof of principle: data can be connected together
 - An extension to the ERNs could prove the efficacy of the system to link data across projects
 - The results of which could be key to convince people of the utility of the system
 - The metrics of such a pilot would be essential so that people can gage application of the system to different networks/diseases
 - ▶ Interestingly, the PPRL topic has been largely discussed during the preparation of the future European Joint Programme for Rare Diseases (EJP RD)
 - When writing the proposal, EUPID system developer (IT as well as partners) were invited to participate
 - The EJP RD proposal includes tasks focused on PPRL to develop solutions that will also link to the ERNs
 - The pilot will provide helpful metrics for the EJP RD
 - ▶ Discussion of potential future collaborations -- connect to other communities once have pilot results
 - Could be interesting to explore the access to the EUPID system by other communities than rare diseases
 - Pan-European pediatric clinical trials network financed by the Innovative Medicine Initiative 2 (IMI2) – this could be a source of collaboration
 - International Consortium for Personalized Medicine (ICPerMed)
 - Equivalent of IRDiRC for personalized medicine
 - Different type of communities (cancer, metabolic diseases, ...)
 - Organized workshops
 - ▶ This would be a good time to promote the EUPID system as there are growing needs particularly surrounding international harmonization of PPRL methods
 - At the ECRD meeting, presentation of the Clinical Patient Management System (CPMS) from the ERNs

- The CPMS will soon add the possibility to have consent to use the data already in the system for research
- This will add a new type of consent
- Number of patients in this collaborative platform is increasing rapidly
- To use that data, it needs to be anonymized in addition to including patient consent to (re)use the data for research
- In the UK, data of patients (from databases) can be used anonymously by default
 - Patients have to actively opt-out
- Would be interesting to involve legal experts to consider the EUPID applications in different settings

2.1.4 Remaining challenges to a more global use of the EUPID system

- ▶ Biggest hurdle is making the EUPID system known
 - Could we use the support of EU Commission?
 - DG Santé has a good visibility
 - If yes, need to complete the pilot beforehand
 - Would it be possible to receive money from the ERN-funded registries to support this pilot? (in case an extension is needed)
 - Could be discussed at the meeting organized with ERNs in June
 - Depending on the pilot results, it would be possible to apply for recognition label to promote the use of the EUPID system
 - IRDiRC Recognized Resources
 - GA4GH is actively looking for additional driver projects
 - Should encourage RD-Connect to apply
 - There is currently no driving project on rare diseases
 - Mutually beneficial
 - If this project becomes a GA4GH driver project, EUPID could become a standard promoted by GA4GH
 - It would increase the project's visibility
- ▶ Implementation of the new EU's new General Data Protection Regulation (GPRD) will be a challenge but could also be beneficial in the precise case of the EUPID system:
 - Organizations are at the moment uncertain of what they can/cannot do
 - Good timing to promote the EUPID system as the best PPRL solution
 - GDPR will also have international consequences in terms of privacy protection
 - Most places in the US must also handle the data of EU residents
 - Therefore, there is an international need to adapt to GDPR
- ▶ It will be important to prevent fragmentation when trying to apply PPRL solutions worldwide
 - Notion of federated model

- Emphasize on the need to be global (especially for rare diseases) to actively prevent further fragmentation
- The project is already a federated model in the sense that data are held by different entities
- It would be important to federate the broker to localize the costs
- Each partner could then build their own instance

2.1.3 Next steps

- ▶ Important to continue communication re recommendations of the PPRL TF and the EUPID system
 - Global vision has been promoted
 - Via the two primers (technical and ethical-legal)
 - Can be downloaded from the IRDiRC website
 - Were publicized in the IRDiRC newsletter
 - A peer reviewed publication has been accepted for publication in the *EEE/ACM Transactions on Computational Biology and Bioinformatics (TCBB) Journal* and will be published soon
 - Presentation at conferences
 - GA4GH meeting will take place in Basel on October 3, 2018
 - In connection with the annual GA4GH meeting, the International Conference on Genome Privacy is taking place on October 2, 2018. The audience is interested in PPRL.
 - Increase publicity for the project

- ▶ Next steps of the PPRL TF
 - Publicize PPRL manuscript as a way « to sell » the vision – *Scientific Secretariat*
 - RD-Connect pilot moving forward; expand pilot with ERNs – *RD-Connect pilot team*
 - Submit abstract for GA4GH / GenoPri Conference in Oct. – *RD-Connect pilot team*
 - Develop/publish other methods for endorsement and recommendations – *PPRL TF members?*
 - Promote the EUPID system by applying to different label to increase its visibility
 - GA4GH driver project
 - Develop into IRDiRC Recommended Resource

2.2 Model Consent Clauses (MCC) TF

- ▶ The overarching purpose of this Task Force is to gather international policy researchers in rare diseases to develop model consent clauses specific to rare diseases that are comprehensive, harmonized, readily-accessible, and internationally applicable, enabling the recruitment and consent of rare disease research participants around the world. The objectives of the Task Force:

- Develop a series of core elements for consent forms
- Collect a compendium for each afore-mentioned core element, to provide examples out of consent forms used around the globe
- Develop a series of model consent clauses specific for rare disease researchers based on robust bioethical and legal approaches, addressing the complexity of the scientific, ethical and legal issues that arise when conducting rare disease research
 - Address issues such as participant privacy, use of identifiable images, and return of results to participants
 - Enable rare disease researchers to use clauses specific to their research context and participant populations, consequently assisting in the customization of their own consent documents
- ▶ This Task Force is composed of multi-stakeholders, including lawyers, ethicists, expert patients, patient representatives, researchers, health policy advisors, and industry representatives from around the world.

2.2.1 Task Force: status update

- ▶ First step of the Task Force was to ask IRDiRC members to send example model consent forms used at/by their respective organization
- ▶ Next, the Task Force defined a set of core elements that are indispensable for model consent clauses:
 - Objective
 - Return of results
 - Matchmaking databases (opt-in/opt-out?)
 - Ongoing analysis/research (indefinite use of data/samples)
 - Limiting research to the "cause of the disease" only (exclude other results)
 - Participation in registries
 - Commercialization/for profit
 - International data/sample sharing
 - Withdrawal mechanisms
 - Facial imaging
 - Identifiability
 - Familial/pedigree consenting
 - De-duplication
 - Re-contact/re-consenting
 - Patient responsibility to maintain contact (update coordinates and contact info)
 - Specific clauses for pediatric/incompetent adults

- ▶ The Scientific Secretariat sorted out the elements of these consent clauses by topic, thereby creating a compendium of examples of consent forms around the globe.

2.2.2 Next steps

- ▶ Currently, the Task Force is analyzing the compendium of information included within the categories described above (document provided by the Scientific Secretariat).
- ▶ Next, the Task Force will develop a series of model consent clauses specific to rare diseases
- ▶ The face-to-face meeting will take place on September 6-7, 2018 in Paris in order to:
 - Finalize consent form language
 - Develop recommendations
- ▶ Suggested ideas for the Task Force to keep in mind:
 - Look at the new *General Data Protection Regulation (GDPR)* law very carefully, and determine its potential impact on research, not yet from a retroactive approach
 - Consider publishing consent elements on IRDiRC website, thereby determining sample consent language considered useful
 - Importance of the length of the consent form
 - Form should not be too long
 - Important not to add too many clauses
- ▶ Potential follow up:
 - Would be interesting to propose an automatized platform to centralize all the consent forms' verbiage that will be recommended by this TF
 - Could be developed in the same manner as the Automatable Discovery and Access Matrix (ADA-M)
 - The ADA-M matrix provides a standardized way to unambiguously represent any and all consent and other conditions of use, making such information computer-readable and hence directly available for digital communication, searching, and automation activities.
 - Idea would be to have a platform:
 - Includes the harmonized verbiage for the different consent form categories described above
 - Researchers could obtain a customized consent form by selecting only the verbiage for the categories relevant to their project

3. Roadmap 2018 activity

3.1 Clinical Research Networks for Rare Diseases (CRNRD) TF (Activity G)

3.1.1 Presentation

- ▶ Task Force proposed by
 - The Chair of the ISC
 - The Chair of the FCC
 - The Vice Chair of the TSC

- ▶ Objective of the TF
 - The objective of the CRNRD TF is to develop recommendations on guiding principles for national/supra-national policies on clinical research networks within an international context for collaboration and interoperability, and the related funding recommendations

- ▶ Proposal for the TF
 - Originally presented in Tokyo, but not approved because it required more background and clarification
 - Comments and suggestions were added:
 - By the Scientific Secretariat after the last ISC teleconference meeting
 - By the FCC chair

3.1.2 Update of the proposal: discussion

- ▶ Possible key questions for this TF are:
 - What are the recommended functions for the Clinical Research Networks? Which functions could benefit from international alignment?
 - What are the tools used in the different Clinical Research Networks? Which resource, tool or standards could be shared and adopted across the USA / EU / Australia / more
 - Which key policy elements so to link up these national or supra-national clinical research network at international level
 - What are the common goals, functions and selection criteria to include in all public funding strategies?

- ▶ Background of the topic
 - The original proposal included background on the RDCRN
 - Proposed update to include additional language on:
 - Background on ERNs
 - IT platform for sharing health/patient data established to support the ERNs
 - Already 100 cases registered and soon much more
 - Existence of the European Patient Advocacy Group (ePAGs) aligned with the ERNs. Each ePAG is specific to an ERN disease group
 - Description of the Solve-RD project

- Fosters application of genomics and/or –omics and/or other high throughput approaches for the molecular characterization of rare diseases in the view of developing molecular diagnosis for a large number of undiagnosed rare diseases
 - European project
 - Collaboration also with countries outside of Europe
 - Works in close collaboration with the ERNs
 - Expected to provide 19,000 exomes of undiagnosed patients from the ERNs
- ▶ Need to revise the original proposal
- ▶ Discussion during this session
- ▶ What are the realistic expectations of the TF?
- “Recommendations for alignment of protocols for data collection, cost sharing...”
 - Seems possible to achieve
 - Potential goals:
 - Recommend best practices
 - Environmental scan on the organizations and practices of the different Clinical Research Networks
 - How can the networks be connected?
 - Recommendations should be on how the networks could work together
 - Identification of barriers that prevent networks to collaborate:
 - Monitoring methods
 - Quality of data
 - Ethical or legal authorizations
 - ...
 - Important to not duplicate existing work
 - The main challenge to this TF is the collaboration across borders
 - Multi-national clinical trials with some centers in EU and US
 - Recurrent issues not specific to rare diseases
 - Example of collaboration between E-Rare and NCATS
 - Different regulation
 - EU coordinator is considered as sponsor
 - Problem to integrate the US team
 - Multi-national clinical trials are however a must-have for rare diseases
 - Crucial problem that could be tackled by this TF
- ▶ How can we have access to patients?
- Communities based research
 - Companies are already in the communities, they manage to find and recruit patients

- Research naïve institutions
 - New technologies such as genome editing will soon need research subjects
 - More often patients are finding researchers/doctors instead of the reverse
 - Before a product is on the market, only educated guess of the actual number of patients
 - Some patients do not have patients' organization representing them
 - Website called "the Mighty" that brings together patients without patients' organization
 - Access via social media?
 - Need to consider those new models centered on patients more than on research centers
 - Challenge to access patients from developing countries
 - Re identification of patients from data is an important issue
 - Legal restrictions
 - Above are interesting topics that could be addressed during this TF
 - Member(s) from the PACC could participate to this activity to give their input
 - Interesting to have the input of funders on how they recruit patients for clinical trials to align with new ways of finding patients
- ▶ Two possible directions for this TF:
 - Develop guiding principles for networks to facilitate international collaboration
 - Promoting community-based research and data provision using innovative approaches
 - ▶ The TF could be divided in two parts:
 - First topic on existing networks and collaboration is almost ready
 - Second topic on the promotion of community-based research could be studied in parallel
 - This matter will be discussed during the Joint Scientific Committee meeting to decide what will be presented at the Consortium Assembly meeting

3.1.3 Next steps

- ▶ **Two potential directions have been proposed for the TF:**
 - Develop guiding principles for networks to facilitate international collaboration
 - Landscape analysis of already existing efforts
 - Alignment of protocols for data collection, cost sharing
 - Identify barriers to collaboration among CRNs and methods for overcoming them (limitations and opportunities)
 - Promoting community-based research and data provision using innovative approaches:
 - Reaching research-naïve locales
 - Recommendations on innovative models and use of technologies (e.g., social media) for data provision and identification of patients

- ▶ To determine the best direction to take, ISC members decided to present both topics during the Joint Scientific Committees meeting
- ▶ When should this activity be initiated?
 - On one hand, it is a timely moment to start this initiative
 - On the other hand, it would be important to gather more information about what exist
 - Like in the background document written at the beginning of most TF
 - Should this be done before or after submitting the proposal to the Consortium Assembly?
 - It requires manpower
 - It requires the involvement of people not limited to IRDiRC members
 - Maybe best option would be to get the proposal approved and proceed with the background research right after
- ▶ ISC members agree that it is the right time to do this activity
 - If postponed, risk to be too late
 - Important initiatives are well established
 - ERNs are already working
 - IRUD Beyond Initiative in Japan
 - Developed importantly during the last year
 - RDCRN in US
 - Each RDCRN has also a patient advocacy group (PAG) attached
 - In addition, existence of a Consortium patient advocacy group (cPAG)
 - Next RCDRN call will be launched latest end of May 2018
 - Awarded in January 2019
- ▶ What are the next steps needed to more forward?
 - Define precisely the focus of the TF
 - Narrow down and rephrase the outputs of the TF

[Post-Meeting Note: The Consortium Assembly did not approve the proposal as is and would like to evaluate an updated version of the document]

3.2 Natural history and registry (NH/R) platform for use in real world evidence (RWE) data collection (Activity D)

- ▶ Support the definition of standards for use of data collected in health care practice for RWE generation, in particular for disease understanding and treatment monitoring
- ▶ Activity D is a cross committee initiative (CCC, FCC, ISC and TSC)
 - Funders would be interested in funding calls related to natural history and RWE data, but they need to have more details on how to approach the topic

- Companies were interested in natural history studies that represent pertinent data in a drug development context
- ▶ During the last Tokyo meeting, it was proposed that activity D would be led by the CCC
 - CCC was not leading an activity in 2018
 - ISC had already two TF planned for 2018
- ▶ Natural history is a topic that historically fell into the expertise area of the ISC
- ▶ This TF could be conducted by the ISC
 - Importance to keep the cross committees' configuration
 - CCC members could attend some ISC meetings
 - The ISC Vice Chair agreed in principle to lead this new activity
 - Presentation at the Joint SC/CA meeting to discuss the idea with the CCC members present in Vienna
- ▶ Discussion about behavior phenotype
 - Poorly described in textbooks
 - Example of Duchenne muscular dystrophy
 - Doctors would describe the pathology as a muscles impairment
 - Families, patients or teams that treat the disease would more describe behavioral problems
 - Crucial for lots of rare diseases
 - How to capture those in registries?
 - Human Phenotype Ontology has a page on behavioral phenotype
 - How well can people describe the phenotype(s)?
 - In UK, every team working on rare disease wants more clinical psychologists
 - Example of a mum in US that did a video recording of her daughter:
 - Patient should have died already
 - She now developed behaviors that doctors have never seen before
 - Helped to understand the patient's phenotype
 - Is this of interest or out of scope for IRDiRC?
 - Should IRDiRC issue recommendations to promote research on this topic?
 - Should IRDiRC plan activities on this topic?
 - This would an excellent topic/task for the future groups of clinical research networks
- ▶ Sometimes psycho-social needs of patients, families and care-takers are omitted
 - Anxiety and depression are now discussed for cancer patients
 - Those characteristics are also true for rare diseases
 - Enormous problem
 - Impact of rare diseases on families in term of divorces for instance
 - Also linked to the economics and the burden to a society

- Discussion at the last ECRD meeting in the “Quality of life” session
 - Care-takers often see their activities strongly modified that corresponds to the definition of disability
 - Could we consider that care-takers are suffering from a “disability”?
 - Could they pretend to a compensation?

[Post-Meeting Note The change of leadership for the Activity D was discussed and approved during the Operating Committee meeting on June 6, 2018. A leadership call will be organized in July 2018 between the chairs of all the committees interested in participating in this activity.]

4. Potential 2019 activities

4.1 Reflection around metrics to evaluate IRDiRC Goal 3

- ▶ How can we measure the economic impact of the diagnostic odyssey?
 - New discipline that likely should be added to the ISC
 - Health economics/public health
 - Development of a potential TF
- ▶ Concept behind economic impact
 - Economic impact of delayed diagnosis?
 - Economic impact on rare diseases?
 - Promotion of research in health economics to
 - Compare existing systems
 - Demonstrate how some organizations are saving time/resources
- ▶ The former EU funded project “Social Economic Burden and Health-Related Quality of Life in Patients with Rare Diseases in Europe” (BURQOL-RD) was working on similar questions
 - Aim was to generate a model to quantify the socio-economic costs and health-related quality of life (HRQOL), for both patients and caregivers, for up to 10 rare diseases in different European countries
 - Several publications came out from this initiative
 - Funding ended
- ▶ What are we exactly searching for?
 - Economic methodologies?
 - Economic impact?
 - Mission of IRDiRC seems more on methodologies
 - Maybe a TF should be set up to already answer the question of focus
- ▶ Two major complaints from the rare diseases field

- Disease model
 - When new drug is developed, developers always want to know its life time impact
 - Shortly after commercialization, need to model the impact to extrapolate it to a life time scale
 - Assessment of utility
 - Mainly based on the European Quality of life 5 dimensions (IQ5) questionnaire
 - Mobility
 - Self-care
 - Usual activities
 - Pain/discomfort (important weight in the questionnaire)
 - Anxiety/depression
 - This questionnaire was originally developed for the oncologic field
 - Economists say it is appropriate for rare diseases
 - Patients disagree as it does not reflect rare diseases impact of life quality
- ▶ How to measure impact on Quality of Life? if not via economics?
- ▶ Therapies are available but do they have access to the therapies?
- Are HTA people interested in those questions?
 - In rich countries, it is not about can I produce or not economic activities? It is more about the value of an improvement to the patient (utility score)
 - IQ5 questionnaire is the standard
 - Questioned for lots of diseases
 - Measurements of quality of life need to be translated appropriately into a meaningful utility score
 - Crucial for multi-system rare diseases
- ▶ ISC would probably need to extend its expertise. What type of profile would be interesting?
- People from the Centers for Medicare and Medicaid Services (CMS)?
 - HTA community
 - Well organized, easy to identify
 - Payers community
 - More complicated
 - Community is quite closed
 - Decisions are made every day regarding reimbursement/healthcare but you do not hear about those decisions otherwise people get demolished by social media
 - Payers might work with IRDiRC if we keep their privacy
 - Do the payers community relay on the HTA community?
 - It depends
 - UK payers for instance have a rule based on cost per quality adjusted life years' (QALYs). So they use HTA

- Example from Poland where it was long said that there is no tradition of economic evaluation by the state
 - Recently, it was found out that an organization in the state was producing the economic evaluation
 - Both communities are quite different
 - This model is however changing in US
 - IT expert would also be valuable to bring a more practical point of view on health economics questions
- ▶ Important topic for rare diseases
 - Insurers are thinking about this topic:
 - Not everything can be reimbursement
 - Global reflection on what would be appropriate for rare diseases patients
 - A lot of undiagnosed patients will remain undiagnosed, costly we would need to propose solutions
 - Some insurers are investing consequent amount of money to develop IT solutions to identify rare diseases patients before they are diagnosed
 - Statistics of frequency of
 - medical appointments with specialists
 - hospitalizations
 - ISC members agreed this activity could be initiated as soon experts have been identified
- ▶ Next steps for this activity
 - Presentation at the Joint Scientific Committee meeting
 - Identification of experts
 - Writing a TF proposal
 - Identification new members in parallel
 - Experts participating to the TF could become ISC members in a longer term perspective

→ ISC members are asked to send their suggestions of experts for the TF and/or potential new ISC members with expertise in health economics

[Post Meeting Note Given the priority of the goal, the Operating Committee decided to lead this activity and to set a short term working group in close collaboration with all IRDiRC Committees as well as external experts]

4.2 Data provision from different data sources: rare diseases research and social media

- ▶ It seems linked to the second topic proposed in the CRNRD TF

- Namely, the promotion of community-based research and data provision using innovative approaches
- ▶ Examples of existing initiatives based on social media
 - Epidemium initiated by Roche
 - Initiative is a data challenge oriented and community-based open science program in the field on cancer research
 - Identification of environmental factors, risk factors... out of large data set (mathematical modelling)
 - At the last REACT congress, a Brazilian initiative was presented:
 - Website where patients would mention what they observed as symptoms and researchers would go and verify local populations and identify rare diseases patients
- ▶ Examples of initiatives at a country-scale
 - Precision Medicine Initiative (PMI)
 - need to incorporate many different types of data, from metabolomics, genomics, the microbiome and data about the patient collected by health care providers and the patients themselves
 - All genomics data produced are going back to the patient
 - Not focused on rare diseases but methods can be interesting
 - Genomics England
 - Sequencing 100000 DNA codes of patients, leading to better, earlier diagnosis and personalized care, for cancer, rare diseases and infectious diseases
 - This project is for NHS patients who have certain rare diseases, plus their families, or who have cancer. Patients will be invited to take part by their hospital doctor
- ▶ ISC members decided to include at least partially included in the second part/follow up activity of the of the Clinical Research Networks for Rare Diseases TF

Next steps and actions

- ▶ Communicate on the article of the PPRL Task Force as soon it will be online
- ▶ Update the Clinical Research Networks for Rare Diseases TF proposal
- ▶ Send suggestions of experts in health economics