IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Meeting report series

Report of the 6th Patient Advocacy Constituent Committee Meeting

Vienna, Austria
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Participants

Yukiko Nishimura, ASrid, Japan – Vice Chair
Virginie Bros-Facer, EURORDIS – Rare Diseases Europe, France
Ritu Jain, Rare Diseases International, Singapore
Katherine Lambertson, Genetic Alliance, USA
Ramaiah Muthyala, I-ORD, India
Qi Sun, CORD, China

Kym Boycott, EURORDIS – Rare Diseases Europe, France –Chair DSC
Virginie Hivert, EURORDIS – Rare Diseases Europe, France – Vice Chair TSC

Christine Cutillo, NCATS, USA
Marlène Jagut, Scientific Secretariat, France

Apologies

Nicole Boice, Global Genes, USA
Kelly du Plessis, RDSA, South Africa
Prasanna Kumar Shirol, ORDI, India
Nicole Millis, RVA, Australia
Peter Saltonstall, NORD, USA
Eda Selebasto, BORDIS, Botswana
Durhane Wong-Rieger, CORD, Canada

Agenda

REPORT

1. Welcome and roundtable

The PACC Vice Chair welcomed all participants and shortly reminded the core mission/objectives of the committee:

- Mission:
  - Actively contribute to the IRDiRC global vision, goals, and set of actions that will accelerate diagnostic and therapeutic development and deployment for all rare diseases, from the patients' perspective
- Objectives toward the 2027 Goals (evolving over time):
  - Address systemic issues and obstacles to patient participation in research
  - Articulate points in the diagnostic and therapeutic development process where patient involvement is crucial
  - Measure success and impact of patient involvement (particularly in areas contributory to the IRDiRC goals)
  - Focus on patient group deliverables that demonstrably advance the goals and activities of other IRDiRC constituencies

Katherine Lambertson is the Assistant Director of Translational Science at Genetic Alliance. The organization serves the mission of IRDiRC by building capacity of patients' organizations to conduct research.

Yukiko Nishimura is the Founder of ASrid in Japan and Vice Chair of the PACC.

Qi Sun represents the Chinese Organization for Rare Disorders (CORD). Before joining CORD 3 months ago, she worked as a prenatal diagnostic physician.

Kym Boycott is Chair of the Diagnostics Scientific Committee. She attended the meeting as an external expert to provide her input on research.

Virginie Hivert is the Vice Chair of the Therapies Scientific Committee. She works as Therapeutic Development Director for EURORDIS – Rare Diseases Europe. She is particularly involved in the patient engagement activities as well as activities surrounding patient empowerment organized by EURORDIS.

Virginie Bros-Facer works as Scientific Director for EURORDIS – Rare Diseases Europe. She focuses her work on patient engagement in research in the diagnostics area as well as research infrastructures (biobanks, registries…). She is also involved in patient engagement in new technologies such as genome editing. The organization serves the mission of IRDiRC by developing capacity building programs to enable

patient to engage in therapeutic development, regulatory processes, genetics, genomics, diagnostics, data sharing.

Ritu Jain comes from Singapore and represents Rare Diseases International that brings together national/international patients' organizations as well as international rare diseases specific federations (more than 50 members organizations that represent patients in more than 100 countries worldwide). The organization serves the mission of IRDiRC by furthering research policies for the benefits of the larger rare diseases community.

Ramaiah Muthyala is the President of the Indian Organization for Rare Diseases that is now present for 15 years. Its first goal was to define what is a rare disease. Challenges faced by developing countries are very unique and not always understood by developed countries.

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. Action B: Identify barriers to patient participation in RD R&D, offer recommendations to remove them

2.1 Background

The action of the PACC is aimed at the identification of barriers to patient participation in RD R&D and recommendations to remove them

Prior discussion:

- The topic will be investigated by creating a multi-stakeholder survey that will be sent to patients and other stakeholders
- The expected outcome is a set of recommendations on how to empower and enable patient participation in rare diseases research
- These steps agreed upon will be:
  - Determination of the target audience design of the survey
  - Translation of the survey
  - Followed by a survey period, and
  - A workshop in which the outcomes are discussed.
  - Based on this discussion, recommendations will be drafted, and
  - Recommendations will be published

Discussion to prepare for this activity:

- Overall

- What is our goal and vision for this survey? Each member articulates their need for this survey – what would you like to see it achieve for patients in your region? (Reminder, this is not necessarily about furthering your organization, it is about furthering what is best for people.)
- Who will be the recipient of these recommendations? Funders? Policymakers? Researchers? Clinicians? Patients? All? This should follow from goal.
- Barriers run the gamut, including (but not limited to): no rare diseases research available in a region or nation, a complete unawareness of the possibility of participation, competing priorities, too many research projects offered without coordination or concern for the patient populations' most pressing needs. Currently, resources are mainly focused in the western world meaning that a great deal of the world is neglected. In fact, greater numbers of people do not have access to research than do. Can a survey be tiered in such a way as to gather this spectrum without alienating those who have no access at all, or losing the interest of those who have many options? How to structure the survey to manage this myriad?
- If the final desired outcome is to remove the barriers, there are two steps:
  - What crucial opportunities for patient participation in R&D?
  - What are the barriers to participation and how are they alleviated?

- Timeline
  - If we execute a survey, how long do we need to formulate the questions?
  - How do we determine where in the world and through which networks we will deploy the survey?
- Survey
  - Need for interpretation and translation into hundreds of languages?
  - Digital and non-digital deployment?

2.2 Redefinition of the original proposed activity

- The initial project proposed by the PACC in November during the Tokyo meeting was approved as a concept by the Consortium Assembly (CA) via the IRDiRC Roadmap 2018 in January 2018. The full proposal of the Activity is needed to delineate the timeline, output, requirements, stakeholders and metrics necessary to successfully complete the Activity.
  - PACC to develop Activity proposal
  - CA to review and approve proposal

- Similar and/or related recent survey initiatives:
  - **Rare Barometer** from EURORDIS-Rare Diseases Europe:
    - Evidence based advocacy

- Contribute to policy based on patients
- Pool of 7000 patients (only EU for a long time, last two surveys beyond EU)
- Will never become multi-stakeholders
- Large project that requires significant economical and human resources
    - Involves people experienced in survey design/management and methodologists
    - Multi-stakeholder steering group to help in phrasing the questions
    - Translation in 23 EU languages done pro bono by a company
    - If were to do similar approach within the IRDiRC context
        - Need for methodologist
        - Need for survey expert
        - Need for language translation at several levels: questionnaire, analysis, and reporting
        - Because multi-stakeholder in the case of IRDiRC, need to adapt questions to the audience(s) targeted
- Survey (February 2017): "Access to treatment: unequal care for European rare disease patients"
- Survey (February 2018): "Rare disease patients' participation in research"
- Future topic: "Unmet pediatric needs"

- EURORDIS – Rare Diseases Europe is involved in the **PARADIGM** program:
    - Started in March 2018
    - Focus on patient engagement throughout therapeutic development
    - Idea is to provide sustainable and meaningful tools for patient engagement
    - Multi stakeholder project (patients' organizations, industries, regulators, HTA, clinicians)
    - EU focused
    - Not specific to rare diseases
    - Financially supported by IMI (Innovative Medicine Initiatives)
    - Now includes a survey (in the process of being finalized). Barriers encountered:
        - Patient engagement does not have the same meaning for everyone
        - To obtain meaningful answers/data, a lot of detail is required for phrasing questions appropriately across various languages
    - Also involves a group developing templates, recommendations on how to interact with regulators, HTA bodies, and pharmaceuticals companies
    - Also includes a business component: "How to sustain the patient engagement?" It provides good principles on how to compensate patients for their time, and how to deal with conflict of interest when patients have to interact with the industry

- What are the data/information that we want to determine? What are the goals? How do we best go about accomplishing those goals and generating that data/information?

- What are we going to gain?
- How to phrase the questions?
  - Perception/understanding is different depending on education, background, experience, origin…
- What is the best strategy?
  - Asking lots of people?
  - Asking small groups of people from lots of countries?
  - Asking a variety of people (different disease representative, different stakeholders)?
  - To capitalize on the dedication within IRDiRC, it was suggested to work with focus groups formed within IRDiRC's own patient organizations (their constituents)
- Important to consider the time to do the survey
  - If it takes several years, barriers might be different at the moment we analyze the data
  - Want to pursue a strategy with a shorter-term win?

- Identification of exact needs before initiating the survey:
  - Do we want to make recommendations on advocacy side?
    - For example, advocate for more access to policy makers and others stakeholders
  - Do we want to make recommendations on what the funders could/should fund?
    - Identification of topics that funders could address with funding calls
  - Both?
  - Already identified need for more capacity-building programs

- Identification of the target audience for the survey
  - PACC members and the organization(s) they represent
  - All stakeholders within PACC members' organizations
  - Importance to be international
    - Difficult to be global at first
      - Composition of PACC itself will help for this matter
    - Step by step process (expansion phase)
    - Barriers identified:
      - Will be distinct depending on geographical area
      - Some barriers will be common
      - Will help to identify which barrier to tackle in which area
  - Environmental scan survey based on partners within IRDiRC
  - Organization of focus group survey within each PACC members' organization
    - Required personal, facilitators …
  - Critical to expand audience to:
    - medical doctors
      - Medical professionals working in "non-digitalized" area is critical to ensure the voice of patients they are treating is heard

- Policy makers
- Funders, academics, industries because of the research focus

- The multi-stakeholders approach is crucial to ensure the high impact of this survey

- Some funders are already aware of barriers to patient engagement in research and already try to put solutions in place (e.g., Canada)

- Creation of a complementary survey to IRDiRC funders/companies
  - Survey can access both barriers and solutions with an assessment of the efficacy of the latest
  - Look at strategies that each of their jurisdictions has used to engage patients in research
  - Ask what are the funders'/companies' objectives in term of patient engagement
  - Perhaps set up as "interviews" with a member of the Sci Sec to alleviate the strain of many free text questions/answers (both taking and analyzing the survey).

- Creation of a complementary survey to IRDiRC Scientific Committees members
  - As an academic, what do you perceive as a barrier to patient engagement when you design your research studies?
  - Perhaps set up as "interviews" with a member of the Sci Sec to alleviate the strain of many free text questions/answers (both taking and analyzing the survey).

- Already great task to engage IRDiRC members and ask for their appropriate feedback after they consult the organization they represent

Conclusion

PACC members raised the following concerns regarding their original project**:**

- Utility
  - Initial suggested approach – potentially not significant added value (too many objectives); can accomplish within a more limited framework
- Resources
  - Requirements of wide-reaching, multilingual survey – significant
- Time
  - Lengthy process – outdated once accomplish outcomes
- Expertise
  - Survey research – complex and requires diverse expertise
- Access
  - Reaching developing nations – hurdles re infrastructure etc.

PACC members are now proposing **an environmental scan survey directed to all IRDiRC members** (and their organizations by extension) to identify:

- Barriers to patients' engagement

- Solutions (existing or not) to incentivize patients' engagement

2.3 Discussion around implementation/outcomes of the new activity

- Possible outcomes
  - Identification of gaps
  - Recommendations around possible area for funding
  - Recommendations to facilitate patient engagement

- Questions to PACC members
  - Barriers/challenges to patient engagement
  - Ideas or solutions to tackle patient engagement (proven efficient or not)

- Questions to funders/companies members
  - Barriers/challenges to patient engagement
  - Ideas or solutions to tackle patient engagement (proven efficient, if easier to share)

- Questions to scientific committees' members
  - Scientific Committees members as a representation of academic researchers
  - Depending on their organization, they can also give feedback on funding
    - Questions on sponsoring by industries or funding agencies
    - Questions on patients' recruitment

- Definition/phrasing of the questions
  - Via a PACC lead Task Force?
  - Need input from others stakeholders to pinpoint the questions
    - At least a representative from each stakeholder
  - Include a methodologist
  - Survey will be mainly done in English
    - Translation will however be needed for some PACC focus groups (before their focus group, analysis and reporting)
    - To avoid bias of translation, it might be important to work with a professional translator instead of relying on each PACC member

- Coordination of different surveys
  - Scientific Secretariat could arrange and manage interviews on the phone for IRDiRC members (funders, companies, scientific committees)
    - Increase response rate
    - More sensitive interpretation of qualitative answer
    - Interview should last max 30 minutes
    - Questions should be provided before the phone interview

- To ease to data collection, could be both a survey and interviews
  - Quantitative data are easier collected via a survey
    - Survey monkey?
    - Qualtrics? (paying software but affordable)
  - Qualitative data are easier collected during interviews

- Need face to face meeting to agree on recommendations
  - Definition of questions can be done by teleconference
  - Even some analysis can be done by teleconference

- Composition of the Task Force
  - PACC members (all?)
  - One member of each scientific (DSC, ISC, TSC) and constituent committees (CCC and FCC)
  - Methodologist(s)
    - Expert in qualitative data analysis
    - Expert in Quantitative data analysis
    - Search for someone working for one of the PACC members' organization? Pro bono?
  - Data protection/ethics expert
    - This aspect has to be carefully evaluated to be able to use the data afterwards
    - Should they be anonymized before analyzed by the experts?
    - For their surveys, EURORDIS – Rare diseases Europe uses the CNIL, a French organism dedicated to data protection
    - In ISC, Dixie Baker has an expertise in data protection. Maybe the PACC could solicit her for feedback.
    - Important to comply with all countries regulations
    - What type of data are we collecting? Where are we storing the data? Who will have access to the data?... We need to answer all those questions
- Timeline
  - Development of the proposal
    - Within PACC
    - By teleconference
    - Before June 30
    - Will be submitted to CA electronic vote as the next CA teleconference might only take place in September
  - In parallel, identification of key members of the Task Forces
    - Identification of a methodologist
      - Via IRDiRC members' network
      - Via IRDiRC newsletter or website
    - Identification of the data analysis expert
    - Identification of the data protection expert

        - Essential to identify members that will have to be remunerated to give a ballpark figure for the budget of this activity
    - Need for a background document?
        - The Scientific Secretariat had already collected documents at the occasion of the previous patient engagement task force
    - Next CA F2F meeting will take place on December 6-7, 2018
        - TF should be initiated at this time
        - Precise budget will be defined then
        - Meeting for this TF in conjunction with F2F?
            - Invite members by September 2018
    - Analysis of data
        - Use IRDiRC spring meeting 2019 for intermediate data analysis
        - Use IRDiRC autumn meeting 2019 for final meeting for recommendations

2.4 Activity B new proposal

Goal:

- Leverage IRDiRC's stakeholder and geographic representation for complementary environmental scan

Justifications:

- Identify barriers from the perspectives of all stakeholders within IRDiRC
- Determine whether existing strategies align with barriers identified by stakeholders

Potential outcomes:

- Create list of the suite of methodologies/strategies used in patient engagement (from Funders/Companies perspective)
    - Developing countries can view the list; see which they potentially could use
- Develop recommendations:
    - Facilitate better patient engagement across geographic areas with shared resources
    - Determine strategic areas for new funding initiatives
    - How do the findings inform future activities of IRDiRC

Proposed steps:

- PACC-led TF to define feasibility & implementation

- Members
  - Include members from PACC, Funders, Companies, and SCs + methodologist (external) + qualitative data analysis expert (external) + data protection expert
- Define design/implementation details
  - Define questions to ask IRDiRC stakeholders (via TC)
  - Instrument: interview only, inclusion of survey, digital?
- Develop budget and reach of focus groups + surveys
  - PACC question development and data analysis would require translation ($$)
- Analysis of results (F2F)
- Ethics and research oversight and data protection?
  - PACC member barriers – gets further into this territory (and away from the environmental scan)
  - Vis-à-vis regulations across various geographical areas
  - Avoid academic survey arena, if possible

- Initiate PACC focus groups
  - Each PACC member goes back to own organization and facilitates focus groups
  - Questions focused around:
    - What are the distinct barriers that your constituents face?
    - What are the solutions that have been shown to be successful?
    - What are new potential solutions for issues faced?

- Initiate Funders, Companies scan
  - Questions focused around: what are the methodologies or strategies to conduct patient engagement in research? What are your solutions?
  - Interviews performed by the Sci Sec (30 minutes max) – easing burden on members

- Initiate SC scan to represent academic researchers across jurisdictions
  - Questions focused how do our industry sponsors deal with this and are they effective/appropriate?
  - Interviews performed by the Sci Sec (30 minutes max)

<u>Timeline:</u>

- Develop proposal (within the PACC)
  - Finalize (include identification of key members of TF) – by June 30
  - Determine members (internal and external) and those than need to be remunerated
  - Present to CA/vote – **via email over summer** (since awaiting until fall for CA TC not optimal/feasible); by Aug
- Initiate TF
  - Send out invitations (internal and external) and hold for F2F Mtg in conjunction with CA – by Sept

- Start work
  - Define design/implementation details (via TC)
  - Finalize budget and reach of focus groups + surveys – at Dec 6-7 CA Mtg
  - Initiate focus groups + surveys – Q1 2019
  - Intermediate review – Q2 2019 (take advantage of May 2019 CA F2F)
  - Review results and develop recommendations – Q3 2019

→ PACC members to go back to their organizations to identify capacity, resources and/or time needed to establish a focus group

→ PACC members to go back to their organizations/networks to identify potential experts that could be involved in this project (translation, data analysis, data protection, methodologist)

3. Action F

- Action F: Issue position statement including specific recommendations on:
  - Model for applying Goal 2 (therapy development) internationally
  - Model for inclusion of patients' perspectives in that therapy development

3.1 Background

- Second action of the PACC, to create a position statement including specific recommendations on:
  - Model for applying Goal 2 (therapy development) internationally, thereby aimed at stimulating drug development equally worldwide
  - Model for inclusion of patients' perspectives in that therapy development
  - The expected outcome is a recommendations or position paper to nations re: multi-stakeholder collaboration on regulatory and therapy development pathways
  - This action is scheduled to take place after Action B has finished

- Members of the PACC expressed a desire to make a simple placeholder statement at this time.
  - What are the basic principles that all can agree on with regard to the inclusion of patient perspectives in therapy development?
    - What other aspects appear to be obvious and the members can agree are essential?
  - Where are areas of either disagreement or places that are impossible to set as baselines given the variation in access to the process?
  - Would this body like to make a preliminary position statement while waiting for the longer process of Action B? If yes, how to proceed?

3.2 Discussion

- IRDiRC goal 2: "1000 new therapies for rare diseases will be approved, the majority of which will focus on diseases without approved options"
  - Difficult to apply worldwide
  - Important to measure the impact on patients more than the number of therapies

- Idea behind the 1000 new therapies is to drive the economic fall and see the consequences

- Notion of impact is embedded in IRDiRC goal 3: "Methodologies will be developed to assess the impact of diagnoses and therapies on rare disease patients"
  - No one knows how to measure the impact practically

- Challenges of expensive therapies
  - Could be sold to more patients and would become cheaper
  - Lots of patients are in developing countries
  - Difficult to access/identify those patients

→ PACC members decided to include this activity partially in their survey

4. Areas of need/potential focus for the Consortium in the future

4.1 Prevention

- Prevention is not part of the current IRDiRC mission, however it is an important topic to be discussed:
  - IRDiRC focuses its action on the present to help people living now with a disease
  - Prevention of next sick children is another question
  - **Important issue to be raised in the future**
  - It is a society issue to also project ourselves in 100 years from now

- Ideas behind prevention:
  - Not all 7000 rare diseases are treatable
  - Philosophical debate about costs of advanced therapies that will not reach most patients vs prevention:
    - How much should the society invest in advanced therapies that will take decades to get to market?
    - Versus prevention for people that want that option
    - Both should probably be developed **in parallel**

- There is no prevention without diagnostics:
  - DSC could work on the prevention issue
  - At the moment, DSC works on carrier screening

- Examples of prevention:
  - For the last 24 years, India developed prevention for skin cells diseases and it has been now expanded to hemophilia
  - China pay more attention to prevent birth defects than develop treatments for economic reasons

- Some "more common" rare diseases have a diagnosis that is expensive and in consequence not accessible to developed countries.
  - Development of cheaper way to diagnose those patients in developing countries is essential
  - Idea could be to already focus on the 2000 monogenic diseases instead of complex ones
  - Economic barrier as it is more difficult to get funding for a project that want to optimize something already existing

4.2 Others

- Data protection/ethics and research oversight

- Capacity building re: patient involvement in research
  - Possibility within IRDiRC to develop capacity building for patients but also for the other stakeholders?
  - Real need
  - Multi-sector/stakeholder (patient, researcher, institution, high level funding agency)
  - E.g. train-the-trainer knowledge platforms

- Access
  - Innovative instruments/technologies
    - For data collection (re cost and access)
    - Language translation and/or pictorial representation

5. Annex document

The following graph was provided to PACC members to help them visualize how applicable on a global level are the actions they are proposing.

Next steps and actions

- Draft a proposal for Activity B
- Validation of the activity B proposal by teleconference
- Identify capacity, resources and/or time needed to establish a focus group
- Identify a methodologist
- Identify a data protection expert
- Identity a data analysis expert (qualitative/quantitative/both?)