IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Meeting report series

Report of the 10th Funders Constituent Committee Meeting

Leiden, Netherlands
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Agenda

1. Welcome and introduction
2. Follow up **Activity A**: Establish process to coordinate and prioritize research funding efforts
    a. Presentation of database of projects by *MyScienceWork*
    b. Live test and discussion on next steps
3. Presentation of Terms of Reference for confidential sharing of information on forthcoming funding opportunities
4. Data management requirement implemented by funders – presentation
5. FCC roadmap for 2020
    a. State of the art of FCC activities accomplished so far
    b. FCC actions to contribute to IRDiRC goals – preparatory document
    c. FCC & CCC joint discussion on subjects of interest – possibly Chrysalis Task Force (boosting research for promising RDs – key criteria for RD to be picked up by pharma)
    d. Decision on actions to implement in 2020

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REPORT

1. Welcome and introduction

The Chair of the Funders Constituent Committee (FCC) thanked and welcomed participating members to the meeting, aimed to discuss the results of the MSW survey for collecting required data for the funding project database, that is part of Activity A and the next steps in this project, as well as to provide an overview of existing data-sharing policies to move forward in the implementation of a working group addressing this topic, and the agenda for 2020.

2. Follow up Activity A: Establish process to coordinate and prioritize research funding efforts

Aim is to systematically track and analyze global rare disease funding landscape, and coordinate that of all IRDiRC members.

Expectation is that this effort will provide a tool that allows for in-depth analysis of funded projects and the rare diseases research funding landscape at an international level – to enable better understanding, address the gaps in research, and provide a basis for further funding coordination.

2.1. Presentation of database of projects

MyScienceWork (MSW) presented the outcome of the funders survey, and provided a description on the development progress of the tool.

Topics covered included:

- Overview of how the solution works
- Project timeline
  - Call for tenders launched in July 2018
  - MSW selected as tender in Nov 2018
  - Funders survey sent out in Feb 2019
  - Currently testing data curation
- Data curation process
  - To automatize data capture and improve data quality
  - One algorithm for detecting diseases in research projects, and another for distinguishing rare diseases from non-rare conditions (currently working with 80% accuracy)
  - Minimum set of information required:
    - Type (national or multinational)
    - Title in English
    - Abstract
    - Abstract url

- Country (coordinating if multinational)
- Start date
- End date
- Funding institution

- Survey results (22 respondents)
  - For the majority, data is available on a database (72,7%), and allow manual extraction only (59,1%)
    - Manual extraction does not pose a problem, as long as the minimum set of required information is provided
  - The majority (69,2%) can provide data in a suitable format
    - Among funders with data available on the website, only some (37,5%) would allow MSW to craw freely: the majority (62,5%) request permission
    - MSW needs to know **where** to find the data, **how** they will collect the data and **what** information is available; minimum set of information is required (see above)
  - The tool will allow to analyze all of the following information:
    - Total number of rare disease related research projects and clinical trials
    - Distribution research projects/CTs per medical domain
    - Comparison of the weight of the medical domain over the total number of RD and the weight of the research in that domain
    - Research coverage of RD in total and by medical domain
    - Distribution of research projects/CTs by classes of prevalence
    - Distribution of research projects/CTs by disease
    - Distribution of research projects by category of research (in total and by medical domain)
    - Distribution of CTs by category and by phase (in total and by medical domain)
    - Distribution of the total budget funded by medical domain, by disease, by category of research/CTs
    - Comparison between countries and over time (respect to domain/diseases /categories covered)
    - Comparison between funders and over time (respect to domain/diseases /categories covered)
    - Comparison over time (respect to domain/diseases/categories covered)

- An overview of the database interface and a demonstration of the tool was also provided

2.2. Questions asked by funders

- How to indicate prevalence correctly?
- For the rate of currency, is it possible to link to a specific API that will convert them automatically at the moment of the analysis?

- Does multilingual support mean that you can translate from Japanese to English automatically? → it does not currently work with Chinese, Japanese or Korean
- Colleagues from China propose to connect to their API that translates Chinese to English
- What about the curation on the type of project? Will the tagging be done manually if not completed from the start? What about the projects that include several aspects, e.g. translational research and drug development? How to tag them?
- How to tag multi-rare diseases projects? (that cover more than one RD)?
- What about the projects in which IRDiRC members are the only funders, but the project includes also teams funded by other funders not being part of IRDiRC consortium?
- There is an absolute need for indication on multinational funding (of one project) and not imposing of one main funder per project!
- Same as above for funding amounts (per country but also per funder, as there are several funders from the same country and we should be able to distinguish them)
- Is URL really mandatory?

2.3. Next steps:

- Survey still open
- Test the analytics with funders' data
- Define a common currency
- Set the exchange rates

3. Presentation of Terms of Reference for confidential sharing of information on forthcoming funding opportunities

This will be discussed later on.

4. Data management requirement implemented by funders

In 2018, all FCC members were asked to fill out a funding collaboration questionnaire in order to investigate a first step towards stronger funding collaboration: 20 out of 25 respondents indicated the existence of a dedicated policy on data sharing as part of their standard funding procedures. Data sharing was also pointed as an important item for the IRDiRC Roadmap.

For this breakout session of the FCC, the Sci Sec prepared a presentation based on a literature report exploring 27 data-sharing policies. This introductory analysis was intended to answer the following questions:

- What are the requirements other funders have adopted in their data-sharing policies?
- What are the commonalities and differences in procedures?
- What are the gaps/bottlenecks to make the strategies more harmonized?
- Which of the recommendations FCC members already apply?

- Whether more in depth analysis among IRDiRC funders is needed to work on the next steps?
- What steps FCC members can take to enhance/facilitate data sharing?

4.1. Review of Funder Policies and Practices

The common elements of DSPs are:

- Data Management Plan (DMP)
  - 21 out of 27 funders require grantees to submit plans for sharing data
    - 19 out of 21 funders require a DMP with every funding request
    - *NIH* grants over $500K
    - *Wellcome Trust* grants which produce data of value for further research
- Data
  - 11 out of 27 funders ask grantees to share data underlying published research
  - 6 policies ask grantees to share data collected during the course of research, whether or not the data is used in a publication
  - 6 agencies ask grantees to share publication data as a minimum standard but may ask for further data to be shared depending on its likely value for re-use
  - Some funders (18 out of 27) specify that further materials should be shared, including metadata needed to interpret the data.
  - Funders do not specify in their policies exactly which elements about the data or study should be shared, in the vast majority of cases.
- Repositories
  - The majority (19 out of 27) of funders specify that data should be shared in a publicly accessible data repository.
  - 8 funders specify that grantees should share data in a subject-specific repository (also called a “domain” repository), if a relevant one is available.
- Persistent identifiers and data citation
  - A handful of funders (9 out of 27) mention that grantees should obtain a persistent identifier (e.g. a DOI) so that their datasets may be uniquely identified and cited, and that they should ensure that their publications cite and link to their data.
- Time limits:
  - The vast majority of funders (24 out of 27) specify when data should be shared.
  - The most common timeframe is to require data-sharing with publication or soon after (12 out of 27 policies), or 12 months following publication (2 policies).
  - 5 funders specify the minimum duration of time that data should be made available. The timeframes include: 10 years (2 policies), (7 years (1 policy), 5 years (2 policies).
- Confidentiality and informed consent
  - 20 out of 27 funders mentions safeguarding confidentiality of participants when sharing data publicly
  - Six policies mention obtaining informed consent that permits data collected as part of the study to be de-identified, used for future research purposes and shared broadly

- Compliance
    - 11 out of 27 policies mention that they will consider compliance with the data-sharing requirement in future funding applications.
    - The most common method of potential enforcement is to consider failure to comply in future funding decisions (7 out of 11).
- Costs
    - Many funders (16 out of 27) mention covering the costs that grantees incur while preparing and sharing data.
    - All but two of the funder policies ask that grantees describe these anticipated costs within their data management plan and budget for them in the initial funding application.

3.1.2. Policy considerations

- Should funders ask grantees to share a plan for sharing data with grant application?
- Submission of DMPs for all data-generating research projects, or only research which yields data likely to be of high value?
- What data should grantees share?
- How much data should be shared?
- Where data should be shared?
- When data should be shared and how long it should be preserved?
- whether compliance is monitored or action taken such as withholding funds
- Budget support, if any, grantees will receive for data management / sharing costs

3.1.3. Recommendations

- Funders request DMPs along with the funding application
- Costs of preparing and sharing data are included in the budget
- Asked grantees to submit a plan for how they will prepare and share data, along with their grant proposal
- Funders ask grantees to share publication data as minimum standard but also materials needed to interpret the data, at the time of publication.
- Sharing of more data on a case by case basis, depending on the likely re-use value of the data.
- Asked grantees to share data in appropriate publicly accessible repositories, preferably in domain repositories in order to promote data discoverability
- Committed to financially support the preparation and sharing of data
- Considered compliance with the policy in future funding decisions

4.2. Discussion – FCC inputs:

- Whether to mandate or recommending specific repositories? → grantees have their preferred depository.
- If funders mandate for sharing data they are expected to pay for that

- IRDiRC funders could recommend repositories that are specific to RDs? → Telethon recommends RD-Connect
- AMED has data sharing policy on human genome studies. Grantees are asked for data management plans but terms such as what is meant by data are not defined. The common practice is to share data through GeneBank and DDBJ (DNA DataBank of Japan) → data is kept up to 5-10 years.
- The GEM Japan, a GA4GH driver project, aspires to facilitate sharing of genomic and phenotypic information from completed and ongoing Japanese research efforts with the domestic and global communities
- At AFM-Telethon, only 1% of the budget is dedicated to data sharing
- In Spain, clauses for data sharing have not been clearly established
- EJP RD funded projects must submit a DMP along with the research proposal, and there are recommendations on which repositories to share data. The costs of data sharing for the life time of the project can be included in the proposal but there is no dedicated budget defined.
- There is a discussion within EJP RD and in Europe at large on putting some policies in place with part of the budget (5%) dedicated to data management and sharing, regardless the type of the project.
- The central questions are:
    - How to ensure the long-term preservation?
    - Where to deposit the data?
    - Who will pay for that?

4.3. Conclusions

There is an interest to set up a working group, and engage with other organizations such as GA4GH, to decide on the further steps to be taken.

- One action might include recommendations in relation to repositories, sustainability, and budget

5. FCC roadmap for 2020

In 2017, the FCC initiated an exercise to identify short, medium and long-term actions in need of implementation for achieving the IRDiRC Goals. The state of the art of activities were discussed.

4.1. FCC activities accomplished so far

- Action 2: Coordinate and utilize RD networks, infrastructures and sustain projects to create global R&D ecosystem → medium term → **Joint Activity G = Clinical Research Networks for RDs (ISC, TSC, FCC)**
- Action 3: Establish processes whereby funders can coordinate and prioritize efforts on research and avoid unnecessary duplication → short term → **Activity A = Database of funded projects with analytic tool**

- Action 7: Formulate and disseminate standards and guidelines including promotion of natural history studies → short term → **Joint Activity D = Natural History Studies (ISC, TSC, FCC)**

- Working group on ELSI in rare diseases. → **Outputs:**
  - Paper submitted to EJHG
  - E-Rare/IRDiRC workshop on Social Sciences & Humanities (Sep 20, 2019 in Gdansk, Poland)

4.2. FCC actions put on hold

- Action 1: Establish mechanisms whereby research toward better diagnosis and treatment is integrated into all clinical care of RD and long-term undiagnosed patients → medium term → **No actions taken by the Committee**
  - Identify actions that could be implemented by FCC members separately
- Action 4: Promote RD biomarkers and modifier discovery and validation→ medium term→ **No actions taken by the Committee**
  - Explore how individual FCC members are tackling this topic
- Action 5: Incorporate undiagnosed disease evaluation into the RD diagnostic paradigm→ medium term → **No actions taken by the Committee**
  - To be pursued at the level of IRDiRC; tackled by RD-connect (concluded)
- Action 6: Foster RD research, diagnosis and treatment in developing countries → short term → **No actions taken by the Committee**
  - Could be incorporated into the ISC-led transversal activity on the availability of drugs in low- and medium-income countries
- Action 8: Formulate and disseminate standards and guidelines including data and biospecimen sharing, data integration and consent processes→ medium-term→ **No actions taken by the Committee**
  - Pursue the discussion on data-sharing with other organizations addressing this topic, such as GA4GH
- Action 9: Accelerate identification and recruitment of RD patients in studies→ medium-term→ **No actions taken by the Committee**
  - This topic is partially being addressed by EURORDIS through the European Disease specific Federations, as well as other individual disease-specific patient organizations
- Action 10: Improve post-approval real world data collection→ long-term→ **No actions taken by the Committee**
  - Will wait the outcome of the Clinical Research Networks Task Force
- Action 11: Formulate and disseminate standards and guidelines on patient engagement in RD research and product development → **No actions taken by the Committee**
  - This topic is being addressed by the PACC through Activity B = Identification of barriers to and recommendations for patient participation in RD research. Also, the Paradigm project co-led by EPF and EFPIA will disseminate patient engagement guidance and tools
- Action 12: Create globally inclusive methodology for counting RD diagnostics and therapies→ medium-term→ **No actions taken by the Committee**
  - This topic will be addressed by the Working Group on Goal 3

- Action 13: Qualify the number of RD patients who receive diagnosis and treatment to ensure that research reaches and benefits patients → medium-term→ **No actions taken by the Committee**
  - This topic will be addressed by the Working Group on Goal 3
- Action 14: Promote RD methodology development for health technology assessment and health economics research to evaluate disease burden and access of patients to diagnostics and therapies → long-term → **No actions taken by the Committee**
  - This topic will be addressed by the Working Group on Goal 3

4.3. FCC & CCC joint discussion on topics of interest

The most envisaged joint action between FCC and CCC relates to the Penumbra Project (now Chrysalis project) that came out from discussions within the CCC. This joint action is aimed at defining what are the criteria that must be fulfilled for a RD to enter the pharma pipeline (CCC) and where are the gaps in the research pipeline for specific RDs (FCC), so as to:

- Boost research for promising RDs
  - Based on key criteria for RD to be picked up by pharma
  - & the capacity of the FCC to have a good overview of the state of the art and progress of research on specific RD (database of funded projects)
- With possibility to set up targeted funding opportunities to fill the gaps in the research « pipeline » to obtain complete portfolio necessary for the industrial partner

The Chrysalis project has connections with other IRDiRC activities, including the Molecular Etiology (ISC) and Neglected RDs (TSC)

4.4. Decision on actions to implement in 2020

Two items came up from this breakout session:

- Possibility for a working group on data-sharing
- The Chrysalis project as a joint Task Force with the FCC and CCC

5. Next steps FCC

The FCC is currently working on different topics:

- Activity A: Database of funded projects with analytic tool
  - With MyScienceWork and Orphanet
- Activity G: Clinical Research Networks
  - Joint Activity of ISC, FCC and TSC
  - Was formally approved at the CA meeting in Vienna, and will start in Q3 2019
- Activity D: Natural History Studies
  - Joint Activity of ISC, FCC, TSC
  - Was formally approved at the CA meeting in Brussels, and will start in Q4 2019
- ELSI Working Group

- Activity within FCC with some external experts
- Paper submitted to EJHG

Future actions to be implemented in 2020:

- Working Group on Data Sharing
  - First steps were made via the presentation provided by the Sci Sec on data-sharing policies landscape
- Chrysalis Project
  - Will be developed into a full proposal for approval at the CA teleconference by early September

Action Items and deliverables

- Continue analysis of the funders tool/database
- Set up a Working Group on data sharing
- Draft proposal for the Chrysalis project