INTERNATIONAL
RARE DISEASES RESEARCH
CONSORTIUM

Minutes of the 10th Executive Committee meeting

16 June 2014

IRDiRC

EXECUTIVE SUMMARY

The Executive Committee (Exec Com) of the International Rare Diseases Research Consortium (IRDiRC) met on 16 June 2014 by teleconference. The tenth meeting of the Exec Com brought together 21 participants including Exec Com members and representatives of two Scientific Committees (Sci Com).

Four proposals for tools to be funded were presented by the Sci Com to the Exec Com:

- Proposal to develop Model Consent clauses for rare diseases research (Interdisciplinary Sci Com)
- Proposal to develop a data standards clearinghouse for rare diseases (Interdisciplinary Sci Com)
- Proposal to develop resources for Community Development of the Human Phenotype Ontology (Diagnostic Sci Com)
- Proposal: enabling RD gene discovery Matchmaker exchange: pilot of v1.0 and development of v2.0 (Diagnostics Sci Com)

The Exec Com then discussed the possibilities for funding of these proposals. Two strategies were envisaged:

- Broad call to put money in a common pot.
- Gather volunteers or groups of volunteers interested in participating to fund a project individually.

Several members have constraints for the financing of such projects. However, there may be a possibility of funding of the tasks to be conducted in Canada. In addition, some tasks are part of work packages of projects funded by the European Commission and a re-allocation of resources is conceivable.

Further discussion is necessary if the decision to develop a funding framework is taken.

REPORT

Proposals for project funding from the Scientific Committees

Two proposals from the Interdisciplinary Sci Com and two proposals from the Diagnostics Sci Com were briefly presented to the Exec Com. A discussion on the possibilities to fund these proposals, without the presence on the Sci Com representatives, ensued.

Proposal to develop Model Consent clauses for rare diseases research (Interdisciplinary Sci Com)

Localization: Canada
Duration: a few months

The purpose of this proposal is to develop model consent clauses for rare disease researchers based on robust bioethical and legal approaches. This "one- stop-shop" resource of consent tools will allow rare disease researchers to select relevant consent clauses based on their research contexts and participant populations and consequently, assist in the customization of their own consent documents. This small proposal specifically addresses the consent needs of the various subpopulations within the rare diseases community by providing a tool kit for researchers in the field.

This short project is significant as there is a general need in the community in spite of recent development made in this area. For example, RD-Connect is not dealing with paediatrics issues per se or rare diseases as such (this proposal was approved by the project coordinator of RD-Connect and chair of the Interdisciplinary Sci Com). In the US, existing NIH projects are mostly specific to return of results issues. High number of hit on the International Policy interoperability and data Access Clearinghouse (IPAC) website, work with researchers (including European one) and experience from Forge Canada/Care for Rare demonstrate that clauses are helpful for researchers to be interoperable across jurisdiction.

There are several deliverables:

- Literature search on articles and tools that exists in terms of the specific needs of rare diseases (paediatrics, adults, and incompetent adults, including family members) will lead to the publication of a short article.
- Generic consent templates to be customized by researchers according to research, national or international needs of their project and specific clauses if they have difficulties with only one issue such as international sharing of samples across border.

This proposal only necessitates funding for one person for a few months to write the content for rare diseases portfolio (rare diseases and pediatrics rare diseases) as there is the infrastructure (IPAC) to do research.

Consent templates will be circulated to the IRDiRC WG on Ethics and Governance and the Interdisciplinary Sci Com for validation of specific clauses and generic templates before publication on IRDiRC and P3G-IPAC websites.

Proposal to develop a Data Standards Clearinghouse for Rare Diseases (Interdisciplinary Sci Com)

Localization: USA
Duration: over a year

Many groups are developing and/or posting standards for individual applications, some of which are applicable to rare diseases. However, there is no crosstalk and an absence of User supply information regarding how standards have been adapted or adopted for specific use cases projects or target populations.

The aim of this proposal is to collect standards from sponsor and user and to create a dynamic clearinghouse website, i.e., a central location for researchers and others to review what exists and be able to get reference from individuals to learn from adoption of standards moving forwards.

Key features of the website:

- The essential elements of the Clearinghouse include taxonomy of standards, a compendium of existing standards, use cases for standards, the standards themselves and references to sources.
- The Clearinghouse will be database driven, enabling searches by standards type, use and contributor
- Any visitor will be able to "deposit" a standard by completing a submission form

This proposal is much broader than proposal to develop resources for the Human Phenotype Ontology (see below).

Proposal to develop resources for Community Development of the Human Phenotype Ontology (Diagnostic Sci Com).

Localization: Australia/Canada/Germany
Duration: over 1 year

The objective is to improve the universality of the Human Phenotype Ontology (HPO) by expanding its impact and its uptake, and to ensure that HPO is meeting the need of the community for all area of rare diseases.

HPO was created 7 years ago and became a standard for rare diseases. However, it is a complex ontology that needs tools for use and sharing data as it is not accessible to most day-to-day users. In addition, there are some deficit within cancers, neurodevelopment disorders and psychiatric disorders.

There are three deliverables:

- To improve HPO website: enable community input, extend the ontology and implement tools for exchange between ontologies.
- To improve the interface called PhenoTips, which is a popular tool for the use of the HPO to capture patient data: addition of functionalities to capture novel terms, to review and convert entered free text forms to standard terms, etc.
- To improve the annotation of HPO terms in free text documents with further development of the BioLark Concept Recognizer tool.

Work done in this project will be partly distributed to the international community through the Clearinghouse.

Proposal: enabling RD gene discovery Matchmaker exchange: pilot of v1.0 and development of v2.0 (Diagnostics Sci Com)

Localization: Canada/USA
Duration: over a year

In order to facilitate the diagnosis of unsolved genetic diseases, the MatchMaker Exchange (MX) initiative, co-lead by IRDIRC and the Global Alliance for Genomics and Health has been developing an Application Program Interface (API) over the past 6 months to allow both phenotypic and genotypic data exchange between existing databases.

The initial version of the MX API (API 1) was developed in collaboration between GeneMatcher and PhenomeCentral, and involves the specification of a patient profile for which a “match” is requested.

The objectives of this proposal is to identify the correct amount of information to be transferred to establish a confident match, and then to develop the version 2 of API to be implemented by other initiatives (Café Variome, DECIPHER, and GEM.app).

Sequence of events:

- Assessment of the version 1.0 of the Matchmaker Exchange API for 6 months
- 2-days workshop to evaluate version 1 and draft version 2.0 of API
- Implementation and evaluation of API version 2.0

This is an international project but all the funding will go in Canada. The support needed in USA will be provided through exchange of work between Canada and USA.

Members of the Exec Com should keep in mind that proposals are flexible. There is a possibility to dialogue back and forth between Exec Com and Sci Com to adapt the proposals to ensure their implementation. These proposals are also an opportunity for IRDiRC to stamp their name on innovative work.

Discussion of Exec Com

General framework for funding proposal

Members of the Exec Com underlined two points:

- There is a challenge for funders in trying to understand the gaps - what are the gaps, what are we trying to solve, and what is the best way to fill them in. A gap analysis with clear identification of projects that are designated to fill the gap would be incredibly helpful to funders.
- It would be best to define and agree on a framework before awarding any project. Moreover, an estimation of future proposals and a system of timely call for application would allow competition and would avoid that proposals coming later cannot be funded despite their good quality.

The role of Sci Com is to identify the gaps and to define tools/projects necessaries to fill these gaps. The aim of this teleconference was to have a sense of possible projects to fill the gaps, and to discuss possible frameworks and mechanisms for funding, as there are yet no mechanisms or budget for this purpose. The goal is to move IRDiRC beyond the organization that talks to an organization trying to facilitate a better coordination as there is a need to move forward now.

There are several possibilities for funding these proposals:

- Common broad call: It would require setting up a process for evaluation. This would be the easiest way but there are constraints for most public funders.
- Gather volunteers or groups of volunteers among the funding bodies, interested in participating to fund a project individually (into their own processes and keeping in mind the international dimension of these proposals), with some attempt to coordinate so that the same players are not carrying the cost all the time. This would require less complicated agreement for each project.

It was specified that:

- To get funding by one of the members, Sci Com will certainly have to write a full proposal explaining uniqueness, overlap with other initiatives, etc.

- Spirit of IRDiRC is that each member participates as it can or wants.
- Rare diseases are the primary interest of IRDiRC but members hope implement tools/actions compatible with broader efforts such as Global Alliance for Genomics and Health and the Cancer community for example. It is thus worth discussion with these communities to have better compatibility.

Members with constraints will have difficulty to help funding projects. For example, NIH does not have any mechanisms for this type of funding for the moment and cannot fund international project unless there is no resources in US. Any process would need to be peer-reviewed and thus the timing would be longer than what is anticipated and hoped for by Sci Com. The European Commission system is based on open call for proposal for specific research topics. Topic for next call is already defined and it will be impossible to fund proposal from those calls. The next opportunity would be to include topics addressing these issues in the call for 2016, which is far away. There may be however the possibility to incorporate some of these elements in ongoing projects.

Possibilities for specific projects

Canada: Model Consent, Matchmaking and part of HPO projects

Genome Canada has reserved a budget to be spent on a project or mixture of projects for Global Alliance for Genomics and Health, with the purpose to fill gaps related to data sharing from institution, from problem between jurisdictions, etc. within Canada, with the idea of commonalities of system between the different communities (rare diseases, cancer, etc.). Some proposals presented here have direct or indirect link to some of the work ongoing for Global Alliance. There are indeed overlaps between IRDiRC and Global Alliance and there may be the possibility of funding tasks presented in the proposals, to be conducted in Canada, from the reserved fund for Global Alliance. Evaluation of projects would go through the usual process of international peer review.
CIHR would be partner of Genome Canada.

Clearinghouse
There is an overlap between the Clearinghouse project and a Work Package of Support-IRDiRC project (identify data standard and determine which ones should be developed). Support-IRDiRC would be able to offer support to the project by providing workforce.
RD-Connect is working on standards. The budget is already fulfilled with other activities, and there may not be any space for more activities under the defined budget, although there are overlaps between the proposal and RD-Connect work on Standards. A possibility would be to consider what is proposed here as to steer the current activities of RD-Connect to take into consideration parts of the proposed ideas here. This would necessitate peer-review to avoid overlap.

Representative of the European Commission recommended further discussion with the project coordinators as there is the possibility of resources re-allocation as long as there is no fundamental change in the aims and general objectives of the projects. This should be done in agreement with the whole consortium behind the projects.

Action items

- Discussion concerning the funding of the tasks to be conducted in Canada should be followed up in Canada
- Scope for discussion between the European Commission and RD-Connect to be defined
- Agenda item for next teleconference: update on the progression of the discussions.

Update on Shenzhen conference

- Website is ready.
- Program is being finalized.
- Chinese and English registration sites are open.
- Draft communication is in preparation for dissemination of information to various stakeholders.
- Executive Committee meeting will be held on Nov 6th.

Annex - List of participants

Members	**Representative**
IRDiRC Chair Executive Committee, Canadian Institutes of Health Research, Canada	Paul Lasko
Genome Canada, Canada	Pierre Meulien
E-RARE-2 (E-Rare Group of Funders), Europe	Daria Julkowska
European Commission, (DG Health and Consumer Protection), EU	Stefan Schreck
European Commission, (DG Research and Innovation), EU	Iiro Eerola
Academy of Finland, Finland	Heikki Vilen
Children's New Hospitals Management Group, Georgia	Oleg Kvlividize
Telethon Foundation, Italy	Lucia Monaco
The Netherlands Organisation for Health Research and Development, The Netherlands	Sonja van Weely
Carlos III Health Institute, Spain	Rafael de Andrès Medina
Food and Drug Administration, USA	Katherine Needleman
National Human Genome Research Institute, NIH, USA	Jeff Schloss
Office of Rare Diseases, USA	Pamela Mc Innes
NKT Therapeutics, USA	Robert Mashal
PTC Therapeutics, USA	Diane Goetz
Scientific Committees	
Chair Diagnostic Sci Com	Kym Boycott
Member Interdisciplinary Sci Com	Bartha Knoppers and Jeffrey Krischer
IRDIRC Scientific Secretariat	
SUPPORT-IRDiRC project	Ségolène Aymé, Barbara Cagniard and Lilian Lau

Apologies

Members	**Representative**
Western Australian Department of Health, Australia	Hugh Dawkins
BGI, China	Ning Li
Chinese Rare Disease Research Consortium, China	Qing Wang
EURORDIS (Patient Advocacy Group), Europe	Béatrice de Montleau
AFM- French Association against	Marie-Christine Ouillade

Myopathies, France	
ANR- French National Research Agency, France	Natalia Martin
FFRD – French Foundation for rare diseases, France	Nicolas Lévy
Lysogene, France	Karen Aiach
Federal Ministry of Education and Research, Germany	Ralph Schuster
Shire, Ireland	Phil Vickers
Istituto Superiore de Sanita, Italy	Enrico Garaci
Korea National Institute of Health, Korea	Hyun-Young Park
Prosensa, The Netherlands	Luc Dochez
National Institute for Health Research, United Kingdom	Willem Ouwehand
Genetic Alliance, USA	Sharon Terry
Genzyme, USA	Carlo Incerti
Isis Pharmaceuticals, USA	Brett Monia
National Cancer Institute, NIH, USA	Edward Trimble
National Eye Institute, NIH, USA	Santa Tumminia
National Center for Advancing Translational Sciences, NIH, USA	Christopher Austin
National Institute of Arthritis and Muskoloskeletal and Skin Diseases, NIH, USA	Stephen Katz
National Institute of Child Health and Human Development, NIH, USA	Melissa Parisi
National Institute of Neurological Disorders and Stroke, NIH, USA	Danilo Tagle
NORD, USA	Peter Saltonstall
Sanford Research, USA	David Pearce
Scientific Committees	
Chair Therapies Sci Com	Yann Le Cam

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