IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Meeting report series

Report of the 13th Interdisciplinary Scientific Committee Meeting

Lyon, France
14 March 2016

Participants

Prof Hanns Lochmüller, Newcastle, UK (Chair)
Prof Jack Goldblatt, Perth, Australia
Dr Stephen Groft, Bethesda, USA
Dr Petra Kaufmann, Bethesda, USA
Dr Jeffrey Krischer, Tampa, USA
Ms Samantha Parker, Paris, France
Prof Rumen Stefanov, Plovdiv, Bulgaria
Dr Domenica Taruscio, Roma, Italy

Dr Christopher Austin, Executive Committee Chair, Bethesda, USA
Dr Lilian Lau, Scientific Secretariat, Paris, France

Apologies

Dr Angel Carracedo, Santiago de Compostela, Spain
Ms Gema Chicano, Murcia, Spain
Prof Bartha Maria Knoppers, Montreal, Canada

Agenda

1. Welcome and introduction
2. The Interdisciplinary Scientific Committee
3. Task Forces implementation and proposals
4. “IRDiRC Recommended” implementation and feedback
5. RARE-Bestpractices
6. Any other business

REPORT

1. Welcome and introduction

The Chair of the Interdisciplinary Scientific Committee (ISC) welcomed its members to the meeting, and extended the apologies of members unable to attend due to prior commitments and health issue.

2. The Interdisciplinary Scientific Committee

2.1 Co-Chair of the ISC

Dr Petra Kaufmann was unanimously voted as the Co-Chair by members present at the meeting. She accepted the vote, and this was announced to the Executive Committee (Exec Comm) and other Scientific Committees (Sci Comms) members who attended the Joint Meeting.

2.2 The way the Committee runs

The members of the ISC were happy with the way things work: one face-to-face meeting per year, with several teleconferences when required. New member(s) should be briefed by current member(s) of ISC and IRDiRC activities, preferably through face-to-face meeting, at either IRDiRC or non-IRDiRC meetings.

2.3 Presentations about IRDiRC and its activities

ISC members who attend meetings and present IRDiRC should inform the Scientific Secretariat (Sci Sec) so their activities can be tracked. In addition, members could request for slide decks from the Sci Sec; alternatively, regularly updated standard slide decks in PowerPoint format are also available from the IRDiRC private website. Members may download them and modify for use accordingly.

2.4 Health technology assessment (HTA)-related expertise

HTA-related expertise is highly relevant to IRDiRC and its activities, and health assessment issues are increasingly implicated in early stages of research and drug development (e.g. in early dialogue for pre-clinical plans). The ISC would like to include this expertise in its Sci Comm to advice on research and methodology (e.g. how to do HTA and adapt it to measure and evaluate rare disease treatments), and to develop a related Task Force that can work on guidelines and recommendations to ensure sustainable future for rare disease research and development as well as patient access to treatments. [*Post-meeting note: see section 3.5 for related Task Force proposal.*]

The ISC's request of HTA-related expertise will be refined to emphasize the importance of HTA in research and methodology aspects prior to presentation to the Exec Comm for approval.

3. Task Forces implementation and proposals

3.1 Interaction with Task Forces

Different IRDiRC Task Forces have different work processes; the general steps were outlined in the accompanying preparatory document. The background documents developed by the Sci Sec to date for use by Task Forces have been useful to help focus on relevant issues; however, with changing leadership at the Sci Sec, scientific guidance from IRDiRC Sci Comms is needed. Sci Comm members interested in specific topic(s) should get involved with the Task Force(s), or contribute at the point when documents are ready for review to provide their feedback.

The ISC strongly emphasized that the endpoint of each Task Force should be a publication in a peer-reviewed journal, and not just publication of Task Force reports and/or recommendations on the IRDiRC website. Where needed, the Sci Sec is ready to provide support in the writing of articles which the Task Force Chair(s) and/or members will lead and validate before submission.

3.2 Participant Unique Identifier (PUID) Task Force

The Exec Comm has signed off on the PUID Task Force, a collaborative effort with GA4GH, which will be co-chaired by Petra Kaufmann and Bartha Knoppers. An invitation letter to Task Force members was in preparation and would be sent out shortly. This Task Force will do its preparatory work via teleconferences, and if things run to plan, a workshop will take place at the end of the year, likely in Paris. [*Post-meeting note: the invitation letters have been sent out.*]

3.3 Best Practices in Patient Group/Stakeholder Engagement

A discussion on Best Practices was started in Glasgow but the Chair of the Therapies Sci Comm (TSC) thought the topic on patient engagement should be led by the TSC and patient groups. However, ISC believes it would be good to have collaborative discussion to include perspective from more than one non-therapy-centric areas (e.g. how patient groups could and should be engaged along drug development process; how patient groups help drive the Toolkit Project – details to be presented at the Joint Exec/Sci Comms meeting – and to identify gaps in resources that serve the needs of the patients). There are issues on ethics, transparency and conflicts of interest to consider. This Task Force could encompass more than just policy recommendations. See Joint Committees report for further action.

Moreover, CTTI has produced recommendations on best practices in patient engagement in clinical trials. This proposal could benefit from a further discussion with the TSC to work out overlaps and identify perspectives which should be addressed.

3.4 Independent Orphan Drug Post-Marketing Registries

A need for independent orphan drug post-marketing registries was discussed. Some drugs, despite use following marketing approvals (e.g. for Gaucher's – 20 years), still lack safety and efficacy data. In cases where regulators request post-marketing data, the registries set up are proprietary to companies which

collect the data. Registries should be developed in a process that is collaborative, industry-independent, and sustainable. Data sharing helps drive development costs down, enables better assessments for payment decision, and in the long term, provides sustainable system.

Industry is considering how to run registries post-marketing authorization, and a concept paper by EUCERD for orphan drug development has been taken up by the European Federation of Industry. However there are issues revolving funding of these registries and mechanism to ensure sustainability. A suggestion: build an independent registry on initial public grant which companies can use, then negotiate with companies that a certain percentage of the profit to be put into registry development and maintenance. Key elements to collect across studies for consideration: continuum pre- and post-approval data, data standards, core set of outcome measures, off-label uses.

This proposal should be enriched following this discussion, and stakeholders to move this forward should be identified. Advisors to FDA or EMA on post surveillance system would be good representatives to have from regulators.

3.5 Proposal received post-meeting via email

The discussion on the need to make drugs affordable for payers while balancing the incentives to keep companies developing therapeutics highlights an important issue which may exacerbate with precision medicine. The issue could be approached without going into reimbursement, e.g. through looking at burden of disease (consideration not only for patients but also carers), or research data collection based on meaningful measures not only for regulators but also payers.

4. "IRDiRC Recommended" implementation and feedback

"IRDiRC Recommended" was launched in 2015 and a set of rules set out at the start have been tweaked so to refine the process along the way. A number of applications have been received and reviewed to date by the members of IRDiRC Sci Comms. Approved applications are recommended for a period of 3 years, after which it will be re-evaluated.

ISC members who have been involved in the review process found the criteria set out are clear and the review form well laid-out, therefore the applications straight forward to review and the process runs smoothly. The kind of resources that are applying for the label also shows encouraging progress.

However, the value of "IRDiRC Recommended" to approved resources is currently unclear, and a strategy should be proposed to audit this, e.g. look at website statistics, the recipients could be surveyed if "IRDiRC Recommended" label makes a difference to their resources.

[*Post-meeting note: "IRDiRC Recommended" page is the 4th most consulted page on the IRDiRC website since its launch in March 2015, with 2,606 views. For the same period of March 2015-March 2016, the most viewed page is the landing page with 21,487 views, followed by Members page with 5,237 views, IRDiRC goals page with 3,220 views, and the fifth is IRDiRC-Related calls page with 2,056 views.*]

While IRDiRC Exec Comm does not directly endorse "IRDiRC Recommended" resources, in order to give value to these resources, it was raised if research funders could integrate "IRDiRC Recommended" resources to their funding calls, e.g. suggest applicants of funding check on recommended resources, identify if any could be used in their proposed projects thus not reinventing the wheel, and if not, briefly explain why. This step may help push for operability, where applicants could set up their research to be interoperable with recommended resources, or develop resources more suited to their needs while bearing in mind interoperability to enable users to transition from one resource to another with reasonable ease.

It was suggested there be call for resources of interest in specific areas, so investigators in these areas could submit for recommendations. This not only populates resources in a comprehensive manner, it also enables identification of areas without recommendations and appropriate calls can be issued.

On the dissemination front, resources that receive "IRDiRC Recommended" are published in a list on the IRDiRC website and the status announced in the OrphaNews. Nonetheless, as the initiative evolves, it is imperative to see the metrics and literature on its utility and value to the rare disease research community.

For a complete list of applications received, whether accepted or not for recommendation, a page on the private website can be consulted. Documents related to the application (application form, reviews received) are also made available on this page.

5. RARE-Bestpractices (RBP)

RARE-Bestpractices (RBP) is a 4-year (2013-2016) EU project coordinated by the ISS in Italy. It contains a specific work package devoted to the collaboration between RBP and IRDiRC. The goals and objectives of RBP can be found on http://www.rarebestpractices.eu/pagine-1-project_description.

Two public databases have been built through the RBP project, which are available for use and input:

- RareGUIDELINES (http://www.rbpguidelines.eu/), a database of rare disease guidelines on 43 disease topics of which their quality was appraised using AGREE II instrument
- RareGAP (http://www.rbpresearch.eu/), a database of validated research recommendations for diagnosis and treatment of rare diseases identified from systematic reviews; this is a tool which institutions and funding agencies can use to identify gaps in research and structure their calls

Additional resources provided by RBP:

- Training courses to acquire skills to appraise healthcare guidelines for rare diseases
- Training courses for health care guidelines developers on diagnosis and treatments of rare diseases
- Training tools, e.g. tutorial of AGREE II instrument on guidelines for rare diseases, methodology on how to structure guidelines
- Newsletter: Guidelines International Network, GIN

- RARE Journal: open access, online, peer-reviewed journal published thrice yearly, with no publishing fees

Proposed ways to contribute to RBP:

- Community effort is needed to feed the databases
- Crowdsourcing in order to open up to more diseases
- Raise awareness of RBP with IRDiRC community and beyond
- Application to be "IRDiRC Recommended"

6. Any other business

Acknowledgement of IRDiRC: Identifying IRDiRC-related metrics through publications is challenging as scientific papers, even those published on work carried out under funding to advance IRDiRC goals, often only acknowledge funding provenance without the mention of IRDiRC. Funders should be encouraging their grantees to include the mention of IRDiRC.

State-of-Play (SoP) report: the SoP is a deliverable of the SUPPORT-IRDiRC contract and is prepared annually by the Sci Sec. The target audience is the IRDiRC Committee members. A number of funders used it to guide their funding calls, while industry members have found it to be a useful report. However, in its current format, it has little value to scientists. The ISC proposed the report to be shortened, and to include list of "IRDiRC Recommended" resources, recommendations from Task Forces, and new funding programs.

European Reference Networks (ERNs): Centers of expertise for rare diseases have been set up in EU member states jointly with the European Commission, but the model is not sustainable as healthcare issues fall under the remit of member states. The DG SANTÉ launched the ERNs to create a clearer structure for knowledge sharing and care coordination across the EU through formation of networks of centers of expertise. It is yet unclear how this initiative will work out, and the first call for interest had just been launched.

Action points

- Refine HTA-related expertise requirement document
- Enrich the proposal on post-marketing registries
- Discussion with TSC on Patient Engagement proposal
- Draft HTA-related Task Force proposal
- IRDiRC communication to promote RBP