

Meeting report series

Report of the 1st Meeting of the Working Group on Chemically-derived products including repurposing

16 January 2014

Organization

Organized by: Scientific Secretariat

Hosted by: GoToMeeting

Participants

Mr Yann Le Cam, Brussels, Belgium (Chairman of the TSC)

Dr Fred Marin, Paris, France

Dr Ramaiah Muthyala, Minneapolis, USA

Dr Nick Sireau, Cambridge, UK

Dr Stelios Tsigkos, London, UK

Apologies

Dr Diego di Bernardo, Naples, Italy

Prof Christopher McMaster, Halifax, Canada

Karin Rademaker, Utrecht, Netherlands

Agenda

16 January 2014

- 1) Overview of IRDiRC
- 2) Role and support of IRDiRC secretariat
- 3) Review of WG mandate
- 4) Election of the WG co-chairs
- 5) WG Deliverables and timing for next call

REPORT

1) Overview of IRDiRC

The WG on Chemically-derived Products including Repurposing is linked to the TSC, which is one of the three Scientific Committees of IRDiRC. Amongst the main goals of IRDiRC, this WG is mainly related to the one that aims to deliver 200 new therapies for RD by 2020 (see governance document: http://www.irdirc.org/?page_id=11). This aim has to be reached for example by boosting the preclinical and clinical translational research and streamlining ethical and regulatory procedures.

The role of this WG is to propose to the TSC recommendations in view of defining common policies between all the members of IRDiRC, in order to guide them to allocate funding of RD research activities. The organizations who joined the Consortium will contribute to the policy development and to the establishment of priorities, thus even there is no obligation, they will probably be committed to apply these policies. One of the first examples is the recent launch by the European Commission of the programme Horizon 2020 which includes in certain calls for proposals a statement that the application has to be in line with the recommendations of IRDiRC.

2) Role and support of IRDiRC secretariat

The IRDiRC Secretariat is located in Paris. The team is composed by 4 people, including a project manager, a communication officer, an information scientist and an assistant. Support in kind is also given by people from the French Rare Diseases Foundation and from Orphanet. The role of the IRDiRC secretariat is to help organizing the meeting and teleconference of the Committees and Working Groups (WGs), to take the minutes and propose a report, but also to prepare some documents upon request, including extraction of data from the Orphanet database or literature survey when needed.

3) Review of WG mandate

General mandate and main tasks

As previously stated, the main mandate of the WG is to issue concise recommendations in order to guide the future programs of the funding research agencies in a synergetic and coordinated way at international level. The new insights and strategy have to be brought to the TSC which will then make recommendations to the IRDiRC Executive Committee.

The key points are defined in page 1 of the briefing document. Point #1 refers to the mapping of expertise that will be shared via the IRDiRC website (www.irdirc.org). For the point #2, the WG will work based on the expertise of its members but may also ask support to the Scientific Secretariat in order to identify opportunities or gaps by requesting data for analysis, extraction from the Orphanet database, literature search, etc. Emphasis was also put on point #3, 4 and 6.

Specific topics to be addressed by the WG

These topics are presented on page 3 of the briefing document. The crucial points are #2, 3, and 4. The members of the WG have first to agree on the scope of their forthcoming discussions and recommendations. They will then express their needs in order to best analyze the areas that deserve additional funding. They would finally focus on priorities and criteria.

- ▶ The first discussion concerned the mechanisms to be put in place in order to detect the drugs that could be available for development purpose and how they are linked to clinical conditions, i.e., to identify which drug could be useful for which disease by examining properties of the drugs, history of the diseases and by expanding knowledge on connections between drugs and new indications, before going to the clinical trials step. An EC funding project which uses animal models in order to achieve this goal was mentioned. The Scientific Secretariat also notified that Orphanet has recently started to explore this topic by discussing with PubChem. The aim of this collaboration is to find a way to use the content of these two databases: properties of drugs and physiological pathways that are targeted, regulatory status of drugs where clinical proof may have been established, history of rare diseases, including which physiological pathways are involved, etc.

As some initial work has already been done, the WG may want to formulate the policy recommendations in a realistic and pragmatic way to make sure not to waste the resources but to get meaningful output from research projects.

- ▶ The WG discussed the possibility to adopt a scope of discussion limited to drugs that have already been registered, chemically-derived or not, rather than focused exclusively on all chemically-derived drugs, because the time scale to the IRDiRC deadline is quite short. Following this first step, the WG wishes to remain flexible and to be able to enlarge the scope if some additional needs are identified.

In order to identify drugs that could be of interest for development, the Scientific Secretariat will provide the WG with the list published by the FDA gathering drugs with a potential for repurposing.

- ▶ It was suggested to have a look to products that have been developed within FP7 projects but have never reached the market. For these potential treatments, some work has already been done and probably published and could be interesting for new short term projects. The Scientific Secretariat will explore how to analyze outcomes from FP6, FP7 and E-Rare funded projects which had a drug development aspect in order to understand the reasons of success or failure. This will probably require contacting the principal investigators.

Regarding the projects funded by NIH or FDA, the OOPD and the National Center for Advancing Translational Sciences should be contacted to ask whether they can handle this.

- ▶ It has been raised that sometimes it is difficult to identify who is doing what and at which stage, especially in the field of repurposing/repositioning and especially for SMEs. So it is good that IRDiRC help to gather this information and display it on the IRDiRC website. This could help SMEs to join a consortium willing to apply for Horizon 2020 calls. The Scientific Secretariat mentioned

that help to join consortium for Horizon 2020 calls could also be obtained through the ECRIN network (European Clinical Research Infrastructure Network).

- ▶ Part of the discussion followed on the issues related to the diversity within the sponsors. Sponsors have different needs and different profiles of development. This issue could be further investigated by the EMA through their resources (surveys, annual reports and SME office resources).
- ▶ Having gathered the previous points, the WG is willing to brainstorm onto the market access issue for SMEs. On one hand, the WG asked if the Scientific Secretariat would be able to perform a meta-analysis from literature on existing incentives (not only financial) for SMEs, some information may be available in the EUCERD state-of-the-art or through members of IRDiRC. On the second hand, the WG will explore how to make the best use of the annual report provided by SMEs to the regulatory Agencies, in order to monitor which companies are in which stage of development and the reasons why some products having been granted an orphan designation never reached the market. This could lead to identify potential hurdles such as lack of proper design of the clinical trial for example.
- ▶ There is a disconnection between designation(s) and approval(s). This needs to be investigated and learn how to speed up the process of converting designations to products. A study has already been performed jointly by Eurordis, the EMA and the FDA but some additional data could be provided by the Agencies. The WG is waiting for feedback from the EMA regarding the optimal use of the annual report on orphan designated products. If the issue is a lack of resources and if the same outcome is obtained from the FDA, this analysis could be useful to establish a recommendation. The point was raised that the quality of the feedback provided by the companies is highly variable, even though the format of EMA annual report templates has been streamlined.
- ▶ Coming back to the discussion on how to establish clusters of compounds, a first set of data could be prepared by the Scientific Secretariat, i.e., a list of products with orphan designation in EU and US and the corresponding diseases. The next steps of the discussion would include a further analysis to identify clusters that would deserve more investments. More than 10,000 drugs are available for repurposing for the last a decade or more. Yet only small numbers of them have been investigated; and have been developed as drugs for new indication. There is a gap. Understanding this gap and how to fill the gap will allow reaching 200 drugs by 2020.
- ▶ Finally the WG highlighted the fact that no matter the fact that the goal is to deliver 200 new drugs, what is important is that these drugs would serve as therapies for new conditions.

5) Election of the WG co-chairs

Dr Ramaiah Muthyala and Dr Fred Marin have been elected as the two co-chairs of this WG and will be responsible of formulating the recommendations to the TSC.

6) WG Deliverables and timing for next call

Timeline

The timeline for the WG is to write recommendations by the beginning of March in shape of few bullet points to be communicated to the TSC. This set of recommendations will be consolidated with the ones from the other WGs and be discussed by the TSC during a face-to-face meeting in March. The TSC will then draft recommendations for the Executive Committee.

A second meeting of this WG will be scheduled the third week of February in order to elaborate the few bullet points. A doodle will be sent next week by the Scientific Secretariat.

Summary of data which could be useful for the WG – Comments from the Scientific Secretariat

- ▶ The list published by the FDA gathering drugs with a potential for repurposing will be provided to the WG by the Scientific Secretariat
- ▶ The Scientific Secretariat could try to improve the data collection of projects in the field of repurposing/repositioning.
- ▶ Meta-analysis on existing incentives (not only financial) for SMEs (literature survey, EUCERD state-of-the-art...) could be performed by the Scientific Secretariat
- ▶ The Scientific Secretariat may also provide the list of products that have been granted so far with an orphan designation in EU and US and the medical conditions concerned
- ▶ The WG has expressed the willingness to have access to the outcomes of FP6, FP7 and E-Rare funded projects and of projects funded by NIH or FDA. The list of those projects could be provided by the Scientific Secretariat, except that it would not be comprehensive for the US. But in any case, accessing to the outcomes would require contact the principal investigators of each project. The recommendations of the WG could be to ask the European Commission or the NIH whether they have assessed the outcomes of their programs or to recommend realizing such a survey.