



RD Platform Expert Workshop on Rare Disease Research Funding

Summary Report

Paris, 3rd December 2009

1. Introduction – The RDPlatform Project

RareDiseasePlatform (RDPlatform) is a three-year support action project of the European Union's Seventh Framework Programme (HEALTH-F2-2008-201230), which began in May 2008.

RDPlatform is dedicated to developing a project-building platform to help researchers in the field of RD set up efficient, multidisciplinary teams to tackle RD research challenges. This project offers the opportunity for potential multinational teams to exchange ideas and strategies in order to structure future research proposals in the 27 EU member states.

The first product of RDPlatform is a database of publicly funded research projects accessible through the research tab of the Orphanet website. Each of the thirteen participating countries is responsible for collecting the information at national level. France carries out the data collection in France, and the remaining Orphanet countries (25 countries). During the first year, this area of the website has been newly conceived to fulfil the previously unmet needs of the European RD research community, which were highlighted during the development of the previous European project. The second product is a database of academic research projects seeking partnership with industry. In the first project this database was accessible from a separate website at the address www.orphanxchange.org. This website has been integrated in the Orphanet Research & Trials tab of the Orphanet website.

Among the objectives of the partners of RDPlatform was the organisation of two workshops with top experts to analyse areas in need of collaborative research projects, based on an analysis of the current situation. The first workshop took place in Paris, on the 3rd of December 2009.

2. Session 1: Research in the field of rare diseases and orphan drugs: where do we stand in Europe?

The first session introduced the state of art of research in the field of rare diseases and orphan drugs in Europe. Ségolène Aymé opened the workshop by presenting the aims of the workshop and giving an overview of rare disease policy in the European Union, whilst highlighting issues such as the concept of unmet medical needs, the 'death valley' gap between research and development and the need to improve collaboration between interested parties: several areas for discussion were highlighted such as the need for public funding into RD research, the need to bridge the gap between basic and clinical research, and the importance of registries in the field of RD research.

Natalia Martin, in charge of data collection for RD research at Orphanet for the RDPlatform project, then presented a report on rare diseases research and its determinants in Europe based on analysis of the Orphanet database content (including the classification of rare diseases, epidemiological data, the orphan drugs database, and the research and trials database): the goal of the report was to provide an overview of on-going research on rare diseases in Europe, especially in the field of therapy development, to identify new avenues for research and to provide recommendations to target calls for proposals at EC and Member State level.

The results of this analysis, along with the results of a statistical analysis of the respective weight of possible determinants and tentative conclusions, were presented and commented upon by the Orphanet team and the workshop participants. The analysis of the distribution of number of diseases by number of treatments in development (estimated through orphan designations or through ongoing clinical trials) showed that most RD (276, representing 6 M people affected by RD) have no more than 3 orphan designations, whereas 53 RD have over three orphan designations (representing 2.2 M people affected). Similar results were obtained when the

clinical trials, the marketed drugs, the patient registries and the preclinical/epidemiological/basic research were analysed. Some of the diseases over-represented upstream in the process of R&D (with a treatment in the market or drugs on development) are also well represented regarding the ongoing research, like Cystic fibrosis, pulmonary arterial hypertension and some rare cancers. It is anticipated that the diseases with more treatments in development are those with a higher prevalence, an assumption which is not backed up by our data analysis. The best represented medical domain in terms of percentage of diseases with MA and OD is Oncology, followed by Systemic and Rheumatologic diseases, Haematology, Gastro-enterology, metabolic diseases and Pneumology. It seems that the most mature fields keep on investing in research and are also the strongest ones regarding the products in development, and even in basic research for some of them. Other fields, however, like Neurology, seem to be essentially in development, since the percentage of diseases with MA is low compared to other domains and to the percentage of neurologic diseases with OD, clinical trials and research. The absence of orphan designations for some medical domains, like Cardiology, could be explained by the fact that the Cardiology rare diseases (mainly cardiomyopathies and rhythm diseases) benefit from treatments already available for common forms of these diseases.

Discussion revolved around the classification and analysis by medical domain (including the interest of analysing separately rare cancers and eliminating neglected diseases from the analysis), the completeness of data analysed, the trends presented by this first analysis and possible explanations for why certain medical domains were poorly, or better, represented in RD research. Other topics of discussion included the possible reasons for success or failure of drug development for RD and the need for private/public partnership.

Natalia Martin also presented the new “Research and Trials” tab of the Orphanet website and explained to participants the different options and searches available to users.

3. Session 2: European Networks/Platforms

Pr. Kate Bushby, coordinator of a FP6 funded Network of Excellence (NoE) presented a successful example of European networks: the Treat-NMD network. A Network of Excellence is an EC instrument for strengthening excellence by tackling the fragmentation of European research. The Treat-NMD network of excellence aims at sharing expertise between basic and clinical research academics and industrial partners in order to develop technological and methodological tools with a view to accelerate the elaboration of new therapies for rare neuromuscular diseases. The main deliverable is a durable structuring and shaping of the way that neuromuscular research is carried out. The main outcome of this NoE is the establishment of patient registries, not only essential tools for trial-readiness, but which are also useful for all stakeholders: patients, clinicians, researchers, and industry. Treat-NMD has defined a mandatory dataset and the means to share registries' data concerning more than 10,000 DMD patients.

The Treat-NMD NoE can be considered as a successful program which has significantly contributed to the acceleration of R&D for NMD. Similarly to other successful EC funded networks, the main issue is related to the sustainability of the structures which have been created during the development of these collaborations, such as patient registries, biobanks, and technological platforms.

Participants thoroughly discussed this issue and proposed potential solutions for the sustainability of these kinds of structures once EC funding is over, and which represents a small budget compared to the budget which is necessary for their construction. These suggestions included: EC involvement in the financing of the coordination and maintenance of these structures through a specific call for proposals (through the E-RARE instrument or a DG Research instrument to allow for the transposition from a research project to a tool for public health -for registries and biobanks for example) or that these databases be allocated to learned societies (only valuable for some databases).

4. Session 3: Funding mechanisms/ types of calls/ areas to be promoted

DG Research

Catherine Berens of the EC DG Research gave a presentation of available funding mechanisms of RD research in the scope of the DG Research framework programme. The Seventh Framework Programme for research and technological development (FP7) is their instrument for funding research over the period 2007 to 2013. The total

budget of the FP7 is € 54,582 billion. There are 7 Specific Programmes under FP7: Cooperation, Ideas, People, Capacities, Euratom and two Specific Programmes for the Joint Research Centre (JRC). The Cooperation Specific Programme of FP7 is sub-divided into 10 Thematic Priorities, which includes the Health theme (€ 6,1 billion of budget).

Research on RD is funded through Sub-theme 2 (Translating research in major diseases) of the Health theme. There have been 4 calls for proposals published for the Health theme, and the rare diseases area was open to proposals in the 1st, 3rd and 4th calls. The research topics of the rare diseases area should focus on Europe-wide studies of natural history, patho-physiology and on development of preventive, diagnostic and therapeutic interventions. This sector includes rare Mendelian phenotypes of common diseases.

The expected impact of the RD area should help identify and mobilise the critical mass of expertise in order (i) to shed light on the course and/or mechanisms of rare diseases, or (ii) to test diagnostic, preventive and/or therapeutic approaches, to alleviate the negative impact of the disease on the quality of life of the patients and their families, as appropriate depending on the level of knowledge concerning the specific (group of) disease(s) under study.

The future calls for proposals for RD research will try to fill the gaps in the research portfolio bearing in mind the EU added value and the EU research potential. They will be based on: results from previous calls, contribution to EU policy objectives, priorities discussed with the Health Theme Advisory Group (scientific community representatives, providing independent advice for the implementation of a Theme) and the Health Theme Programme Committee (Member States representatives).

The evaluation criteria of the FP7 projects include: Scientific & Technological Excellence, Implementation : are the management and financial plans good enough to accomplish the goals, and Impact: what will this project contribute to the European community. The individual evaluation of these criteria must reach at least 3/5 for each, and a total of 10 point must be obtained in order to select it for further evaluation.

E-Rare: Networking research programmes on rare diseases in Europe

Sophie Koutouzov, Coordinator of the E-Rare network, presented an overview of the E-Rare project. E-Rare is the ERA-Net program for research on rare diseases. The ERA-Net scheme is supported by the European Commission under the Sixth Framework Program for a 4-year period (starting June 1st 2006). The main goal of the E-Rare program, as part of the ERA-Net, is to support cooperation and coordination of national or regional research. E-Rare is a network of ten partners – public bodies, ministries and research management organisations – from eight countries, responsible for the development and management of national/regional research programs on rare diseases and for the development of joint and strategic activities in order to: harmonise and develop synergies between the 8 national research programmes (on rare diseases), to develop common research policy on rare diseases and to coordinate national actions in order to reduce fragmentation.

One of the achievements of E-Rare is the development of a framework and tools for the implementation of transnational research funding. Two different Joint Transnational Calls (JTC) for research on RD have already been launched. In addition, best practice recommendations that optimise the use of data management systems and biobanks in common calls have also been created.

A total of 502 research groups in 6 countries (FR, IT, DE, ES, TR, IL) applied for 123 eligible projects for the JTC of 2007. An increase in the number of research groups (566), countries (10: NL, PT, AT and GR participated together with the other countries), and projects (137) was observed during the second call (2008-2009). The average rate of success for the E-Rare funded projects is 10% (13/123 consortia funded in 2007 and 16/137 in 2009), which is unsatisfactory if we compare this to the FP success rate (18-25%), and we consider the work invested by the applicants and the agencies. The success of the E-Rare JTC (2006-2010) reflects the expectations and needs of the transnational RD research community. The JTC general process can be considered as successful, with 120-150 proposals and a great flexibility in the inclusion of new partners (AT, GR, PT). However, the translational call has leverage funds from agencies of countries without RD national plans. It was proposed that lobbying should be carried out so that the national plans include the national participation to the E-Rare projects as an efficient mean to fund RD research.

An extension of E-Rare is planned under the FP7, for the period of 2010-2014. The main goal will be the development of a joint translational RD research programme, with a wider European collaboration, an increase in communication, the creation of indicators, the launch of yearly JTCs, the development of a strategic research policy (increasing the national funds), and the elaboration of plans for the sustainability of the E-Rare network.

5. Conclusions and next steps

Participants at the workshop agreed that networks are essential tools in the field of rare diseases and that additional instruments should be put in place to ensure the continuity of previously funded RD projects/networks and to fund coordination activities. It was agreed that a report of the workshop be produced and validated by workshop participants and identified experts in the field of RD research, using results of the workshop and a second analysis of the data. This second analysis should separately analyse rare cancers and should be carried out using certain data sets (orphan drug designations, clinical trials, registries etc.) and excluding uncertain data (pre-clinical and basic research). The multi-variate analysis should be repeated by medical domain by disease. It was also suggested that an annex listing all DG Research FP 5, 6 and 7 projects and DG Sanco financed European Reference Networks for RD be added to the report and that all networks for RD be approached to assess their perception of the problem of sustainability. It was also suggested that three to five successful networks for RD be selected and analysed in order to investigate the determinants for a successful RD network

This report will be produced and sent to participants and the tentative list of experts at the start of 2010.

Annex: List of Participants

RD Platform – Orphanet France

AYME, Ségolène
DOULET, Nicolas
HIVERT, Virginie
MARTIN, Natalia
RODWELL, Charlotte

RD Platform - Partners

CASSIMAN, Jean-Jacques (BE)
DALLAPICCOLLA Bruno (IT)
DONNAI Dian (UK)
GAVHED Désirée (SE)
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PRONICKA Ewa (PL)
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VAN OVERVELD Petra (for VAN OMMEN, Gert-Jan) (NL)
VOIGTLANDER Till (AT)

RD Platform - Advisory Board

KOUTOUZOV Sophie (FR)

Invited experts

ANDREU Antoni (ES)
ASHTON-KEY Martin (UK)
BERENS Catherine (DG Research)
BURTON Hilary (UK)
BUSHBY Kate (UK)
DE VRUEH Remco (NL)
HINTER Helmut (AT)
HIORT Olaf (DE)
LOVATT Brian (UK)
RAY COQUARD Isabelle (for Jean-Yves BLAY)
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SCHUSTER Ralph (DE)
TANNER Stuart (UK)
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WESTERMARK Per (SE)
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