

## Why joining the ERA-Net “E-Rare-2” on Research on Rare Diseases

### **1 - The need for transnational collaboration and coordination in the field of rare disease research**

Rare diseases are a prime example of a research area that will strongly profit from coordination on a transnational scale. By definition a rare disease affects no more than 5 per 10 000 persons in the European Union (EU), still rare diseases affect or will affect at least 29 million persons in the EU. These figures stand approximately the same for the US where a rare disease is defined as one affecting fewer than 200,000 people. The 6-8,000 identified rare diseases represent a major health issue since a large percentage of these diseases lead to a significant decrease in life expectancy, and most of them cause chronic illness with a large impact on quality of life and the health care system of each EU country. Although both the Orphan Drug Act in the US (1983) and the European legislation on Orphan Drugs (2000) have accelerated the development of specific therapeutics for rare diseases, still thousands of rare diseases remain without any specific treatment. Recent research has shown that development of orphan drugs is clearly increased when more biomedical research on the specific diseases has been performed. Thus, biomedical research is definitely needed to understand rare diseases and to discover new treatments. Due to the small number of patients per disease and the scattering of these patients over large geographical areas, research on rare diseases is scarce, hampered by lack of resources, and is fragmented in different laboratories throughout the EU and across Atlantic. Thus, it is crucial to fight this fragmentation and foster research on rare diseases, including cross-border cooperation and collaboration to maximize the potential of scientific resources of each country.

### **2- Actions taken by the European Commission to favour European collaboration in the field of rare disease research**

- A workshop “Identifying the research needs of the rare diseases community” organised by the EC - Directorate General for Research - in 2005 with stakeholders in the field of rare diseases was aimed at providing the EC with specific recommendations in relation to the field of research on rare diseases. The discussion highlighted many priorities on type and sizes of the research projects and on infrastructures and topics (e.g. natural history of diseases, physiopathology, therapeutic interventions, etc.).
- Rare diseases were one of the priorities of the Community’s 6th Framework Programme (FP) for research, technological development and demonstration activities (2002-2006), and continue to be a priority for action in the 7th FP for research, technological development and demonstration activities (2007-2013).
- The conference “Rare disease research: Building on Success” organised by the EC in 2007 aimed at raising awareness at the level of Member States and European Parliament on the needs of research on rare diseases, as well as promoting rare diseases as a priority of the European Union’s political research agenda.

- The Communication from the Commission<sup>1</sup> (Nov. 2008) indicated that fostering of research on rare diseases, including cross-border cooperation and collaboration is important to maximise the potential of scientific resources across the EU.

- The Council Recommendation of 8 June 2009 on an action in the field of rare diseases (2009/C 151/02)<sup>2</sup>. In this Recommendation, rare disease research is specifically emphasised and it is suggested that the coordination of Community, national and regional programmes for rare disease research should be improved. Furthermore, the needs and priorities for basic, clinical, translational and social research in the field of rare diseases and modes of fostering them should be identified, and interdisciplinary cooperative approaches to be complementarily addressed through national and Community programmes should be promoted.

### 3 - **Actions taken by the European Commission to favour European coordination in the field of rare disease research:** **“E-Rare”: The European Research Area Network (ERA-Net) on rare diseases**

#### A/ E-Rare: Missions and objectives

The first E-Rare project (2006-2010) was supported by the EC FP6 and comprised ten partners from eight different European and associated countries and two associate partners. The major goal of E-Rare project was ***to build the foundation for a transnational research programme on rare diseases***. To reach this goal, the E-Rare network, which was composed of **8 representatives** of the main research funding Agencies/Ministries: **France (CO)**, INSERM/ANR; **Belgium**, FRS-FNRS; **Germany**, BMBF and PT-DLR; **Italy**, ISS; **Spain**, ISCIII; **the Netherlands**, ZonMw; **Israel**, CSO/MOH, and **Turkey**, TUBITAK, focused on the coordination of national/regional research programmes on rare diseases, and the development of transnational cooperation for research funding activities.

#### B/ E-Rare achievements: building on success

During the 4-years of E-Rare running programme, the partner countries have set up a ***systematic exchange of information and best practices***. Surveys conducted amongst the E-Rare partner countries, but also in Australia, Japan, Korea and the USA which aimed at comparing the research programmes for rare diseases in these countries have contributed to building a common understanding among the E-Rare partners and enabling a long-term cooperation. They have increased awareness on rare diseases programmes inside and outside of the consortium, not only to national research funding agencies, but also to other stakeholders and decision makers. Furthermore, the examples given by the different national rare disease programmes, and the cooperation with E-Rare, have contributed to the development of the future Dutch programme for rare disease research, scheduled to open in 2010.

E-Rare has also worked out the ***definition of strategic priorities*** to develop and influence the research policy on rare diseases and shape future programmes and research activities on national, transnational and European levels. Four major workshops have been organised by E-Rare, which typically gathered high-level scientists (researchers and clinicians) on rare

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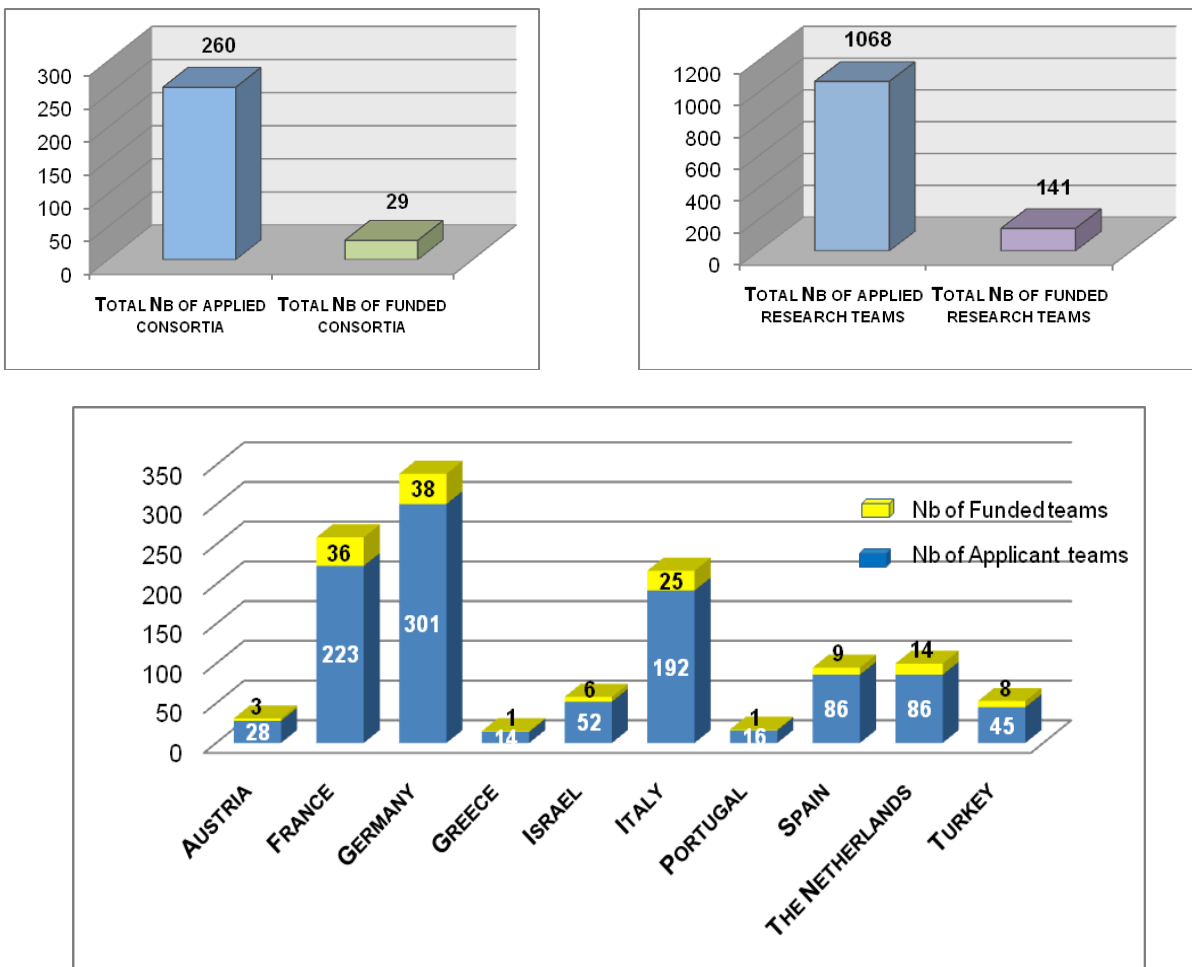
<sup>1</sup> Communication from the Commission to the European Parliament, the Council, the European Economic and social Committee and the Committee of the regions on Rare Diseases: Europe's challenges {SEC(2008)2713/2712} of November 2008

<sup>2</sup> Council Recommendation of 8 June 2009 on an action in the field of rare diseases (2009/C 151/02), published in the Official Journal of the European Union, C 151/7 on 3.7.2009

diseases and representatives from funding agencies, regulatory bodies, the EC, and European patient associations. These workshops have been decisive in shaping the scientific focus of the E-Rare joint transnational calls and in defining priorities, for the E-Rare network, as well as for the EC, for research on rare diseases funding.

The most important achievement and success of E-Rare concerns the **implementation of a transnational cooperation between E-Rare partners for the funding of transnational research projects on rare diseases**. Within less than 3 years of the consortium's runtime, the partners have succeeded in launching, implementing and completing **two full-fledged joint transnational calls (JTC)** for joint multidisciplinary research projects on rare diseases. As a result, six out of eight of the E-Rare partners not only have launched a first JTC a few months after the start of the project (March 2007), but also succeeded, - despite research budget restrictions due to the world-wide financial crisis - to launch a second JTC in December 2008 attracting 4 additional funding organisations from 4 Member States (**Austria, Greece, Portugal, and the Netherlands**). As a whole, the financial input of each partner funding agency has allowed the funding of **29 transnational research consortia** (≈ 10-12% success rate) with 147 participating (141 funded) research teams from 13 countries, for a total budget of 19.6 Mio. €<sup>3</sup>.

**Fig 1: E-Rare-1 Joint Transnational Calls (JTC) for research projects on rare diseases: Compilation of JTC 2007 & 2009<sup>4</sup>**



<sup>3</sup> see annex at the end of document

<sup>4</sup> Note that Austria, Greece and Portugal have participated to only JTC 2009

The lessons learnt from this initiative are several-fold: firstly, in both instances this initiative has received **tremendous feedback** from the transnational research community on rare diseases. Secondly, the number and high quality of the submitted applications attest the **huge need** of the scientific research community on rare diseases **for funding** transnational networking, collaboration and multidisciplinary. Finally, the success of the two E-Rare joint transnational calls is an **exemplary illustration** of the attraction that a common European initiative can develop as shown by E-Rare not only in the addition of new call partner countries inside and outside the consortium, but also, and even more significantly, of partner countries that do not have a specific national research programme on rare diseases.

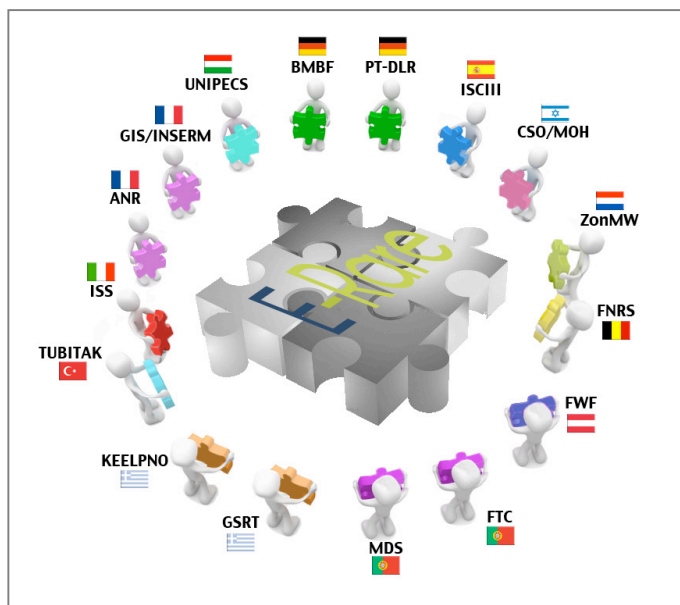
#### 4 - E-Rare-2 (2010-2014): the new EC FP7-funded ERA-Net on rare diseases

##### E-Rare-2: Mission and objectives

Based on the success of the first E-Rare programme, the E-Rare partners' countries, together with 5 new countries (Austria, Greece, Poland and Portugal as full partners, and Poland as an observer) have submitted a new project (E-Rare-2) in response to the 4<sup>th</sup> Health Call from the EC, which has been accepted by the EC with an outstanding evaluation.

E-Rare-2, **composed now of 12 full partners countries** (AT, BE, DE, ES, **FR (Co)**, GR, HU, IL, IT, NL, PT, TR) and one observer country, PL – represented by **16 main Agencies/Ministries for Research** (see Picture below) – aims at tackling further the different needs and challenges of rare disease research outlined above by building on the experience and results of the previous ERA-Net. The integration of five additional countries will broaden the basis of experience and the impact of joint actions. The cooperation and coordination among the partners will be deepened by **systematic exchange of information, joint calls, thorough assessment of the funding mechanisms and results of the funded research projects** and, finally, **strategic activities** aimed at a sustainable development and extension of the network.

The most important and effective **joint activity between the 12 E-Rare-2 partners countries** will be achieved by funding transnational collaborative research through **yearly joint transnational calls: two “general” joint calls (2011 and 2013)** with broad and open topics are foreseen to allow researchers to choose their projects based on state of the art and research demand for the specific disease; **two “focused” joint calls (2012 and 2014)** will enable E-Rare-2 to address themes of research on rare diseases which needs special attention and a focused approach (e.g. access to technology research platforms, harmonization/merging of existing national biobanks and registry databases, etc.).



The E-Rare-2 project has been definitely accepted by the EC and has started on October 1<sup>st</sup>, 2010 for 4 years. Our first joint call (JTC 2011) has been launched in December 2010 with final results expected in October 2011.

## 5 - How does the EC financially support E-Rare-2? What for?

The financial support from the EC for E-Rare activities (2 Mio €) is meant for the **coordination activities** between E-Rare-2 full partners countries (e.g. “glue” money), including travels for joint meetings, organisation of workshops, call secretariat (call implementation and organisation). Therefore, the participation of a given funding agency to E-Rare-2 does not require any initial budget commitment.

## 6 - Can countries participate in E-Rare-2 joint transnational calls without being a full partner?

As the **funding of successful transnational research projects is insured by Member States** (usually through national funding agencies), it is the decision of each E-Rare-2 partner country to participate or not in the joint transnational calls according to the “variable geometry principle”. For instance, the Netherlands and Belgium, two E-Rare full partners, did not participate in the JTC 2007 because they did not reach an agreement with their respective national research agency at time the call was launched.

Countries outside the E-Rare consortium (and outside Europe (e.g USA)) can join E-Rare-2 call activities anytime before the official date of launching. Indeed, the updated call documents and procedures E-Rare has established all along these years are of high quality and meet the international standards that allow easy inclusion of new partners to a call. In this regard, 3 new partner countries (Austria, Greece, and Portugal) have joined the 2009 call (JTC 2009) without being members of the E-Rare-1 consortium.

### ***- What are the call evaluation steps and rules?***

All call partners agree (e.g signature of a Memorandum of Understanding) that the joint research projects in response to the call(s) will be evaluated and ranked by a common international Scientific Evaluation Committee (SEC). The management of the call (secretariat) is assigned to a full E-Rare partner (e.g., France for the JTC 2007, Germany for the JTC 2009, and France for JTC 2011).

### ***- What are the call funding rules and call partners' commitments?***

Funding of the joint call (i.e. funding of the selected research projects) is based on the principle of the “virtual common pot”.

At time of decision to participate in the call, each partner country makes a provisional statement of their respective funding capacity. The funding capacity may vary substantially between partner countries. The provisional funding made by each call partner country remains virtual until the end of the evaluation process of the joint proposals.

**The rule of funding is that each call partner country (i.e. funding agency) funds its own national research teams within the successful joint proposals (i.e national money does not travel across border)**

## 7 - Why your country should join E-Rare-2 joint research funding activities on rare diseases

In many European countries, academic research on rare diseases is funded in programmes that may not be specifically dedicated to rare disease research, because RTD ways of programming varies according to national legal and RTD framework for policing. In some EU member states though, dedicated programmes for rare disease research are present. The linking of the responsible funding organisations and ministries in the first E-Rare project and the subsequent joined activities have increased both the **awareness of the funding agencies on rare disease research**, and the amount of information available on what kind of rare disease research was funded in the different national programmes and on the procedures used in the national programmes.

A first appraisal of the E-Rare-1 funded research projects on rare diseases showed that the proposed research and proposed approaches often cover the whole spectrum of research on a rare disease, going from clinical research (patient databases, biobanks), through genetics and physiopathology up to pre-therapeutical research. Therefore, E-Rare-2 by launching four joint transnational calls will further **contribute to the progresses in research essential for opening routes for new treatments**. Indeed, progress in understanding the cause and natural history of the diseases and well-defined patient cohorts of sufficient size is crucial for better drug development. In Europe, Orphan drug development is often carried out by small and medium enterprises specialized in specific technical platforms to develop innovative therapeutics and fostered by the EU Orphan Drug Regulation. The strengthening of European cooperation for rare disease research brought about by E-Rare-2 will therefore also boost the economy with regard to pharmaceutical and biotechnological industry. This will be of great benefit to the patients who can expect better treatments in the future.

The first E-Rare project has also shown that there is an obvious **need for collaboration between researchers in Europe**. The interest of the researchers to collaborate with each other and apply for funding in the E-Rare Joint Transnational Calls in 2007 and 2009 exceeded by far the expectations of the E-Rare partners. Altogether, 260 eligible proposals with the participation of over 1000 research groups were submitted. Even researchers in some of the projects that were not granted have indicated to funding organisations that they would like to continue their new collaboration despite the fact that they did not get funding via the E-Rare Joint Transnational Calls. Thus, the collaboration of the funding organisations has already resulted in new collaborations of researchers for future activities.

Likewise, the participation **of your country as partner** in E-Rare-2 research funding activities will amplify European collaboration on research on rare diseases under a common umbrella, allowing national research teams to foster collaborations with several EU countries within the same single project, to share data, infrastructures, approaches and expertises, and thus will contribute to the development of research without which there is little, if any, development of new therapeutics.

Finally, E-Rare-2 will meet with many of the **challenges that have been raised in the Communication and Recommendation on rare diseases**. Indeed, the Council Recommendation of 8 June 2009 on an action in the field of rare diseases (2009/C 151/02) specifically emphasizes the importance of research on rare disease. It is suggested that the coordination of Community, national and regional programmes for rare disease research should be improved and interdisciplinary cooperative approaches to be complementarily addressed through national and Community programmes be promoted.