NEEDS AND PRIORITIES FOR RARE DISEASE RESEARCH

Rare disease research (RDR) represents a broad range of scientific investigations to establish knowledge on rare diseases (RD). Basic RDR involves the biochemical study of underlying pathophysiological mechanisms and their genetic and molecular characterisation. Clinical research focuses on the development of diagnostic tools and therapeutic solutions. Translational research accelerates the transfer of knowledge from basic "bench-side" research into clinical "bedside" applications. Equally important, in this multidisciplinary field of research, are studies of social consequences of the disease, health economy, communication and culture as well as epidemiological studies and research into the natural history of the disease. These studies equally help enlighten solutions towards better standards of care and treatment and higher quality of life for RD patients. Specific and careful allocation of budgets and coordination of activities at the national, regional and European levels are imperative for accelerating the attainment of the ultimate goal - effective treatments for patients.

WHY IS RD RESEARCH REQUIRED?

The EU Regulation on Orphan Medicinal Products[1] is a true success. Still, in the last 10 years, only approximately 100 new RD medicines – with an orphan drug designation or not – have been approved in the EU[2]. The number of RD projects funded by the European Commission Directorate General for Research Framework Programmes (FP), in particular FP6 and FP7, is steadily growing[3]. Approximately 5,000 research projects in EU currently cover 2,000 different RDs. In addition over 650 clinical trials are ongoing for more than 300 RD (including for designated orphan drugs)[4]. However, there are thousands of RD for which there is no ongoing research activity. In particular, for RD with a prevalence of <1/10,000, therapeutic research is very limited or non-existent.

The Commission Communication on Rare Diseases[5] proposes that Member States put in place strategies to foster RD research, including cross-border cooperation and collaboration to maximise scientific resources across the EU.

The Commission's Council Recommendation[6] recommends that Member States establish and implement plans or strategies to ensure provisions aimed at fostering research in the field of RD. Both documents call for a RDR policy which is both comprehensive (covering a large scope from basic to clinical research) and integrated (EU and national levels)

The European Project for Rare Diseases National Plans Development (EUROPLAN) further specifies guidelines and recommendations[7] for the elaboration of national action for RDR in the context of a national plan. The E-RARE project provides an important forum for Member states to exchange about their respective RDR policy and to coordinate their strategies.

WHY IS RESEARCH IMPORTANT TO RARE DISEASE PATIENTS?

The greatest barrier to prevention, diagnosis and treatment of RD is insufficient knowledge. A lack of RDR has delayed in the establishment of fundamental scientific knowledge needed to understand the causes and mechanisms for the majority of RD, resulting in under-diagnosis, misdiagnosis, delays in diagnosis and inappropriate treatment, whether drug therapy or other medical attention. The key to developing this knowledge is supporting and developing all elements of RDR. Investment in RDR can improve the identification of, understanding of and ›

1 EC Regulation 141/2000 on Orphan Medicinal Products
2 http://www.orpha.net/orphacom/cahiers/docs/GB/List_of_marketing_orphan_drugs_in_Europe.pdf
3 See References. EURORDIS. European Workshop on RDR, Presentation - Manuel Hallen, DG Research, European Commission
4 Ibid, Presentation - Research activities in Europe: Trends and determinants, Ségolène Aymé, Director of Orphanet
5 COM (2008) 679 Communication from the Commission to the European Parliament, the Council the Economic and Social Committee and the Committee of the Regions on Rare Diseases: Europe's challenges.
6 Council Recommendation of 8 June 2009 on an action in the field of rare diseases.
7 Final recommendations available on the EUROPLAN website, www.europlanproject.eu

- development of therapeutic options for many RD - subsequently reducing global public health expenses by avoiding expensive and ineffective treatments.

Due to their low individual prevalence, their complexity and requirement for a multidisciplinary approach, the field of RDR is one in which benefits of a specific and targeted coordination and collaboration are most obvious and pressing. Traditional funding mechanisms including "normal" market conditions, patient organisation fundraising efforts, and public funds are not adapted to the reality of RDR requirements, which include concerted efforts at both the national and international levels.

How should the need for more RD research be addressed?

Developing National Plans and Strategies

Fostering research should be included as one of the major pillars of a national plan or strategy on RD and should include:

- Facilitation of research cooperation, exchange of information and sharing of expertise (especially in smaller Member States where resources to create networks at the national level are scarce)
- Creation of specific national RDR programmes with specific dedicated funds and participation in international consortia such as E-RARE[8], to better coordinate research and research policy at the country level
- Identification of on-going research and resources and dissemination of information about research calls
- Identification of priorities for basic, clinical, translational and social research and modes to foster them
- Creation of specific platforms and infrastructures for RDR and ensuring their long-term functioning
- Overcoming economic unattractiveness by supporting research on new or existing orphan drugs with specific programmes through public funding, public-private partnerships, and incentive programmes
- Increasing career attractiveness in this field by creating recruitment and training programmes and additional incentives for young scientists

Supporting the Determinants of Research

Three main determinants identified in promoting a significant level of research activity in a given RD include the existence of (a) patient organisations (b) patient registries (c) European networks (of centres of expertise or of research) in which all actors are involved[9].

Patients should be partners in research not only as subjects, but also as advocates for fundraising and key stakeholders in the drafting of guidelines and policies, and should always be consulted in the drafting and evaluation of national research policy in the context of RD plans.

Identifying Priorities

Depending on the RD or group of RD in question and maturity of the specific field, RD priorities in allocation of resources should include:

- Research to determine the incidence, prevalence, natural history and clinical nosology
- Basic research concerning the aetiology and genetic links of the disease and potential causes of mutations
- The development of improved screening and diagnostic techniques
- Basic and clinical research for the development and evaluation of new standards of care, medical devices, and orphan medicinal products
- Social and human research related to needs of rare disease patients
- Information to the general public and education programmes for health care professionals based on the findings of this research

Related issues

- Investment in RDR should occur at two levels:
  - Specific RD budget lines for funding networking (national and EU level) and infrastructures such as biobanks and registries
  - Participation of RD projects in competitive allocation of funds under general health research budget lines, where projects are not selected on the basis of rarity, but according to the criteria of excellence, innovative ideas, concepts and technologies.
- The wider community benefits from research on RD as it often advances medical research in general and drives novel approaches. Public health systems may also develop specific solutions and innovative approaches to address rare disease patients' needs.

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- Rare Disease Platform (ORPHANET): A European Platform of Integrated Information Services for Researchers in the Field of Rare Diseases and Orphan Drugs Supporting Team and Project Building. www.rdplatform.org

8 Network of public bodies, ministries and research management organizations responsible for the development of national/regional research programmes on RD and supported by the EC under the DG Research Framework Programme ERA-Net scheme.
9 See footnote 4.

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