EURORDIS
European Organisation for Rare Diseases

EURORDIS Position Paper on the Research Priorities for the 7th Framework Programme

Eurordis – the European Organisation for Rare Diseases – is a patient-driven pan-European network of more than 220 rare disease organisations from 23 countries (15 of which are EU member states). On behalf of the 30 millions patients affected by rare diseases in the enlarged Europe, Eurordis would like to put forward some priorities for the Seventh Framework Programme of Research.

This position paper is based on the policy work performed by the Working Group nominated by the French Health Ministry to develop proposals for research in the framework of the French Rare Disease Plan 2005-2008. This group, composed of clinicians and scientists working in the field of rare diseases, policy makers, and rare disease patient representatives, was coordinated by the *Institut des Maladies Rares*; Eurordis was one of its members. The paper has been further developed based on Eurordis advocacy work between 2002 and 2004, on the recent DG Research consultation on FP7 and on the experience gained through the participation of Eurordis as an Observer in the E-rare project, and Era-net involving the French, Spanish and German public partners funding rare disease research; this paper doesn't represent their views. This document was finalised through consultation with the 25 patient organisation representatives involved in the *Eurordis European Public Affairs Committee*, representing a broad range of rare diseases and EU Member States.

Lisbon Strategy, competitiveness and employment

At the UNICE Competitiveness Day, on 9 December 2004, Commissioner for Enterprise and Industry, M. Verheugen, underlined once again the importance of innovation for the promotion of the Lisbon Strategy. "Innovation can be encouraged in a number of ways. Europe must find a way in which education and research can be brought to the forefront of our society again. Research and Development is possibly the most important vehicle of innovation. We find that differences in R&D expenditure explain much of the innovation gap between Europe and the US. So it is in this area that the Lisbon project needs new impulses and therefore the target set out in the Strategy of spending 3% of our GDP on research and development deserves our full commitment".

In this context, it is of fundamental importance not to underestimate the potential of new technologies developed in the Health sector, such as biotechnology and nanotechnologies, to increase European competitiveness, foster employment and support the research-driven SMEs.

Specificities of Rare Diseases

Due to the great number of rare diseases, their low prevalence (less than 1/2000) and their heterogeneity, rare diseases represent by definition an area of research that has to be developed at the European level, rather than in isolation within single laboratories scattered throughout the EU. As it is difficult at this stage to develop projects for each of the 5000 rare diseases, it is important to establish both horizontal cross-cutting platforms and vertical disease-specific projects, based on excellence, to be used as models for other rare or common diseases. It is therefore crucial to create European structures of excellence through networking and cooperation between laboratories. The selection process of projects funded through the EU Framework Programmes, based on the excellence of the objectives and methods, will raise the quality standards of European research. It is necessary to integrate European research teams in a pan-European space and develop a truly European culture for research.

While in some areas huge networks of excellence and large integrated projects are possible, in the specific domain of rare diseases, competent European research groups (including SMEs) working on the same topic are few and can only be supported through other instruments, such as smaller size international projects.

Research on rare diseases has proven to be very difficult as it often implies a multi-disciplinary approach, associating teams of clinical research, genetics, physiopathology, patient organisations, therapeutic, social and human scientists as well as the optimal use of technological platforms (such as sequencing platforms, facilities for transgenic animals and imaging, etc.). The status of research on rare diseases varies greatly according to the different pathologies. It is therefore fundamental to keep a global vision of all research fields in order to ensure rapid reactivity to the development of knowledge and technological tools.

The organisation and financing of technological platforms go well beyond the framework of research on rare diseases. It is important to ensure their functioning and viability in the long run as technological platforms represent a strategic investment for the whole of R&D in Europe, and the basic tool to achieve concrete advances in the future.

Definition of six main strategic orientations for research on rare diseases

1. Descriptive and analytical epidemiology, natural history of the disease and clinical nosology.

This field of research has been insufficiently developed even though it constitutes the prerequisite of any therapeutic advance. It includes different aspects:

- The collection of information on rare diseases in terms of incidence, prevalence or distribution (age, sex, environment, etc…);
- The definition of new nosological entities through in-depth analysis, at clinical /genetic level, of apparently homogeneous diseases, also taking advantage of the huge source of information represented by patient organisations.
- The study of the natural history of the disease, of its risk factors, its severity and associated complications. The identification of factors that could explain various phenotypes, including the studies of genotype/phenotype correlation.

Actions to be undertaken:

- To facilitate the development of multidisciplinary networks associating clinicians, geneticians, epidemiologists, patients, relying on the centres of reference that are currently being established in some Member States.
- To facilitate the constitution of cohorts and observatories.
- To facilitate the development of tools needed to implement these studies, in particular data management tools for shared databases.

2. Genetic and molecular characterisation

Around 1200 genetic anomalies responsible for rare diseases have been identified. There are probably more than 4000 diseases for which the genetic characterisation remains to be done. It is of fundamental importance to pursue the efforts in this field in order to allow the development of diagnostic tests and to initiate pathophysiological studies of these diseases.

Actions to be undertaken:

- To assemble sufficient collections of biological material corresponding to families and/or cohorts of patients, whose phenotypic characteristics have been correctly analysed. As was recently underlined during the Conference on Basic Research for Life Sciences (Brussels, 13 December 2004), the collection of data and high quality

biological samples, as well as their storage and dissemination, are of fundamental importance at EU level, in particular concerning rare diseases.
- Mapping and cloning of the disease responsible genes. Identification of mutations. Detection of gene deletion or other anomalies of gene dosage.

3. Pathophysiology

Even though much remains to be done, many genes involved in a large number of diseases have been identified in the last 15 years. However, a significant number of rare diseases (approximately 20%) are not of genetic origin. In all these cases, and more than for monogenic diseases, it is necessary to understand the mechanisms participating to the development of the disease and the phenotypes observed in the patients. This research mobilises different approaches common to all projects: establishment of pathological cell lines to be used as models, transcriptome, proteome, in vivo imaging, etc.

Actions to be undertaken:

- The development of animal transgenic facilities.
- The analysis of data from the transcriptome and proteome technology represents a major challenge and should be supported.
- The identification of the appropriate non-genetic markers, biological, functional etc., to be used for diagnosis, and evaluation of disease progression.
- The development of research on animal models different than mice should also be encouraged.

4. The improvement of diagnostic performances

In order to improve the timely care of people affected by rare diseases it is of fundamental importance to enhance the diagnostic performances in terms of delays, reliability and accessibility. This would also reduce the costs and human consequences associated with diagnostic delays. The development of new diagnostic tools, the transfer of knowledge from research development to clinical use, as well as the implementation and evaluation of new diagnostic methods, all these elements have to be taken into account. Advances are expected from new technologies, in particular from nanotechnologies, which offer opportunities for performing genetic and/or biological diagnostics.

Actions to be undertaken:

- To support large-scale screening projects of gene mutation in order to develop diagnostic tools and diagnostic applications of nanotechnologies, where there is a demonstrated benefit for patients
- To support common projects with the industry and to facilitate the development of joint DG Research/ DG Enterprise projects.
- To support projects aimed at developing evaluation methods for diagnostic tools: performances, clinical utility…

5. Therapeutic research

The development of therapeutics for patients living with a rare disease is of course the ultimate objective, with a particular focus on children. The diversity of the pathological situations, associated with the lack of knowledge of the physiopathology of a great number of rare diseases and the relative lack of interest from the pharmaceutical industry, illustrate the complexity of research in this field, which entails a large variety of approaches. Four main sectors may be identified: a) Development of innovative devices aimed at alleviating or compensating disabilities linked with the disease; b) Development of Orphan Medicinal Products (OMP) including specific paediatric formulations; c) Cell therapy; d) Gene therapy.

Actions to be undertaken:

- To facilitate the establishment of partnerships with various technological fields for the development of symptomatic treatments.
- To support projects aimed at searching for chemical molecules potentially interesting in the treatment of rare diseases, following two approaches: on the one hand high

output molecular screening; on the other hand research of therapeutic molecules based on physiopathological knowledge of the diseases.
- To support projects on cell and gene therapy in view of application to rare diseases;
- To develop projects of pre-clinical therapeutic research and proof of concept studies, which are specifically relevant to orphan drugs and rare diseases: animal models, including large animals
- To develop joint DG Research/DG Enterprise/EMEA projects for funding designated orphan drugs at early stage of clinical development.
- Specific actions should be undertaken aimed at developing orphan medicinal products for indications, which include the paediatric population.

6. Research in social and human sciences

Few research teams work in the area of Social and Human Sciences (SHS) in the field of health, and even fewer on rare diseases. It seems important to mobilise specialists in the following disciplines: sociology, economy, anthropology, history of sciences, law and public health. Several lines of research could be privileged, such as: a) Society and rare diseases: social perception and representations, problems of accessibility to care - notably concerning underprivileged populations - economic evaluation and equity; b) rare diseases, research and innovation: public/private scientific cooperation, the role of patients organisations; c) care practices, the day-to-day experience of the disease: self-managed medical care, family implication, health education policy, evaluation of techniques and organisation methods; d) Public health and rare diseases: research policies, health care policies, prospective public health policies. Research conducted in these fields should not only be descriptive but also analytic, and aimed at measuring various parameters related to the progress of EU research on rare diseases, such as: evaluation of the efficacy of incentives to attract scientists and research laboratories in the field of rare diseases, and to stimulate the interest of the pharmaceutical industry in the development of projects on orphan drugs. The results obtained from these studies would offer important clues for evaluating the middle and long-term efficacy of the research strategies chosen by the EU.

Actions to be undertaken:

- To support research projects in the above-mentioned fields of SHS.
- To attract young researchers in SHS towards these themes by clearly showing willingness to support research projects, including funding of scholarships.

Importance of concerted actions in the field of research on rare diseases

The specificities of research on rare diseases justify a concerted action between different national policies of financing and management, in order to optimise the use of funding, infrastructures and technological platforms, as well as the coordination of the participants.

The objectives identified are the following ones:

- To ensure a global vision and a strategic coordinated reflection in the field of research on rare diseases.
- To facilitate the development of a European Policy of research on rare diseases.
- To stimulate new programmes of multidisciplinary research and encourage new teams to become involved in research on rare diseases.
- To attract young researchers towards this field of research.
- To ensure that different departments and institutions involved in research do work together in a concerted way in order to coordinate relevant activities and programmes, avoiding duplications.
- To ensure high reactivity towards new scientific and technological developments.
- To guarantee a sufficient visibility with patients, researchers and health professionals.
- To facilitate the industrial developments of results from research in the fields of diagnostics and therapeutics.
- To disseminate new knowledge acquired from research by implementing training and information for the scientific community, the health professionals and the patients.