Comments about ” Rare diseases: Europe’s challenge” from the Public and Professional Policy Committee of the European Society for Human Genetics.

The European Society of Human Genetics (www.eshg.org) is a non-profit organization. Its aims are to promote research in basic and applied human and medical genetics, to ensure high standards in clinical practice and to facilitate contacts between all persons who share these aims, particularly those working in Europe. The Society will encourage and seek to integrate research and its translation into clinical benefits and professional and public education in all areas of human genetics.
The Public and Professional Policy Committee (PPPC) formulates the professional and scientific view on social, ethical and legal issues, on behalf of the Society when asked to do so by the Board or the membership.
Several ESHG members were involved in EUROGENTEST. EuroGentest is an EU-funded Network of Excellence (NoE) with 5 Units looking at all aspects of genetic testing - Quality Management, Information Databases, Public Health, New Technologies and Education. Through a series of initiatives EuroGentest encourages the harmonization of standards and practice in all these areas throughout the EU and beyond.

The PPPC of ESHG recognizes the Communication on Rare Diseases as an important strategic document that will help the development of high quality and equitable national services for patients with rare diseases. All topics raised in the 14 questions below are relevant to the ESHG institutional aims so collaboration between European Commission and ESHG executive and/or commissions should certainly be considered. ESHG is the organization on which all the National Genetic Scientific societies, support groups and possibly other groups do converge. Many rare diseases are genetic conditions. It is not difficult to find points why geneticists emphasize the importance of concerted actions:
- rare diseases receive little attention (low individual population frequency, little is known about many of them, only some specialists are familiar with the details, etc);
- scientific developments in the last decades, like the human genome projects and other ’omics, gave clues to analyse rare diseases in order to find precise diagnostic tools, better care and therapy;
- the informational revolution in the last decades (internet, e-learning, e-communication, etc) gave us means and possibilities to create national experts groups and international networks to achieve a critical mass of operational partners in order to increase the research activities, enrolment of patients in clinical research, etc;
- research on rare diseases may result in findings and discoveries which could be converted into the care of common disorders as well;
- these concerted actions can be effective on wide societal base only (networking of research teams, organized health care systems involving clinics, laboratories, reference centres, harmonized cooperation between expert groups, health politicians, civil support groups, industry, etc)

We will answer the specific questions raised in the document ”Rare diseases: Europe’s challenge” below.

Question 1: Is the current EU definition of a rare disease satisfactory?

The PPPC of the ESHG supports the current EU definition for the whole of Europe.
However, the problem with a strict numerical definition is obviously that for many rare diseases the prevalence is not known. Apart from the definition of less than 5 per 10 000, “diseases that are so rare that concerted efforts are needed” could be considered. If a long period of time elapses before diagnosis or no expertise on the disease is available on the disease, concerted actions are warranted. From an epidemiological point of view, it should be mentioned that diseases that are rare in the general population (*low population prevalence*) can be frequent in certain age groups (for instance certain breathing problems in premature babies) or in certain geographic areas or ethnic/population groups (e.g. thalassemia). We suggest that the interpretation of the definition is that diseases with *population* prevalence less than 5 per 10 000 are considered rare. That would include some

disorders with somewhat higher prevalence in specific subpopulations. A final comment is that very rare disorders with unknown prevalence still risk receiving least attention.

Question2: Do you agree that there is a pressing need to improve coding and classification in this area?

Yes. For health policy as well as individual health care access to accurate information depends on adequate and standardized coding and classification. Existing coding and classification systems need to be integrated and updated. Both the *development* of coding and classification schemes and their *use* in clinical practice need improvement.

Question 3: Can a European inventory of rare diseases help your national/regional system to better deal with RD?

The most important thing (because of language, distances, different diseases in different populations) is to have a national plan on how to organize the health care of rare diseases. In some countries good information sources exist, but most EU countries would profit from initiatives such as www.orpha.net. A single source pulling together scientific and clinical information for European clinicians would be a key tool in enhancing recognition and care of rare diseases throughout Europe, and to support research. Guarantee sustainability of the activities by long-term funding.

Question 4: Should the European Reference Networks privilege the transfer of knowledge? The mobility of patients? Both? How?

The transfer of knowledge/experience is of primary importance. The mobility of patients has also problems and should be used only in exceptional cases (or in case of very small countries like Luxembourg), mainly in rare surgical operations, gene therapy trials, possibly preimplantation diagnostics, second opinion at diagnosis, etc.

Question 5: Should on-line and electronic tools be implemented in this area?

Yes. Information technologies already have opened up sources of information and advice, improved access to genetic tests, and contributed to contacts with others affected by the same condition. Apart from improvement of existing applications, further possibilities such as online consultation using video techniques should be developed.

Question 6: What can be done to further improve access to quality testing for RD?

Continue the work that Eurogentest has started to guarantee optimal quality for genetic testing in rare diseases. Set a network of highly qualified European laboratories which can provide genetic tests for very rare diseases.
Contribute to funding possibilities for countries with a limited health care budget or patients without adequate insurance.
Exchange information (Orpha.net).
Guarantee the quality of genetic counselling associated with genetic testing.

Question 7: Do you see a major need in having an EU level assessment of potential population screening for RD?

Yes and no. The WHO criteria (Wilson and Jungner 1968) form the basis of many schemes for the assessment of new possibilities for screening and testing in populations at low risk. These schemes include analytic validity, clinical validity and utility of test, but also ethical, legal, economical, cultural, political and societal aspects. Some of the information needed to weigh pros and cons can be generated at an EU level, but some other aspects will differ between countries (availability of resources, cost-effectiveness in countries with higher or lower prevalences of disorders, political choices, priorities). The parameters needed for evaluation in each member state (such as test sensitivity, specificity, effectiveness of the intervention, effects at long term follow up of patients) can certainly be better assessed at EU level. Evidence generated in this way can support decision making in Member States.

Question 8: Do you envisage the solution to the orphan drugs accessibility problem on a national scale or on an EU scale?

On a EU scale regulation and stimulation of development should take place. As reimbursement takes place on a national scale, EU can only facilitate information on reimbursement issues and research on orphan drugs. Accessibility in low income countries might be addressed at EU level as well.

Question 9: Should the EU have an orphan regulation on medical devices and diagnostics?

Yes and no.
Current medical devices regulation focuses on quality and safety, but should ensure clinical utility is properly taken into account. Information on the test properties and the interventions needed in case of unfavourable results need to be communicated and evaluated.
Meanwhile companies operating in the field of rare disease diagnostics need incentives to further develop products in this area. New regulations should not become another threshold for the development of useful medical devices and diagnostics.

Question 10: What kind of specialised social and educational services for RD patients and their families should be recommended at EU level and at national level?

Reliable information on rare diseases should be available in such a way that the patient can easily distinguish officially reliable information from non-reliable information.

Question 11: What model of governance and of funding scheme would be appropriate for registries, databases and biobanks?

As rare diseases are rare, it might be difficult to fund the work via everybody paying when using such a database etc. Thus PPPC would like to see that funding comes from public money. In case of biobanks: ESFRI/BBMRI, P3G, OECD among other players are creating the best practices for biobanking. PPPC does not see rare diseases databases/biobanks more problematic than biobanking/health data in general, except for funding.

Question 12: How do you see the role of partners (industry and charities) in an EU action on rare diseases? What model would be the most appropriate?

Both sectors should be involved, as well as universities. Public-private partnerships supported by EU might be best appropriate. Patient/family associations should be involved as well.

Question 13: Do you agree with the idea of having action plans? If yes should it be at national or regional level in your country?

There definitely have to be a national action plans but having European recommendations and a European level of action plan might support the national efforts.

Question 14: Do you consider it necessary to establish a new European Agency on RD and to launch a feasibility study in 2009?

PPPC-ESHG recognizes the need to ensure sustainable activity and funding in the field of rare diseases. Innovation of health care in this area should not rely on 3 to 5 year projects. We also believe that it would be helpful in following and supporting the efforts in different Member States. It would also be useful in order to coordinate the Member States' health facilities on RD and to achieve a homogeneous access to diagnosis and therapy for all the European citizens.

On behalf of the Public and Professional Policy Committee of the European Society for Human Genetics,

Prof. Martina Cornel, chair.